Blood

Dr. Ali Ebneshahidi
Functions of Blood

1. Transport of substances
   - **O2**: blood transports oxygen from the lungs to tissue cells, so that cellular respiration is possible.
   - **Co2**: blood transports carbon dioxide from tissue cells to the lungs, so that this harmful gas can be eliminated from the body.
   - **Nutrients**: blood transports water, glucose, amino acids, fatty acid, vitamins, and minerals from the digestive tract to tissue cells, so that energy can be generated by oxidizing these nutrients.
   - **Wastes**: blood transports urea, uric acid, ammonia, creatinine, and excessive vitamins and minerals from tissue cells to the kidneys and skin for disposal.
   - **Heat**: blood transport body heat from skeletal muscles to other regions and help distribute body heat evenly.
   - **Hormones**: blood transports most hormones from endocrine glands to target tissues.
Other Functions of Blood

2. Protection

– Blood maintains normal PH in body fluids, preventing acidosis or alkalosis.

– Blood maintains normal body fluid volume.

– Blood prevents excessive blood loss by events in hemostasis using thrombocytes, fibrinogen, calcium, and other clotting factors.

– Blood helps fight infections using white blood cells and antibodies.

– Blood maintains a relatively stable chemical composition, and helps in maintenance of stable internal equilibrium - a phenomenon known as homeostasis.
Hemostasis
Physical Properties of Blood

1. Blood has a higher **viscosity** (thickness) than water.
2. Blood **temperature** is about 100.4 F (38 C).
3. Blood **PH** is 7.35 – 7.45.
4. Blood constitutes about 8% of body **weight**.
5. Blood **volume** ranges from 4 to 6 liters (slightly over 1 gallon).
6. Blood is pigmented because of a pigment protein called **hemoglobin** in erythrocytes – blood turns red when hemoglobin binds with O\(_2\), and turns dark red or blue when hemoglobin binds with CO\(_2\).
Chemical Composition of Blood

– Blood is a connective tissue made of blood cells suspended in a liquid matrix.

– Using a centrifuge, components of blood can be separated into layers based on molecular weight (heavier substances will be forced to the bottom of the test tube due to centrifugal force).

– Top layer is blood plasma (about 55% of total blood volume), middle layer is the "Buffy coat" composed of leukocytes and thromboocytes (about <1% of total blood volume), and bottom layer is the erythrocytes (about 45% of total blood volume).

– Blood cells in this centrifuged tube are called "formed elements" which provide a clinical indicator known as hematocrit (HCT) where HCT lower than 40% may be classified as anemia, while HCT greater than 55% may be polycythemia.
1. Withdraw blood and place in tube.
2. Centrifuge the blood sample.

- **Plasma**
  - 55% of whole blood
  - Least dense component

- **Buffy coat**
  - Leukocytes and platelets
  - <1% of whole blood

- **Erythrocytes**
  - 45% of whole blood (hematocrit)
  - Most dense component
(b) Photomicrograph of a human blood smear, Wright’s stain (610×)
Erythrocytes

- Blood cells specialized to deliver oxygen to tissue cells, using a protein called hemoglobin.

- Small (7.5 μm in diameter), round (from top view), biconcave shaped (from side view), and lack a nucleus [the biconcave shape in RBC is thought to allow RBC to slip through small capillaries, provide larger surface area for diffusion of gases, and to allow hemoglobin to be closer to the cell membrane of RBC. The lack of nucleus in RBC provides a larger cytoplasmic volume, and because RBC do not reproduce using mitosis during their short life span of 120 days].
• 1/3 of the cytoplasm volume is filled with hemoglobin.
• Red Cell Count (RCC) is a clinical measurement of erythrocytes in each mm$^3$ of blood – male's RCC range is 4.6 -6.2 x $10^6$/mm$^3$, female's range is 4.2-5.4 x $10^6$/mm$^3$.
• RCC increases after exercising, after a large meal, when a person is at high altitudes, or when body temperature rises.

(a) Hemoglobin consists of globin (two alpha and two beta polypeptide chains) and four heme groups.

