Lecture Outline: Blood, Hemopoiesis, and Hemostasis

I. **Introduction to the Circulatory System and Blood**

A. Official Organ Systems

1. 11 official organ systems exist
2. The **circulatory system** is an official organ system
3. The **cardiovascular system** is NOT an official organ system
   a. Cardiovascular refers to the heart (cardio) and vessels (vascular)
   b. It does not include blood
   c. It is not considered a complete organ system
   d. The circulatory system, however, includes the heart, vessels, AND blood

B. Lecture Structure

1. The circulatory system lecture is split into two slideshows
2. The first slideshow focuses on **Blood**
3. The next slideshow will cover the cardiovascular system, which comprises the rest of the circulatory system after blood

C. Blood as a Connective Tissue

1. Blood is histologically categorized as a connective tissue
2. All connective tissues contain two major components:
   a. A cellular component
   b. An extracellular matrix
3. Blood adheres to these guidelines, having both components

II. **Components of Whole Blood**

A. The **Formed Elements** (Cellular Component)

1. Constitute slightly less than half of whole blood volume
2. They include all blood cells and platelets
3. There are six major kinds of formed elements:

a. **Red Blood Cells (Erythrocytes)**

(1) Only one kind is found in each human

(2) They vastly outnumber white blood cells and platelets

(3) Approximately 5 million are present per cubic millimeter of blood

e. **White Blood Cells (Leukocytes)**

(1) There are five different kinds

(2) They fall into two main categories

h. **Platelets**

(1) They are not truly complete cells, lacking a nucleus

(2) They are cell fragments with a cellular origin

(3) They are included in the formed elements due to their cellular origin and membrane

(4) There are typically 150,000 to 400,000 platelets per cubic millimeter

(5) They are very tiny, contributing little to the overall volume of blood

B. The **Extracellular Matrix** (Plasma)

1. It comprises everything else besides the formed elements
2. It makes up a little over half of whole blood volume

3. After centrifugation, it floats above the formed elements because it is less dense
4. Its composition includes:
    a. **Mostly water** (90%)
    b. Various **solutes**:
        (1) **Salts** (electrolytes)
        (2) **Plasma proteins** (dissolved proteins carried in the blood)
    e. **Transported substances**, whose levels can fluctuate:
        (1) **Nutrients**: such as glucose, fatty acids, amino acids, and vitamins
        (2) **Waste products**: including urea and uric acid, resulting from the breakdown of proteins
        (3) **Respiratory gases**: primarily oxygen and carbon dioxide
        (4) **Hormones**: picked up from glands and distributed throughout the body, affecting only cells with specific receptors

III. **Red Blood Cells (Erythrocytes)**

A. Appearance and Structure

1. In prepared slides, they appear as small brown or pink circles and are far more numerous than white blood cells
2. A healthy red blood cell has a **biconcave disc shape**
    a. It is caved in on both sides, resembling a donut without a complete hole
    b. This shape allows for the maximum possible hemoglobin content
3. Mature red blood cells **lack a nucleus**

   a. The nucleus is lost during their development
   b. This leads to a short lifespan, requiring millions to be replaced daily
   c. They are an exception among most body cells, as most cells have one nucleus, and some are multi-nucleated
4. Red blood cells are packed with **hemoglobin**, containing millions of molecules per cell
   a. Hemoglobin is a protein
   b. It is produced based on instructions stored in DNA, specifically hemoglobin genes
   c. The unique sequence of amino acids dictates the protein's specific shape

B. Function
1. The **main job of red blood cells is to carry respiratory gases**
   a. They pick up **oxygen** at the lungs and deliver it to body cells through reversible binding
   b. They pick up **carbon dioxide** from body cells and deliver it to the lungs for exhalation, also through reversible binding
2. Oxygen is essential for **cellular respiration**, serving as the final electron acceptor in the process
3. A circulatory system is necessary in large organisms for efficient oxygen delivery to deep cells, as diffusion alone is insufficient

C. Sickle Cell Disease (Abnormal Red Blood Cells)
1. This disease is caused by a **mutation in the DNA**, specifically a single nucleotide error in the hemoglobin gene
2. This genetic error results in a **wrong amino acid sequence**

for hemoglobin

3. The abnormal hemoglobin causes the red blood cells to adopt a **sickle shape**
4. The consequences include:
    a. Hemoglobin performs poorly in carrying oxygen and carbon dioxide
    b. Hemoglobin molecules clump together, leading to the symptoms of the disease
5. This illustrates the critical importance of the information contained in DNA for determining protein shape and function

