18. Cardiovascular System: Blood

With this chapter we begin our study of the cardiovascular (circulatory) system. This system consists of a fluid that circulates throughout the body (blood), a pump (the heart), and a series of tubes through which the blood flows (arteries, capillaries, and veins).

I. Functions and General Composition of Blood

Blood is a type of connective tissue. Cells (i.e., formed elements) of the blood are located within a liquid matrix, which is known as the plasma. Formed elements of the blood include white blood cells (leukocytes), red blood cells (erythrocytes), and platelets.

The plasma and formed elements together constitute whole blood (Fig. 18.1). Erythrocytes account for about half of the volume of whole blood. The percentage of blood volume occupied by erythrocytes is called the hematocrit. Nearly all of the remainder of whole blood is plasma. Leukocytes and platelets account for less than 1% of blood volume. How is the hematocrit of a blood sample measured?

Functions of blood

A. Blood is important for transportation of materials throughout the body. This includes the following functions:
   1. Delivery of oxygen and nutrients to the tissues of the body.
   2. Transport of carbon dioxide and other waste products from the tissues.
   3. Transport of hormones throughout the body.

B. Blood plays various roles in regulation of homeostasis:
   1. Blood helps maintain body temperature by distributing heat.
   2. Various chemicals in the blood help to regulate pH in the body.
   3. Blood is important in regulating water and salt balance in the body.

C. Blood plays an important role in protection of the body:
   1. Platelets and blood proteins help prevent blood loss.
   2. Leukocytes and other components of the immune system help defend the body against infection.

Physical characteristics of blood

Because the blood contains formed elements and a variety of dissolved solutes, blood is considerably more viscous (about five times more viscous) than pure water and more resistant to flow. Blood pH is slightly alkaline, with a pH between 7.35 and 7.45. Would you consider blood with a pH or 7.25 to be acidic or alkaline?

The color of blood ranges from bright scarlet red (when well oxygenated) to a dark red (when poorly oxygenated). The volume of blood in a typical adult man is 5 to 6 liters. The volume in a typical adult woman is slightly less, about 4 to 5 liters.
II. Composition of Blood Plasma
Normal blood plasma contains over 100 different chemicals. However, water accounts for about 92% of the plasma volume. Proteins make up a significant fraction of the substances found in the plasma, approximately 8 g per 100 ml of plasma. Some of the more important plasma proteins are as follows:

**Albumins** account for about 60% of the plasma proteins. These proteins are generally involved in transporting lipids within the blood stream. Why do lipids need assistance for transport in the blood?

**Globulins** are important for transport and protection. Transport globulins carry thyroid hormones, metal ions, triglycerides, and steroids. **Immunoglobulins** are proteins made by the immune system to help attack foreign invaders.

**Fibrinogen** and **prothrombin** are used in the process of blood clotting. You will learn more about them later in this chapter.

Most plasma proteins are produced in the liver, and certain liver disorders can therefore alter the properties of the blood.

You should be generally familiar with the plasma solutes listed in Tables 18.3 and 18.4.

III. Formed Elements in the Blood

**Hemopoiesis**

Formed elements in the blood arise via the process of **hemopoiesis (or hematopoiesis)**. In embryonic humans, this process occurs in the liver, spleen, thymus, and bone marrow. As humans mature into adults, bone marrow becomes the primary site of both red and white cell production.

Although the book places hemopoiesis in its own section, I will address the topic as we discuss the various types of formed elements.

**Erythrocytes**

The most abundant cells in the blood are the erythrocytes (Fig. 18.5). Mature erythrocytes are **anucleate** cells containing little more than a cytoskeleton and the protein, **hemoglobin**. Without a nucleus and other cellular machinery, the life span of a mature erythrocyte is short, about 120 days. How would you describe the shape of an erythrocyte?