(b) Iron-containing heme pigment.
Formation of Erythrocytes (Erythropoiesis)

- After birth, blood cells are formed in red bone marrow of long bones, sternum, ribs, cranial bones, vertebrae, and pelvis.
- Stem cells called hemocytoblasts give rise to erythroblasts, which develop into reticulocytes (during this stage, the nucleus is extruded), then finally matured to become erythrocytes.
- Regulated by factors such as erythropoietin (a hormone from the kidneys to stimulate proliferation of erythrocyte precursors).
- Nutritional factors are also critical – vitamin $B_{12}$ and folic acid (for DNA synthesis) and iron (for hemoglobin synthesis).
RBC Disorders

- **Anemia** (a condition where the oxygen-carrying capacity of blood is reduced due to RBC or hemoglobin deficiency, and result in lack of energy in the person).
  - **nutritional anemia** – caused by a diet lacking sufficient iron, essential amino acids, or vitamin $B_{12}$.
  - **pernicious anemia** – caused by insufficient erythropoietin due to the inability of the stomach to produce "intrinsic factor“ for vitamin $B_{12}$ absorption in the small intestine.
  - **hemorrhagic anemia** – caused by excessive loss of RBC through internal bleeding.
  - **hemolytic anemia** – caused by rupturing of RBC due to defects in hemoglobin, enzymes, RBC cell membrane, or agents such as parasites, toxins, and incompatible blood transfusion.
  - **aplastic anemia** – caused by destruction of red bone marrow due to toxins, radiation, or certain drugs.
- sickle – cell anemia – caused by an abnormal kind of hemoglobin called "Hb-S" that bends the RBC into sickle shape, which can rupture the cell easily, reduce oxygen delivery, and lodge RBC in capillaries [this genetic disease has the highest frequency, 1/250, in the African – American group].

(a) Normal erythrocyte has normal hemoglobin amino acid sequence in the beta chain.

(b) Sickled erythrocyte results from a single amino acid change in the beta chain of hemoglobin.
Leukocytes (WBC)

- Constitute less than 1% of all blood cells in formed elements, and have nuclei.
- Spherical, slightly larger than erythrocytes, and generally function in the lymphatic system for body defenses.
- Divided into 2 groups based on the presence of granules in cytoplasm – **granulocytes** (WBC that contain granules in their cytoplasms with their nuclei divide into lobes) and **agranulocytes** (WBC that lack granules in their cytoplasms).
- Granulocytes include **neutrophils** (small, pinkish granules; 54-62% of all WBC), **eosinophils** (large, red granules; 1-3%), and **basophils** (large, blue granules, 0.4-1%).

- Agranulocytes include **lymphocytes** (large, round nucleus; 25-33%) and **monocytes** (irregular or kidney-shaped nucleus; 3-9%).
<table>
<thead>
<tr>
<th>CELL TYPE</th>
<th>ILLUSTRATION</th>
<th>DESCRIPTION*</th>
<th>CELLS/µL (mm³) OF BLOOD</th>
<th>DURATION OF DEVELOPMENT (D) AND LIFE SPAN (LS)</th>
<th>FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes (red blood cells, RBCs)</td>
<td><img src="image" alt="Illustration" /></td>
<td>Biconcave, anucleate disc; salmon-colored; diameter 7–8 µm</td>
<td>4–6 million</td>
<td>D: about 15 days LS: 100–120 days</td>
<td>Transport oxygen and carbon dioxide</td>
</tr>
<tr>
<td>Leukocytes (white blood cells, WBCs)</td>
<td></td>
<td>Spherical, nucleated cells</td>
<td>4800–10,800</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Granulocytes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Neutrophil</td>
<td><img src="image" alt="Illustration" /></td>
<td>Multilobed nucleus; inconspicuous cytoplasmic granules; diameter 10–12 µm</td>
<td>3000–7000</td>
<td>D: about 14 days LS: 6 hours to a few days</td>
<td>Phagocytize bacteria</td>
</tr>
<tr>
<td>• Eosinophil</td>
<td><img src="image" alt="Illustration" /></td>
<td>Bilobed nucleus; red cytoplasmic granules; diameter 10–14 µm</td>
<td>100–400</td>
<td>D: about 14 days LS: about 5 days</td>
<td>Kill parasitic worms; complex role in allergy and asthma</td>
</tr>
<tr>
<td>• Basophil</td>
<td><img src="image" alt="Illustration" /></td>
<td>Bilobed nucleus; large purplish-black cytoplasmic granules; diameter 10–14 µm</td>
<td>20–50</td>
<td>D: 1–7 days LS: a few hours to a few days</td>
<td>Release histamine and other mediators of inflammation; contain heparin, an anticoagulant</td>
</tr>
</tbody>
</table>