IV. **White Blood Cells (Leukocytes)**

A. General Characteristics

1. They are less numerous than red blood cells
2. They are crucial for **immunity**, protecting the body from harm

B. **Granulocytes** (characterized by visible granules under a microscope)

1. **Neutrophils**
    a. They are the most numerous white blood cell, making up 40-70% of all WBCs
    b. Their occurrence is typically 3,000-7,000 per cubic millimeter
    c. Their **function is as phagocytes**, meaning they perform "cell eating"
        (1) They engulf and remove harmful substances from the body
2. **Eosinophils**
    a. They are less numerous, comprising about 2% of WBCs
    b. Their **functions include killing various kinds of**

parasitic worms and playing roles in allergy attacks

3. **Basophils**
   a. They are the rarest type of white blood cell
   b. They stain well with basic (alkaline) dyes
   c. Their **function is in the inflammatory response**
      (1) They release **histamine**, a chemical signal that causes vasodilation (widening of blood vessels), increasing blood flow to an inflamed area
      (2) They also release **heparin**, an anticoagulant that prevents blood clots from forming

C. **Agranulocytes** (do not have visible granules)

1. **Monocytes**
   a. They are the largest of all white blood cells
   b. Their **function is as phagocytes**, acting as a "cleanup team"
      (1) They leave the bloodstream
      (2) They engulf debris and potentially harmful things outside the bloodstream
2. **Lymphocytes**
   a. There are several different categories of lymphocytes, such as B lymphocytes and T lymphocytes
   b. **B lymphocytes** are responsible for producing **antibodies**, which are vital for immunity
   c. **T lymphocytes** mature in the thymus, which is where their "T" designation comes from
   d. All blood cells, including lymphocytes, originate in the bone marrow

V. **Platelets**

A. Description

1. They are cell fragments, not complete cells
2. They originate from huge cells that break into many smaller pieces
3. Though very tiny, they are numerous, ranging from 150,000 to 400,000 per cubic millimeter

B. Function: **Hemostasis** (the stoppage of bleeding)

1. They are important in the formation of blood clots

VI. **Hemopoiesis (Blood Cell Formation)**

A. **Stem Cells**: These are cells capable of developing into several different kinds of cells

1. This contrasts with non-stem cells, such as skin cells, which typically only produce copies of themselves

B. **Hemocytoblasts** (also known as Hemopoietic Stem Cells)

1. These are the stem cells responsible for producing all the formed elements of the blood
2. They are located in the **red marrow** of bones
3. When activated by specific signals:
   a. One stem cell will replace itself
   b. The other will differentiate and develop into one of several formed elements

C. Developmental Pathways from Hemocytoblasts

1. **Myeloid stem cells**: These can develop into basophils, eosinophils, neutrophils, monocytes, platelets, or erythrocytes
2. **Lymphoid stem cells**: These can develop into the major kinds of lymphocytes

D. **Erythropoiesis** (The Specific Production of Red Blood Cells)

1. This process is regulated by the **oxygen level in the blood**,

maintaining homeostasis

2. The **stimulus** for erythropoiesis is a decreased oxygen level in the blood, which can be caused by factors like a reduced red blood cell count due to bleeding, insufficient hemoglobin production, or low oxygen availability
3. The **kidneys** are responsible for sensing low oxygen levels
4. In response, the **kidneys release the hormone Erythropoietin (EPO)** into the bloodstream
5. The **target tissue** for EPO are the cells in the red marrow (hemocytoblasts)
6. The **effect** of EPO binding to these cells is the activation of stem cells to specifically produce more red blood cells
7. The **result** is an increase in red blood cells, which enhances the blood's oxygen-carrying capacity, thereby returning the oxygen level in the blood to normal through negative feedback

VII. **Hemostasis (Stoppage of Bleeding)**

A. Definition: Hemostasis is the body's natural, built-in ability to stop bleeding after an injury occurs

B. It occurs in sequential steps:

1. **Step 1: Vascular Spasm**
    a. The **stimulus** is a tear in a blood vessel, which exposes connective tissue to the blood that is normally only in contact with epithelial cells
    b. The **response** is a contraction of the smooth muscle lining the blood vessel
    c. The **result is vasoconstriction**, or narrowing of the vessel
        (1) This makes it harder for blood to flow through the

injured area

(2) It immediately reduces blood loss

2. **Step 2: Platelet Plug Formation**
   a. The **process** involves chemical signals released at the injury site, which instruct platelets to stick together
   b. The **mechanism** is the interaction of proteins located on the surface of these platelets
   c. The **result** is the formation of a **platelet plug**

      (1) This provides a quick, initial seal for the hole

      (2) However, it is not very strong and serves only as a temporary solution

3. **Step 3: Coagulation** (Blood Clotting)
   a. This step **involves** numerous plasma proteins
   b. A **key protein** is **fibrinogen**, which is normally a dissolved protein in the plasma
   c. An **enzyme** called **thrombin**, which is itself a protein, plays a crucial role

      (1) Thrombin is produced in response to the injury

      (2) It catalyzes the rapid conversion of fibrinogen into fibrin

   f. **Fibrin** is different from fibrinogen because it is insoluble and precipitates out of the plasma
   g. The **result** is that fibrin molecules form a strong **mesh**

      (1) This mesh traps red blood cells, which then die and harden, along with platelets

      (2) This collective structure forms what is called a **clot**, which is significantly stronger and provides a long-term solution compared to the platelet plug

(3) The clot continues to harden over time, improving its effectiveness

C. **Clot Dissolution**: Eventually, once the epithelial cells of the vessel heal and replace themselves, the body chemically dissolves the clot.

