BLOOD

Dr. Ali Ebneshahahidi
Functions of blood


2. Protection: maintenance of normal Ph, normal body fluid volume, hemostasis, fight infection, and maintain homeostasis.


4. Blood volume ranges from 4 to 6 liters (slightly over 1 gallon). Ph range of blood is 7.35-7.45.

5. Blood is pigmented because of a pigment protein called hemoglobin in erythrocytes – blood turns red when hemoglobin binds with O2, and turns dark red or blue when hemoglobin binds with CO2.
Chemical composition of blood

1. Withdraw blood and place in tube
2. Centrifuge

Plasma (55% of whole blood)

Buffy coat: leukocytes and platelets (<1% of whole blood)

Erythrocytes (45% of whole blood)

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Blood

- Blood spun in a centrifuge tube containing anticlotting substances will separate into an upper clear liquid phase (55%, plasma) and a lower denser cellular phase (hematocrit, 45%).

- Plasma contains $\text{H}_2\text{O}$, proteins, electrolytes, hormones, and nutrients.

- The Hematocrit consist of red & white blood cells platelets.

- A drop of blood outside the body clots, separates into a clear liquid phase (serum) and a reddish dense mass of cells and fibers (clot). Serum composition is similar to plasma minus fibrinogen. The clot resembles the hematocrit plus fibrin.
sources

- The source of plasma water is ingested $\text{H}_2\text{O}$.
- The source of plasma protein is the liver.
- The source of blood cells is the bone marrow.
- Primary: In adults, blood cells are formed by the red bone marrow, the primary source is the marrow in the sternum, ribs, vertebrae, skull, and pelvis.
- Secondary: Blood cells can be formed by the marrow in the femur & Tibia (if necessary).
- Tertiary: In E.R. (excessive blood loss) blood cells can be formed in liver and spleen. In the embryo, these organs are the primary source of blood cells.
Erythrocytes (red blood cells)

- 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 PBC to slip through capillaries more effectively to provide a larger surface area for diffusion of gases, and to allow hemoglobin to be closer to the cell membrane of RBC, and the lack of nucleus in RBC is believed to allow RBC have a larger cytoplasm volume to fill with hemoglobin, and because RBC do not reproduce using mitosis during their short life span of 120 days].
Erythrocytes

RCC increases after exercising, after a large meal, when a person is at high altitudes, or when body temperature rises. Nutritional factors in our diet are critical in the formation of RBC (vitamin B-12, folic acid, and iron). The hormone Erythropoietin from the kidney stimulates RBC production from the bone marrow.
Protection

- Blood prevents blood loss by:
  - Activating plasma proteins and platelets
  - Initiating clot formation when a vessel is broken
- Blood prevents infection by:
  - Synthesizing and utilizing antibodies
  - Activating complement proteins
  - Activating WBCs to defend the body against foreign invaders
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\textsubscript{12}.

- **pernicious anemia** – caused by insufficient erythropoietin due to the inability of the stomach produce "intrinsic factor" for vitamin B\textsubscript{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, 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].

• **Policythemia**: (a disorder where HCT is greater than 55% increasing the viscosity of blood, and results in sluggish circulation, hypertension, thrombosis, or hemorrhage) divided into primary and secondary policythemia and policythemia vera.
Leukocytes (white blood cells)
Lekocytes

- Constitute less than 0.1% of all blood cells in formed elements.
- 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 cytoplasm's 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%).
- A granulocytes include **Lymphocytes** (large, round nucleus; 25-33%) and **Monocytes** (irregular or kidney-shaped nucleus; 3-9%).
- **Phagocytes**: are leukocytes that have the ability to engulf foreign substances for body defense purposes. These include the eosinophil, neutrophil, and monocyte.

- 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).
Specific Functions of WBC

- Neutrophils phagocytize small particles in blood or connective tissues.

- Eosinophils in the blood, control inflammation and allergic reaction.

- Basophiles release anticoagulant (to prevent spontaneous blood clotting) and histamine (to enhance inflammation).

- Monocots 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)

- Critical in forming **platelet plugs** in hemostasis, and along with fibrinogen, in forming blood clots.
- Also can perform amoeboid motion.
- Averaged life span is 5-9 days.
- Normal range is 130,000-360,000 / mm$^3$. 
Plasma plasma

- **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 include triglycerides, phospholipids, and cholesterol, they combine with proteins (globulins) and form lipoproteins.

- **Very low density lipoproteins (VLDL)** have a high amount of triglyceride. It transports triglycerides synthesized in the liver from carbohydrates to adipose cells (bad cholesrol).

