

Hematology

OUTLINE

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OBJECTIVES

After studying this chapter, readers should be able to:

1. Distinguish between the formed elements and the liquid portion of the blood.
2. Explain the characteristics of red blood cell counts.
3. Describe *erythropoiesis* and the sites of production of erythropoietin.
4. Distinguish between the five types of white blood cells and discuss their functions.
5. Describe the functions of each of the major components of blood plasma.
6. Describe the characteristics of platelets and their functions.
7. Define *hemostasis* and explain the mechanisms that help achieve it.
8. Explain what prevents the formation of massive clots throughout the cardiovascular system.
9. Explain blood typing and how it is used to avoid adverse reactions to blood transfusions.
10. Distinguish between a thrombus and an embolus.

KEY TERMS

Agglutination: The clumping of red blood cells following a transfusion reaction.

Agranulocytes: Leukocytes without granular cytoplasm.

Albumins: The smallest of plasma proteins; they make up around 60% of these proteins by weight.

Antibodies: Agglutinins; gamma globulin proteins that respond to specific antigens.

Antigens: Agglutinogens; red blood cell surface molecules that react with antibodies from the plasma.

Basophils: Leukocytes that have fewer granules than eosinophils, which become deep blue in basic stain.

B cells: Lymphocytes that are responsible for humoral immunity.

Bilirubin: An orange pigment formed from biliverdin that has potent antioxidant activity; bilirubin is orange and excreted along with biliverdin in the bile.

Biliverdin: A green pigment created from decomposing heme, which is converted to bilirubin.

Coagulation: The formation of a blood clot.

Colony-stimulating factors (CSFs): Glycoproteins that can cause the proliferation and differentiation of leukocytes.

Embolus: A clot that dislodges or fragments, to be carried away in the blood flow.

Eosinophils: Leukocytes with coarse, same-sized granules that appear dark red in acid stain.

Erythropoiesis: The process of developing erythrocytes (red blood cells), which mostly occurs in the red bone marrow (myeloid tissue).

Erythropoietin: A hormone that uses negative feedback to control the rate of red blood cell formation.

Fibrin: Insoluble threads of protein made from the plasma protein fibrinogen.

Fibrinogen: A plasma protein that is important for blood coagulation. It is the largest plasma protein.

Globulins: Antibodies made by the liver or lymphatic tissues that make up around 36% of the plasma proteins.

KEY TERMS CONTINUED

Granulocytes: Leukocytes with granular cytoplasm, including neutrophils, eosinophils, and basophils.

Hematocrit (HCT): The volume percentage of red blood cells in a sample of whole blood.

Hematology: The study of blood and blood disorders.

Hemoglobin: The substance in red blood cells that carries oxygen.

Hemostasis: The stoppage of bleeding.

Interleukins: Hormones upon which many of the effects of leukocytes depend.

Leukocytes: White blood cells; they protect the body against disease and develop from hemocytoblasts in red bone marrow.

Leukocytosis: A condition of white blood cells exceeding 10,000 per cubic millimeter (microliter), indicating an acute infection.

Leukopenia: A condition of the total white blood cell count being below 5,000 per cubic millimeter (microliter); this signifies conditions such as influenza, AIDS, and others.

Lymphocytes: Leukocytes with large, round nuclei inside a thin cytoplasm rim.

Macrophages: Cells that phagocytize and destroy damaged red blood cells, mostly in the liver and spleen.

Mast cells: Connective tissue cells that, during allergic reactions, release histamine and heparin.

Megakaryocytes: Red bone marrow cells that fragment to produce platelets.

Monocytes: Leukocytes that are the largest type of blood cells, with varied nuclei.

Natural killer (NK) cells: Lymphocytes responsible for immune surveillance; they are important in preventing cancer.

Neutrophils: Leukocytes with small granules that appear light purple in neutral stain; older neutrophils are called *segs* while younger neutrophils are called *bands*.

Nonprotein nitrogenous substances: Amino acids, urea, and uric acid in the plasma.

Plasma: The liquid portion of blood.

Plasma cells: Specialized B cells that form and secrete antibodies.

Plasma proteins: The most abundant solutes (dissolved substances) in the plasma.

Platelets: Thrombocytes; platelets are cytoplasm fragments of megakaryocytes that are important in blood clotting.

Polymorphonuclear leukocytes: White blood cells with segmented lobular nuclei, such as neutrophils.

Prothrombin: An alpha globulin made in the liver that is converted to thrombin.

Red blood cells (erythrocytes): Those red blood cells that transport gases, including oxygen.

Serotonin: A substance that contracts smooth muscles in blood vessels, reducing blood loss.

Serum: The clear, yellowish liquid that remains after clot formation; serum is plasma minus fibrinogen and some, but not all, of its clotting factors.

T cells: Lymphocytes that are responsible for cell-mediated immunity.

Thrombin: A substance that causes fibrinogen to be cut into sections of fibrin and then joined into long threads as part of the clotting process.

Thrombocytes: See *platelets*.

Thrombopoietin: A hormone that causes megakaryocytes to develop from hemocytoblasts, resulting in eventual platelet (thrombocyte) formation.

Thrombus: A clot that forms abnormally in a vessel.

Vasospasm: An action of muscle contraction in a small blood vessel that occurs after it is cut or broken; this action can completely close the ends of a severed vessel.

White blood cells: See *leukocytes*.

Introduction

The blood is made up of cells, fragments of cells, and dissolved biochemicals containing nutrients, oxygen, hormones, and wastes. It helps to distribute body heat and maintain stable interstitial fluid. Blood is actually a connective tissue with its cells suspended in a liquid, extracellular matrix. It is heavier and thicker than water. Blood contains erythrocytes (red blood cells), platelets, and leukocytes (white blood cells). Red blood cells (RBCs), white blood cells (WBCs), and platelets are collectively called *formed elements*. The liquid portion of blood is called **plasma**. Blood volume represents about 7% of a person's body weight.

Plasma contains water, amino acids, carbohydrates, lipids, proteins, hormones, electrolytes, vitamins, and cellular

wastes (see **Figure 6–1**). An average adult has approximately 4 to 6 L of blood.

Hematology

Hematology is the branch of medicine that is concerned with the study of blood and blood disorders. The blood transports oxygen, nutrients, cellular waste products, and hormones throughout the body. It is involved in heat distribution, protection against infection, and the regulation of acid–base balances. Hematology is a major component of the clinical laboratory. Phlebotomists must be familiar with the composition and normal values of the blood. They must also understand common blood diseases and conditions. This chapter will examine the structure and functions of the blood, which