In a typical adult male there are 5.1-5.8 million erythrocytes per mm$^3$ of whole blood; in females the value is 4.3-5.2 million per mm$^3$. The normal range for the hematocrit of adult males is 40-54%, and the normal range for females is 37-47%. What factors contribute to these differences between men and women?
The functional part of an erythrocyte is the hemoglobin molecule (Fig. 18.6). Each molecule of
hemoglobin contains four polypeptides (two “alpha” chains and two “beta” chains). Attached to
each polypeptide is a structure called a heme. Each heme unit contains an iron atom (Fe), which
can bind to a molecule of oxygen (O\textsubscript{2}). Thus, each hemoglobin molecule can bind up to four
molecules of oxygen. Hemoglobin bound to oxygen is referred to as oxyhemoglobin, and
hemoglobin without any oxygen bound is referred to as deoxyhemoglobin.

Carbon dioxide also is able to bind directly to the polypeptides of hemoglobin. About 20% of
the CO\textsubscript{2} in the blood is bound to hemoglobin.

Erythrocyte production (Fig. 18.7) in adults occurs primarily in the red bone marrow.
Production of erythrocytes is controlled largely by the peptide hormone erythropoietin (EPO).
Production of EPO is, in turn, largely stimulated by hypoxia in the kidneys and periphery. Why
is EPO used by certain athletes, such as cyclists?

What are some potentially life-threatening side effects of “blood doping”?

Refer to Fig. 18.3 for the specific steps of erythrocyte formation. I want you to know the
following steps: Hemocytoblast cells (stem cells) in the marrow divide into myeloid stem cells,
which in turn give rise to erythrocytes and several types of leukocytes. Myeloid stem cells
destined to become erythrocytes first become proerythroblasts, then erythroblasts, which
begin the production of hemoglobin. The erythroblasts lose their nuclei to become reticulocytes, which enter the blood and become mature erythrocytes.

Cells in the liver, spleen, and bone marrow typically phagocytize dead and dying erythrocytes
(Fig. 18.8). These cells process hemoglobin, recycle the amino acids, and prepare the heme
units for excretion. Free iron ions are toxic, and iron removed from hemoglobin needs to be
stored safely. These iron ions are bound to the protein transferrin and transported through the
blood stream to the liver and spleen where they are stored. Iron is stored in these organs bound
to the proteins ferritin and hemosiderin. Iron can then be transferred by transferrin to the bone
marrow, where it is incorporated into new erythrocytes. The remainder of the heme unit is
converted to bilirubin, a yellow pigment that is picked up by the liver, secreted into the small
intestine, and converted to a brown pigment called stercobilin, which is excreted from the body.

Failure to process erythrocytes properly can result in a variety of clinical conditions:
hemoglobinuria is an excess of hemoglobin in the urine, which results from excess breakdown
of erythrocytes in the blood without adequate processing; jaundice is an excess of bilirubin,
which may result from inability of the liver to excrete the products of heme breakdown.
Leukocytes
Leukocytes are much less numerous than erythrocytes, about 5,000-11,000 per \( \text{mm}^3 \). They are divided into five types (Table 18.6). Review the functions and appearance of each type in your textbook and lab manual, and learn which of the five types are \textit{granulocytes} and which are \textit{agranulocytes}. I will get you started here:

A. \textbf{Neutrophils} are also referred to as \textit{polymorphonuclear leukocytes} (PMN’s) because of the shape of their nuclei. These are the most numerous of the leukocytes. They are phagocytic, and partial to killing bacteria. The number of neutrophils in the body rises dramatically in response to acute bacterial infections.

B. \textbf{Eosinophils} respond to infections by multicellular parasites. They gather around these organisms and release digestive enzymes onto them.

C. \textbf{Basophils} are the least numerous of the leukocytes. They migrate to injury sites where they release histamine and heparin.

D. \textbf{Monocytes} enter the tissues and become phagocytic cells called \textit{macrophages}. They are especially important in fighting chronic infections (\textit{e.g.}, tuberculosis), and they are partial to killing viruses and some bacteria.

E. \textbf{Lymphocytes} come in three types: \textit{T cells}, \textit{B cells}, and \textit{natural killer cells}. These cells are primarily responsible for the body’s specific immune response.

