chapter

15 Blood

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Key Terms

albumin (p. 285)
anemia (p. 286)
basophils (p. 294)
coagulation (p. 296)
eosinophil (p. 294)
erythrocytes (p. 285)
erythropoietin (p. 290)
fibrin (p. 296)
hematocrit (p. 285)
hemoglobin (p. 288)
hemolysis (p. 290)
hemopoiesis (p. 286)
hemostasis (p. 295)
leukocytes (p. 285)
lymphocytes (p. 286)
monocytes (p. 286)
neutrophil (p. 292)
plasma (p. 285)
platelets (p. 285)
red blood cells (p. 285)
reticulocyte (p. 287)
serum (p. 285)
thrombocytes (p. 285)
white blood cells (p. 285)

Objectives

1. Describe three functions of blood.
2. Describe the composition of blood, including:
   - Describe the three types of blood cells: erythrocytes, leukocytes, and thrombocytes.
   - Explain the formation of blood cells.
3. Explain the composition, characteristics, and functions of red and white blood cells and platelets, including the breakdown of red blood cells and the formation of bilirubin.
4. Identify the steps of hemostasis.
5. Describe the four blood types.
6. Describe the Rh factor.

Long before modern medicine, blood was viewed as the part of the body that possessed the life force. This belief arose from the observation that severe bleeding episodes often ended in death, suggesting that the life force flowed out of the body with the blood. Blood was also credited with determining personality traits and emotions. For example, the wealthy were called *blue bloods*. Feuding groups often attributed the cause of the troubled relationship to bad blood. Anger was said to cause the blood to boil, whereas fear could generate blood-curdling screams. The qualities of blood seemed so magical that a sharing of a few drops of blood could make one's friend a blood brother. Although we no longer speak of blood in such terms, we do recognize that an adequate blood supply is essential for life. We are still fascinated by blood and have a fancy word for its study: hematology.

Blood flows through a closed system of blood vessels. The force that pushes the blood through the vessels is the pumping action of the heart (see Chapter 16).

WHAT BLOOD DOES

Blood performs three general functions: transport, regulation, and protection. First, the blood transports many substances around the body. For example, blood delivers oxygen from the lungs to every cell in the body. Blood picks up waste material from the cells and delivers the waste to organs that eliminate it from the body. Nutrients, ions, hormones, and many other substances use blood as the vehicle for movement throughout the body. Second, blood participates in the regulation of fluid and electrolyte balance, acid–base balance, and body temperature. Third, blood helps protect the body from infection. Blood also contains clotting factors, which help protect the body from excessive blood loss.

COMPOSITION OF BLOOD

CHARACTERISTICS

Blood is a type of connective tissue that has a liquid intercellular matrix. The color of blood varies from a bright red to a darker blue-red. The difference in color is caused by the amount of oxygen in the blood; well-oxygenated blood is bright red, whereas oxygen-poor blood is blue-red. The amount of blood varies,

8. Hyperglycemia, polyuria, polydipsia, polyphagia, and ketoacidosis are characteristic of a deficiency of
   a. cortisol.
   b. insulin.
   c. catecholamines.
   d. neurohypophyseal hormones.
9. Which of the following is not a steroid?
   a. Adrenal cortical hormones
   b. ACTH
   c. Estrogen
   d. Androgens
10. Which of the following is not true of antidiuretic hormone (ADH)?
   a. Secreted by the neurohypophysis
   b. Also called *vasopressin*
   c. Stimulates the kidney causing water reabsorption
   d. Is the salt-retaining hormone

Go Figure

1. **According to Figure 14-1**
   a. All endocrine glands are located in the abdominal cavity.
   b. No endocrine glands are located in the pelvic cavity.
   c. The pituitary gland is located within the thoracic cavity.
   d. The thyroid and parathyroid glands are located in the neck.

2. **According to Figure 14-4 which of the following is not true?**
   a. The adenohypophysis secretes TSH, growth hormone, prolactin, the gonadotropins, and ACTH.
   b. The posterior pituitary gland secretes ADH and oxytocin.
   c. The hypothalamic-hypophyseal portal system allows the anterior and posterior pituitary glands to "swap" hormones.
   d. Hypothalamic-releasing hormones control the secretion of the adenohypophysis.

3. **According to Figures 14-4 and 14-8**
   a. ACTH stimulates the secretion of catecholamines.
   b. Cortisol stimulates the adenohypophyseal secretion of ACTH.
   c. ACTH is a hypothalamic-releasing hormone.
   d. ACTH secretion decreases as plasma levels of cortisol increase.

4. **According to Figure 14-5**
   a. T_3 and T_4 are adenohypophyseal hormones.
   b. TSH stimulates the parathyroid glands.
   c. T_3 and T_4 stimulate the thyroid gland to secrete thyroxine.
   d. The secretion of TSH is inhibited by increased plasma levels of T_3 and T_4.

5. **According to Figures 14-6 and 14-7**
   a. PTH increases plasma calcium levels by its effects on bone, kidneys, and intestine.
   b. The stimulus for the release of PTH is hypercalcemia.
   c. Carpal spasm is a sign of hypercalcemia.
   d. As plasma levels of calcium increase, PTH levels increase.

6. **According to Figure 14-9**
   a. The pancreas secretes insulin and glucagon in response to hyperglycemia.
   b. Insulin is secreted in response to an increase in the blood glucose.
   c. Glucagon lowers the blood glucose level.
   d. Glucagon is secreted in response to hyperglycemia.

depending on body size, gender, and age. The average adult has 4 to 6 L of blood.

Do You Know...

Why George Washington's 9 Pints of Blood Went Down the Drain?

You probably remember George Washington for chopping down the cherry tree, for his penchant for truth, and for being the first president—but here is something you probably didn't know about George's medical history. George had been quite ill with a long winter cold, pneumonia, and throat infection. Despite many home remedies and much attention, the infection lingered and worsened. Enter the "quacks"! Immediately before his death, George was bled of 9 pints of blood in an attempt to rid his body of disease. This commonly used procedure was called *bloodletting*.

The practice of bloodletting had been around since before the days of Hippocrates (a long, long time ago). Bloodletting grew out of the belief that health was the result of a balance of the four body humors (fluids): blood, phlegm, black bile, and yellow bile. Disease was therefore attributed to an imbalance of the humors. By draining George's blood, the bloodletter hoped to balance George's unbalanced humors. (Not funny!) The fact that George died immediately after being drained of 9 pints is not surprising. At a time when he needed all the help he could get from his blood, he was literally drained and probably plunged into a state of low-volume circulatory shock. Although the practice of bloodletting, as described in this case, has been discredited, the practice of bloodletting hasn't completely died out. It has, however, been cleaned up and refined. "Therapeutic phlebotomy," or the removal of blood for therapeutic purposes, is routinely performed in the treatment of polycythemia vera and hemochromatosis, conditions characterized by excess RBCs, iron, and blood volume. And our little leech on page 298 is a natural born phlebotomist when it comes to maintaining blood flow in edematous tissues.

We retain a friendly reminder of our former bloodletting ways in the barbershop pole. Barbers and surgeons were the early bloodletters, and the pole advertised their trade. The barbershop pole is striped red and white. Red represents blood, white represents the tourniquet, and the pole itself represents the stick that the patient squeezed to dilate the veins for easy puncturing. Fortunately, today's barbers go for your hair and not your jugular.

Other characteristics of blood include pH (normal, 7.35 to 7.45) and viscosity. Blood viscosity (vis-KOS-i-tee) refers to the thickness or stickiness of the blood and affects the ease with which blood flows through the blood vessels. Viscosity is best demonstrated by comparing the flow of water and molasses. If water and molasses are poured out of a bottle, the molasses flows more slowly. Molasses is said to be more viscous, or thicker, than water. Blood is normally three to five times more viscous than water. Although blood viscosity does not normally fluctuate widely, an increase in viscosity can thicken the blood so much that it puts an extra burden on the heart, thereby causing the pumping action of the heart to fail.

BLOOD HAS TWO PARTS

Blood is composed of two parts: the plasma and the formed elements (blood cells and cell fragments). The **plasma** is a pale yellow fluid composed mostly of water; it also contains proteins, ions, nutrients, gases, and waste. The plasma proteins consist of **albumin** (al-BYOO-min), various clotting factors, antibodies, and complement proteins. In general, the plasma proteins help regulate fluid volume, protect the body from pathogens, and prevent excessive blood loss in the event of injury. **Serum** is the plasma minus the clotting proteins.

The blood cells and cell fragments include the following:

- **Red blood cells** (RBCs) are also called **erythrocytes** (eh-RITH-roh-sytes) (from *erythro,* meaning "red"). RBCs are primarily involved in the transport of oxygen to all body tissues.
- **White blood cells** (WBCs) are also called **leukocytes** (LOO-koh-sytes) (from *leuko,* meaning "white"). WBCs protect the body from infection.
- **Platelets** (PLAYT-lets) are also called **thrombocytes** (THROM-boh-sytes). Platelets protect the body from bleeding.

The two parts of blood can be observed in a test tube. If a sample of blood is collected in a tube and spun in a centrifuge, two phases appear; the heavier blood cells appear at the bottom of the tube, whereas the lighter plasma accumulates at the top.

The separation of blood into two phases forms the basis of a blood test called the *hematocrit* (Hct) or *packed cell volume* (Figure 15-1). The **hematocrit** (hee-MAT-oh-krit) is the percentage of blood cells in a sample of blood. A sample of blood is normally composed of 45% blood cells and 55% plasma. The blood cells are

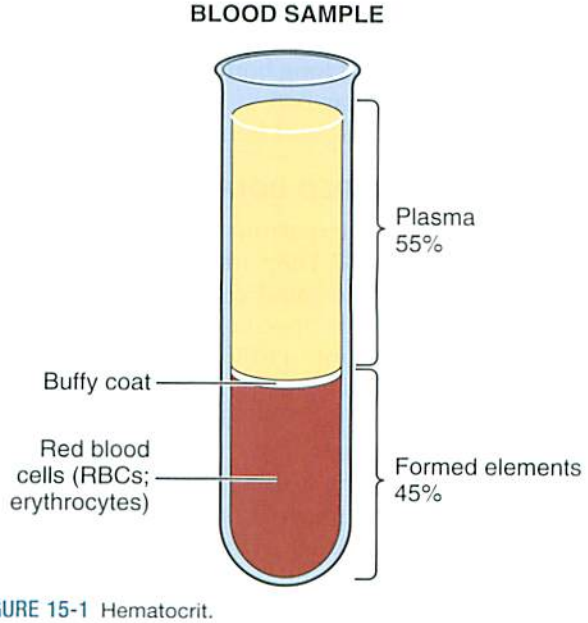


FIGURE 15-1 Hematocrit.

composed mainly of RBCs. A small layer of cells between the plasma and the RBCs is called the *buffy coat* and consists of WBCs and platelets. Because the buffy coat is so thin, any change in the Hct is generally interpreted as a change in the numbers of RBCs. For example, a person with a low Hct is considered to be anemic, with a lower than normal number of RBCs. A word of caution! Because the Hct is expressed as a percentage (%), any change in blood volume affects the Hct. For example, a dehydrated patient has a diminished blood volume. Thus, the ratio of RBCs to blood volume increases. The elevated Hct therefore represents not an increase in RBCs but a decrease in blood volume. Conversely, an expanded blood volume, as occurs in heart failure, decreases the Hct. The lowered Hct represents not a decrease in RBCs but an increase in blood volume. In essence, the RBCs have been diluted by the excess water in the blood. An expanded blood volume causes a "dilutional anemia."

? Re-Think

1. List the two parts of blood.
2. List the three types and functions of blood cells.
3. Describe the effect of dehydration on the hematocrit.

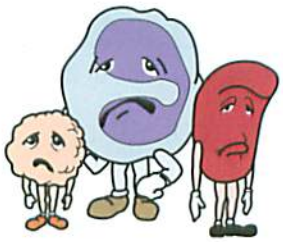
ORIGIN OF BLOOD CELLS

The process of blood cell formation is called **hemopoiesis** (hee-moh-POY-ess-iss). The three types of blood cells (RBCs, WBCs, and platelets) are made in hemopoietic tissue. The two types of hemopoietic tissue in the adult are the red bone marrow and the lymphatic tissue, which is found in the spleen, lymph nodes, and thymus gland.

Blood formation in the red bone marrow is called *myeloid hemopoiesis*. (Myeloid comes from the Greek word meaning "bone marrow.") Blood formation in the lymphatic organs (described in Chapter 21) is called *lymphoid hemopoiesis*. Red bone marrow is found primarily in the ends of long bones, such as the femur, and in flat and irregular bones, such as the sternum, cranial bones, vertebrae, and bones of the pelvis.