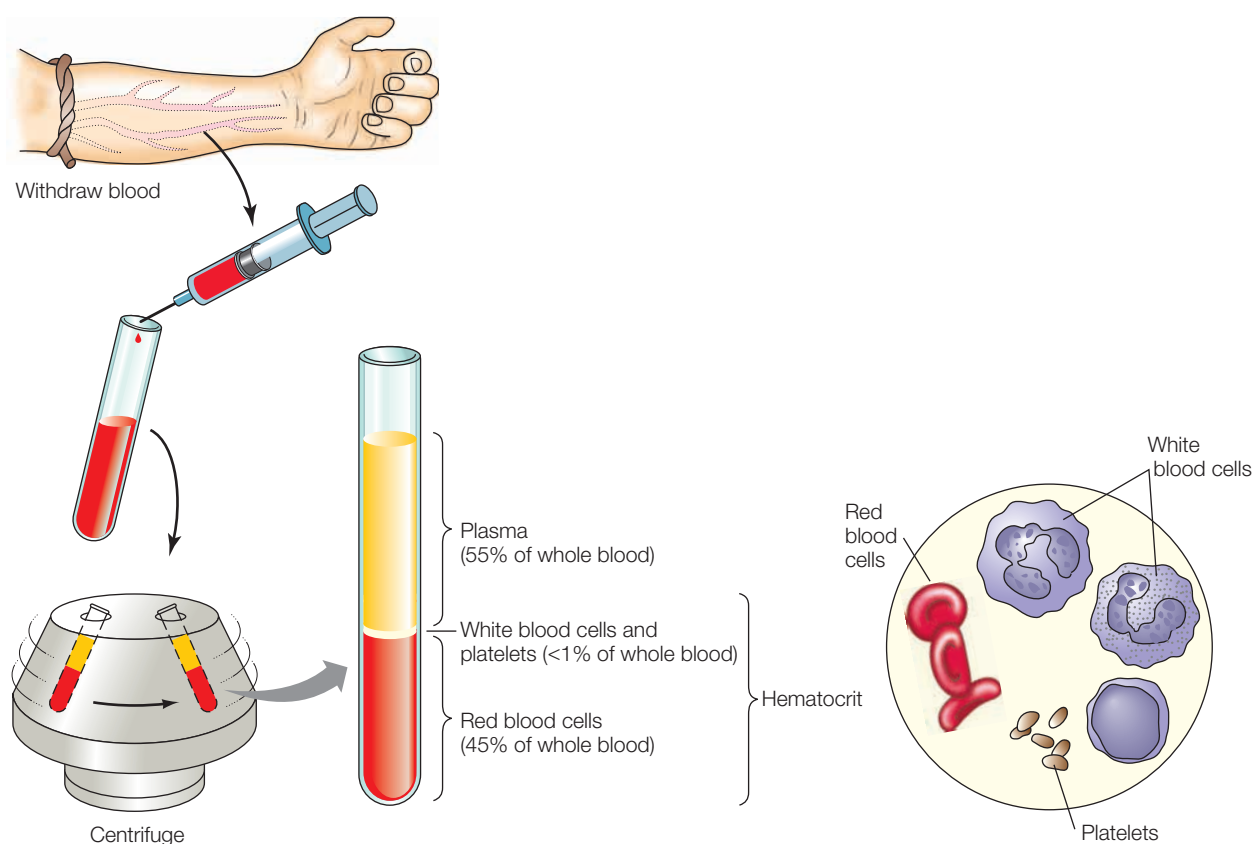


Figure 6-1 The composition of whole blood

is a specialized fluid connective tissue containing cells suspended in a fluid matrix.

Red Blood Cells

Red blood cells (erythrocytes) have a biconcave shape, meaning that they are basically round, with a center that is depressed in comparison with their edges. They are approximately 7.5 micrometers (μm) in diameter and $2\ \mu\text{m}$ thick at the rim. This shape helps them to transport gases by increasing the surface area of the cell, allowing greater diffusion (see **Figure 6-2**).

The shape of erythrocytes also ensures that the cell membrane is nearer to the **hemoglobin** (which carries oxygen) inside the cell. The cytoplasm of an RBC consists mainly of a 33% solution of hemoglobin. This is the red pigment that gives an RBC its color and name. Erythrocytes make up about 45% of blood volume—this portion is known as the **hematocrit** (HCT). When it binds with oxygen, *oxyhemoglobin* is formed. Oxyhemoglobin is bright red. When oxygen is released, *deoxyhemoglobin* is formed. Deoxyhemoglobin is darker red, and blood rich in deoxyhemoglobin may appear bluish when seen through blood vessels. The cytoplasm of erythrocytes contains an enzyme, *carbonic anhydrase* (CAH), that catalyzes the reaction of carbon dioxide (CO_2) plus water (H_2O) into hydrogen (H_2) and carbon trioxide (CO_3).

Erythrocytes have nuclei that are shed as they mature, allowing more room for hemoglobin. Lacking nuclei, mature

RBCs cannot synthesize proteins or divide to form more cells. They produce ATP through glycolysis because they do not have mitochondria, and they use none of the oxygen carried in their hemoglobin.

A *red blood cell count* is the number of RBCs in a microliter of blood. Normal ranges of RBCs are as follows:

- Adult males: 4.6 million to 6.2 million cells per microliter
- Adult females: 4.2 million to 5.4 million cells per microliter

Increased numbers of circulating RBCs increase the blood's *oxygen-carrying capacity*, which can affect health. Red blood cell counts are taken to diagnose many diseases and evaluate their courses. However, the opposite is also true: decreased RBC counts lead to decreased oxygen-carrying capacity, which is more likely to be seen on a regular basis than increased counts.

In humans, RBCs are mostly developed in spaces within bones that are filled with red bone marrow (myeloid tissue). This process is called **erythropoiesis**. Erythrocytes usually live for 120 days, with replacement cells created to maintain a relatively stable RBC count. The rate of red blood cell formation is controlled by negative feedback via the hormone **erythropoietin**. It is released by the kidneys and liver in response to prolonged oxygen deficiency (see **Figure 6-3**).

Production of red blood cells (erythropoiesis) continues at a heightened rate until the amount of them in the blood

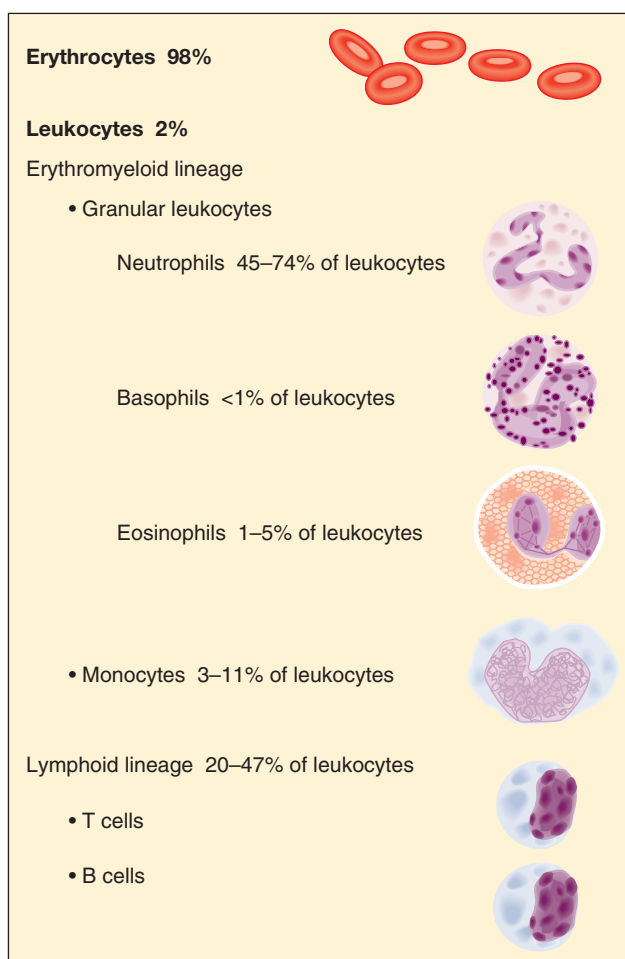


Figure 6–2 Various blood cells

circulation is enough to supply oxygen to the body tissues. The stages of formation of RBCs and other blood cells from hemocytoblasts are shown in **Figure 6–4**.

B-complex vitamins such as *vitamin B₁₂* and *folic acid* greatly influence RBC production and are necessary for DNA synthesis. Hematopoietic (blood-cell-forming) tissue is very vulnerable to deficiency of both of these vitamins. Iron is required for normal red blood cell production and for hemoglobin synthesis. Iron is slowly absorbed from the small intestine, and the body reuses much of the iron released by the decomposition of hemoglobin from damaged RBCs. Only small amounts of iron must be taken in via the diet.

Anemia has various causes, but sometimes it is caused by too little hemoglobin, or by too few RBCs. People with anemia may appear pale and lack energy because their blood is not able to carry enough oxygen. Iron-rich foods are important for the pregnant woman especially, in order to supply enough oxygen to her blood supply as well as to the blood supply of the developing fetus. However, not all anemia is due to iron deficiency. Because a pregnant woman's blood volume will increase due to fluid retention that supports the fetus, it decreases her hematocrit levels. *Hemochromatosis* is a condition that involves normal to increased RBCs. It is an iron handling disorder in which the small intestine absorbs

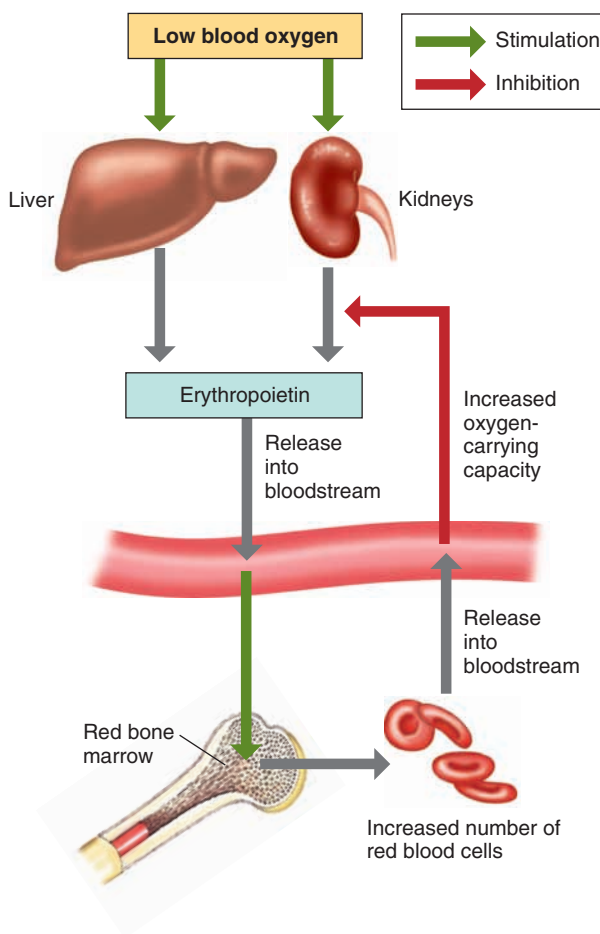


Figure 6–3 Erythropoietin is released by the kidneys and liver in response to prolonged oxygen deficiency.

iron at 10 times the normal rate, building up to toxic levels. This is treated by periodic blood removal.

