Hematology L1

- Hematology is defined as the study of blood; the term (hemo or hemato) is derived from the Greek word for blood.
- Hematology studies normal and pathologic aspects of blood and **blood cells.**

Blood

- It is highly specialized tissue, along with the circulatory sys.
- The blood is the fluid of life about (7-8%) of human B.w, is highly specialized circulating tissue, and is adapted to meet the needs of the body tissues and organ systems.

The primary function of blood is

- Transport of O_2, CO_2, nutrients, and waste products, hormones.
- protection plays roles in inflammation, phagocytosis, antibody & complements and platelet factors
- Regulation act as a buffer, water balance, acid-base balance & internal communication.
- Regulation and equalizing of internal body temperatures

The ancient presumed that blood carries a mysterious (vital force), and Roman gladiators drank it to fortify themselves for battle.

From ancient Egypt to the 19^{th} century, physicians drained bad blood from their patients to treat everything from gout to headaches.

Little information was known about blood until the first microscopes revealed the blood cell.

SELECTED SCIENTIFIC DEVELOPMENTS RELEVANT TO HEMATOLOGY

1628	Blood circulation described by William Harvey (1578-1657) in England
1674	First description of red blood cells, by Antonj van Leeuwenhoek (1623-1723) in Holland
1772	Plasma clotting factors described by William Henson (1739-1774)
1773	First descriptions of white blood cells, by William Henson in England
1830	Compound microscope developed
1843	First hematology monograph published, in France by Gabriel Andral (1797-1876)
1845	Leukemia described as a distinct disease by Rudolf Virchow (1821-1902) in Germany and John Bennett (1812-1875) in Scotland
1851	Hemoglobin discovered by Otto Funke in Germany; first blood cell counts published, by Karl Vierordt in Germany
1858	Fibrinogen isolated by Denis de Commercy in France and Olaf Hammarsten in Uppsala
1865	Red blood cell function described by Felix Hoppe-Seyler (1825-1895) in Germany
1869	Bone marrow identified as source of blood cells by Ernst Neumann (1834-1918) in Germany and Giulio Bizzozero (1846-1901) in Italy
1870	Leukemia identified as a disease of the bone marrow by Neumann
1879	Paul Ehrlich (1854-1915) in Germany develops white blood cell differential count and tri-acid staining technique
1886	Phagocytosis described by Ilya Metchnikov (1845-1916), a Russian
1890	Anticoagulants based on calcium removal described by Arthus and Pages in Switzerland
1900	ABO blood groups discovered by Karl Landsteiner (1868-1943) in Austria
1902	May-Grünwald stain and Wright stain (1906) introduced for blood smears
1905	Common coagulation pathway proposed by Paul Morawitz (1879-1936) in Germany
1906	Platelets accurately characterized by James Wright (1869-1938) in Boston
1910	Sickle-cell anemia presented as a disease by James Herrick in Chicago
1925	Thalassemia described by Thomas Cooley in Detroit
1926	Studies on lymphocytes and cell-mediated immunity by James Murphy in New York
1927	Sternal puncture technique utilized by Mikhail Arinkin (1876-1948) in Russia; makes possible routine bone marrow examination
1929	Closed-tube hematocrit introduced by Maxwell Wintrobe in the United States
1931-1949	Red cell metabolism and enzymes detailed by Otto Warburg (1883-1970), Gustav Embden (1874-1933), and Otto Meyerhof (1884-1951) in Germany
1936	Prothrombin assays introduced; expand understanding of coagulation mechanism
1950	Ferrokinetic studies used to study iron turnover
1957	Introduction of automated cell counters to the clinical laboratory
1961	Hematopoietic stem cell demonstrated by transplantation and irradiation techniques; platelet aggregation with ADP studied in Sweden
1969	T and B lymphocytes characterized
1975	Kohler and Milstein describe the production of monoclonal antibodies by cells in tissue culture

- Blood is a connective tissue composed of two portions: The liquid portion is called plasma, about (55% of the whole blood), and the solid part is called cellular components, about (45%).
- **Plasma (**55%**)** is a liquid portion of the blood and consists of a large number of organic & inorganic substances (solutes (9%)) dissolved in water (solvent (91%)).
    - **Water**, The most important part of a plasma, represents about 91% of the plasma and about 9% represent other solutes.

The primary function of water

__ acts as a polar solvent for blood cells and other components of the blood

__ acts as temperature regulation of the body in two ways 1- radiation and 2- evaporation of water from the skin.

Different solutes (9%) include mostly

P. protein, salts, ions (Na^+, K^+, Ca^{+2}, Mg+, Zn+, Cl^- and HCO_3 plays an essential role in acid-base in the body) 's balance of gasses, hormones, nutrients, wastes (uric acid, urea & creatinine), and enzymes.

A- Plasma protein (7%) is formed mainly in the liver and classified according to (or function, structure) their solubility in the water

Albumins (soluble in water) are the smallest & most abundant p. protein.

- - Which contribute to viscosity, osmotic pressure, & blood volume.
- - helps buffer blood
- - transports many solutes by binding to them, like drugs, penicillin, pigments, fatty acids, bile salts and hormones.

Globulins (not soluble in water)

Some are involved in clotting.

Some are enzymes.

Globulins are divided into 3 types (α, β, γ) according to their speed in the electrophoretic medium.

- **alpha globulins** (α1 and α2)(e.g., the proteins that transport thyroxine and retinol [vitamin A])

- **beta globulins** (e.g., the iron-transporting protein **transferrin**). **Fibrinogen** is a soluble precursor to fibrin. That forms the framework of a blood clot. **LDL** and **plasminogen**
- **Gamma globulins**.
    - Gamma globulins are the least negatively-charged serum proteins.
    - Most antibodies are gamma globulins. Therefore gamma globulins become more abundant following infections or immunizations.

