

System physiology - Animal

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7.A Blood and circulation

7.A.1 Blood corpuscles

Blood is the fluid component of the cardiovascular system. Small embryos don't need cardiovascular systems, because diffusion across their exposed surfaces provides adequate oxygen and removes waste products as rapidly as they are generated. By the time a human embryo reaches a few millimeters in length, however, developing tissues are consuming oxygen and nutrients faster than they can be provided by simple diffusion. It is the first system to become fully operational. The heart begins beating at the end of the third week of embryonic life, when many other systems have barely begun their development.

When the heart starts beating, blood begins circulating. In adults, circulating blood provides nutrients, oxygen, chemical instructions, and a mechanism for waste removal to each of the roughly 75 trillion cells in the human body. The blood also transports specialized cells that defend peripheral tissues from infection and disease.

The cardiovascular system is extensively integrated with the lymphatic system. The two systems are interconnected and interdependent. Fluid leaves the bloodstream, enters the tissues, and returns to the blood within the vessels of the lymphatic system. For this reason, the cardiovascular and lymphatic systems are often said to be components of a single circulatory system.

Functions of Blood

- The transportation of dissolved gases, nutrients, hormones, and metabolic wastes.
- The regulation of the pH and ion composition of interstitial fluids.
- The restriction of fluid losses at injury sites.
- Defense against toxins and pathogens. Blood transports white blood cells, specialized cells that migrate into peripheral tissues to fight infections or remove debris. Blood also delivers antibodies, special proteins that attack invading organisms or foreign compounds.
- The stabilization of body temperature. Blood absorbs the heat generated by active skeletal muscles and redistributes it to other tissues.

7.A.2 Haemopoiesis and formed elements

➤ Composition of blood

Blood is a fluid connective tissue with a matrix called **plasma**. Plasma is similar to interstitial fluid, although it contains a unique assortment of suspended proteins. There is a continuous exchange of fluid from the tissues into the blood and vice versa, driven by a combination of hydrostatic pressure, concentration gradients and osmosis.

Formed elements are blood cells and cell fragments that are suspended in plasma.

Three types of formed elements exist

- i. **Red blood cells (RBCs)** or erythrocytes are the most abundant blood cells. These specialized cells are essential for the transport of oxygen in the blood.
- ii. **White blood cells** The less numerous white blood cells (WBCs) or leukocytes are cells involved with the body's defense mechanisms. There are five classes of leukocyte, each with slightly different functions.
- iii. **Platelets** are small; membrane bound cell fragments that contain enzymes and other substances important to the process of clotting.

Formed elements are produced through the process of hemopoiesis or hematopoiesis.

Hemocytoblasts, or pluripotent stem cells, divide to produce myeloid stem cells and lymphoid stem cells. Lymphoid stem cells are responsible for lymphocyte production, whereas myeloid stem cells are responsible for the production of all other kinds of formed elements. Together, the plasma and the formed elements constitute whole blood. The components of whole blood can be fractionated, or separated, for analytical or clinical purposes.

- i. **Red Blood Cells** The most abundant blood cells are the red blood cells (RBCs), which account for 99.9 percent of the formed elements. These cells give whole blood its deep red color. Red blood cells contain the red pigment hemoglobin, which binds and transports oxygen and carbon dioxide.

Abundance of RBCs A standard blood test reports the number of RBCs per micro liter of whole blood as the red blood cell count. In adult males, 1 micro liter, or 1 cubic millimeter of whole blood contains 4.5–6.3 million RBCs; in adult females, 1 micro liter contains 4.2–5.5 million. A single drop of whole blood contains approximately 260 million RBCs, and the blood of an average adult has 25 trillion RBCs. The number of RBCs thus accounts for roughly one-third of all cells in the human body.

The hematocrit is the percentage of whole blood occupied by cellular elements. The normal hematocrit in adult males averages 46 (range: 40–54); the average for adult females is 42 (range: 37–47). The gender difference in hematocrit primarily reflects the fact that androgens (male hormones) stimulate red blood cell production, whereas estrogens (female hormones) do not.

Whole blood contains roughly 1000 red blood cells for each white blood cell. After centrifugation, the white blood cells and platelets form a very thin Buffy coat above a thick layer of RBCs. Because the hematocrit value is due almost entirely to the volume of RBCs, hematocrit is commonly reported as the volume of packed red cells (VPRC), or simply the packed cell volume (PCV).

Many conditions can affect the hematocrit. For example, the hematocrit increases in cases of dehydration, owing to a reduction in plasma volume, or after erythropoietin (EPO) stimulation. The hematocrit can decrease as a result of internal bleeding or problems with RBC formation. As a result, the hematocrit alone does not provide specific diagnostic information. Yet a change in hematocrit is an indication that other, more specific tests are needed.