HEMOPOIESIS AND RED BONE MARROW

How does the red bone marrow produce three different types of blood cells? They are produced in the red bone marrow from the same cell, called a *stem cell*. Under the influence of specific growth factors, the stem cell differentiates into a RBC, a WBC, or a platelet. Note the stem cell in Figure 15-2. In line 1, the stem cell differentiates into the RBC (erythrocyte). In lines 2, 3, and 4, the stem cells form five different types of WBCs (leukocytes). The **lymphocytes** and **monocytes** originate in the bone marrow; some of the lymphocytes mature and reproduce in the lymphatic tissue. In line 5, the stem cell differentiates into a megakaryocyte (meg-ah-KAIR-ee-oh-syte), a large blood cell that breaks up into tiny cell fragments called *platelets* or *thrombocytes*.



BONE MARROW MISERY

BONE MARROW DEPRESSION

Cheer up! Even bone marrow gets depressed. Under certain conditions, the bone marrow cannot produce enough blood cells. Bone marrow depression is called *myelosuppression*. What happens if the bone marrow is depressed? Depressed bone marrow leads to a severe deficiency of RBCs, causing a serious form of **anemia** called *aplastic anemia*. Myelosuppression can also cause a deficiency of WBCs (leukocytes) called *leukopenia* (loo-koh-PEE-nee-ah). The leukopenic person is defenseless against infection and may die from a common cold. Depressed bone marrow may also produce inadequate numbers of platelets, or thrombocytes. This condition is called *thrombocytopenia* (throm-boh-sye-toh-PEE-nee-ah). The thrombocytopenic person is at high risk for hemorrhage. Why the concern for bone marrow depression? Because many drugs, especially cytotoxic cancer drugs, and certain procedures, such as radiation, depress the bone marrow, a person exposed to any of these therapies must be monitored for symptoms of myelosuppression. Clinically, this is a huge problem.

BONE MARROW OVERACTIVITY

Then, there is the hyperactive bone marrow known as *polycythemia vera*, or the overactivity and excess production of blood cells—bone marrow gone wild! The excess thickened blood (increased viscosity) burdens the heart, overwhelms the clotting system, and produces a beet-red, ruddy face (caused by the increase in RBC production). To help this condition, the patient may be given a drug that depresses the bone marrow or undergo therapeutic phlebotomy (fleh-BOHT-oh-mee) to remove excess blood. The myelosuppressed anemic patient appears pale and has a low RBC count, low hematocrit, and low hemoglobin. The patient with polycythemia vera has an elevated RBC count, elevated hematocrit, and an elevated hemoglobin, and has a ruddy or red face.

? Re-Think

1. Where does most hemopoiesis occur?
2. What are three consequences of myelosuppression?

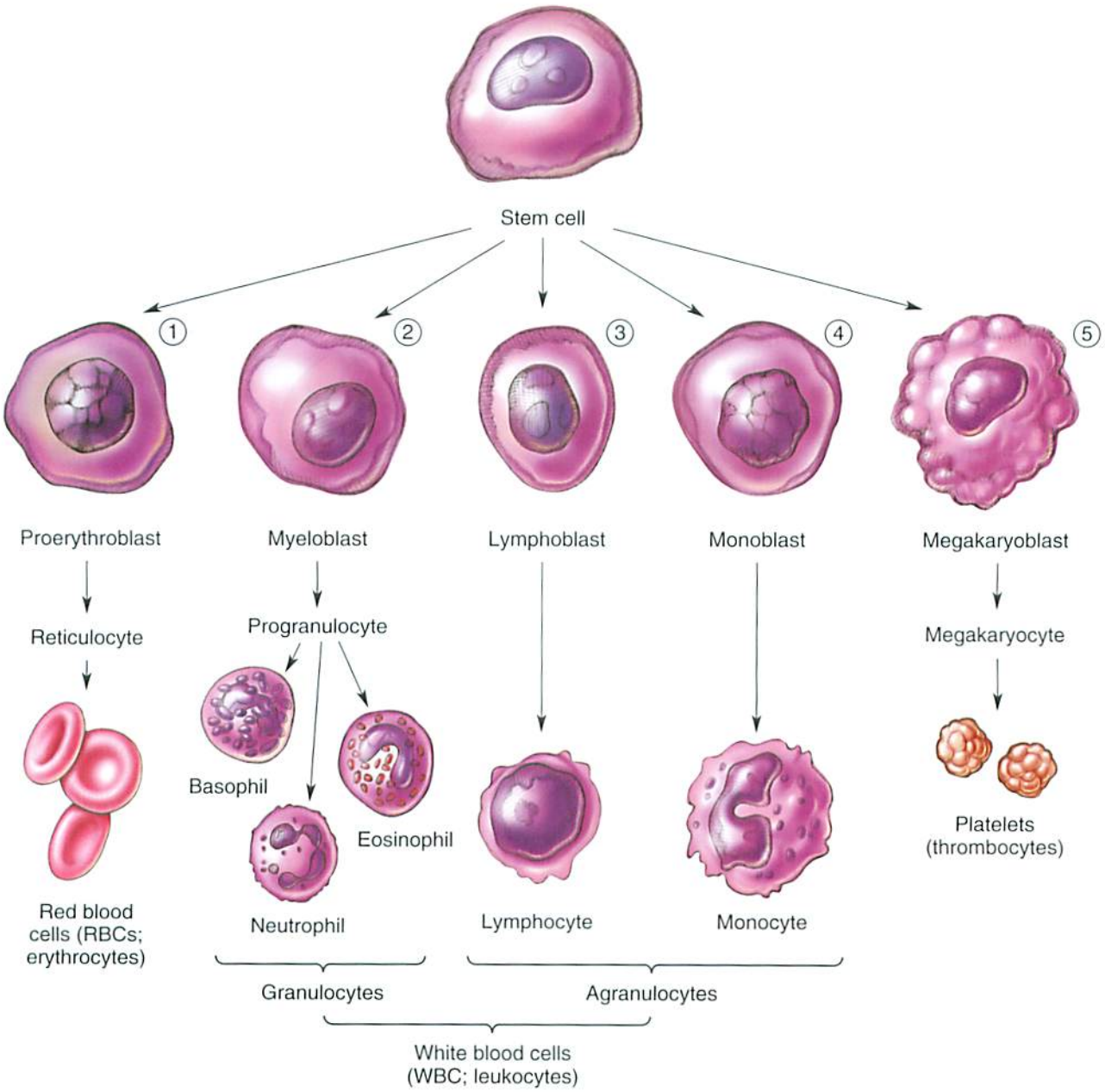


FIGURE 15-2 Differentiation of a stem cell into RBCs, WBCs, and platelets.

2+2 Sum It Up!

Blood is composed of plasma and blood cells. The RBCs (erythrocytes) carry oxygen; the WBCs (leukocytes) protect against infection and the platelets (thrombocytes) prevent bleeding. The hematocrit is a measure of the ratio of the blood cells to blood volume. Myelosuppression and polycythemia are two examples of altered bone marrow activity.

BLOOD CELLS

RED BLOOD CELLS

The RBCs are the most numerous of the blood cells. Between 4.5 and 6.0 million RBCs are in one microliter of blood. The rate of production by the red bone marrow is several million RBCs per second. The production of RBCs is called *erythropoiesis* (eh-rith-roh-poy-EE-sis). RBCs are primarily concerned with the transport of oxygen and carbon dioxide.

"RETICS"

The immature RBC is called a **reticulocyte** (reh-TIK-yoo-loh-syte) (clinical nickname, retics; see Figure 15-2). The number of reticulocytes in blood is normally very small (0.5% to 1.5%). Reticulocytes can develop into mature RBCs within 48 hours of release into the blood. Why measure the reticulocyte count? A high reticulocyte count may indicate blood loss or another iron-deficient state. Why? A loss of blood stimulates the bone marrow to make more RBCs. The greater the

bone marrow activity, the higher the number of reticulocytes prematurely added to the circulation. The reticulocytes simply don't have time to mature in the bone marrow. Conversely, a low reticulocyte count might indicate that the patient's bone marrow is unable to make RBCs, as in myelosuppression or severe iron deficiency. Hence, changes in the reticulocyte count can provide valuable diagnostic clues.

SHAPE AND CONTENTS

What do RBCs look like? First, RBCs are large. The large RBCs stay in the blood vessels and do not roam around the tissue spaces, as do the WBCs. Second, RBCs are flexible disc-shaped cells that have a thick outer rim and a thin center (Figure 15-3). Because the RBC can bend, it can squeeze its way through tiny blood vessels. This flexibility allows the RBC to deliver oxygen to every cell in the body. The RBC's ability to bend is important. If the RBC were not able to bend, it would not fit through the tiny blood vessels, and tissue cells would be deprived of oxygen and die. Decreased oxygenation and cell death occur in a condition known as *sickle cell disease*. Instead of bending, the RBCs assume a sickle or C shape and block blood flow through the tiny blood vessels.

Red blood cell size and shape matter! While reading the results of a blood smear, you may come across the terms *anisocytosis* and *poikilocytosis*, which pertain to shape. Anisocytosis (ahn-ISS-oh-syte-OH-sis) refers to unequal-sized RBCs, whereas poikilocytosis (poy-KEE-loh-syte-OH-sis) refers to irregularly shaped RBCs. Both are found in anemia and other blood disorders (dyscrasias).

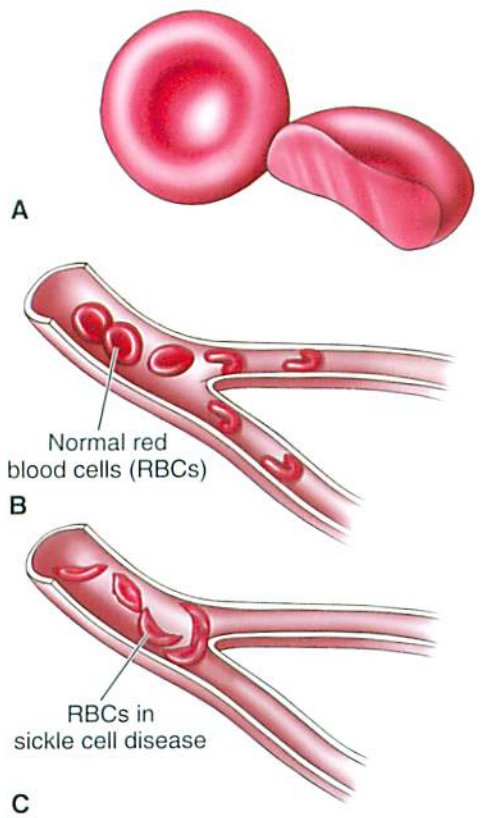


FIGURE 15-3 **A,** The RBCs are large and doughnut shaped. **B,** The RBCs must bend to fit through the blood vessel. **C,** Sickled RBCs blocking the flow of blood through the blood vessel.

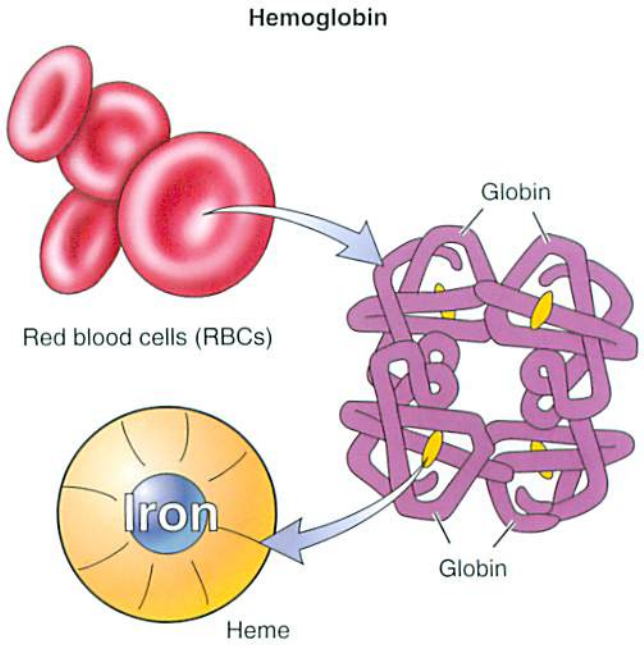


FIGURE 15-4 Hemoglobin and iron.

The content of the RBC is also unique. The RBC normally loses almost all its organelles as it develops. Having no mitochondria, the RBC is not powered aerobically; rather, it produces adenosine triphosphate (ATP) anaerobically. Think about it; the RBC does not metabolically use up the oxygen that it is transporting throughout the body. Also, the RBC, lacking a nucleus and DNA, cannot replicate; the "old" RBC is removed from the blood and replaced by a new RBC made in the bone marrow. We now know what the RBC does not contain, so what does it contain? It contains mostly hemoglobin. Read on.