- **Low density lipoproteins (LDL)** have a high amount of cholesterol. Delivers cholesterol to various cells, including liver cells (bad cholesterol).
HDL

- High density lipoprotein: (HDL – good cholesterol)

  characteristics: Relatively high conc. of protein and low conc. of lipids.

  Function: Transports to the liver remnants of chylomicrons that have given up their cholesterol.

  Note: A high ratio of HDL to LDL cholesterol appears to ward off plaque formation and Heart disease.
Major events in red blood cell destruction

1. Squeezing through the capillaries of active tissues damages red blood cells.

2. Macrophages in the liver & spleen **phagocytize** damaged red blood cells.

3. Hemoglobin from the red blood cells is decomposed into heme and globin.

4. Heme is decomposed into **iron** and **biliverdin**.

5. Iron is made available for reuse in the synthesis of new hemoglobin or is stored in the liver as **ferritin**.

6. Some biliverdin is converted into **bilirubin**.

7. Biliverdin and bilirubin are excreted in bile as bile pigments.
Hormonal control of red blood cell production

- The kidney & liver tissue experience an $O_2$ deficiency.
- These tissues release the hormone erythropoietin.
- Erythropoietin travels to the red bone marrow and stimulates an increase in production of red cells.
- As increasing number of red blood cells are released into the circulation, the $O_2$ – carrying capacity of blood rises.
- The $O_2$ concentration in the kidney and liver tissue increases, and the release of erythropoietin decreases.
Bone marrow

The bone marrow, hidden within the bones of the skeleton, is easily overlooked as a tissue, although collectively, it is nearly the size and weight of the liver.

Marrow is a highly vascular tissue, filled with blood sinuses, widened regions lined with epithelium.
**Dietary Factors Affecting RBC Production:**

- **Vitamin $\text{B}_{12}$**: (requires intrinsic factor for absorption via small intestine)
  - Source: Absorbed from small intestine.
  - Function: DNA synthesis

- **Iron**: (requires vitamin C for absorption in small intestine)
  - Source: Absorbed from small intestine; conserved during red cell destruction and made available for reuse.
  - Function: Hemoglobin synthesis

- **Folic acid**:
  - Source: Absorbed from small intestine
  - Function: DNA synthesis
Hemostasis

- The Term hemostasis refers to the stoppage of bleeding.
- Blood clotting involves a series of Rxs wherein each reaction stimulates the next Rx, which may be initiated by extrinsic or intrinsic mechanisms.
- The extrinsic clotting mechanism is triggered when blood contacts damaged tissue.
- The intrinsic clotting mechanism is triggered when blood contacts a foreign surface.
- Clot formation depends on the balance between clotting factors that promote clotting and those that inhibit clotting.
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Physiology of blood clotting

1. Injury to wall of blood vessel:

Injury (cut) to a blood vessel is followed by a series of reactions that result in the formation of a blood clot, which seals the injured opening & prevents the loss of blood.

2. Vasoconstriction:

Adhesion of blood platelets to the exposed collagen fibers (in the wall of the injured vessel) cause the release of serotonin from platelets, which induces strong vasoconstriction and decrease blood flow.
3. **platelet plug formation**:

- Contact of the platelets with collagen in the injured wall releases **thromboxane A2**, which induces aggregation of more platelets in the plug area and stimulates the formation of platelet pseudopods. These enable the platelet aggregates to bind together, forming a temporary plug to stop blood loss. (Platelets adhere to rough surfaces and to each other, forming a plug).
**Platelet plug formation**

1. Exposed collagen binds and activates platelets.
2. Release of platelet factors.
3. Attracts more platelets.
4. Aggregate into platelet plug.

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- *Lumen of blood vessel*
- *Intact endothelium*
- *Smooth muscle cells*
- *Collagen in subendothelial layer*
- *Exposed collagen in damaged blood vessel wall*

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4. clot formation: To strengthen the plug. Fibrinogen, a blood protein is converted to fibrin; fibrin forms a net over the platelets. Red cells in the center and exterior of the plug adhere to this net. The combination of platelets and red cells entangled within a thight fibrin net forms a blood clot, a stronger and more permanent plug to stop blood loss.
Blood Coagulation

- regulated by extrinsic (from injured tissue) and intrinsic (from blood) mechanisms.

- in **extrinsic mechanism**, damaged blood vessels in the injured area release "tissue thromboplastin", which after a series of chemical reaction, produces "prothrombin activator".

- in **intrinsic mechanism**, blood being exposed to collagen fibers or other foreign substances after blood vessels are opened, will release the "Hageman factor", which will also produce the "pro thrombin activator".

- "prothrombin activator" converts **prothrombin** (produced by liver) into **thrombin**, which in turn converts fibrinogen into **fibrins**. These steps require calcium and "clotting factors" (proteins that facilitate blood coagulation).
- To dissolve the clot, the enzyme plasmin lyses (breaks up) the fibrin net; plasmin is formed from an inactive precursor, plasminogen.