*Appearance when stained with Wright's stain.

© 2016 Pearson Education, Inc.
### Table 17.2 Summary of Formed Elements of the Blood (continued)

<table>
<thead>
<tr>
<th>CELL TYPE</th>
<th>ILLUSTRATION</th>
<th>DESCRIPTION*</th>
<th>CELLS/µL (mm³) OF BLOOD</th>
<th>DURATION OF DEVELOPMENT (D) AND LIFE SPAN (LS)</th>
<th>FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Erythrocytes</strong></td>
<td></td>
<td>Biconcave, anucleate disc; salmon-colored; diameter 7–8 µm</td>
<td>4–6 million</td>
<td>D: about 15 days LS: 100–120 days</td>
<td>Transport oxygen and carbon dioxide</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Agranulocytes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Lymphocyte</td>
<td></td>
<td>Spherical or indented nucleus; pale blue cytoplasm; diameter 5–17 µm</td>
<td>1500–3000</td>
<td>D: days to weeks LS: hours to years</td>
<td>Mount immune response by direct cell attack or via antibodies</td>
</tr>
<tr>
<td>• Monocyte</td>
<td></td>
<td>U- or kidney-shaped nucleus; gray-blue cytoplasm; diameter 14–24 µm</td>
<td>100–700</td>
<td>D: 2–3 days LS: months</td>
<td>Phagocytosis; develop into macrophages in the tissues</td>
</tr>
<tr>
<td><strong>Platelets</strong></td>
<td></td>
<td>Discoid cytoplasmic fragments containing granules; stain deep purple; diameter 2–4 µm</td>
<td>150,000–400,000</td>
<td>D: 4–5 days LS: 5–10 days</td>
<td>Seal small tears in blood vessels; instrumental in blood clotting</td>
</tr>
</tbody>
</table>

*Appearance when stained with Wright's stain.
© 2016 Pearson Education, Inc.
Formation of Leukocytes

- All granulocytes are developed from **myeloblasts** in red bone marrow, and they have an averaged life span of about 12 hours.
- Lymphocytes are developed from **lymphoblast** in red bone marrow and lymphatic tissues, and they survive for years.
- Monocytes are developed from **monoblasts** in red bone marrow, and they live for weeks or months.
- Normal WBC count is about 5,000-10,000 / mm$^3$. When the count is above 10,000, it is called **leukocytosis** where acute infections, vigorous exercises, emotional disturbances, or loss of body fluids may be the cause. When the count is below 5,000, it is called **leukopenia** which is usually due to anemia, poisoning, or certain immune – suppressing infections.
Note: All Blood cells arise from the same *stem* cell, the hemocytoblast.

© 2016 Pearson Education, Inc.
• **Phagocytes** are leukocytes that have the ability to engulf foreign substances for body defense purposes. These include the *eosinophil*, *neutrophil*, and *monocyte*. Eosinophil always remain in the blood and engulf bacteria, parasites, and other substances; while neutrophils and monocytes can squeeze themselves through capillary walls (a process called "**diapedesis**") and engulf substances in connective tissues.