Red blood cells bend as they move through blood vessels, but aging causes them to become more fragile. Cells called **macrophages** phagocytize and destroy damaged red blood cells, mostly in the liver and spleen. Hemoglobin from RBCs is broken down into *heme*, which contains iron, and the protein *globin*. The heme then decomposes into iron and **biliverdin**, a green pigment. The blood may transport the iron to synthesize new hemoglobin. Most of the iron that is removed from degraded hemoglobin is recycled to the bone marrow. Biliverdin is converted into **bilirubin**, an orange pigment, and excreted along with biliverdin in the bile. The life cycle of RBCs is summarized in **Figure 6–5**.

White Blood Cells

Leukocytes, also known as **white blood cells**, protect the body against disease and develop from hemocytoblasts in the red bone marrow in response to hormones. These hormones are either **interleukins** or **colony-stimulating factors (CSFs)**. Interleukins are organized by number, while most of the CSFs are named for the type of cells they stimulate. White blood cells are transported to sites of infection and may then leave the bloodstream.

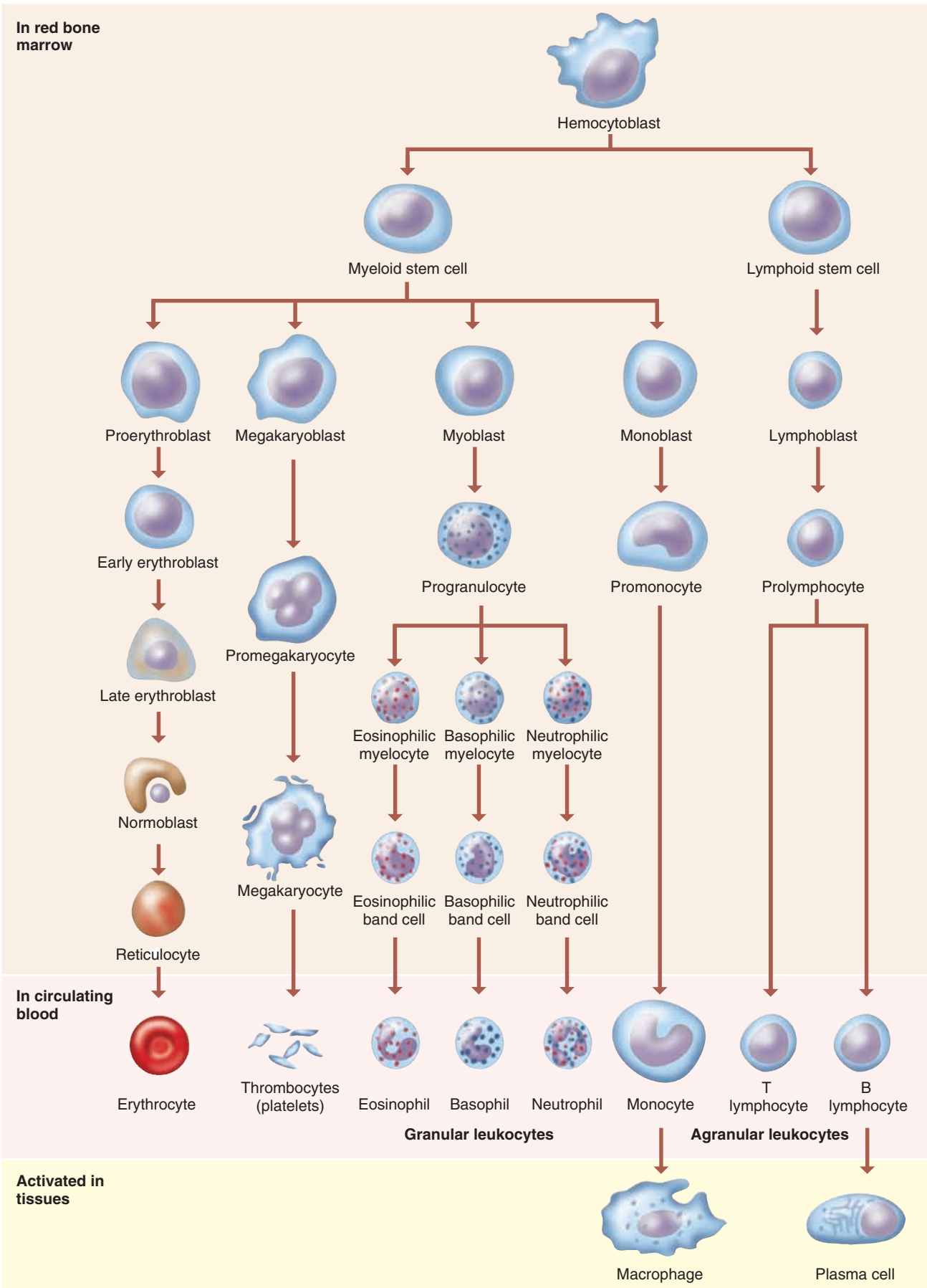


Figure 6-4 The stages of formation of the blood cells from hemocytoblasts
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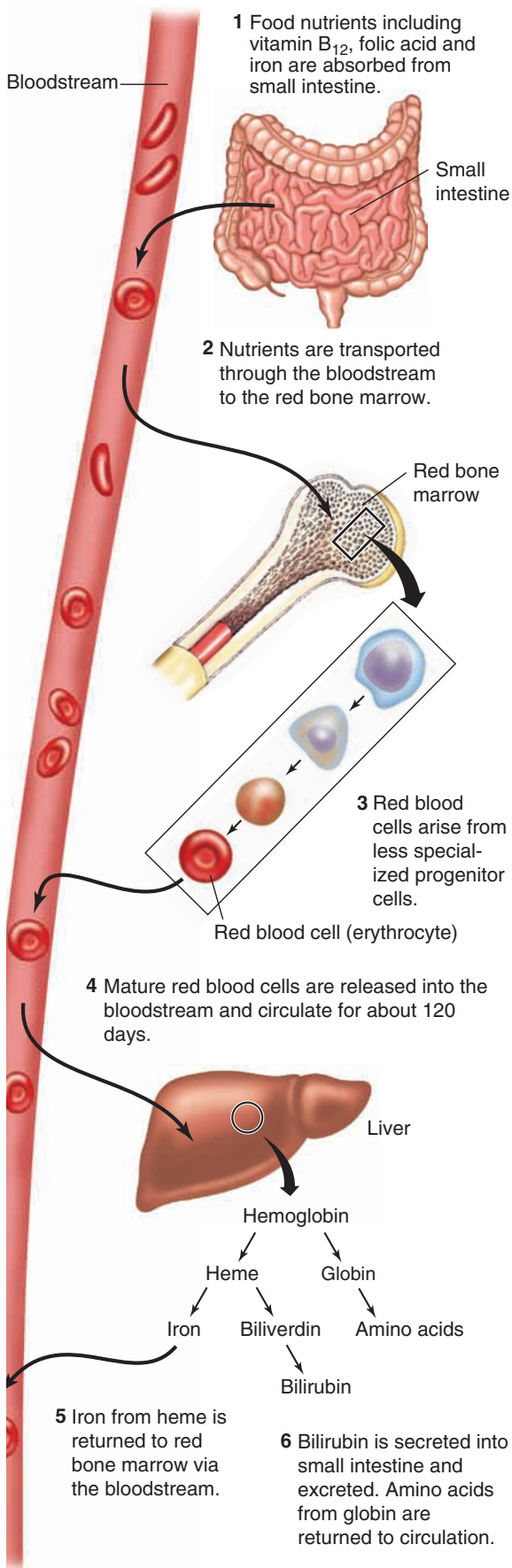


Figure 6-5 The life cycle of RBCs

There are usually five types of WBCs in circulating blood, differing in size, cytoplasm nature, nucleus shape, and staining characteristics. Leukocytes with granular cytoplasm are called **granulocytes**, while those without granular cytoplasm are called **agranulocytes**. Most granulocytes are about twice as large as a red blood cell, including eosinophils, basophils, and neutrophils. Granulocytes also develop in the red bone marrow, as RBCs do, but they only live about 12 h.