**Clotting Factors:**

<table>
<thead>
<tr>
<th>I. Fibrinogen</th>
<th>VIII. Antihemophilic factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>II. Prothrombin</td>
<td>IX. Plasma Thromboplastin</td>
</tr>
<tr>
<td>III. Tissue Thromboplastin</td>
<td>X. stuart-prower factor</td>
</tr>
<tr>
<td>IV. Calcium</td>
<td>XI. Plasma Thromboplastin-a</td>
</tr>
<tr>
<td>V. Proaccelerin</td>
<td>XII. Hageman factor</td>
</tr>
<tr>
<td>VI. Proaccelerin precursor</td>
<td>XIII. Fibrin stabilizing factor</td>
</tr>
</tbody>
</table>
Coagulation Cascade

**Intrinsic pathway:**
Vessel endothelium ruptures, exposing underlying tissues (e.g., collagen)

Platelets cling and their surfaces provide sites for mobilization of factors

- XII
- XI
- IX
- Ca²⁺
- Ca²⁺
- VIII
- VIIIa
- IXa/VIIIa complex
- Ca²⁺
- PF₃ released by aggregated platelets

**Extrinsic pathway:**
Tissue cell trauma causes exposure of blood to

Tissue factor (TF)

- Ca²⁺
- VII
- VIIa
- X
- Xa
- Ca²⁺
- PF₃
- Prothrombin activator

- Prothrombin (II)
- Thrombin (IIa)
- Fibrinogen (I)
- Fibrin
- XIII
- XIIIa

**Cross-linked fibrin polymer**
Factors that inhibit blood clot formation

1. Smooth lining of blood vessel – prevents activation of intrinsic blood clotting mechanism.
2. Prostacyclin- inhibits adherence of platelets to blood vessel wall.
3. Fibrin threads- absorbs thrombin.
5. Heparin from mast cells and basophils- interferes with the formation of prothrombin activator.
6. Aspirin- inhibits prostaglandin production resulting in a defective platelet release reaction.
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, 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%).
Blood group & Transfusion

- 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.

- Type O, the universal donor, can be donated to any other blood groups since it has no antigens and will cause only minimal agglutination. By the same token, 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 groups

<table>
<thead>
<tr>
<th>BLOOD GROUP</th>
<th>FREQUENCY (% U.S. POPULATION)</th>
<th>RBC ANTIGENS (AGGLUTINOGENS)</th>
<th>PLASMA ANTIBODIES (AGGLUTININS)</th>
<th>BLOOD THAT CAN BE RECEIVED</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB</td>
<td>4  4  5  &lt;1</td>
<td>A  B</td>
<td>None</td>
<td>A, B, AB, O (Universal recipient)</td>
</tr>
<tr>
<td>B</td>
<td>11  20  27  4</td>
<td>B</td>
<td>Anti-A (a)</td>
<td>B, O</td>
</tr>
<tr>
<td>A</td>
<td>40  27  28  16</td>
<td>A</td>
<td>Anti-B (b)</td>
<td>A, O</td>
</tr>
<tr>
<td>O</td>
<td>45  49  40  79</td>
<td>None</td>
<td>Anti-A (a)</td>
<td>O (Universal donor)</td>
</tr>
</tbody>
</table>

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Rh blood grouping system

- "Rh" is named after the rhesus monkey, whom we did the scientific research on this blood grouping.

- In addition to antigens A and B, erythrocytes might also carry another surface protein called Rh factor.

- 10 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\(^-\).
# Blood Typing

<table>
<thead>
<tr>
<th>Blood type being tested</th>
<th>RBC agglutinogens</th>
<th>Serum Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Anti-A</td>
</tr>
<tr>
<td>AB</td>
<td>A and B</td>
<td>+</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>–</td>
</tr>
<tr>
<td>A</td>
<td>A</td>
<td>+</td>
</tr>
<tr>
<td>O</td>
<td>None</td>
<td>–</td>
</tr>
</tbody>
</table>
Clinical terms

- Elevated lymphocytes
  - Hair cell leukemia, whooping cough, mononucleosis

- Elevated eosinophils
  - Tape worm infestation, hook worm infestation

- Elevated monocytes
  - Typhoid fever / malaria T.B.

- Too few helper T cells
  - AIDS

- Hemophilia: A hereditary disorder marked by greatly prolonged coagulation time.

- Leukemia: A malignancy of the blood forming cells in the bone marrow.

- Thalassemia: Group of hereditary hemolytic anemias resulting from very thin, fragile erythrocytes.