Major Functions of Blood

- The body contains 4 to 6 liters of blood with an average pH of 7.35 to 7.45.
  Functions include:
- Transport Oxygen, Carbon Dioxide, Nutrients, Hormones, Heat, and Metabolic Wastes
- Regulation of pH, Body temperature, and water content of cells
- Protection against blood loss through clotting
- Protection against diseases through phagocytic white blood cells and antibodies
Components of Normal Adult Blood

Measured via Hematocrit: female 38% to 46%, male 40% to 54%

Abnormal Hematocrits

- **Polycythemia**: Increased RBC production.
- **Physiologic Polycythemia**: Increase in RBC production due to hypoxic tissues, like what occurs at high altitudes.
- **Polycythemia Vera**: genetic mutation in the hemocytoblastic cell line that increases RBC production. Hematocrit values can reach 70%
Components of Normal Adult Blood

Formation of Blood cells

Hemopoiesis

Hormones:
RBC: Erythropoietin
Platelets: Thrombopoietin
WBC’s: Colony stimulating Factors (4)
Red Blood Cells or Erythrocytes

- Contain hemoglobin to carry oxygen
- 4.8 to 5.4 million RBC’s per microliter
- Produced at a rate of 2 million RBC’s per second
- Lack a nucleus
- Biconcave to increase surface/volume ratio
- Diameter of 7 – 8 microns

RBC Shape and the Structure of Hemoglobin

- RBC’s pass through capillary beds in single file.
- Hemoglobin is made of four polypeptides: Two Alpha and two Beta that contain a heme unit
- Each heme can carry an O2
- There are about 280 million hemoglobin molecules in each RBC
- Other molecules such as CO2 and NO are also carried by hemoglobin
Formation and Destruction of RBC’s

Changes in hemoglobin

- **Anemia**: A deficiency of RBCs, which can be caused by either too rapid loss or slow production.
  - **Blood loss Anemia**: Due to hemorrhage, plasma is replaced in 1-3 days, but, RBC replacement takes longer.
  - **Microcytic Hypochromic Anemia**: Low levels of hemoglobin in RBCs due to chronic blood loss resulting in low Fe3+ levels in newly produced RBCs.
  - **Aplastic Anemia**: Decreased RBC production in bone marrow due to chemical, drug, or radiation exposure.
  - **Pernicious Anemia**: Chronic illness caused by impaired absorption of Vitamin B-12 because of a lack of intrinsic factor (IF) in gastric secretions. Vitamin B12, in turn, is necessary for the formation of red blood cells.
Changes in Hemoglobin

- **Anemia**: A deficiency of RBCs, which can caused by either too rapid loss or slow production.
  - **Hemolytic Anemia**: Different abnormalities of RBCs that make RBCs fragile and rupture easily.
  - **Hereditary Spherocytosis**: RBC develop as small spherical cells rather than being biconcave. These spherical cells easily rupture by slight compression.
  - **Sickle-cell Anemia**: Genetic mutation causing abnormal beta chains. When this hemoglobin is exposed to low O2 concentrations, it precipitates into long crystals that cause the cells to become sickle-shaped.

<table>
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<th>ABO Blood Types</th>
<th>Group</th>
<th>O</th>
<th>A</th>
<th>B</th>
<th>AB</th>
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</table>
Hemolytic Disease of Newborns (HDN) or Erythroblastosis Fetalis

WBC Anatomy and Function
Neutrophil

- Make up 60 to 70% of WBC’s
- 10–12 um. In diameter
- Nucleus 2-5 lobes (increase with cell age)
- Fine granular cytoplasm
- Phagocytic cells that engulf bacteria
- Increase: (lymphocytosis) stress, burns, bacterial infections
- Decrease: (lymphopenia) Radiation exposure, B12 deficiency
WBC Anatomy and Function  

**Eosinophil**

- Make up 2-4% of WBC’s
- 10 –12 um in diameter
- Nucleus 2–3 lobed
- Cytoplasm filled with large red granules
- Combat histamines in allergic reactions
- Phagocytic on antigen/antibody complexes
- Destroy certain parasitic worms
- Increase: *(Eosinophilia)* allergic reactions, parasitic infections, autoimmune disease
- Decrease: *(Eosinopenia)* bacterial infections, steroid use, Cushing’s disease

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**Basophil**

- Make up .5 to 1% of WBC’s
- 8- 10 um in diameter
- Cytoplasm filled with large deep blue-purple granules
- Liberate heparin and histamines during allergic reactions
- Intensify inflammatory response
- Increase: *(Basophilia)* Allergic reactions, leukemia, cancers, hypothyroidism
- Decrease: *(Basopenia)* Pregnancy, ovulation, stress, hyperthyroidism
WBC Anatomy and Function

Monocytes

- Make up 3-8% of WBC’s
- 12 – 20 um in diameter
- Nucleus is kidney-shaped
- Cytoplasm is non-granular
- Phagocytic cells
- Increase: (Monocytosis) Viral and fungal infections, tuberculosis, and some leukemias
- Decrease: (Monocytopenia) Bone marrow depression, treatment with cortisol

WBC Anatomy and Function

Lymphocytes

- Make up 20 to 25% WBC’s
- Small: 6-9 um in diameter
- Large: 10-14 um
- Nucleus is round or slightly indented
- Cytoplasm forms rim around nucleus
- B cells produce antibodies
- T cells attack viruses, cancer cells, and transplanted tissues
- Natural killer cells attack infectious microbes and tumor cells
WBC Anatomy and Function