HEMOGLOBIN

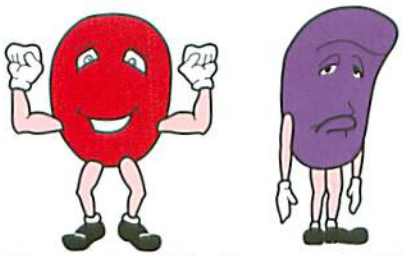
Red blood cells are filled with a large protein molecule called **hemoglobin** (Figure 15-4). Hemoglobin (hee-moh-GLOH-bin) consists of two parts: globin (protein) and heme, an iron-containing substance. Hemoglobin contains four globin chains, with each globin having a heme group. The hemoglobin molecule is responsible for RBC function.

What is so important about heme? As the RBCs circulate through the blood vessels in the lungs, oxygen (O_2) attaches loosely to the iron atom in the heme. The oxygenated hemoglobin is referred to as *oxyhemoglobin*. Then, as the blood flows to the various tissues in the body, the O_2 detaches from the hemoglobin. The unloaded oxygen diffuses from the blood to the cells, where it is used during cellular metabolism.

The globin portion of hemoglobin also plays a role in gas transport. Globin transports some of the carbon dioxide (CO_2) from its site of production in the metabolizing cells to the lungs, where it is excreted. The CO_2-hemoglobin complex is called *carbaminohemoglobin* (kahr-bam-ih-no-hee-moh-GLOH-bin). To repeat: Hemoglobin carries both O_2 and CO_2 but at different sites.

WHY BLOOD CHANGES ITS COLOR

The color of blood changes from bright red to blue-red. When hemoglobin is oxygenated, blood appears bright red. When hemoglobin is unoxygenated, blood assumes a darker blue-red color. Thus, blood coming from the lungs is well oxygenated and appears red. Blood leaving the tissues has given up its oxygen and appears blue-red. When a person is deprived of O_2, the blood is a blue-red color, causing the skin to look blue, or cyanotic. Cyanosis is a sign of hypoxemia, a deficiency of O_2 in the blood. Cyanosis is always cause for concern and should prompt a search for the underlying cause of the hypoxemia.



Oxygenated RBC Unoxygenated RBC

Why can a person have cherry-red blood and be hypoxemic at the same time? It's a carbon monoxide (CO) thing. Blood is bright red when the hemoglobin is saturated with O_2. CO, like O_2, binds to the iron and also makes the blood appear bright cherry red. When CO occupies the iron site, however, no O_2 can be carried by the hemoglobin. Therefore, the person with CO poisoning can be both cherry red and hypoxemic. CO poisoning is deadly and very common. By the way, 20% of the hemoglobin of a cigarette smoker is unavailable for O_2 transport because of the presence of CO in the smoke.

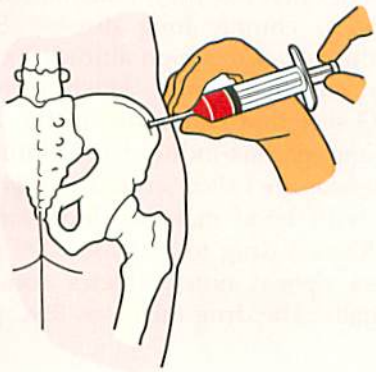
SUBSTANCES ESSENTIAL FOR HEMOGLOBIN PRODUCTION

What does the body need to make adequate amounts of hemoglobin? In addition to healthy bone marrow, the body requires certain raw materials. Iron, vitamin B_{12}, folic acid, and protein are essential for hemoglobin synthesis. Recall that the heme, the O_2-carrying component of hemoglobin, contains iron. A diet deficient in iron can result in inadequate hemoglobin synthesis and a condition called *iron deficiency anemia*. Young women are more prone to iron deficiency anemia than young men, as might be expected. Women not only are more apt to get caught up in rigorous and unhealthy dieting, but they also tend to lose more iron because of the blood loss associated with menstruation and fetal demands during pregnancy. Persons with a low income also have a higher incidence of iron deficiency anemia because iron-rich foods such as meat are expensive. The RBCs of a person with iron deficiency anemia are microcytic (small cell size) and hypochromic (pale).

Do You Know...

Why There Is a Needle in This Hip Bone?

Because the red bone marrow is the site of blood cell production, certain abnormalities of blood cells can be detected through a bone marrow biopsy. In this procedure, a needle is inserted into the red bone marrow, usually at the iliac crest (hip bone). A sample of bone marrow is withdrawn, or aspirated, and then studied microscopically. The analysis includes the numbers and types of blood cells and the specific developmental characteristics of each cell type.



A deficiency of other raw materials can cause other specific anemias. A deficiency of folic acid, for example, causes folic acid deficiency anemia. In addition to adequate dietary intake, raw materials must be absorbed from the digestive tract. Absorption of some of the raw materials requires special transport proteins. Adequate absorption of vitamin B_{12}, for example, requires a transport protein called *intrinsic factor*. Intrinsic factor is normally secreted by the lining of the stomach. The inability to secrete adequate intrinsic factor in some persons results in inadequate absorption of vitamin B_{12}. This condition results in a form of anemia called *pernicious anemia*. Why pernicious? Pernicious comes from the Latin word meaning "violent death," a reference to the painful neurological consequences of vitamin B_{12} deficiency. Today, pernicious anemia is easily treated with vitamin B_{12} and patients no longer die a violent death. Both folic acid deficiency and pernicious anemia are characterized by RBCs that are macrocytic (large RBCs) and normochromic (normal

RBC color). Note how the size and color of the RBCs can provide diagnostic clues about the different types of anemias.

REGULATION OF RBC PRODUCTION

New RBCs are constantly added to the circulation, and old, worn-out RBCs are constantly removed from the circulation. Figure 15-5 indicates that the RBC count is maintained through negative feedback control. When the O_2 in the body tissues decreases, the kidneys sense the need for additional O_2 and secrete a hormone called **erythropoietin** (eh-RITH-roh-POY-eh-tin). The erythropoietin (EPO) stimulates the bone marrow to produce additional RBCs. The increase in the number of RBCs causes an increase in the amount of oxygen transported to the tissues. As tissue O_2 increases, the stimulus for EPO release diminishes, and the bone marrow slows its rate of RBC production.

Three clinical thoughts about EPO follow:

- Note what happens in a person who is chronically hypoxemic, such as a person with emphysema (a chronic lung disorder). The low oxygen in the blood stimulates the secretion of excess EPO, causing additional RBC production. Thus, a person with emphysema often has polycythemia (excess RBCs) secondary to chronic lung disease. Similarly, a person who moves to a high-altitude location experiences a mild hypoxemia, which, in turn, stimulates EPO secretion and a rise in the RBC count. Both the emphysema-induced and altitude-induced polycythemias are called *secondary polycythemias*.
- Patients with bone marrow depression may be given EPO as a drug to increase RBC production. On a less upbeat note, athletes sometimes use EPO illegally. The drug increases RBC production, thereby increasing the amount of O_2 delivered to exercising muscle. The administration of EPO under this condition is a form of blood doping.
- Patients with declining kidney function do not produce enough EPO and therefore become anemic. This type of anemia is called the *anemia of chronic renal (kidney) failure*. It is treated with the administration of EPO.

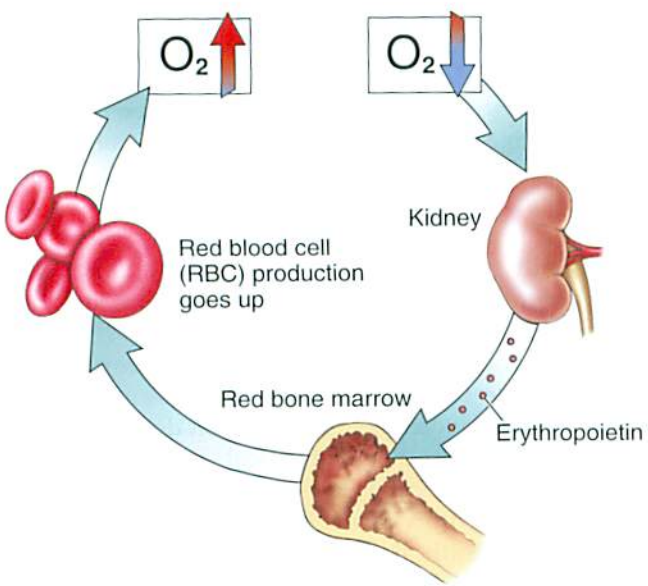


FIGURE 15-5 Regulation of RBC production by erythropoietin.

REMOVAL AND BREAKDOWN OF RED BLOOD CELLS

How does the body know when an RBC needs to be removed from the circulation? The life span of a RBC is about 120 days. Because the mature RBC has no nucleus, it cannot reproduce and must be replaced as it wears out. The signal for RBC removal? With time, as it performs its job, the RBC eventually gets misshapen, ragged around the edges, and fragile; the poor thing looks worn out! The ragged RBC membrane is detected by the macrophages that line the spleen and liver. The macrophages, or big eaters, remove the RBCs from the circulation and phagocytose them. Sometimes, the RBCs are broken down very rapidly in a process called **hemolysis**, exceeding the rate of RBC replacement. This results in hemolytic anemia and jaundice. Why is the yellow hue called jaundice? Look in the "recycle bin" in Figure 15-6.

RECYCLE!

As the old, worn-out RBC is dismantled, its components are recycled. The hemoglobin is broken down into globin and heme (see Figure 15-6). The globin is broken down into various amino acids that are later used in the synthesis of other proteins.

The heme is further broken down into iron and bile pigments. The iron is stored in the liver until it is needed by the bone marrow for the synthesis of new hemoglobin. The liver removes bile pigments, especially bilirubin, from the blood and excretes them into the bile. Bile eventually flows into the intestines and is excreted from the body in the feces. What if RBC breakdown is excessive, as in hemolysis? The excess bilirubin in the blood, called *hyperbilirubinemia*, is deposited in the skin, causing it to appear yellow or jaundiced. Because the jaundice is caused by hemolysis, it is called *hemolytic jaundice*, as opposed to *obstructive jaundice* (described in Chapter 23).

2+2 Sum It Up!

RBCs are filled with hemoglobin; the heme (iron) portion carries O_2 as oxyhemoglobin, while the globin portion carries CO_2 as carbaminohemoglobin. Normal RBCs are formed only in the presence of adequate raw materials, normal genetic information that directs hemoglobin synthesis, and healthy bone marrow. RBC production is regulated by erythropoietin, which in turn responds to tissue levels of oxygen. Hemoglobin is degraded into globin and bilirubin. The iron is recycled and the bilirubin is excreted in the bile.

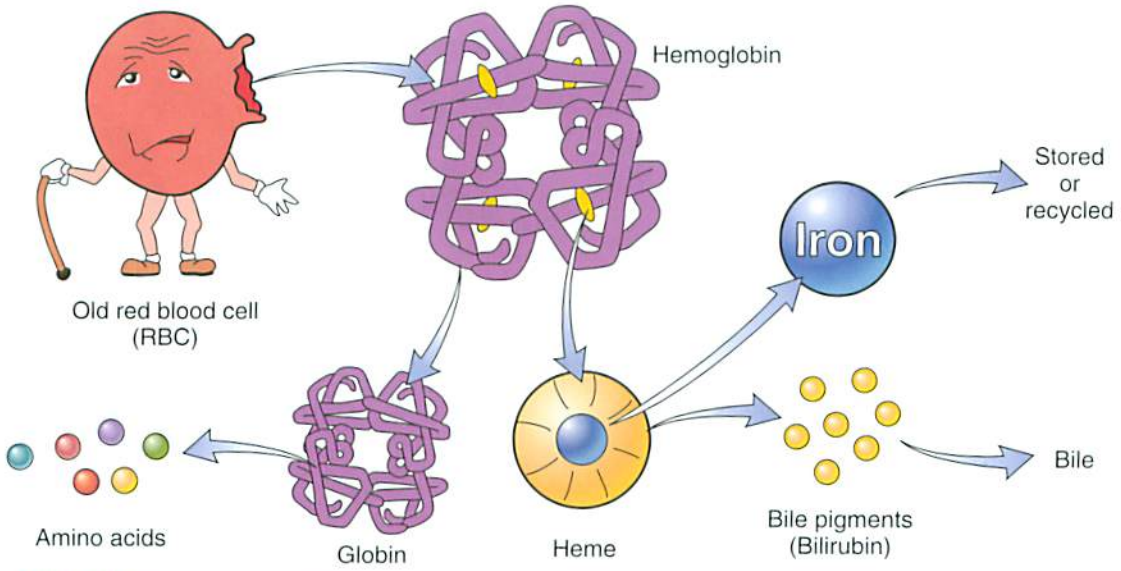
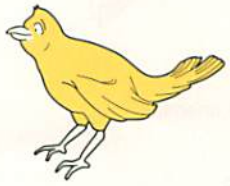


FIGURE 15-6 Breakdown of old RBCs. Note the recycling of amino acids and iron and the excretion of bilirubin.