Like erythrocytes, leukocytes arise from \textbf{hemocytoblasts} (Fig. 18.3). Also like erythrocytes, neutrophils, eosinophils, basophils, and monocytes develop from \textbf{myeloid stem cells}. Lymphocytes arise from hemocytoblasts that differentiate into \textbf{lymphoid stem cells}. The life spans of leukocytes vary greatly: granulocytes typically live for just a few hours or days; agranulocytes may live for just a few hours or for many years.

Platelets
Blood typically contains 150,000 to 400,000 platelets per \( \text{mm}^3 \). While most platelets circulate in the blood stream, approximately one-third of the platelets in the body are held in the spleen as a reserve.

Platelets provide the following functions:
\begin{itemize}
  \item \textit{A. Release of chemicals required for blood clotting.}
  \item \textit{B. The formation of a temporary patch in a damaged blood vessel.}
  \item \textit{C. Active contraction after clot formation to reduce the size of a break.}
\end{itemize}

Platelets form in the bone marrow from large cells called \textbf{megakaryocytes} (Fig. 18.3). (Notice from the figure that, like erythrocytes and leukocytes, megakaryocytes arise from hemocytoblasts.) Megakaryocytes produce the various enzymes and other materials required by platelets, and shed cytoplasm in membrane-enclosed packets, which are the platelets that enter the bloodstream.
IV. Hemostasis
Clotting of the blood, which occurs to heal damaged blood vessels, is referred to as hemostasis. In addition to healing the vasculature, hemostasis establishes a framework for tissue repair. Hemostasis occurs in three phases: (1) vascular spasms, (2) platelet plug formation, and (3) coagulation.

Vascular spasm
Damage to the blood vessel wall causes contraction of the smooth muscle cells of the vessel wall. This results in a “vascular spasm” that reduces or may stop the flow of blood through the vessel. This process may last for about 30 minutes. During this process, endothelial cells that line the inside of the blood vessel release a variety of chemicals. Some of these chemicals enhance contractions of the smooth muscle layer and stimulate division of endothelial cells, smooth muscle fibers, and fibroblasts. In addition, the endothelial cell membranes become sticky.

Platelet plug formation
Platelets stick to surfaces at the site of the injury (adhesion) and to each other (aggregation). This forms a plug that may close the wound, if the wound is not very large. Adhesion and aggregation stimulate the platelets to release a variety of chemicals, including calcium ions and chemicals called clotting factors. These various chemicals promote adhesion and aggregation, vascular spasms, and blood clotting. You should see that hemostasis is enhanced by positive-feedback loops.

Coagulation
Coagulation, which is the true blood-clotting phase, begins 30 seconds or more after the injury. This is a complex process (Fig. 18.13), which may follow two pathways: the intrinsic pathway results from damage to the inside of the vessel, and the extrinsic pathway is initiated by damage to tissue outside the vessel. Most of the chemicals needed for clot formation ("clotting factors") are proteins produced by the liver and require an adequate supply of vitamin K. We’ll skip the details until we get to the final stages:

Both pathways lead to the formation of a substance called prothrombin activator, which converts the plasma protein prothrombin into an enzyme called thrombin. Thrombin catalyzes a reaction that causes fibrinogen molecules to link together into a mesh of protein called fibrin. Fibrin covers the platelet plug and traps additional cells and platelets in its fibrous network.

Elimination of the clot
Blood clots are stabilized by a process called clot retraction. Platelets contain the proteins actin and myosin, and (like muscle cells) platelets can contract. As clot retraction is occurring, healing of the blood vessels also takes place as platelet-derived growth factor (PDGF) promotes vessel repair. Eventually, the blood clot dissolves in a process called fibrinolysis.

Blood clotting is inhibited by various factors, including antithrombin-III, which specifically inhibits several clotting factors. Heparin, released by basophils and mast cells, accelerates the activation of antithrombin-III. Tubes used to collect blood samples typically contain either heparin or EDTA (a chemical that binds calcium ions). Why?