• Neutrophils usually remain in close proximities, while monocytes develop into *macrophages* and travel longer distances to find foreign substances (using movements called **amoeboid motion** which relies on the pseudopods of macrophages).
Phagocytosis

1. Phagocyte adheres to pathogens or debris.

2. Phagocyte forms pseudopods that eventually engulf the particles, forming a phagosome.

3. Lysosome fuses with the phagocytic vesicle, forming a phagolysosome.

4. Toxic compounds and lysosomal enzymes destroy pathogens.

5. Sometimes exocytosis of the vesicle removes indigestible and residual material.

(b) Events of phagocytosis.
Specific Functions of WBC

• Neutrophils phagocytize small particles in blood or connective tissues.
• Eosinophils in the blood, control inflammation and allergic reaction.
• Basophils release anticoagulant (to prevent spontaneous blood clotting) and histamine (to enhance inflammation).
• Monocytes phagocytize larger particles in connective tissues.
• Lymphocytes attack foreign agents directly (under cell mediated immunity) or by forming antibodies (under antibody mediated immunity).
Thrombocytes (Platelets)

- Small remnant fragments of megakaryocytes in red bone marrow.
- Formed by a process called thrombopoiesis in the red bone marrow where the hormone thrombopoietin from the liver stimulates the fragmentation of megakaryocytes (thrombocytes are anucleated).
- Critical in forming platelet plugs in hemostasis, and along with fibrinogen, in forming blood clots.
- Also can perform amoeboid motion and their average life span is 5-9 days. Normal range is 130,000-360,000 / mm³.
Blood Plasma

- The aqueous non-cellular matrix of blood.
- Contain 92% water, 7% plasma proteins (albumin, globulin, and fibrinogen), and 1% chemical substances such as inorganic salts, glucose, amino acid, fatty acids, vitamins, minerals, hormones, enzymes, urea, ammonia, and antibodies.

**Albumin** is critical in maintaining osmotic pressure in blood and body fluids. **Globulin** serves as protein transporters (e.g. for steroid hormones). **Fibrinogen** is converted into fibrins in the formation of a blood clot.
Plasma Lipids

- Plasma lipids include triglycerides, phospholipids, and cholesterol. They combine with proteins (globulins) and form lipoproteins. Since lipids are less dense than proteins, the higher amount of lipids in a lipoprotein will result in a lower overall density of the lipoprotein molecule.
  - **very low density lipoproteins (VLDL)** have a high amount of triglyceride [bad cholesterol].
  - **low density lipoproteins (LDL)** have a high amount of cholesterol [bad cholesterol].
  - **high density lipoproteins (HDL)** have a small amount of lipids [good cholesterol].
  - Plasma also contain nitrogenous substances such as amino acids, ammonia, urea, uric acid, creatine, and creatinine.
  - Electrolytes normally found in blood plasma include Na\(^+\), K\(^+\), Ca\(^{++}\), Mg\(^{++}\), Cl\(^-\), and HCO\(_3^-\). The most abundant are Na\(^+\) and Cl\(^-\).
Blood Grouping

• Blood grouping is critical in blood transfusion, so that **agglutination** (clumping of erythrocytes) caused by binding of antigens to antibodies can be prevented.

• Blood is grouped based on the presence of surface proteins on erythrocytes called **antigens** (agglutinogens), that are genetically inherited.

• **ABO blood grouping system**
  - based on the presence of **antigen A** or **antigen B** on the surface of RBC.
  - 4 possible blood types in this system: **type A** (carries antigen A; 27-41% of population), **type B** (carries antigen B; 10-20%), **type AB** (carries both antigens A and B; 4-7%), and **type O** (carries neither antigens; 45-50%).
  - these antigens are synthesized during fetal development. About 2-8 months after birth, the immune system will spontaneously develop specialized proteins called **antibodies** to be "compatible" with these antigens: type A develops **anti-B antibodies**, type B developed **anti-A antibodies**, type AB will have no antibodies and type O develops both anti-A and anti-B antibodies.
<table>
<thead>
<tr>
<th>BLOOD GROUP</th>
<th>RBC ANTIGENS (AGGLUTINOGENS)</th>
<th>PLASMA ANTIBODIES (AGGLUTININS)</th>
<th>BLOOD THAT CAN BE RECEIVED</th>
<th>FREQUENCY (% OF U.S. POPULATION)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB</td>
<td>A</td>
<td>None</td>
<td>A, B, AB, O “Universal recipient”</td>
<td>4.00  4.00  7.00  2.00  &lt;1.00</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>Anti-A (a)</td>
<td>B, O</td>
<td>11.00  19.00  25.00  10.00  4.00</td>
</tr>
<tr>
<td>A</td>
<td>A</td>
<td>Anti-B (b)</td>
<td>A, O</td>
<td>40.00  26.00  28.00  31.00  16.00</td>
</tr>
<tr>
<td>O</td>
<td>None</td>
<td>Anti-A (a)</td>
<td>O “Universal donor”</td>
<td>45.00  51.00  40.00  57.00  79.00</td>
</tr>
</tbody>
</table>