Do You Know...

Who This Little Yellow Bird Called *Icterus* Is?

The term *icterus* is a Greek word for "little yellow bird." Icterus is the same as jaundice. The ancient Greeks thought that a jaundiced person could be cured by gazing at the yellow bird. We now know that bird watching is not the cure. Jaundice is caused by an elevation of bilirubin in the blood (hyperbilirubinemia). The hyperbilirubinemia can be caused by excessive blood cell destruction (hemolysis) or the reduction in the elimination of bilirubin from the blood (via the liver and bile). When jaundice is present, it is essential to determine the cause of the hyperbilirubinemia. The cure? Treat the underlying cause of the jaundice.



THE ANEMIAS...AS A SUMMARY OF RED BLOOD CELL REQUIREMENTS AND CONDITIONS

Figure 15-7 is meant to draw attention to the various conditions and raw materials essential for RBC production. Failure to provide the necessary conditions and essential raw materials results in anemia, a deficiency of RBCs. For example, deficiencies of raw materials, such as iron, folic acid, and vitamin B_{12}, decrease the RBC count. Incorrect genetic information results in malformed and dysfunctional hemoglobin and numerous types of anemia; the best known is sickle cell anemia. Impaired organ function, such as kidney disease and bone marrow depression, decreases the production of RBCs. Finally, anemias are caused by excess destruction (hemolytic anemia) or loss (bleeding) of RBCs (hemorrhagic anemia).

Re-Think

1. Explain why excess hemolysis causes jaundice.
2. Why must you know the underlying cause of anemia before treating it? Provide three examples in your explanation.

WHITE BLOOD CELLS

White blood cells (WBCs), or leukocytes, are large round cells that contain nuclei. WBCs lack hemoglobin and are less numerous than RBCs. WBCs function primarily to protect the body by destroying disease-producing microorganisms (pathogens) and removing dead tissue and other cellular debris by phagocytosis. When an infection is present in the body, the numbers of WBCs generally increase. This increase in the number of WBCs is called *leukocytosis* (loo-koh-syte-OH-sis). A few infections cause leukopenia, a decrease in the numbers of WBCs. Leukocytes vary widely with respect to life span: granulocytes may live only a few hours, whereas some lymphocytes may live for years.

Normally, 1 µl (microliter) of blood contains 5000 to 10,000 WBCs (Table 15-1). This number is somewhat misleading because the WBCs spend less than 12 hours in the blood; they leave the blood vessels and migrate to connective tissue or to the site of an infection or inflammation, where they work and live out their lives (Figure 15-8). Thus, the number of WBCs distributed

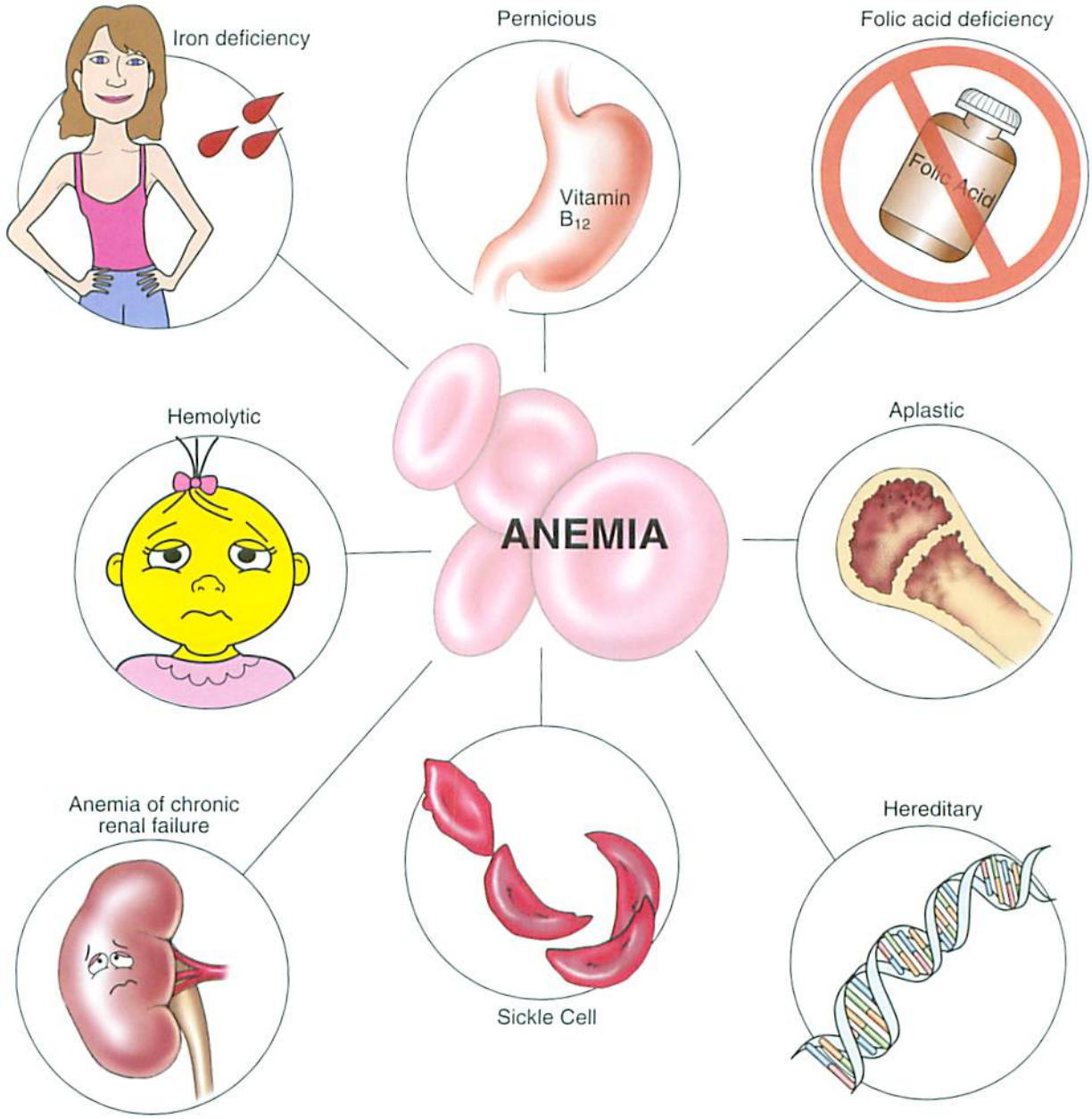


FIGURE 15-7 Summary of red blood cell formation and anemias.

throughout the body is much larger than what is suggested by the WBC count in the blood.

TYPES OF WHITE BLOOD CELLS

WBC production is called *leukopoiesis* (loo-koh-poy-EE-sis) (see Figure 15-2). Each of the five types of WBCs has a different name, appearance, and function (Table 15-2). How do we tell the difference? WBCs are classified according to granules in their cytoplasm. WBCs that contain granules are called *granulocytes*. Other WBCs do not have granules in their cytoplasm and are called *agranulocytes*. Granulocytes are produced in the red bone marrow and are classified according to their staining characteristics. The three types of granulocytes are neutrophils, basophils, and eosinophils.

NEUTROPHILS

The **neutrophil** (NOO-troh-fil) is the most common granulocyte. Neutrophils (which are pale or stain lavender) account for 55% to 70% of the total WBC population and usually remain in the blood for about 10 to 12 hours. The neutrophil's most important role is phagocytosis. These cells quickly move to the site of infection, where they phagocytose pathogens and remove tissue debris. The battle between the neutrophils and pathogens at the site of infection creates pus, a collection of dead neutrophils, parts of cells, and fluid.

Sometimes, the body can wall off the collection of pus from the surrounding tissue, forming an abscess. Abscess formation is one way that the body can prevent

Table 15-1 Types and Functions of Blood Cells

CELL TYPE	NORMAL RANGE	PRIMARY FUNCTION
Red blood cells (RBCs)	Men: 4.5–6.0 million/μL Women: 4.2–5.4 million/μL	Transport oxygen and carbon dioxide
Hemoglobin (Hgb)	Men: 13.5–17.5 g/100 mL Women: 12–16 g/100 mL	
Hematocrit (Hct)	Men: 40%–50% Women: 37%–47%	
Reticulocytes	0.5%–1.5%	
White blood cells (WBCs)*	5000–10,000/μL	Protect the body from infection
Platelets (thrombocytes)	150,000–450,000/μL	Help control blood loss from injured blood vessels

μL, Microliter.
*See Table 15-2 for the WBC differential count.

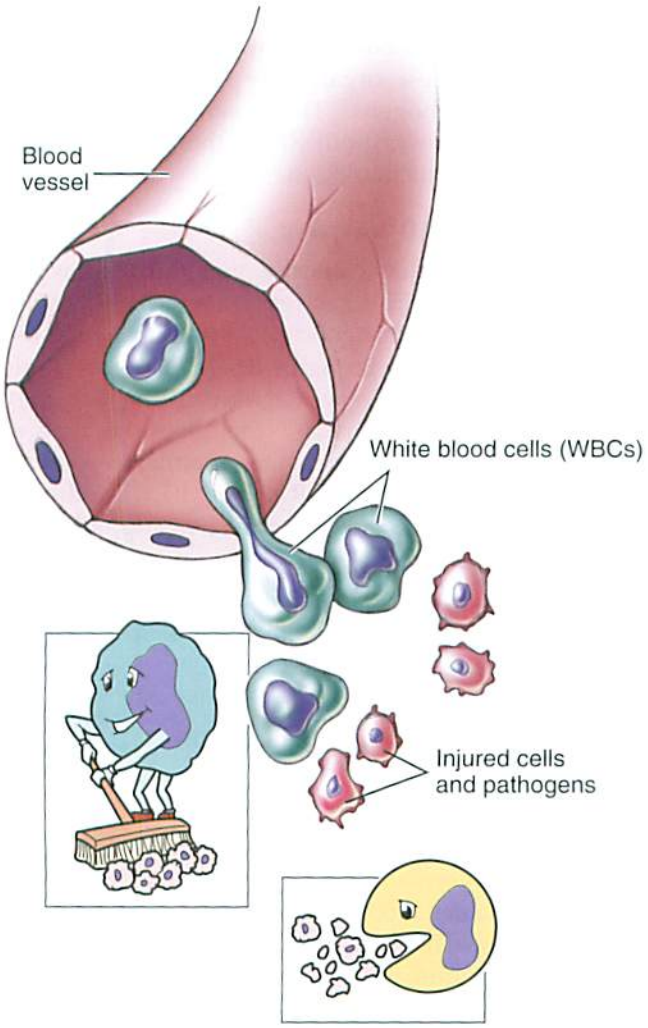


FIGURE 15-8 White blood cells are involved in phagocytosis.

the spread of infection. The neutrophil plays such an important role in the defense of the body that a deficiency of neutrophils (neutropenia or granulocytopenia) is considered life threatening. Unless resolved, the person may die from an overwhelming infection. Be sure that you understand these terms: *leukopenia*, *granulocytopenia*, and *neutropenia*. In what way are the terms similar and different?

Naming the Neutrophil

Because it plays such an important role in protecting the body from infection, the neutrophil is often the center of attention. Depending on its age, appearance, and its actions at the moment, the neutrophil has many nicknames.

Polys, Polymorphs, or Polymorphonuclear Leukocytes. The neutrophil is a round cell that contains a nucleus. The nucleus can have many shapes and different sizes. Because of the many-shaped (polymorphic) nucleus, neutrophils are called *polymorphs*, or *polymorphonuclear leukocytes* (PMNs). Sometimes, they are simply called *polys*.

Segs. The nucleus of the mature neutrophil appears segmented when viewed under a microscope. Mature neutrophils are therefore called *segs*.

Band Cells, Staff Cells, and Stab Cells. The nucleus of the immature neutrophil looks like a thick curved band—hence the name *band cells*. Because the band resembles the shape of a staff, the band cells are also called *staff cells*. Neutrophils are also called *stab cells*.

What Is a "Shift to the Left"?