- **Structure of RBCs** Red blood cells are among the most specialized cells of the body. Each RBC is a biconcave disc with a thin central region and a thicker outer margin. An average RBC has a diameter of $7.8\mu\text{m}$ and a maximum thickness of $2.6\mu\text{m}$ although the center narrows to about $0.8\mu\text{m}$. This unusual shape has three important effects on RBC function
 - i. **RBC has a large ratio of surface area to volume** oxygen must be absorbed or released quickly as the RBC passes through the capillaries of the lungs or peripheral tissues. The greater the surface area per unit volume, the faster is the exchange between the cell's interior and the surrounding plasma. The total surface area of the RBCs in the blood of a typical adult is about 3800 square meters, roughly 2000 times the total surface area of the body.
 - ii. **It enables RBCs to form stacks, like dinner plates** that smooth the flow through narrow blood vessels. An entire stack can pass along a blood vessel only slightly larger than the diameter of a single RBC, whereas individual cells would bump the walls, bang together, and form logjams that could restrict or prevent blood flow.
 - iii. **It enables RBCs to bend and flex when entering small capillaries and branches** during their differentiation, the RBCs of humans and other mammals lose most of their organelles, including nuclei; the cells retain only the cytoskeleton. Because they lack nuclei and ribosome's, circulating mammalian RBCs cannot divide or synthesize structural proteins or enzymes. As a result, the RBCs cannot perform repairs, and their life span is relatively short—normally less than 120 days. With few organelles and no ability to perform protein synthesis, their energy demands are low. In the absence of mitochondria, they obtain the energy they need through the anaerobic metabolism of glucose absorbed from the surrounding plasma. The absence of mitochondria ensures that absorbed oxygen will be carried to peripheral tissues, not stolen by mitochondria in the cell.
- **RBC Production** Embryonic blood cells appear in the bloodstream during the third week of development. These cells divide repeatedly, rapidly increasing in number. The vessels of the embryonic yolk sac are the primary site of blood formation for the first eight weeks of development. As other organ systems appear, some of the embryonic blood cells move out of the bloodstream and into the liver, spleen, thymus, and bone marrow. These embryonic cells differentiate into stem cells that produce blood cells by their divisions. The liver and spleen are the primary sites of hemopoiesis from the second to fifth months of development, but as the skeleton enlarges, the bone

marrow becomes increasingly important. In adults, red bone marrow is the only site of red blood cell production as well as the primary site of white blood cell formation.

Red blood cell formation, or erythropoiesis, occurs only in red bone marrow, or myeloid tissue. This tissue is located in portions of the vertebrae, sternum, ribs, skull, scapulae, pelvis, and proximal limb bones. Other marrow areas contain a fatty tissue known as **yellow bone marrow**. Under extreme stimulation, such as severe and sustained blood loss, areas of yellow marrow can convert to red marrow, increasing the rate of RBC formation.

- **Stages in RBC Maturation** During its maturation, a red blood cell passes through a series of stages. Divisions of hemocytoblasts in bone marrow produce (i) myeloid stem cells, which in turn divide to produce red blood cells and several classes of white blood cells, and (ii) lymphoid stem cells, which divide to produce the various classes of lymphocytes. Cells destined to become RBCs first differentiate into proerythroblasts and then proceed through various erythroblast stages.

Erythroblasts, which actively synthesize hemoglobin, are categorized on the basis of total size, the amount of hemoglobin present, and the size and appearance of the nucleus.

After roughly four days of differentiation, the erythroblast, now called a **normoblast**, sheds its nucleus and becomes a reticulocyte, which contains 80 percent of the Hb of a mature RBC. Hb synthesis then continues for two to three more days. After two days in the bone marrow, reticulocyte enters the bloodstream. At this time, reticulocyte normally accounts for about 0.8 percent of the RBC population in the blood and can still be detected by staining. After 24 hours in circulation, the reticulocyte completes their maturation and become indistinguishable from other mature RBCs.

- **Regulation of Erythropoiesis** For erythropoiesis to proceed normally the red bone marrow must receive adequate supplies of amino acids, iron and vitamins (including folic acid) required for protein synthesis. For example, we obtain vitamin B₁₂ from dairy products and meat, and its absorption requires the presence of intrinsic factor produced in the stomach. If vitamin B₁₂ is not obtained from the diet, normal stem cell divisions cannot occur and pernicious anemia results.

Erythropoiesis is stimulated directly by the peptide hormone erythropoietin and indirectly by several hormones, including thyroxin, androgens and growth hormone. Estrogens do not stimulate erythropoiesis.

Erythropoietin, also called EPO or erythropoiesis-stimulating hormone, is a glycoprotein that appears in the plasma when peripheral tissues, especially the kidneys, are exposed to low oxygen concentrations.

Erythropoietin is released

- During anemia
- When blood flow to the kidneys declines
- When the oxygen content of air in the lungs declines, owing to disease or to high altitudes
- During the respiratory surfaces of the lungs is damaged.