Lymphocytes

- Increase: *(Lymphocytosis)* Viral infections *(Toxoplasmosis, Epstein-Barr, Hepatitis, and Rubella)*, inflammation, and some leukemias
- Decrease: *(Lymphopenia)* Prolonged illness, immunosuppression

Diseases of Leukocytes

**Leukemia**’s are cancers of the tissues that form white blood cells in the bone marrow.

**General Symptoms and Signs of Leukemia**
- Fever
- Lymphadenopathy – *swollen lymph nodes*
- Joint pain
- Enlarged spleen and lymph nodes
- Easy bruising
- Hemorrhaging
Diseases of Leukocytes

Types of Leukemia

Myelogenous – originates in the bone marrow. Can be acute or chronic. Acute forms progress rapidly and have a poor prognosis. Chronic forms progress more slowly and are more susceptible to treatment.

Lymphocytic – originates in lymphoid tissue. Has acute and chronic forms.

Malignant Lymphoma – several malignancies of lymphoid tissues. Viruses have thought to be the causative factor.

1. Hodgkin's lymphoma - also known as Hodgkin's disease, is a type of lymphoma first described by Thomas Hodgkin in 1832. Hodgkin's lymphoma is characterized clinically by the orderly spread of disease from one lymph node group to another. Hodgkin's lymphoma was one of the first cancers to be rendered curable by combination chemotherapy.

2. Non-Hodgkin lymphoma (NHL) describes a group of cancers arising from lymphocytes. It is distinct from Hodgkin lymphoma in its pathologic features and treatment. The non-Hodgkin lymphomas are a diverse group of diseases with varying courses, treatments, and prognoses. Aggressive lymphomas, also known as intermediate and high-grade lymphomas, tend to grow and spread quickly and cause severe symptoms.

Indolent lymphomas, also referred to as low-grade lymphomas, tend to grow quite slowly and cause fewer symptoms.

Non-malignant disorder of leukocytes

Infectious Mononucleosis – due to Epstein Barr herpes virus. It results in an abnormal increase in atypical lymphocytes that resemble monocytes. Symptoms include mild fever, fatigue, sore throat and swollen lymph nodes and spleen which is subject to rupture. The treatment is usually bed rest.
Platelet Anatomy and Function

- Disc-shaped 2 – 4 um in diameter
- 150,000 to 400,000 per uL of blood
- Alpha Granules: contain clotting factors, platelet-derived growth factor
- Dense Granules: contain ADP, ATP, Ca2+, serotonin, and fibrin-stabilizing factor
- Increase: (Thrombocytosis) myeloproliferative disease, hemorrhage, iron deficiency, and hyposplenism.

Steps in Vascular Damage and Clotting Responses

- Vascular Spasm: contraction of smooth muscle in arteriole walls to reduce blood flow.
- Platelet plug formation:
  1. Platelet adhesion:
     Platelets contact and stick to free collagen fibers of the damaged blood vessel
  2. Platelet release reaction:
     Activated platelets extend many projections that enable them to contact and interact with one another. They then liberate their granules.
Steps in Vascular Damage and Clotting Responses

Liberated ADP and thromboxane A2 help activate other platelets. Serotonin and thromboxane A2 function as vasoconstrictors helping to decrease blood flow.

3. Platelet aggregation: Liberated ADP makes new platelets sticky; these newly-recruited and activated platelets adhere to the originally-activated platelets. The process causes the formation of a platelet plug.

The Blood Clotting Cascade

- **Extrinsic Pathway** (Fast acting)
  1. Tissue Factor (TF) or Thromboplastin is released by tissue cells outside of the damaged vessel.
  2. TF begins a chemical reaction pathway that activates Thrombokinase (F10). F10 combines with Proaccelerin (F5) to form the enzyme Prothrombinase.
The Blood Clotting Cascade

- **Intrinsic Pathway (slow acting)**
  Activated by factors within the blood or vessels.
  Antihemophilic factor D or Hageman factor (F12) is activated by contact with collagen fibers.
  F12 starts a chemical cascade that ultimately activates F10 or Thrombokinase.
  F10 combines with Proaccelerin (F5) to form the enzyme Prothrombinase.

The Blood Clotting Cascade

- **The Common Pathway**
  Prothrombinase catalyzes the conversion of Prothrombin (F2) to Thrombin.
  Thrombin converts the soluble plasma protein fibrinogen in the insoluble protein fibrin (loose threads).
  Thrombin also activates Fibrin Stabilizing Factor (F13) which converts the loose threads into stable threads.
The Problems with Clotting Cascade

• **Hemophilia A:** Deficiency of Factor VIII accounts for 85% cases.
  – Almost exclusively in males. Females are usually carriers
  – caused by a gene mutation on the “X” chromosome. Occurs in about 1/10,000 male births

• **Other Hemophilias** account for another 15%
  – **Hemophilia B** (Factor IX)
  – **Hemophilia C** (Factor XI)
  – **Hemophilia D** (Factor XII)

The Problems with Platelets and Abnormal Clotting

• **Thrombocytopenia:** Abnormally low levels of platelets. Usually below 50,000/ul of blood.
  – folic acid deficiency, leukemia or myelodysplastic syndrome, and dengue fever.
  – In many cases, specific antibodies are produced against platelets destroying them

• **Thrombus:** Abnormal clot that develops in a blood vessel.

• **Embolus:** Free thrombic clots carried in the blood that usually get caught in arterioles in the brain, kidney, and lungs.