This is a clinical phrase illustrating the response of the WBCs to a pathogen. As the body tries to mount an attack against a pathogen, it needs more neutrophils. The production of the neutrophils may be so rapid that the time for cells to mature is inadequate. A greater proportion of the neutrophils is therefore immature and appears banded. When immature neutrophils (bands) become prominent in the differential WBC count (lab test), the condition is termed a *shift to the left*. The term is derived from early studies that used tabular headings to report the numbers of each cell

Table 15-2 White Blood Cells (WBCs) (Differential Count)*

TYPE OF WBC	PERCENTAGE OF TOTAL WBC COUNT	FUNCTION OF CELL
Granulocytes		
Neutrophils	55–70	Phagocytosis
Eosinophils	1–3	Inflammatory responses, parasitic infection, allergies
Basophils	0–1	Inflammatory responses, release of heparin
Agranulocytes		
Lymphocytes	25–38	Immunity
Monocytes	3–8	Phagocytosis

*A differential WBC count indicates the percentage of each type of WBC.

type. The cell types were listed across the top of the printout, starting with bands on the left and the more mature neutrophils on the right. Thus, a shift to the left indicates an infection.

BASOPHILS

The second type of granulocytic WBCs, called **basophils** (BAY-so-fils), is normally present in small numbers. Basophils make up less than 1% of the WBCs and absorb a dark blue stain. The basophil plays a role in the inflammatory response, primarily through its release of histamine. The basophil also releases heparin, an anticoagulant. Because basophils are found in abundance in areas with large amounts of blood, such as the lungs and liver, the release of heparin is thought to reduce the formation of tiny blood clots.

EOSINOPHILS

The third type of granulocytic WBC is the **eosinophil** (ee-oh-SIN-oh-fil). The prefix eos- means rosy and refers to the staining characteristic of the eosinophil. Eosinophils are present in small numbers, constituting only 1% to 3% of the WBCs. They are involved in the inflammatory response, secreting chemicals that destroy certain parasites, engage in phagocytosis, and become elevated in persons with allergies.

AGRANULOCYTES

The two types of agranulocytes are lymphocytes and monocytes. The lymphocytes are produced in the red bone marrow; some migrate to, mature, and reproduce in the lymphoid tissue (lymph nodes, liver, spleen). Lymphocytes constitute 25% to 38% of the WBCs and perform an important role in the body's immune response. (Immunity will be discussed further in Chapter 21.) Monocytes are the second type of agranulocyte. Like the neutrophil, the monocyte is phagocytotic. Although the neutrophils are more abundant (55% to 70% of the WBCs), the monocytes (3% to 8% of the WBCs) are more efficient phagocytes.

Monocytes differentiate, or change, into macrophages. These macrophages become wandering or fixed. Wandering macrophages travel or wander about the body, patrolling for pathogens and cleaning up debris. Wandering macrophages are particularly abundant under the mucous membranes and skin, where they destroy pathogens that gain entrance through cuts and abrasions. In contrast, fixed macrophages reside in a particular organ, such as the liver, spleen, lymph nodes, or red bone marrow. As blood or lymph flows through these organs, the fixed macrophages phagocytose pathogens. These same macrophages also phagocytose worn-out RBCs, thereby helping to remove them from circulation.

GOOD NEWS, BAD NEWS

The bad news is that clinically, you must know the names and classifications (granulocytes, agranulocytes) of the WBCs. The good news is that you can use the monkey business in Figure 15-9. "**N**aughty **L**ittle **M**onkeys **E**at **B**ananas," says **GRAN**pa **BEN**. "Naughty Little Monkeys Eat Bananas" identifies the type of WBCs—**n**eutrophils, **l**ymphocytes, **m**onocytes, **e**osinophils, and **b**asophils. **GRAN**pa **BEN** indicates that the granulocytes are **b**asophils, **e**osinophils, and **n**eutrophils.

? Re-Think

1. Classify the neutrophil and identify its function.
2. Why can't you diagnose granulocytopenia or thrombocytopenia from a hematocrit reading?

PLATELETS

Platelets are tiny cell fragments of the larger megakaryocytes. Normally, each microliter of blood contains between 150,000 and 450,000 platelets or thrombocytes. They are produced in the red bone marrow (see Figure 15-2) and have a life span of 5 to 9 days. The production of the platelet is called *thrombopoiesis* (THROM-boh-poy-EE-sis).

Platelets prevent blood loss. (Platelet function is more fully described later in the "Hemostasis" section.) Failure of the bone marrow to replace platelets at an adequate rate results in a deficiency called *thrombocytopenia*. This condition is characterized by petechiae—little pinpoint hemorrhages under the skin—and potentially lethal bleeding episodes.

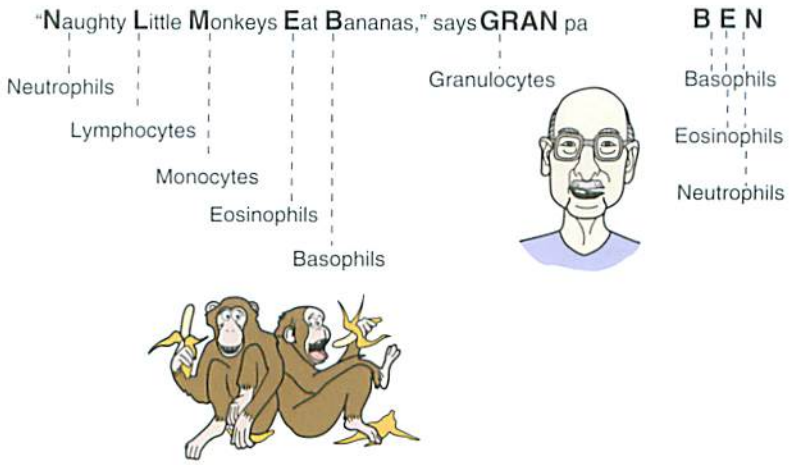


FIGURE 15-9 Naming white blood cells.

BLOOD COUNTS

A complete blood count (CBC) is a laboratory test that provides information about the composition of the blood. A CBC provides the normal range of the numbers of RBCs, WBCs, and platelets. In addition to the numbers of blood cells, the CBC provides information specific to each cell type. Relative to the RBC, the CBC indicates the normal hemoglobin content of the RBC, the normal Hct, and the percentage of the reticulocytes (the immature RBCs). With regard to information concerning the WBCs, a CBC indicates the percentage of each type of WBC (the differential WBC count).

DIFFERENTIAL COUNT

A differential WBC count indicates the percentage of each type of WBC (see Table 15-2). The differential count provides valuable diagnostic information because it indicates which specific WBC is involved. For example, one infection may cause an elevation primarily in the numbers of neutrophils, but a different infection may cause an elevation in the monocytes.

2+2 Sum It Up!

The WBCs (leukocytes) protect the body by destroying pathogens and removing dead tissue and other cellular debris by phagocytosis. The five types of WBCs are granulocytes (neutrophils, basophils, and eosinophils) and agranulocytes (lymphocytes and monocytes).

HEMOSTASIS: PREVENTION OF BLOOD LOSS

Injury to a blood vessel causes bleeding. Bleeding usually stops spontaneously when the injury is minor. What causes the bleeding to stop? The process that stops bleeding is called **hemostasis**, which literally means that the blood *(hemo)* stands still *(stasis)*. Hemostasis involves three events: blood vessel spasm, the formation of a platelet plug, and blood clotting (Figure 15-10). (Do not confuse the words *hemostasis* and *homeostasis*.)

BLOOD VESSEL SPASM

When a blood vessel is injured, the smooth muscle in the blood vessel wall responds by contracting in a process called *vascular spasm*. (*Vascular* refers to blood vessels.) Vascular spasm causes the diameter of the blood vessel to decrease, thereby decreasing the amount of blood that flows through the vessel. In the smallest vessels, vascular spasm stops the bleeding completely. In the larger vessels, vascular spasm alone may slow bleeding but is generally insufficient to stop bleeding.

FORMATION OF A PLATELET PLUG

When a blood vessel is torn, the inner lining of the vessel activates the platelets. The platelets become sticky and adhere to the inner lining of the injured vessel and to each other. By sticking together, they form a platelet plug, which diminishes bleeding at the injured site. Over several minutes, the plug will be invaded by activated blood-clotting factors and will eventually evolve into a stable, strong blood clot. In addition to forming a plug, the platelets also release chemicals that further stimulate vascular spasm and help activate the blood-clotting factors. Thus, the platelets participate in all three phases of hemostasis. Good news! Exercise decreases platelet stickiness and the formation of deadly blood clots. Bad news? Stress increases platelet stickiness.

ANTIPLATELET DRUGS AND BLEEDING

Aspirin and other antiplatelet drugs such as clopidogrel (Plavix) slow vascular spasm and prevent platelet stickiness; they are commonly used to suppress

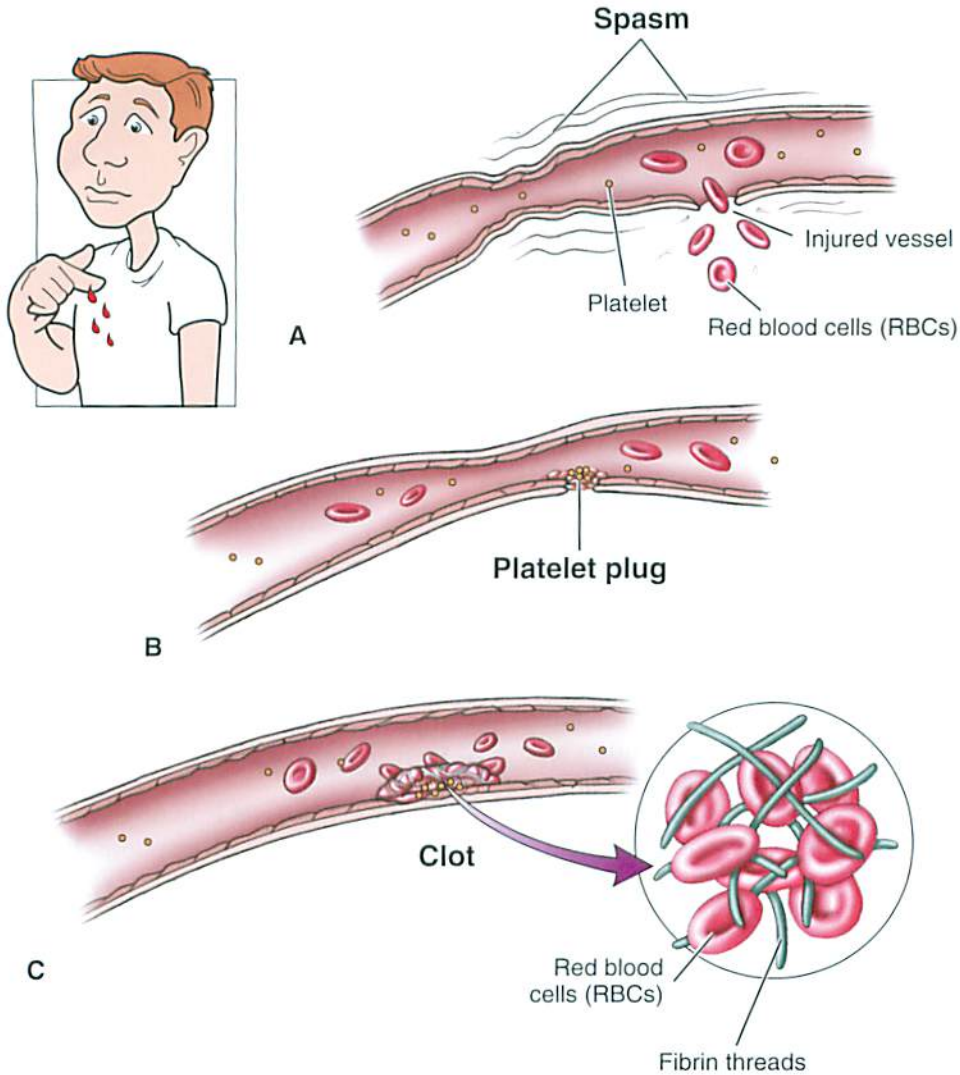


FIGURE 15-10 Steps in hemostasis. **A,** Blood vessel spasm. **B,** Formation of the platelet plug. **C,** Blood clotting (coagulation).

hemostasis. (A baby aspirin a day keeps the heart doctor away.) Excess antiplatelet therapy, however, can cause serious bleeding episodes, especially in a person who is thrombocytopenic or who is taking anticoagulant drugs.

BLOOD CLOTTING

Vascular spasm and a platelet plug alone are not sufficient to prevent the bleeding caused by a large tear in a blood vessel. With a more serious injury to the vessel wall, bleeding stops only if a blood clot forms. Blood clotting, or **coagulation**, is the third step in the process of hemostasis. A blood clot is formed by a series of chemical reactions that result in the formation of a netlike structure. The net, or framework, of the clot is composed of protein fibers called **fibrin**. As blood flows through the fibrin net, large particles in the blood, such as RBCs and platelets, become trapped within it. The fibrin net and the trapped elements are called a *blood clot*. The blood clot seals off the opening in the injured blood vessel and stops the bleeding.