Once in the bloodstream, Erythropoiesis (EPO) travels to areas of red bone marrow, where it stimulates stem cells and developing RBCs.

Erythropoietin has two major effects

- It stimulates increased cell division rates in erythroblasts and in the stem cells that produce erythroblasts
- It speeds up the maturation of RBCs, mainly by accelerating the rate of Hb synthesis.

Under maximum Erythropoiesis (EPO) stimulation, bone marrow can increase the rate of RBC formation tenfold, to about 30 million per second.

If Erythropoiesis (EPO) is administered to a healthy individual, such as in the case of rule-breaking athletes, the hematocrit may rise to 65 or more. Such an increase can place an intolerable strain on the heart. Comparable problems can occur after blood doping, a practice in which athletes attempt to elevate their hematocrit by reinfusing packed RBCs that were removed and stored at an earlier date. The goal is to improve oxygen delivery to muscles, thereby enhancing performance. The strategy can be dangerous, however, because it elevates blood viscosity and increases the workload on the heart. A Helsinki police officer displays syringes and empty infusion bags of banned blood-thinning agents that officials suspect may have been used by the Finnish cross-country ski

team. Blood-thinning agents are often employed to counteract the increase in blood viscosity caused by blood doping or the use of Erythropoiesis (EPO).

➤ Blood Types

Antigens are substances that can trigger an immune response, a defense mechanism that protects us from infection. Most antigens are proteins, although some other types of organic molecules are antigens as well. Our cell membranes contain surface antigens, substances that our immune defenses recognize as normal. In other words, our immune system ignores these substances rather than attacking them as foreign. Our blood type is a classification determined by the presence or absence of specific surface antigens in the RBC cell membranes. The surface antigens involved are integral membrane glycoprotein or glycolipids whose characteristics are genetically determined. The surface antigens of RBCs are often called **agglutinogens**.

Red blood cells have at least 50 kinds of surface antigens. Three of particular importance are A, B, and Rh (or D). They have been designated as surface antigens.

The RBCs of an individual have

- i. Either A or B surface antigens
- ii. Both A and B surface antigens
- iii. Neither A nor B surface antigens.

- **Blood Typing** The blood type depends on the presence of surface antigens (agglutinogens) on RBC surfaces. The plasma contains antibodies (agglutinins) that will react with foreign surface antigens. In a cross-reaction, antibodies that encounter their target antigens lead to agglutination and hemolysis of the affected RBCs.

Type A blood has surface antigen A only, Type B has surface antigen B only, Type AB has both A and B, and Type O has neither A nor B. These blood types are not evenly distributed throughout the population. For example the average values for the U.S. population are as follows: Type O, 46 percent; Type A, 40 percent; Type B, 10 percent; and Type AB, 4 percent. The term Rh positive indicates the presence of the Rh surface antigen, sometimes called the **Rh factor**. The absence of this antigen is indicated as Rh negative when the complete blood type is recorded, the term Rh is usually omitted and the data are reported as O⁻ A⁺ and so on. As in the distribution of A and B surface antigens, Rh type differs by race and by region.

We are probably aware that our blood type must be checked before we can give or receive blood. Our immune system ignores the surface antigens on our own RBCs. However, our plasma contains antibodies, sometimes called **agglutinins** that will attack the antigens on "foreign" RBCs. When these antibodies attack, the foreign cells agglutinate, or clump together; the process is called **agglutination**. The plasma of a Type A, Type B, or Type O individual always contains either anti-A or anti-B antibodies, or both, even if the person has never been exposed to RBCs that carry foreign surface antigens. If we have Type A blood, our plasma contains anti-B antibodies, which will attack Type B surface antigens. If we have Type B blood, our plasma contains anti-A antibodies. The RBCs of an individual with Type O blood have neither A nor B surface antigens, and that person's plasma contains both anti-A and anti-B antibodies. A Type AB individual has RBCs with both A and B surface antigens, and the plasma does not contain anti-A or anti-B antibodies.

In contrast to the situation with surface antigens A and B, the plasma of an Rh-negative individual does not necessarily contain anti-Rh antibodies. These antibodies are present only if the individual has been sensitized by previous exposure to Rh-positive RBCs. Such exposure can occur accidentally during a transfusion, but it can also accompany a seemingly normal pregnancy involving an Rh-negative mother and an Rh-positive fetus.

- **Hemolytic Disease of the Newborn** Both the parents provide Genes controlling the presence or absence of any surface antigen in the membrane of a red blood cell, so a child can have a blood type different from that of either parent. During pregnancy, when fetal and maternal circulatory systems are closely intertwined, the mother's antibodies may cross the placenta, attacking and destroying fetal RBCs. The resulting condition is called **hemolytic disease of the newborn (HDN)**.

This disease has many forms, some so mild as to remain undetected. Those involving the Rh surface antigen are quite dangerous, because the anti-Rh antibodies are able to cross the placenta and enter the fetal bloodstream, whereas the