Neutrophils have small granules that appear light purple in neutral stain. Older neutrophils (sometimes called *segs*) have lobed nuclei in two to five segments connected by thin chromatin strands. Younger neutrophils have C-shaped nuclei and are called *bands* (see Figure 6-4). This structure has given neutrophils other names: **polymorphonuclear leukocytes**, *polymorphs*, or even *polys*. Neutrophils are highly mobile, and usually they are the first type of WBCs to arrive at the site of any injury. These active cells specialize in attacking and digesting bacteria. Neutrophils make up 54 to 62% of the leukocytes in most adults.

Most neutrophils have short life spans, surviving in the bloodstream for only about 10 h. When they actively engulf debris or pathogens, they may live for 30 min or less. A neutrophil will die after engulfing one to two dozen bacteria. As neutrophils break down, they release chemicals that attract other neutrophils to their location. A mixture of dead neutrophils and cellular debris products forms *pus*, which is associated with infected wounds.

Eosinophils have coarse, same-sized granules that appear dark red in acid stain (see Figure 6-4). Their nuclei have usually just two lobes (therefore, they are called *bilobed*), and they make up only 2 to 4% of circulating leukocytes. Eosinophils are particularly effective against multicellular parasites such as flukes or parasitic worms, which are too large to engulf. During a parasitic infection, the number of circulating eosinophils increases dramatically. These cells are sensitive to circulating allergens (materials that trigger allergies) and are also attracted to sites of injury. Once arriving at these sites, eosinophils release enzymes that reduce the degree of inflammation **mast cells** and neutrophils produce.

Basophils are smaller than neutrophils or eosinophils and have lower amounts of granules. They are more irregular and become deep blue in basic stain (see Figure 6-4). They usually account for less than 1% of circulating leukocytes. Basophils migrate to injury sites and cross the capillary endothelium to accumulate in the damaged tissues, where they release *histamine* (which dilates blood vessels) and *heparin* (a compound that prevents blood clotting). Mast cells release the same compounds in damaged connective tissues. Mast cells and basophils exist in distinct populations but have separate origins.

Monocytes are the largest type of blood cell, existing up to twice as large as red blood cells (see Figure 6-4). They have nuclei that may be kidney-shaped, lobed, oval, or round. Monocytes usually make up 2 to 8% of circulating leukocytes, having phagocytic properties prior to movement to the tissues. An individual monocyte is transported through the bloodstream, remaining in circulation for only about 24 h before entering peripheral tissues. Here, a monocyte becomes a tissue macrophage. Macrophages are aggressive phagocytes

that often attempt to engulf items as large as (or larger than) themselves. When phagocytically active, they release chemicals that attract and stimulate neutrophils, monocytes, and other phagocytic cells.

Lymphocytes are usually only a little larger than RBCs, with large, round nuclei inside a thin cytoplasm rim (see Figure 6–4). Lymphocytes make up between 20 and 30% of circulating leukocytes. Lymphocytes continuously migrate from the bloodstream into the peripheral tissues and back into the bloodstream. Circulating lymphocytes constitute only a small fraction of all lymphocytes, and the majority of lymphocytes are in other connective tissues in lymphatic organs. Lymphocytes are vital for immunity. Some of them produce antibodies that attack certain foreign substances.

Circulating blood contains three functional classes of lymphocytes, which cannot be distinguished with a light microscope, as follows:

1. **T cells** are responsible for *cell-mediated immunity*, which is a specific defense mechanism that combats invading foreign cells and tissues. T cells either enter peripheral tissues and attack foreign cells directly or control the activities of other lymphocytes.
2. **B cells** are responsible for *humoral immunity*, which is a specific defense mechanism that involves the production and distribution of antibodies. These antibodies attack foreign antigens throughout the body. Activated B cells differentiate into **plasma cells**, which are specialized to form and secrete antibodies.
3. **Natural killer (NK) cells** are responsible for *immune surveillance*, which involves the detection and subsequent destruction of abnormal tissue cells. NK cells (sometimes known as large granular lymphocytes) are important in preventing cancer.

Normally, there are 4,500 to 10,000 white blood cells in a microliter of human blood. This is called a *white blood cell count (WBC count)*. White blood cell counts are of interest to determine the clinical conditions of patients. If the WBC count is higher than normal, there may be an infection. If WBCs exceed 10,000 per cubic millimeter (mm^3) (microliter, or μL), the condition is called **leukocytosis**, which may indicate an acute infection. It is important to note that microliters are now being used more than cubic millimeters for this type of measurement, with 1 μL equivalent to 1 mm^3 . Also, normal ranges of WBC counts vary slightly from hospital to hospital. Conditions such as leukemia may also be noted as a result of WBC counts.

Appendicitis is an example of an acute infection that an elevated WBC may signify. When the WBC count is greatly elevated, leukemia may exist. **Leukopenia** is defined as a total WBC count below 5,000 per cubic millimeter (microliter). It may be more associated with immune suppression or chemotherapy-related diseases. Leukopenia is associated with diseases such as influenza, measles, mumps, chicken pox, AIDS, poliomyelitis, and typhoid fever.

Percentages of the types of leukocytes in a blood sample are listed in a *differential white blood cell count (diff)*, which is useful to determine the type of condition that exists with greater accuracy. Bacterial infections usually cause neutrophil counts to increase, while certain parasitic infections cause

the number of eosinophils to increase. AIDS causes certain types of lymphocyte counts to drop sharply.

Platelets

Platelets are also known as **thrombocytes**. They are cytoplasm fragments arising from red bone marrow cells (called **megakaryocytes**). Megakaryocytes develop from hemocytoblasts (megakaryoblasts) because of the hormone **thrombopoietin**. Platelets lack nuclei and are not even one-half the size of RBCs. They live for about 10 days and are capable of amoeboid movement. Usually, platelet counts range from 130,000 to 400,000 per microliter. The function of platelets is primarily to block injuries to damaged blood vessels and to start forming blood clots. Therefore, the main event of the platelet phase is the formation of the platelet plug. **Table 6–1** lists the characteristics of RBCs, WBCs, and platelets.

Plasma

Plasma suspends the cells and platelets of the blood. It is a clear, straw-colored liquid made up of 92% water, with organic and inorganic biochemicals. Plasma is close to the same density as water. Plasma makes up 46 to 63% of the volume of whole blood. It helps to transport gases, nutrients, and vitamins while helping to regulate fluid and electrolyte balance as well as pH levels. **Plasma proteins** are the most abundant of the solutes (dissolved substances) in the plasma. They are not usually used as energy sources, remaining in the blood and interstitial fluids. Three primary classes of plasma proteins exist: albumins, globulins, and fibrinogen. These three classes make up more than 99% of the plasma proteins. The remainder consists of circulating enzymes, hormones, and prohormones.

Albumins are the smallest of the plasma proteins, but they make up around 60% of these proteins by weight. They are made in the liver and play an important role in the plasma's *osmotic pressure*. Because plasma proteins are too large to move through capillary walls, they create an osmotic pressure to hold water in the capillaries (known as *colloid osmotic pressure*). This helps regulate water movement between blood and tissues, to aid in controlling blood volume and blood pressure. Albumins are also important in the transport of fatty acids, thyroid hormones, some steroid hormones, and other substances.

Globulins (including *alpha*, *beta*, and *gamma globulins*) make up around 35% of the plasma proteins. Important plasma globulins include antibodies and transport globulins. Antibodies, also called immunoglobulins, attack foreign proteins and pathogens. *Transport globulins* bind small ions and hormones. Alpha and beta globulins are made by the liver to transport lipids and fat-soluble vitamins. Gamma globulins are made by the lymphatic tissues and are a type of antibody. **Fibrinogen** (making up around 4% of the plasma proteins) is important for blood coagulation. It is made in the liver and is the largest (in size) of the plasma proteins. **Table 6–2** summarizes albumin, globulin, and fibrinogen.