FORMATION OF THE BLOOD CLOT

How does the clot form? The clot is the result of a series of reactions in which a number of clotting factors are activated. The series of reactions in which one clotting factor activates another clotting factor is called the *clotting cascade*.

Follow the three stages of blood coagulation identified in Figure 15-11.

- *Stage I.* Injury to the blood vessel wall activates various clotting factors. These clotting factors normally circulate in the blood in their inactive form. When activated, the clotting factors produce prothrombin activator (PTA).
- *Stage II.* In the presence of calcium, platelet chemicals, and PTA, prothrombin is activated to form thrombin.

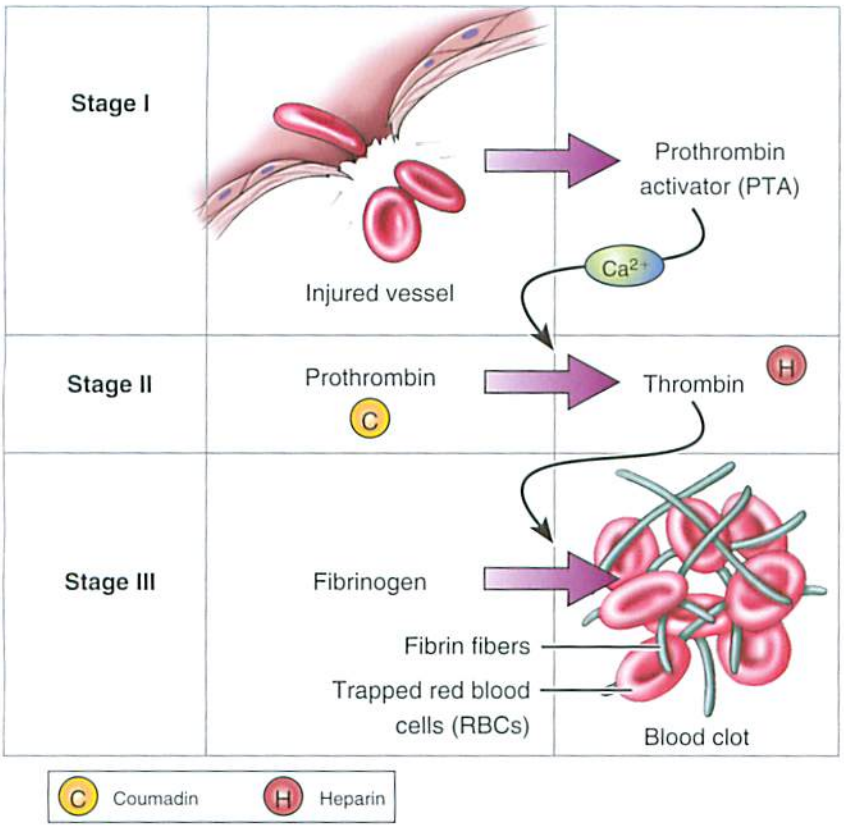


FIGURE 15-11 Three stages of blood clotting. The sites of Coumadin *(C)* and heparin *(H)* activity are indicated.

- *Stage III.* Thrombin activates fibrinogen. Activated fibrinogen forms the fibrin fibers, or fibrin net. The net traps other blood cells and particles to form the clot. Other factors then stabilize and strengthen the clot.

Do You Know...

What Queen Victoria, the "Royal Disease," and Factor VIII Have in Common?

Hemophilia A is a bleeding disorder caused by the deficiency of a clotting factor called *factor VIII*, or the *hemophilic factor*. Hemophilia was common in the royal families of Europe; hence, it was called the "royal disease." Why was hemophilia so prevalent in the royal families? Hemophilia is genetically transmitted. Because of the tendency of the royals to intermarry (e.g., cousin marrying cousin), the gene carrying hemophilia was kept in the family and expressed frequently in the royal offspring. Queen Victoria of England carried the gene for hemophilia. Victoria, being both reproductively prolific and politically astute, placed a descendant on every throne in Europe. As each descendant married and intermarried, the incidence of hemophilia increased. (There are other forms of hemophilia, all caused by deficiencies of clotting factors and characterized by excessive bleeding. Hemophilia B is caused by a deficiency of factor IX, whereas hemophilia C is caused by a deficiency of factor XI.)

ANTICOAGULANTS

Although the body must be able to stop bleeding, it is equally essential for it to prevent excessive clot formation. Several natural mechanisms prevent clot formation. Two of the most important mechanisms are a smooth inner lining (endothelium) of the blood vessels and the secretion of heparin, an anticoagulant.

Endothelium

The inner lining (endothelium) of the blood vessels is smooth and shiny and allows blood to flow easily along its surface. If the surface of the endothelium becomes roughened or lined with cholesterol plaques, however, coagulation factors are activated and blood clots are apt to form.

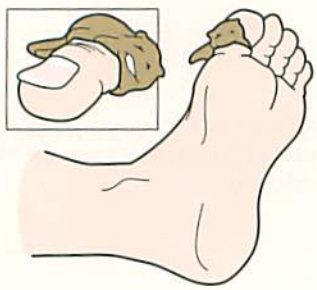
Secretion of Heparin

Heparin is secreted by mast cells. Mast cells are basophils that are concentrated in and around the liver and lungs, sites where the blood is stagnant and therefore apt to clot easily. Heparin acts as an anticoagulant by removing thrombin from the clotting process. In other words, heparin is an antithrombin agent. Note in Figure 15-11 that the formation of thrombin in stage II is crucial for clot formation (the conversion of fibrinogen to fibrin).

Do You Know...

Why This Toe Needs This Leech?

This toe was accidentally severed from its owner. In reattaching the toe to the foot, the surgeon recognized that the toe graft would be successful only if the blood supply to the toe was good. Frequently, after surgery of this type, blood clots and edema (swelling) develop at the graft site, resulting in a decrease in blood flow. Leeches, or bloodsuckers, may be applied to the site of the graft. As the hungry leech attaches to the skin to feed, it injects a potent anticoagulant. The anticoagulant prevents blood clotting at the graft site, thereby maintaining a good blood flow and improving the chances for successful grafting. Enter the celebrities. The rich and famous have discovered that leeches "take away the years." Attach a hungry leech to some puffy *whatever* and presto, the swelling subsides. Leeches are making it big and bringing in big bucks!



Anticoagulant Medications

At times, the administration of anticoagulant drugs may be necessary. Anticoagulants are administered in an attempt to prevent the formation of a blood clot. The blood clot is called a *thrombus;* the process of blood clot formation is called *thrombosis*. The problem? A piece of the thrombus can break off, forming an embolus, a traveling blood clot. The embolus may lodge in the smaller blood vessels of other organs, blocking the flow of blood to the organ and resulting in organ damage, such as a pulmonary infarct (necrosis), heart attack, or brain attack (stroke). A common killer disorder, called *deep vein thrombosis* (DVT), is particularly lethal. A clot in the deep veins of the legs gives rise to an embolus. The embolus travels to the blood vessels of the lungs, where it blocks blood flow and often causes instant death.

Thrombosis may be prevented by the administration of two types of anticoagulants: heparin and warfarin (Coumadin). Heparin, designated "H" in Figure 15-11, acts as an antithrombin agent. Another anticoagulant, Coumadin (warfarin), also prevents clot formation. Like heparin, Coumadin interferes with the clotting scheme but does so at a different step. Coumadin, designated "C" in Figure 15-11, decreases the hepatic (liver) utilization of vitamin K in the synthesis of prothrombin, causing hypoprothrombinemia (hye-poh-pro-THROM-ben-EE-mee-ah), a diminished amount of prothrombin in the blood. Less prothrombin means less thrombin, and less thrombin means that blood clotting is diminished.

Do You Know...

About Harry Clotter, His Spinach Salad, and His PT?

Harry was diagnosed with DVT after a 15-hour nonstop flight on his broomstick. After a 3-day stay in the hospital with heparin therapy, he was discharged on Coumadin (warfarin) and directed not to eat spinach. Why no spinach? The drug Coumadin works by blocking the utilization of vitamin K in the hepatic synthesis of prothrombin. Because spinach contains a lot of vitamin K, it reduces the effectiveness of Coumadin, thereby reversing its anticoagulant effects. So leave the spinach to Popeye, Harry. Harry was also advised to lose the stick and walk.

Harry was also directed to have his prothrombin (PT) time measured regularly. The PT is a blood test that measures the time it takes for a sample of blood to clot. Coumadin blocks the synthesis of prothrombin, so it induces hypoprothrombinemia and prolongs the PT. Because Coumadin can prolong the PT, the person is at risk for bleeding. Conversely, too little Coumadin provides inadequate anticoagulation, predisposing the person to clot formation; hence, the need for regular monitoring. PT values are reported as international normalized ratio (INR) units in an attempt to standardize laboratory test results. Harry's physician would most likely aim for an INR between 2 and 3.

CLOT RETRACTION

What happens to the clot after it forms? It becomes smaller as water is squeezed out. This process is called *clot retraction*. As the clot retracts, the edges of the injured blood vessels are also pulled together. This pulling together slows bleeding and sets the stage for repair of the blood vessel.

CLOT BUSTING: FIBRINOLYSIS

Are you stuck with the clot forever? No! After the clot accomplishes its task, it is dissolved by a process called *fibrinolysis* (fye-brin-OL-is-sis) (Figure 15-12). A substance called *plasmin* dissolves the clot. Plasmin is formed from its inactive form, plasminogen (plaz-MIN-o-jen), which normally circulates within the blood. Tissue plasminogen activator (TPA), formed by injured tissue, activates plasminogen.

TPA can now be administered as a drug to persons with life-threatening conditions caused by clots. TPA is in a category of drugs called *clot busters* or *fibrinolytic agents*. These drugs have revolutionized the treatment of myocardial infarction (heart attacks caused by blood clots in the blood vessels of the heart) and brain attacks (blood clots in the blood vessels of the brain). Long before we started injecting clot-busting drugs, however, the vampire bat had figured out plasmin physiology and had perfected the technique. Vampire bat saliva contains a TPA-like substance that dissolves clots and facilitates its dining activities.

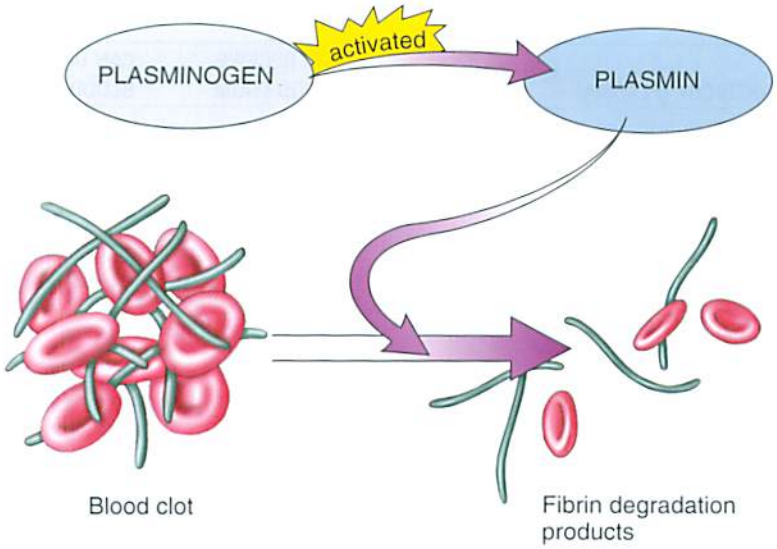


FIGURE 15-12 Fibrinolysis, also called "clot busting."

Re-Think

1. Use the following words to explain the steps in coagulation: fibrinogen, thrombin, fibrin, PTA, and prothrombin.
2. Why might excessive doses of aspirin, heparin, Coumadin, and TPA cause bleeding?

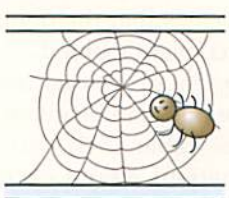
2+2 Sum It Up!

The process that stops bleeding after injury is called *hemostasis*. Hemostasis involves three events: blood vessel spasm, the formation of a platelet plug, and blood clotting (coagulation). Clotting occurs when thrombin causes the conversion of fibrinogen into a fibrin clot. Blood clots are eventually dissolved by plasmin. Three major groups of drugs affect hemostasis: antiplatelet drugs, anticoagulants, and fibrinolytic or clot-busting drugs.

Do You Know...