© 2016 Pearson Education, Inc.
- the shapes of the antigen and antibody in the same blood type do not fit in their binding, as a result spontaneous agglutination is avoided. In unmatched blood transfusion, however, anti-A antibodies binding to antigen A or anti-B antibodies binding to antigen B, could cause agglutination and acute kidney failure.

- in blood transfusions, blood types should be matched carefully and transfused to the identical blood groups. In emergency cases, however, type O, the universal donor, can be donated to any other blood groups since it has no antigens and will cause only minimal agglutination. Type AB, the universal recipient, can receive blood from any other blood groups since it has no antibodies to bind to the donor's antigens and will also cause minimal agglutination.
Blood being tested

Type AB (contains agglutinogens A and B; agglutinates with both sera)

Type A (contains agglutinogen A; agglutinates with anti-A)

Type B (contains agglutinogen B; agglutinates with anti-B)

Type O (contains no agglutinogens; does not agglutinate with either serum)
• **Rh blood grouping system**
  
  – "Rh" is named after the rhesus monkey.
  
  – in addition to antigens A and B, erythrocytes might also carry another surface protein called **Rh factor**.
  
  – 45 Rh factors have been found in human blood, the most important one for transfusion purposes is antigen D.
  
  – people who carry Rh factors are **Rh⁺** (85-100% of population), while people who don't have Rh factors are **Rh⁻**.
  
  – Rh factors are formed during fetal development, but somehow there is no **anti – Rh antibodies** being developed spontaneously after birth. Anti-Rh antibodies are only developed when a person (whether Rh⁺ or Rh⁻) is exposed to foreign Rh factors (usually by blood transfusion).
  
  – when a Rh⁻ person receives blood from a Rh⁺ person several times, the amount of anti-Rh antibodies developed in this Rh⁻ person may be sufficient to cause agglutination with the blood cells from the donor, resulting in critical kidney failures.
Erythroblastosis Fetalis

- During pregnancy, the above danger may also occur where a Rh⁻ mother produces anti-Rh antibodies when her immune system is stimulated by the Rh⁺ fetus. Usually the amount of antibodies is small in the first pregnancy, creating little danger to the fetus. In subsequent pregnancies, however, the risk of agglutination increases which causes erythroblastosis fetalis or hemolytic disease of the newborn (HDN). [An injection of Rh immunoglobulin or RhoGAM into the mother's blood after the first pregnancy can prevent this condition.]
Clinical Terms

**Thrombocytopenia:** due to deficient number of platelets, causing spontaneous bleeding from small blood vessels all over the body.

**Hemophilia:** condition characterize by greatly prolonged coagulation time (failure of blood to clot causing prolonged bleeding).

**Hemorrhage:** means bleeding.

**Hematoma:** accumulated, clotted blood in tissue due to injury (bruises).

**Septicemia:** presence of bacteria and disease causing organism in blood poisoning.

**Polycythemia:** a disorder where HCT is greater than 55% increasing the viscosity of blood, and results in sluggish circulation, hypertension, thrombosis, or hemorrhage. It is divided into primary and secondary polycythemia, and polycythemia vera.
• **Infectious mononucleosis (IM)** is a contagious disease caused by the Epstein – Barr virus where the lymphoid tissues of the patient (usually female) carry infected lymphocytes that have become larger and resemble monocytes.

• **Leukemia** is form of cancer in the blood. Acute leukemia is a malignant tumor of blood – forming tissues with uncontrolled production and accumulation of immature leukocytes. Chronic leukemia is an accumulation of mature leukocytes that seem to have abnormally long life spans.