Oxygen and carbon dioxide are the most important *blood gases*, with nitrogen also contained in the plasma. *Plasma nutrients* include amino acids, nucleotides, lipids, and simple sugars absorbed from the digestive tract. Glucose is

Table 6–1 Characteristics of Blood Cells and Platelets

Type	Function	Amount	Description
Red blood cells (erythrocytes)	Transport carbon dioxide and oxygen	4.2 million to 6.2 million per microliter	Biconcave discs with no nucleus, about one-third hemoglobin
White blood cells (leukocytes)	Destroy parasites and pathogens and remove worn cells	5,000 to 10,000 per microliter	
<i>Granulocytes</i>			<i>About twice the size of RBCs, with cytoplasmic granules</i>
1. Neutrophils	Phagocytize small particles	54 to 62% of WBCs	Nuclei have 2–5 lobes, granules stain light purple
2. Eosinophils	Help control allergic reactions and inflammation and kill parasites	1 to 3% of WBCs	Bilobed nuclei, granules stain dark red
3. Basophils	Release histamine and heparin	Less than 1% of WBCs	Bilobed nuclei, granules stain blue
<i>Agranulocytes</i>			<i>No cytoplasmic granules</i>
1. Monocytes	Phagocytize large particles	3 to 9% of WBCs	2–3 times larger than RBCs, varied nuclei shape
2. Lymphocytes	Provide immunity	25 to 33% of WBCs	Only slightly larger than RBCs, with very large nuclei
Platelets (thrombocytes)	Help control blood loss from broken vessels and begin clotting process	130,000 to 360,000 per microliter	Cytoplasmic fragments

transported in the plasma from the small intestine to the liver.

In the liver, glucose is stored as glycogen or converted to fat. The concentration of glucose in the blood is represented in milligrams per deciliter (mg/dL). When the blood concentration of glucose drops, *hypoglycemia* (a potentially dangerous condition) occurs. When glucose is elevated, it is called *hyperglycemia*, which can lead to diabetes (see **Table 6–3**). Plasma carries amino acids to the liver to manufacture proteins or to be used for energy. Plasma lipids include triglycerides, cholesterol, and phospholipids. Lipids are not water-soluble, but plasma is mostly made of water. Hence, lipids join with proteins to form lipoproteins, which the plasma can carry.

Nonprotein nitrogenous substances have nitrogen atoms, but are not proteins. In the plasma, these include amino acids,

urea, and uric acid. Blood plasma also contains many *electrolytes*, which include potassium, calcium, sodium, magnesium, chloride, phosphate, bicarbonate, and sulfate ions. The most abundant types are sodium and chloride ions. All plasma constituents are regulated so that their blood concentrations remain mostly stable. **Figure 6–6** summarizes blood composition.

Hemostasis

The stoppage of bleeding is known as **hemostasis**. When blood vessels are damaged, this vital process helps to limit or prevent blood loss. Hemostasis consists of three phases: *vascular phase*, *platelet phase*, and *coagulation phase*. When a smaller blood vessel is cut or broken, smooth muscles in its walls contract (**vasospasm**), and loss of blood slows nearly

Table 6–2 The Plasma Proteins

Protein	Origin	Percentage of Total	Function
Albumins	Liver	60	Help maintain colloid osmotic pressure
Globulins Alpha	Liver	36	Transport lipids and fat-soluble vitamins
βBeta	Liver		Transport lipids and fat-soluble vitamins
Gamma	Lymphatic tissues		Constitute a type of antibody
Fibrinogen	Liver	4	Plays key role in blood coagulation

Table 6–3 Blood Glucose Levels

Level	Description	Resulting Conditions
Less than 70 mg/dL	Hypoglycemia	Can be potentially fatal; symptoms include lethargy, impaired mental functioning, irritability, and loss of consciousness
Between 70 and 110 mg/dL	Normal	Levels usually lower in the morning and rise after meals
Between 110 and 125 mg/dL	Borderline hyperglycemia	Does not result in diabetes mellitus
126 mg/dL or greater	Hyperglycemia	If persistent, can result in diabetes mellitus, which can cause eye, kidney, and nerve damage

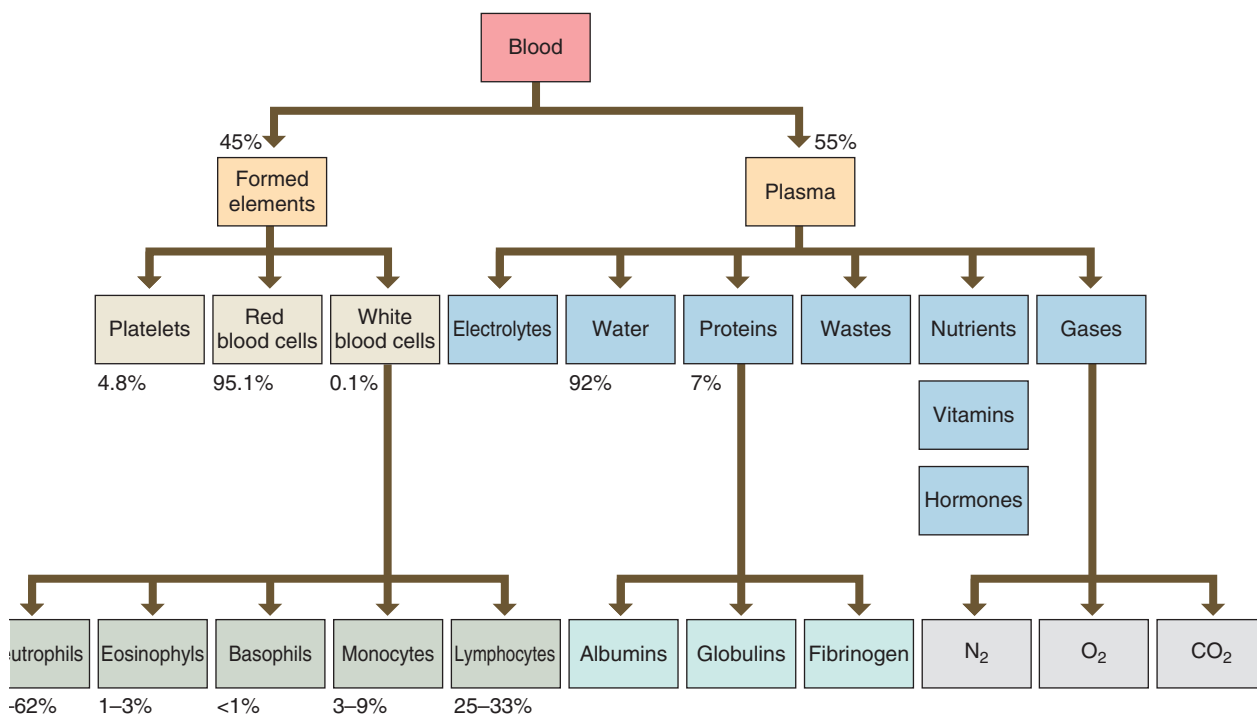


Figure 6-6 Blood composition

immediately. A vasospasm has the potential to completely close the ends of a severed vessel.

The effects of vasospasm may last for a few minutes up to about 30 min. At that time, a *platelet plug* has formed, and blood begins coagulating. Platelets release **serotonin** to contract smooth muscles in blood vessels, reducing blood loss. Platelets stick to rough surfaces and connective tissue collagen under the endothelial blood vessel lining. They also stick to one another to form a platelet plug in the area of the blood vessel injury. Larger breaks may require a blood clot to stop bleeding (see **Figure 6-7**).

The formation of a *blood clot* is known as **coagulation**. It requires many biochemicals known as *clotting factors*. Some clotting factors promote coagulation while others inhibit it, so a delicate balance between these two types is achieved to address the specific injured tissue. The most important event in coagulation is the conversion of the plasma protein fibrinogen to the insoluble threads of the protein called **fibrin**. The first step is the release of *tissue thromboplastin*, which results in the production of *prothrombin activator*. **Figure 6-8** describes the blood-clotting system. There are two pathways to the activation of the clotting system.

Prothrombin is an alpha globulin made in the liver on a continual basis, and it is always present in the blood plasma. Prothrombin activator converts prothrombin to **thrombin**, which causes fibrinogen to be cut into sections of fibrin. This fibrin then joins to form long threads. The threads stick to the surfaces of damaged blood vessels to create a mesh that traps blood cells and platelets. The result is a blood clot. After the formation of the clot, serum remains.

Serum

Serum is the clear, yellow liquid that remains after a clot forms. It is plasma minus some, but not all, of the clotting factors. Because blood is approximately one-half cells and one-half liquid, any test requiring 1 mL of serum would require 2 mL of blood to be collected.