About Miss Muffet, Her Curds, Whey, and Blood Clot?

As you know, little Miss Muffet sat on her tuffet eating her curds and whey—that is, her soured milk. (The lumps in soured milk are called *curds*, and the watery part is called *whey*. So much for Muffet's diet.) What does this have to do with blood? Thrombosis (blood clotting) is from a Greek word meaning "to curdle," as in the curdling of milk. Serum is from a Latin word that refers to whey or the watery residue left after milk has curdled. Miss Muffet didn't really have a blood clot, but her diet inspired blood-clotting vocabulary. Her tuffet and arachnophobic personality are another story!



BLOOD TYPES

The history of medicine has recorded attempted blood transfusions since its earliest days. Although some were successful, others were medical disasters. The earliest physicians recognized that a severely wounded person was in need of blood. They did not realize, however, that blood from one person cannot always be mixed with blood from another. These physicians unknowingly demonstrated by disaster the presence of different blood types.

ANTIGENS AND BLOOD TYPES

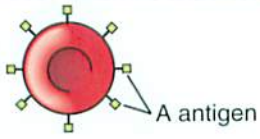
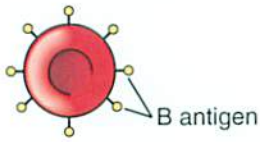
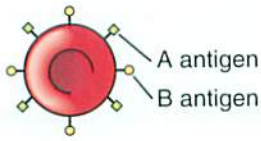
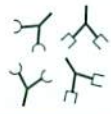
Blood is classified according to specific antigens on the surface of the RBC. An antigen is a substance that the body recognizes as foreign; the encounter evokes an immune response, thereby producing antibodies. As a foreign substance, an antigen stimulates an antigen–antibody response. This response is designed to attack and destroy the antigen.

The ABO grouping contains four blood types: A, B, AB, and O. The letters A and B refer to the antigen on the RBC. Table 15-3 shows what it means to be type A, B, AB, or O.

- A person with type A blood has the A antigen on the RBC.
- A person with type B blood has a B antigen on the RBC.
- A person with type AB blood has both A and B antigens on the RBC.
- A person with type O blood has neither A nor B antigen on the RBC.

Remember that the antigen is located on the RBC membrane.

Table 15-3 ABO Blood Groups

BLOOD TYPE*	ANTIGEN (RBC MEMBRANE)	ANTIBODY (PLASMA)	CAN RECEIVE BLOOD FROM	CAN DONATE BLOOD TO
A (40%)	 A antigen	Anti-B antibodies 	A, O	A, AB
B (10%)	 B antigen	Anti-A antibodies 	B, O	B, AB
AB† (4%)	 A antigen B antigen	No antibodies	A, B, AB, O	AB
O‡ (46%)	 No antigen	Both anti-A and anti-B antibodies 	O	O, A, B, AB

*Number in parentheses indicates the percentage of the population with this blood type.
†Type AB, universal recipient.
‡Type O, universal donor.

ANTIBODIES AND BLOOD TYPE

In addition to the antigens on the RBCs, specific antibodies are found in the plasma of each blood type (see Table 15-3).

- A person with type A blood has anti-B antibodies in the plasma.
- A person with type B blood has anti-A antibodies in the plasma.
- A person with type AB blood has neither anti-A nor anti-B antibodies in the plasma.
- The person with type O blood has both anti-A and anti-B antibodies in the plasma.

ANTIGEN–ANTIBODY INTERACTION

Table 15-3 indicates that type A blood contains the A antigen and anti-B antibodies. What would happen if a person had the A antigen on his or her RBCs and anti-A antibodies in his plasma? The A antigen and the anti-A antibody would cause a clumping reaction much like the curdling seen when milk and vinegar are mixed together.

This clumping of the antigen–antibody interaction is called *agglutination*. Agglutination reactions cause the RBCs to burst or lyse, a process called *hemolysis*. If rapid hemolysis were to occur in the circulation, hemoglobin would be liberated from the RBCs, causing kidney failure and death.

COMPATIBILITY AND INCOMPATIBILITY OF BLOOD TYPES

The curdling, or agglutination, reaction has important implications for blood transfusions. Some blood types mix without undergoing agglutination reactions; they are said to be *compatible blood groups*. Other blood groups agglutinate, causing severe hemolysis. These blood groups are incompatible. To avoid giving a person incompatible blood, donor blood is first typed and cross-matched.

What do blood typing and cross-matching mean? First, the blood type (A, B, AB, or O) is determined. Then, a sample of donor blood (blood from the person who is donating it) is mixed (cross-matched) with a sample of recipient blood (blood from the person who is to receive the donated blood). Any evidence of agglutination indicates that the donor blood is incompatible with the recipient's blood.

Suppose a recipient of a blood transfusion has type A blood. She or he then can be given type A blood and type O blood (see Table 15-3). No antigen–antibody reaction (agglutination) would occur because type A

donor blood has the A antigen and the recipient has only anti-B antibodies (plasma). The type O donor blood does not cause agglutination because that person's RBC has neither the A nor the B antigen. Type A and type O blood are therefore compatible with type A blood.

Note what happens, however, if the type A recipient receives type B blood (see Table 15-3). Type B donor blood has the B antigen on each RBC surface. The plasma antibodies of the recipient are anti-B antibodies. The B antigen and the anti-B antibodies cause agglutination; thus, type B blood is incompatible with type A blood. What happens if the type A recipient is given type AB blood? In this case, the RBC contains both A and B antigens. The plasma of the recipient contains anti-B antibodies. When types A and AB are mixed, an agglutination reaction then occurs; these blood groups are incompatible. The administration of incompatible blood groups forms the basis of hemolytic blood transfusion reactions. The presence or absence of antibodies dictates the compatibility/incompatibility characteristics of the four blood groups (see Table 15-3).

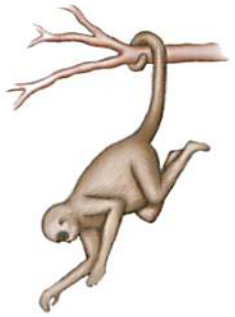
Note in Table 15-3 that type O blood can be given to people in all four blood groups. Type O blood is therefore called the *universal donor*. For this reason, blood banks stock a large supply of type O blood. Note also that someone with type AB blood can receive all four types of blood; this person is called a *universal recipient*. Table 15-3 also indicates the prevalence of the four blood types. Type A blood occurs in 40% of the population, 10% of the population has type B, 4% has type AB, and 46% has type O. Thus, type O is the most common and type AB is the least common. (What blood type are you?)

Re-Think

1. Why can't a person with type O blood safely receive a transfusion of type AB blood?
2. Why can't you change a person's blood type from type A to type O by giving him or her several transfusions of type O blood?

Rh CLASSIFICATION SYSTEM

Blood is also classified according to the Rh factor. The Rh factor is an antigen located on the surface of the RBC. The Rh factor was named for the rhesus monkey, in which it was first detected. If an RBC contains the Rh factor, the blood is said to be Rh-positive (+). If the RBC lacks the Rh factor, it is said to be Rh-negative (–). Thus, A+ blood refers to type A (A antigen) blood that also has the Rh factor, whereas A– blood is type A blood that does not have the Rh factor. Approximately 85% of the population is Rh positive (+).



Plasma does not naturally carry anti-Rh antibodies. In two conditions, however, the plasma of an Rh-negative (–) person can develop anti-Rh antibodies.

Do You Know...

About Bilirubin, Kernicterus, and Sulfa Drugs?

Normally, bilirubin is transported by the plasma proteins, especially albumin, in the blood. In pharmacology terms, bilirubin is said to be tightly bound to albumin. As long as the bilirubin is bound to the albumin, it is not free to leave the blood and stain the tissues yellow. Enter the sulfa drugs. If an infant (younger than 2 months old) is given a sulfa drug to treat an infection, the drug binds to the albumin and displaces or frees the bilirubin. The free bilirubin enters the tissues, staining them yellow. Because the blood–brain barrier of the infant is not fully developed, the bilirubin can enter the central nervous system (CNS), causing brain damage (kernicterus). The same thing happens when a pregnant woman is given a sulfa drug. The drug crosses the placental barrier, enters the fetal blood, and causes an excess of free bilirubin. Thus, the administration of sulfa drugs to an infant or to a pregnant or nursing mother is contraindicated.

The first condition involves the accidental administration of Rh-positive (+) blood to an Rh-negative (–) person. If Rh-positive (+) blood from a donor is administered to an Rh-negative (–) person (the recipient), the Rh antigen of the donor stimulates the recipient to produce anti-Rh antibodies. The recipient is now said to be sensitized. If the Rh-negative (–) person is later given a second transfusion of Rh-positive (+) blood, the anti-Rh antibodies in the plasma of the recipient will attack the Rh antigen of the Rh-positive (+) donor blood, causing agglutination and hemolysis.

The Rh factor may cause a serious problem in a second condition, that of an Rh-negative (–) pregnant mother who is carrying an Rh-positive (+) fetus (Figure 15-13). During this first pregnancy, the baby grows to term and is delivered uneventfully. During childbirth, however, some of the baby's Rh-positive (+) blood crosses the placenta and enters the mother's blood.

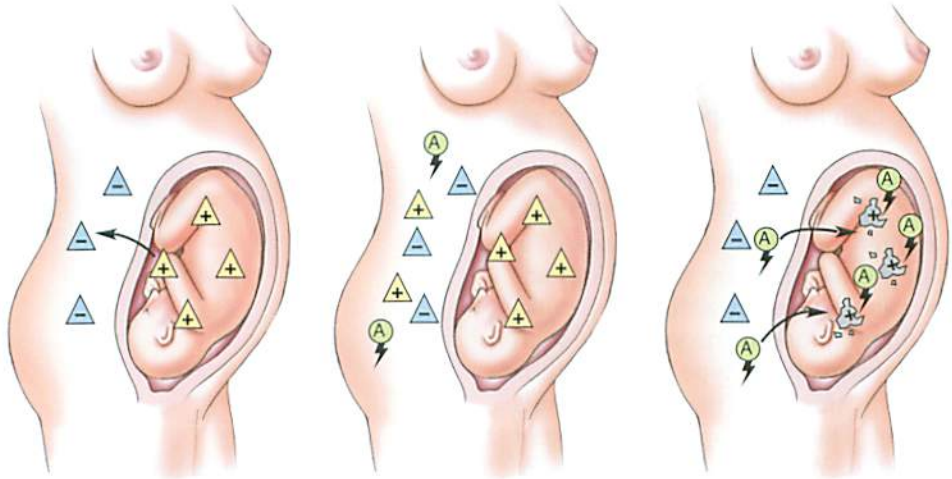


FIGURE 15-13 Rh-negative (–) mother, Rh-positive (+) fetus.

The Rh antigen stimulates the mother's immune system to produce anti-Rh antibodies. In other words, the mother has become sensitized by her first baby. If the mother becomes pregnant for a second time with an Rh-positive (+) baby, the anti-Rh antibodies move from the mother's circulation into the baby's circulation. These anti-Rh antibodies attack the baby's RBCs, causing agglutination and hemolysis. In response, the baby becomes jaundiced and anemic as the RBCs undergo hemolysis.

This hemolytic condition is called *erythroblastosis fetalis*. The hemolysis causes a rapid rise in plasma levels of bilirubin. The hyperbilirubinemia (increased bilirubin in the blood), in turn, causes severe jaundice and a condition called *kernicterus*. Kernicterus (kehr-NIK-tehr-ahs), caused by the staining of a part of the brain with bilirubin, is characterized by severe retardation in mental development. The great tragedy is that kernicterus is preventable. Every woman should know her blood type and recognize the need for early prenatal care!

Erythroblastosis fetalis can be prevented by the administration of the drug RhoGAM. RhoGAM is administered to the Rh-negative mother during pregnancy and within 72 hours after delivery. RhoGAM surrounds, or coats, the baby's Rh-positive (+) antigens, thereby preventing them from stimulating the development of anti-Rh antibodies by the mother.

Other antigens in the maternal and fetal blood are capable of inducing hemolysis, hyperbilirubinemia, and jaundice. Consequently, a newer and more inclusive term than *erythroblastosis fetalis* is *hemolytic disease of the newborn* (HDN). HDN includes all antigen–antibody reactions, including the Rh factor, that cause hemolysis and jaundice.

Visit any newborn nursery and you will see a little yellow baby "sunbathing" in an isolette. What's that about? It has been known for years that ultraviolet radiation (sunlight) hastens the disappearance of jaundice. Phototherapy provides ultraviolet radiation, which helps break down the bilirubin deposited in the skin so that it can be eliminated from the body.

2+2 Sum It Up!