VIII. **Blood Typing (ABO Blood Group)**

A. Importance: The ABO blood group is famous because incorrect blood transfusions can lead to death, unlike many other blood groups that typically do not cause problems

B. Key Components:

1. **Antigens**: These are foreign materials, such as molecules or parts of molecules, that the body is capable of recognizing
2. **Antibodies**: These are proteins produced by the body specifically to recognize and target various kinds of antigens, similar to how vaccines work by stimulating antibody production against inactive antigens

C. Red Blood Cell Antigens (located on the plasma membrane of red blood cells)

1. **A antigens**
2. **B antigens**
3. These antigens are produced based on a person's **genetic makeup**, specifically the genes they possess for A and B antigens

D. Plasma Antibodies (found in the plasma)

1. These antibodies recognize and attack foreign antigens
2. Crucially, a person does NOT produce antibodies against their OWN antigens, to prevent self-destruction

E. **ABO Blood Types and Characteristics**

1. **Type AB Blood**

a. **Antigens**: Possesses both A and B antigens on red blood cells
b. **Antibodies in Plasma**: Has neither anti-A nor anti-B antibodies
c. **Universal Recipient (of red blood cells)**: Can receive red blood cells from Type A, B, AB, or O individuals, because the AB person has no antibodies to attack them
d. **Plasma Donation**: Can donate plasma to anyone, as its plasma contains no antibodies that would interfere with recipient's antigens
e. **Whole Blood Reception**: Can only receive whole blood from another Type AB person, due to potential antibodies in other blood types' plasma

2. **Type B Blood**
    a. **Antigens**: Possesses only B antigens on red blood cells
    b. **Antibodies in Plasma**: Has anti-A antibodies
    c. **Can receive (Red Blood Cells)**: From Type B or Type O (as they do not have A antigens)
    d. **Cannot receive (Red Blood Cells)**: From Type A or Type AB (as they possess A antigens)
    e. **Can receive (Plasma)**: From Type AB (which has no antibodies) or Type B (which only has anti-A antibodies, not affecting B's own B antigens)
    f. **Cannot receive (Plasma)**: From Type A (which has anti-B antibodies that would attack B's own B antigens) or Type O (which has both anti-A and anti-B antibodies, attacking B's own B antigens)
    g. **Can donate (Whole Blood)**: Only to another Type B person

3. **Type A Blood**
    a. **Antigens**: Possesses only A antigens on red blood cells
    b. **Antibodies in Plasma**: Has anti-B antibodies
    c. **Can receive (Red Blood Cells)**: From Type A or Type O (as they do not have B antigens)
    d. **Cannot receive (Red Blood Cells)**: From Type B or Type AB (as they possess B antigens)
    e. **Can receive (Plasma)**: From Type AB (which has no antibodies) or Type A (which only has anti-B antibodies, not affecting A's own A antigens)
    f. **Cannot receive (Plasma)**: From Type B (which has anti-A antibodies that would attack A's own A antigens) or Type O (which has both anti-A and anti-B antibodies, attacking A's own A antigens)
    g. **Can donate (Whole Blood)**: Only to another Type A person
4. **Type O Blood**
    a. **Antigens**: Possesses neither A nor B antigens on red blood cells
    b. **Antibodies in Plasma**: Has both anti-A and anti-B antibodies
    c. **Universal Donor (of red blood cells)**: Can donate red blood cells to Type A, B, AB, or O, because Type O red blood cells lack antigens for antibodies to attack
    d. **Plasma Donation**: Can only donate plasma to another Type O person, as its plasma contains both anti-A and anti-B antibodies, which would be dangerous for other blood types
    e. **Whole Blood Reception**: Can only receive whole blood

from another Type O person

F. Blood Typing Test (Agglutination)

1. The **method** involves taking a drop of a person's blood and adding specific antibodies to observe the reaction
2. **Agglutination**, or clumping together, occurs when antibodies react with their corresponding antigens
3. The test results are **interpreted** as follows:
    a. **Type AB**: Blood shows agglutination with both anti-A and anti-B antibodies
    b. **Type B**: Blood shows no agglutination with anti-A antibodies, but strong agglutination with anti-B antibodies
    c. **Type A**: Blood shows strong agglutination with anti-A antibodies, but no agglutination with anti-B antibodies
    d. **Type O**: Blood shows no agglutination with either anti-A or anti-B antibodies

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