Following the addition of *clot activator* to most vacuum tubes, serum for testing needs to clot for only 15 to 20 min before it is centrifuged. Plasma fibrinogen traps red blood cells to form a fibrin network. Immunological and chemistry tests are performed on serum. A variety of tests can now be performed on either serum or plasma.

Plasma

Plasma is the fluid portion of blood that remains after all blood cells have been removed. It consists of water and dissolved proteins, amino acids, glucose, fats, fatty acids, electrolytes, gases, and metabolic wastes. It is composed of about 90% water, 9% protein, and other chemical substances that total about 1%. Plasma comprises the liquid portion of whole blood that contains active clotting agents. Plasma is used for “stat” chemistry testing and coagulation studies.

A whole blood specimen is centrifuged to separate the various blood components. Red blood cells will settle in the bottom of the tube, with the white blood cells and platelets forming a thin, white “buffy coat” and the plasma remaining above it. At this point, the plasma contains all of the dissolved components of the blood, including the coagulation factors. Plasma specimens contain an anticoagulant, natural heparin, to prevent clotting.

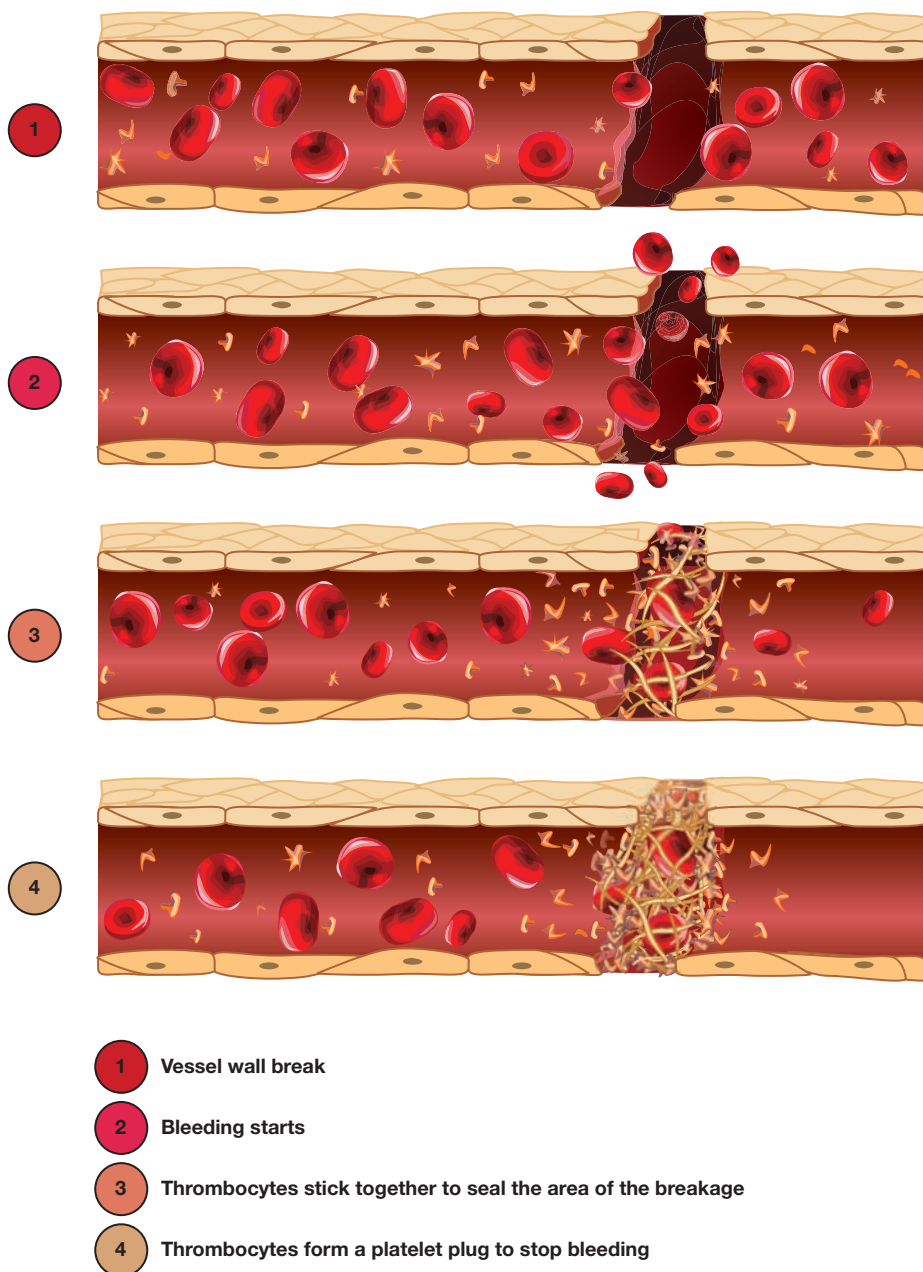


Figure 6-7 Platelet plug

Appearance of Serum and Plasma

Blood serum appears as a yellow or straw-colored fluid. It is seen after blood has been allowed to clot, and it does not contain fibrinogen, which is found in the clotted portion of the blood. Blood plasma is the pale yellowish liquid part of whole blood. It contains coagulation factors that help form clots to stop bleeding.

Blood Clotting

More prothrombin activator becomes present if tissue damage is more severe. Continual clotting occurs to stop greater damage. Positive feedback is used to stimulate more clotting action based on the original clotting action. However, this

continual process can work only for a short time because it interrupts the stability of the body's internal environment. Excess thrombin is normally carried away to avoid the formation of a massive blood clot. As a result, blood coagulation usually occurs in blood that is not moving or that is only moving slowly. Clotting stops because excess thrombin is absorbed on the clot.

Blood clots in ruptured vessels are invaded by *fibroblasts* to produce fibrous connective tissue that helps seal blood vessel breaks. Clots that form in tissues as a result of blood leakage (*hematomas*) disappear over time. This process requires the plasma protein *plasminogen* to be converted to *plasmin*, an enzyme that digests threads of fibrin and other proteins involved in clotting. While plasmin may dissolve entire clots,