Blood is classified according to the antigens on the surface of the RBC. The ABO grouping contains four blood types: A (A antigens), B (B antigens), AB (A and B antigens), and O (neither A nor B antigens). An antigen–antibody reaction, called *agglutination*, occurs when blood is mismatched. Type AB blood is the universal recipient blood. Type O blood is the universal donor blood. The Rh factor is another type of antigen on the RBC. Rh-positive blood has the Rh factor on the RBC, whereas Rh-negative blood does not contain the Rh factor.

As You Age

1. The volume and composition of blood remain constant with age, so most laboratory values remain normal. Alterations in laboratory values for blood usually indicate alterations in other organ systems. For example, the fasting blood glucose level increases with aging. This alteration is not the result of changes in the blood, however. Rather, it is the result of age-related changes associated with insulin. The same is true regarding serum lipid levels. Serum lipid levels increase 25% to 50% after the age of 55, but the increase is caused by an altered metabolism and not by changes of the blood and blood-forming organs.
2. The amount of red bone marrow decreases with age. The total number of blood cells remains normal, but older persons take longer to form new blood cells and hence recover more slowly from bleeding episodes.
3. An age-related decline occurs in white blood cell (WBC) activity. Although WBC activity still increases in response to infection, it does so more slowly.

MEDICAL TERMINOLOGY AND DISORDERS Disorders of the Blood

Medical Term	Word Parts	Word Part Meaning or Derivation	Description
Words			
ecchymosis	ecchy-	From the Greek word *eccym*, meaning "to pour out"	An **ecchymosis** is *a formation of escaped blood in the tissues from a blood vessel that has ruptured (commonly called a* bruise).
	-osis	condition or increase	
hematocrit	hemat/o-	blood	The **hematocrit** is *the ratio of the blood cells to the volume of the blood sample.*
	-crit	to separate	
normochromic	norm/o-	normal	**Normochromic** RBCs contain a normal amount of hemoglobin; therefore the color is normal.
	-chrom/o-	color	
	-ic	pertaining to	
myelodysplasia	myel/o-	bone marrow	Refers to *a group of disorders in which the bone marrow fails to produce blood cells, causing a reduction in RBCs, WBCs, and platelets.*
	-dys-	faulty	
	-plasia	formation	
petechiae		From an Italian word meaning "flea-bite," a reference to the appearance of petechiae	**Petechiae** are *tiny purple or red spots resulting from bleeding under the skin's surface.*
purpura		From a Latin word meaning "purple garment"	**Purpura** are *red or purple splotches under the skin or mucous membrane and are due to bleeding.*
Disorders			
anemia	an-	without	**Anemia** is *a deficiency of red blood cells (RBCs) or hemoglobin, diagnostically indicated by a low hematocrit.* The reduction in RBCs leads to varying degrees of hypoxemia, the basis for most of the signs and symptoms. The etiological classification is based on the causes of anemia. The anemias are described in the text.
	-emia	condition of the blood	

Continued

MEDICAL TERMINOLOGY AND DISORDERS Disorders of the Blood—cont'd

Medical Term	Word Parts	Word Part Meaning or Derivation	Description
hemolytic disorders	hem/o-	blood	**Hemolytic** refers to *the breakdown of RBCs, which leak their contents (hemoglobin, bilirubin, K^+) into the plasma.* There are many causes of hemolysis: infections, especially streptococcus and staphylococcus; antibody-inducing drugs; diseases such as sickle cell anemia (hemolytic crisis); the administration of incompatible blood; and hemolytic disease of the newborn (HDN).
	-lysis-	breakdown	
	-ic	pertaining to	
hemostatic disorders	hem/o-	blood	**Hemostatic** refers *to disorders that impair the ability of the blood to clot.* Disorders can be inherited or acquired (which is more common). **Thrombocytopenia,** *a reduction in platelets,* presents as spontaneous bleeding, such as hematuria, and prolonged bleeding from minor injuries. **Heparin-induced thrombocytopenia and thrombosis syndrome (HITTS),** also known as **white clot syndrome,** is of particular concern because of the frequent use of heparin as an anticoagulant. Heparin induces an immune response that causes platelet aggregation. **Hemophilia** refers to a group of bleeding disorders characterized by delayed coagulation and caused by a deficiency of a coagulation factor. **Hemophilia A,** the most common type, is due to a Factor VIII deficiency. Factor IX deficiency is called **hemophilia B** or **Christmas disease,** named for Stephan Christmas, the first patient diagnosed with factor IX deficiency. The chief symptom is bleeding, often into joints **(hemarthrosis).** Hemophilia (phil/o- = love) literally means "love of bleeding"; in this instance, love should be understood as a tendency to bleed. **Von Willebrand's disease** is the most common hereditary coagulation defect. It is a deficiency of von Willebrand factor, a protein that is necessary for platelet stickiness. **Disseminated intravascular coagulation (DIC),** despite its reference to coagulation, is characterized by excessive bleeding. An underlying condition stimulates accelerated clotting, depleting blood clotting factors and platelets and causing profuse hemorrhage.
	-stasis	stop or stand	
	-ic	pertaining to	
leukemias	leuk/o-	white	Also called *cancer of the blood,* **leukemia** is a hematological malignant condition in which there are excessive, immature ("blasts"), and abnormally functioning leukocytes. There are several classification systems. There are acute and chronic leukemias. There are also lymphocytic and myelocytic leukemias. The **lymphoblastic** or **lymphocytic leukemias** are caused by abnormal changes in bone marrow cells that give rise to B lymphocytes. The **myeloid** or **myelocytic leukemias** are caused by abnormal changes in bone marrow cells that give rise to RBCs, platelets, and some WBCs. Because the bone marrow becomes infiltrated with immature and abnormal leukocytes, hemopoiesis (blood formation) is severely impaired. The patient becomes anemic, thrombocytopenic, and neutropenic.
	-emia	blood condition	

MEDICAL TERMINOLOGY AND DISORDERS Disorders of the Blood—cont'd

Medical Term	Word Parts	Word Part Meaning or Derivation	Description
hemorrhage	hem/o-	blood	**Hemorrhage** refers to *active bleeding*. The patient becomes symptomatic with a loss of 15% to 30% of the total blood volume. **Hemorrhage** is classified in stages depending on the amount of blood loss. Hemorrhage may be internal, as in the loss of blood from a ruptured aneurysm, or external as in bleeding from a laceration on the arm. With severe hemorrhage the patient can "bleed out" or "bleed to death." This is known in medical terminology as **exsanguinations** (*ex* = out of) and (*sanguis* = blood).
	-rrhage	to burst forth	
septicemia	sept-	rotten	Also called *blood poisoning* and refers to *the presence of harmful substances in the blood, such as pathogens and toxins.* Septicemia can cause a life-threatening septic shock.
	-emia	blood condition	

Get Ready for Exams!

Summary Outline

Blood has three main functions: it delivers oxygen to all cells; it helps regulate body functions, such as body temperature; and it protects the body from infection and bleeding.

I. Blood Functions
- A. Transport (O_2, CO_2, nutrients)
- B. Regulation (fluid/electrolyte, acid–base, temperature)
- C. Protection (infection, blood loss)

II. Composition and Characteristics of Blood
- A. Blood is composed of plasma and blood cells.
- B. The blood cells originate in the bone marrow and lymphoid tissue.
- C. Hemopoiesis: erythropoiesis, leukopoiesis, and thrombopoiesis

III. Blood Cells
- A. Red blood cells (RBCs) or erythrocytes
  1. RBCs are filled with hemoglobin.
  2. Oxyhemoglobin transports oxygen and carbaminohemoglobin transports carbon dioxide.
  3. RBC production is regulated by erythropoietin (senses oxygen).
- B. White blood cells (WBCs)
  1. WBCs are classified as granulocytes and agranulocytes.
  2. The granulocytes are neutrophils, basophils, and eosinophils.
  3. The nongranulocytes are the lymphocytes and monocytes.
- C. Platelets
  1. Platelets are thrombocytes.
  2. Platelets are involved in hemostasis.

IV. Hemostasis
- A. Stages of hemostasis
  1. The three stages of hemostasis are blood vessel spasm, formation of a platelet plug, and blood coagulation.
  2. The three stages of blood coagulation are summarized in Figure 15-11.
- B. Dissolving clots and preventing clot formation
  1. Eventually, the clot dissolves by a process called *fibrinolysis;* clot dissolution is achieved primarily by plasmin.
  2. Natural anticoagulant mechanisms include a smooth endothelial lining and heparin.

V. Blood Types
- A. ABO blood types
  1. There are four types of blood: A, B, AB, and O.
  2. The A and B antigens are on the membrane of the RBC.
  3. Blood plasma contains anti-A and anti-B antibodies.
  4. Blood antigen and antibodies are summarized in Table 15-3.
- B. Rh factor
  1. An Rh-positive person has the Rh antigen on the RBC membrane; an Rh-positive person does not have anti-Rh antibodies in the plasma.
  2. The Rh factor must be considered when blood is transfused; an Rh-negative person cannot receive Rh-positive blood.
  3. An Rh-negative mother carrying an Rh-positive baby may give birth to a baby with hemolytic disease of the newborn (HDN).

Review Your Knowledge

Matching: Blood Cells

Directions: Match the following words with their descriptions below. Some words may be used more than once.

a. platelets
b. white blood cells
c. red blood cells

1. ___ Contains the antigens A and B
2. ___ Requires erythropoietin for production
3. ___ The reticulocyte is an immature cell of this type.
4. ___ Includes the neutrophil, eosinophil, and basophil
5. ___ A deficiency causes petechiae and bleeding
6. ___ Stickiness and plug both describe the functional role of this cell type.
7. ___ Primarily concerned with infection
8. ___ Measured as the hematocrit
9. ___ Classified as granulocytes and agranulocytes
10. ___ Primarily concerned with the delivery of oxygen

Matching: Blood Clots

Directions: Match the following words with their descriptions below. Some words may be used more than once.

a. embolus
b. plasmin
c. heparin
d. warfarin (Coumadin)
e. thrombus

1. ___ A blood clot in the leg
2. ___ Drug that interferes with the hepatic utilization of vitamin K in the synthesis of prothrombin
3. ___ A traveling or moving blood clot
4. ___ Enzyme that dissolves clots
5. ___ An anticoagulant that works by removing thrombin (antithrombin activity)

Matching: Blood Types

Directions: Match the following blood types with their descriptions below. Some may be used more than once.

a. A
b. B
c. AB
d. O

1. ___ The blood cells that contain neither the A antigen nor the B antigen
2. ___ The universal donor
3. ___ This blood type can receive type B and type A blood.
4. ___ This blood type contains only anti-B antibodies.
5. ___ This blood type contains both anti-A and anti-B antibodies.

Multiple Choice

1. The erythrocyte
   a. is phagocytic.
   b. contains hemoglobin and transports oxygen.
   c. initiates blood coagulation.
   d. produces antibodies that are involved in the immune response.
2. The neutrophil
   a. is a T lymphocyte.
   b. is a granulocytic phagocyte.
   c. secretes antibodies.
   d. activates plasmin.
3. Thrombin
   a. activates fibrinogen.
   b. is responsible for the formation of the platelet plug.
   c. is inactivated by vitamin K.
   d. is inactivated by prothrombin.
4. What statement is true regarding the administration of type A+ blood to a type O– recipient?
   a. The blood types are compatible; no hemolytic reaction is expected.
   b. Persons with O– blood are allergic to type A+ blood.
   c. The administration of type A+ blood to a type O– recipient causes hemolysis.
   d. Persons with type O– blood can safely receive type A+ blood.
5. Erythropoietin
   a. is synthesized by the kidneys.
   b. stimulates the bone marrow to make RBCs.
   c. is released by the kidney in response to hypoxemia.
   d. All of the above are true.
6. Which of the following is most likely to cause jaundice?
   a. Anemia
   b. A deficiency of erythropoietin
   c. A deficiency of intrinsic factor
   d. Hemolysis
7. Which of the following is a true statement?
   a. The reticulocyte is an immature thrombocyte.
   b. The neutrophil is a phagocytic granulocyte.
   c. The neutrophil, basophil, and eosinophil are fragments of the megakaryocyte.
   d. A deficiency of reticulocytes causes hypoprothrombinemia.
8. Hypoprothrombinemia and a prolonged prothrombin time is
   a. associated with bleeding.
   b. symptomatic of pernicious anemia.
   c. a consequence of heparin therapy.
   d. a consequence of thrombocytopenia.
9. Hyperbilirubinemia
   a. can be caused by hemolysis.
   b. causes jaundice.
   c. can cause kernicterus.
   d. All of the above are true.
10. Which of the following is least related to heme?
    a. Oxygen
    b. Phagocytosis
    c. RBC
    d. Iron