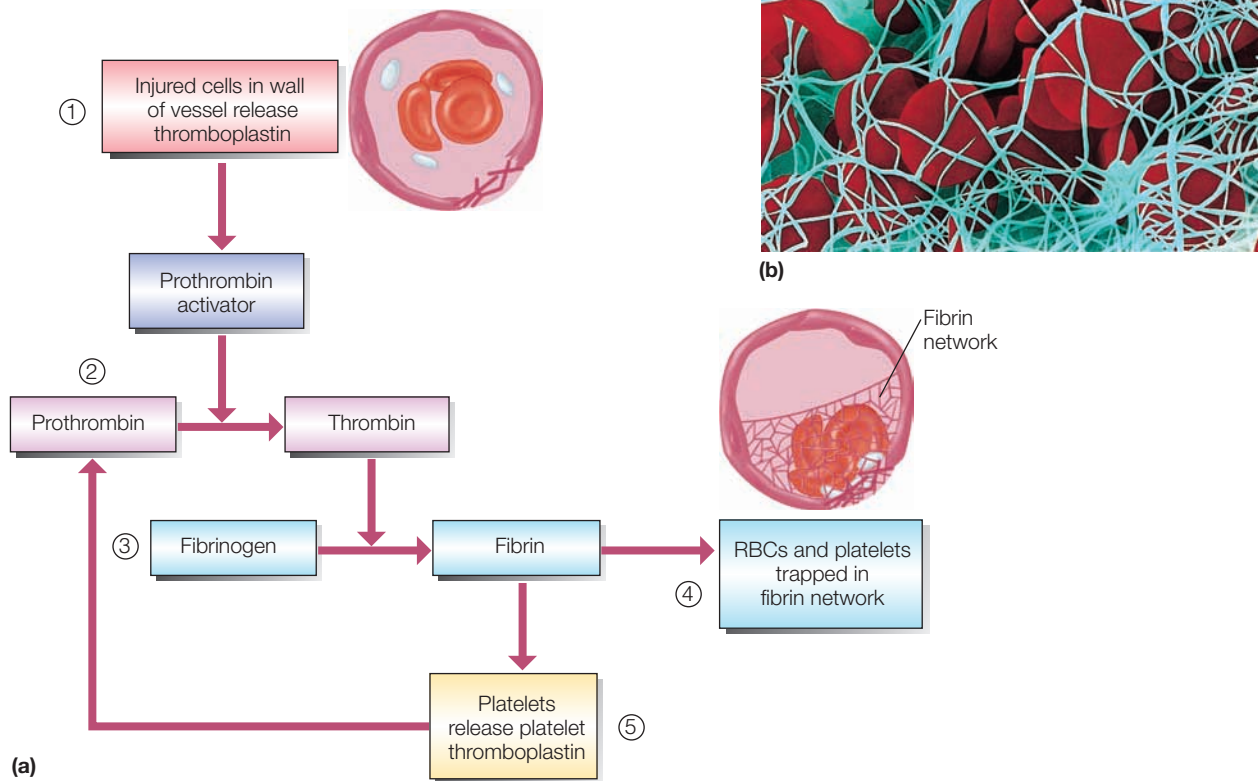


Figure 6–8 Blood Clotting Simplified. (a) Injured cells in the walls of blood vessels release the chemical thromboplastin (1). Thromboplastin stimulates the conversion of prothrombin, found in the plasma, into thrombin (2). Thrombin, in turn, stimulates the conversion of the plasma protein fibrinogen into fibrin (3). The fibrin network captures RBCs and platelets (4). Platelets in the blood clot release platelet thromboplastin (5), which converts additional plasma prothrombin into thrombin. Thrombin, in turn, stimulates the production of additional fibrin. (b) A scanning electron micrograph of a fibrin clot that has already trapped platelets and RBCs, plugging a leak in a vessel. The RBCs are red, and the fibrin network is turquoise.

those that fill large blood vessels are usually not removed naturally.

A **thrombus** is a clot that forms abnormally in a vessel. An **embolus** is a clot that dislodges or fragments to be carried away in the blood flow. Emboli usually move until they reach narrow vessels, which they may block. When a blood clot forms in a vital organ's vessels, it kills the tissues served (*infarction*) by the vessel, a potentially fatal occurrence. If this occurs in the heart, it is known as *coronary thrombosis*. If it occurs in the brain, it is known as *cerebral thrombosis*.

Pulmonary embolism describes a clot blocking a vessel supplying the lungs. In *atherosclerosis*, the endothelial linings of blood vessels change due to fatty deposits that accumulate.

Blood Types and Transfusions

Blood consists of different types, not all of which are compatible. Safe blood transfusions of whole blood depend on matching the blood types of both donors and recipients. The clumping of red blood cells following a transfusion reaction

is called **agglutination**. This involves red blood cell surface molecules called **antigens** (*agglutinogens*) that react with **antibodies** (*agglutinins*) from the plasma. There are more than 260 antigens on RBC membranes. A few of them can produce serious transfusion reactions, including antigens of the ABO group and those of the Rh group.

The *ABO blood group* is based on the presence or lack of two major protein antigens (antigen A and antigen B) on RBC membranes. Erythrocytes may have one of the following four antigen combinations:

- Antigen A only—*type A blood*
- Antigen B only—*type B blood*
- Both antigen A and B—*type AB blood* (the least common type)
- Neither antigen A nor antigen B—*type O blood* (the most common type)

Blood types are inherited. Antibodies related to each type of antigen are produced between 2 and 8 months after birth. For example, if antigen A is absent, the antibody called *anti-A* is produced. Therefore, people with type A blood (meaning that antigen A is present but antigen B is absent) have *anti-B*

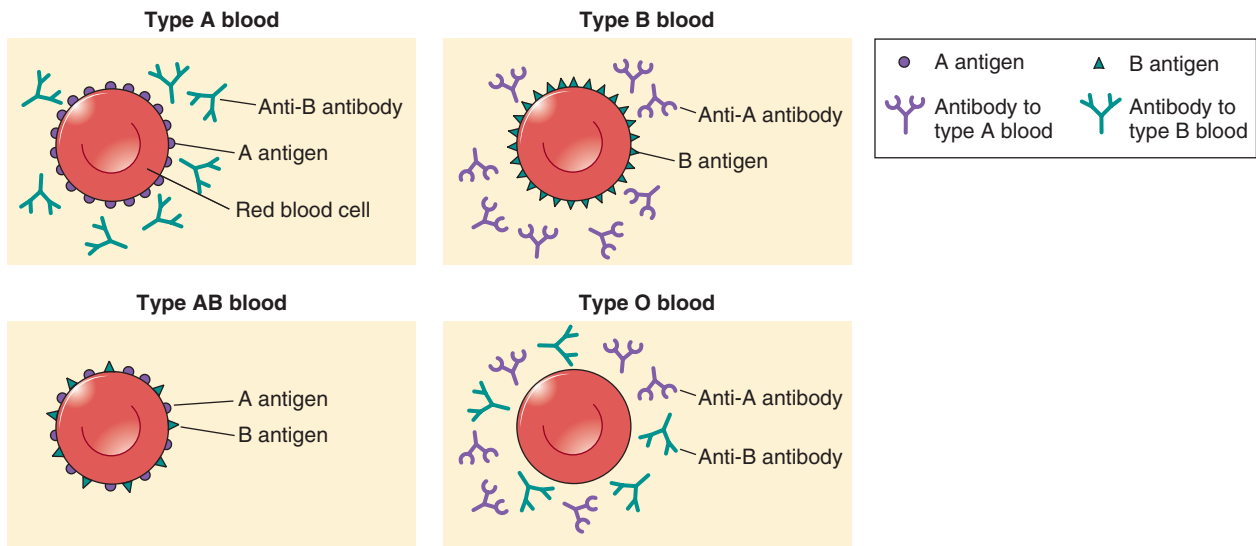


Figure 6-9 Various antigens and antibodies distinguish blood types

Table 6-4 ABO Blood Group Antigens and Antibodies

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

antibody. The opposite is true for people with type B blood. Those with type AB blood have neither of the two antibodies. People with type O blood have both antibodies (see Figure 6-9). Anti-A and anti-B antibodies in blood group O individuals are often IgG class antibodies and *may* cross the placenta, but usually do not. When they do not cross the placenta, a pregnant woman and her fetus may have different blood types, and agglutination in the fetal cells cannot occur. However, when these antibodies do cross the placenta, the result is a mild *hemolytic disease of the newborn (HDN)* because the A- and B-antigens are not fully expressed at birth. Table 6-4 summarizes blood types, antigens, and antibodies.

Antibodies of a certain type will react with antigens of the same type and cause clumping of RBCs, so these combinations must be avoided. For example, a person with type A (anti-B) blood must not receive blood of either type B or type AB in order to avoid clumping. A person with type B (anti-A) blood must not receive type A or type AB blood. A person with type O (anti-A and anti-B) must not receive type A, B, or AB blood. Because type AB blood lacks both anti-A and anti-B antibodies, those with type AB blood can receive transfusions from any other type. Because of this, type AB individuals are called *universal recipients*. Rapid transfusion must be avoided, however, because agglutination can still occur as a result of certain antibodies in the blood being transfused. It is therefore always best to transfer blood from the same type as the person requiring the transfusion (see Table 6-5). Note that the permissible donor types listed in this table should be used only in extreme emergencies. Figure 6-10 illustrates the concept of agglutination.

Because type O blood lacks antigens A and B, it can be transfused, in extreme emergencies, into people with any other type. Because of this, people with type O blood are

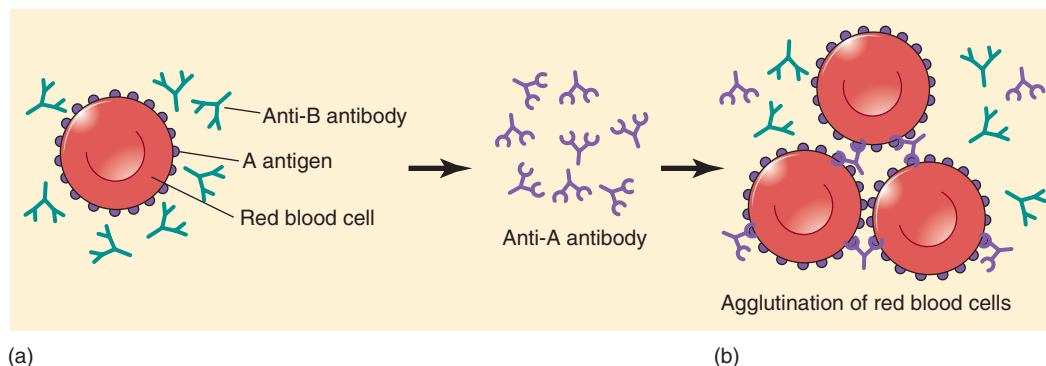


Figure 6-10 Agglutination

Table 6–5 Blood Transfusion Rules

Recipient's Blood Type	Preferred Donor Type	Permissible Donor Type
A	A	O
B	B	O
AB	AB	A, B, and O
O	O	No alternate types

called *universal donors*. Type O blood still should be given to people of other blood types slowly so that it will be diluted by the recipient's blood volume. This will minimize chances of an adverse reaction.

The *Rh blood group* received its name from the rhesus monkey because it was in this type of monkey that it was first studied. There are several Rh antigens (factors) in humans, the most prevalent of which is *antigen D*. If it is present on the RBC membranes, the blood is called *Rh-positive*. If not, it is called *Rh-negative*. Only 15% of the U.S. population is Rh-negative. The presence or absence of Rh antigen is inherited, but the antibodies that react with it (called *Rh antibodies*) are not spontaneous. They form only in Rh-negative people because of specific stimulation.

An Rh-negative person receiving Rh-positive blood will begin producing anti-Rh antibodies (see **Figure 6–11**). The first transfusion usually causes no serious problems. But after that, the Rh-negative person has become sensitized to Rh-positive blood. A second transfusion, even months later, will usually cause the donated RBCs to agglutinate.

A similar condition can occur when an Rh-negative female is pregnant with an Rh-positive fetus. Although the pregnancy

may be normal, at birth (or miscarriage) the placental membranes tear, allowing some of the fetus's Rh-positive RBCs to enter the mother's circulation. This may stimulate her tissues to begin producing anti-Rh antibodies. If she becomes pregnant a second time and the fetus is Rh-positive, these antibodies (*hemolysins*) cross the placental membrane to destroy the fetal RBCs. The fetus develops hemolytic disease of the fetus and newborn, formerly referred to as *erythroblastosis fetalis*. While extremely rare due to the careful management of Rh status, this condition may cause the death of the fetus or infant. Anemia, an enlarged liver or spleen, generalized swelling, and newborn jaundice are signs of this condition.

Summary

Blood is a type of connective tissue. It consists of red blood cells, white blood cells, and platelets suspended in a liquid, plasma, extracellular matrix. Blood transports substances between body cells and the external environment. It helps to maintain a stable internal environment. Blood is separated into formed elements and liquid portions. Red blood cells carry oxygen to the body tissues. White blood cells are important in protecting the body against pathogens and infection. Platelets are vital for blood coagulation.

Blood plasma transports gases and nutrients, helps maintain stable pH, and helps regulate the fluid and electrolyte balance. Hemostasis is the stoppage of bleeding. It involves the steps of blood vessel spasm, platelet plug formation, and blood coagulation. Blood can be typed on the basis of cell surface antigens. The ABO blood group concerns the presence or absence of antigens A and B. The Rh blood group concerns the Rh antigen, which is present on the red blood cell membranes of Rh-positive blood but is not present in Rh-negative blood.

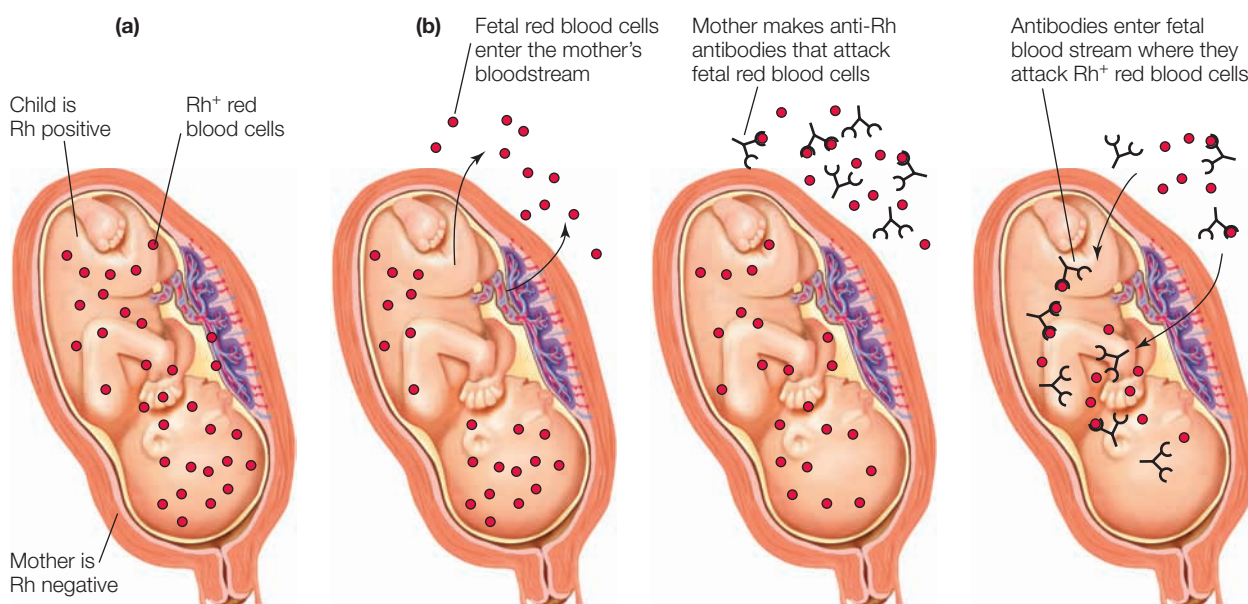


Figure 6–11 The Rh factor and pregnancy

CRITICAL THINKING

An instructor was conducting an oral examination, and he asked a phlebotomist the following questions. How would you respond to each of these?

1. Why is venipuncture a common technique for obtaining a blood sample?
2. How would the hematocrit change after an individual suffered a significant blood loss?
3. How do basophils respond during inflammation?
4. Which blood type or types can be transfused into a person with type O blood?

WEBSITES

<http://surgery.about.com/od/beforesurgery/qt/PTPTTINRtests.htm>

<http://www.hematology.org/>

http://www.mhhe.com/biosci/esp/2002_general/Esp/folder_structure/tr/m1/s7/trm1s7_3.htm

http://www.nhlbi.nih.gov/health/dci/Diseases/bt/bt_what.html

<http://www.purchon.com/biology/plasma.htm>

<http://www.redcrossblood.org/learn-about-blood/blood-types>

<http://www.unomaha.edu/hpa/blood.html>

REVIEW QUESTIONS

Multiple Choice

1. Which of the following terms means “the process of red blood cell production”?
 - A. erythropoiesis
 - B. erythrocytosis
 - C. erythropenia
 - D. hemocytosis
2. *Immature* red blood cells are found in peripheral blood samples and are referred to as
 - A. myeloblasts
 - B. erythroblasts
 - C. reticulocytes
 - D. erythrocytes
3. The formed elements of the blood are called
 - A. clotting proteins
 - B. lipoproteins
 - C. albumins
 - D. blood cells
4. Which of the following are the most abundant proteins in blood plasma?
 - A. fibrinogens
 - B. albumins
 - C. lipoproteins
 - D. globulins
5. Which of the following white blood cells produce antibodies?
 - A. monocytes
 - B. lymphocytes
 - C. eosinophils
 - D. basophils
6. Platelets are formed from cells in the bone marrow known as
 - A. megakaryocytes
 - B. erythroblasts
 - C. lymphoblasts
 - D. myeloblasts
7. Which of the following vitamins is needed for the formation of clotting factors?
 - A. vitamin A
 - B. vitamin D
 - C. vitamin K
 - D. vitamin E
8. Thrombocytes are
 - A. small cells that lack a nucleus
 - B. small cells with many-lobed nuclei
 - C. fragments of large megakaryocytes
 - D. large cells with prominent nuclei
9. Which of the following white blood cells release histamine and heparin?
 - A. basophils
 - B. monocytes
 - C. neutrophils
 - D. eosinophils
10. Erythrocytes are formed in
 - A. the spleen
 - B. red bone marrow
 - C. yellow bone marrow
 - D. the liver
11. Which of the following hormones regulates production of red blood cells?
 - A. erythropoietin
 - B. thymosin
 - C. epinephrine
 - D. somatotropin
12. Which of the following is the major protein in a red blood cell?
 - A. myoglobin
 - B. fibrinogen
 - C. albumin
 - D. hemoglobin
13. Older erythrocytes are broken down by the
 - A. kidneys
 - B. lungs
 - C. spleen
 - D. pancreas
14. Allergies stimulate an increased _____ count.
 - A. erythrocyte
 - B. eosinophil
 - C. monocyte
 - D. neutrophil
15. People of which of the following blood groups are known as universal recipients?
 - A. group O
 - B. group A
 - C. group B
 - D. group AB