Functions of plasma proteins

- Carrier proteins; many plasma proteins act as carriers for many compounds (called carrier proteins).
- Regulation of the movement of water between the intravascular and extravascular fluid components (osmotic pressure of the albumins maintains the balance between them)
- Coagulation; - is carried out by the same plasma proteins ((plugging any breaks in the circulatory system).
- Immunoglobulins (antibodies produced by certain lymphocytes against pathogens)

Table 2.1 Components of the Blood

Liquid phase: plasma
- Water
- Electrolytes (e.g., Na^+, Ca^{2+}, HCO_3^-, Cl^-)
- Proteins
- Miscellaneous: sugars, fats, vitamins, hormones

Solid phase: formed elements
- Erythrocytes
- Leukocytes
    - Granulocytes
        - Neutrophils
        - Eosinophils
        - Basophils
    - Lymphocytes
    - Monocytes
- Platelets

Table 2.2 Electrolyte Composition of Blood (mEq/L)

Cations	Plasma	Anions	
Na^+	142	HCO_3^-	27
K^+	5	Cl^-	103
Ca^{2+}	5	Protein	16
Mg^{2+}	3	Miscellaneous	9
Total	155		155
	Erythrocytes		
K^+	125	HCO_3^-	20
Na^+	30	Cl^-	74
Mg^{2+}	12	Miscellaneous	73
Total	167		167

Table 2.2 Summary of the Major Plasma Proteins

Plasma Protein	Plasma Concentration (g/L)	Molecular Weight (daltons)	Functions
Albumin	40.0	69,000	Regulation and maintenance of plasma volume and distribution of extracellular fluid. Also functions as a carrier protein.
α_1-Globulins			
α_1-Antitrypsin	3.0	45,000	Anticoagulant effect
HDLs (high-density lipoproteins)	0.5	200,000	Lipid transport
α_2-Globulins			
Ceruloplasmin	0.4	160,000	Copper transport
Haptoglobins	1.2	95,000	Types of glycoproteins that bind free hemoglobin to conserve iron.
α_2-Macroglobulin	3.0	800,000	Anticoagulant effect
VLDLs (very low-density lipoproteins)	1.0	10,000,000	Lipid transport
β-Globulins			
Transferrin	3.0	90,000	Iron transport
Hemopexin	1.0	80,000	Binds ferriheme
C_3 (β_{1C}-globulin)	1.2	220,000	Component of complement pathway
C_4 (β_{1E}-globulin)	0.4	240,000	Component of complement pathway
Plasminogen	0.7	140,000	Fibrinolysis
Fibrinogen	3.0	350,000	Fibrin formation
LDLs (low-density lipoproteins)	1.0	2,300,000	Lipid transport
γ-Globulins			
Immunoglobulins			
IgA	2.5	170,000	Each Ig group has different antibody functions. They move mainly as γ-globulins on zone electrophoresis, but some migrate as β-globulins or as α_2-globulins.
IgD	0.03	180,000	
IgE	Trace	200,000	
IgG	10.0	150,000	
IgM	1.0	900,000	

Cellular components (about 45% of blood) are include

a- Red blood cells or erythrocytes (95%)

These corpuscles lack a nucleus and organelles; they contain hemoglobin & distribute oxygen. RBC is marked by proteins that define different blood groups.

__ Biconcave disc thin center, thick edges (2.0 μm thick and 7.5 μm diameter)

__ High surface area/volume ratio

__ Flexible easily deforms to fit through narrow capillaries

b- Leukocytes (WBC) 3% of blood cells

Are true cells, larger than RBC, about 8 µm in diameter, the main function in the protection of the body as part of the immune system, attack & destroy bacteria & pathogens and remove dead cells and tissues

Most WBC has pseudopodia; they squeeze out of capillaries into tissue spaces. They are classified according to their structure and affinity for various dyes.

- **Granulocyte**
  - Neutrophils, Band cells or PMNs, about (60-70%). Are multi-lobed nuclei and abundant cytoplasmic granules, they have little affinity for either dye or called microphage outside blood vessels
  - Eosinophils (1-4%).The granules take up red dye eosins. Attack parasites and phagocyte antigen-antibody complexes.
  - Basophils (0.1%). The granules have an affinity for blue dye. They secrete anticoagulant and vasodilator substances as histamines and serotonin.
  - **Monocyte** (2-8%).
- They are long-lived cells &
- largest of the circulating WBC, with a diameter of 17-24 µm,
- they have large C or S-shaped nuclei,
- The pale cytoplasm and several granules are called macrophages outside blood vessels.

Lymphocytes

- A second most common type of WBC (20-35%)
- Small cells / large round dense stained nuclei occupy the cells.

1- B Lymphocytes (10-15%) produce antibodies and act as humoral immunity (B= bursa of Fabricius in the bird)

2- T Lymphocytes (75-80%)

- cytotoxic T (T_c) acts as cell-mediated immunity
- Helper T cells (T_H), activate B cell and T cells (T= matured in the thymus)

3- Natural killer cells (10%)

Are large lymphocytes present, the cytoplasm contains several reddish-purple granules

- **Platelets 1 % (250x 103 platelet/µm)**

Are fragments of cytoplasm produced from megakaryocytes, round or oval, have a very invaginated surface area and short life span1-2weeks

Platelet functions are

__ Secrete vasoconstrictors

__ Promote homeostasis

__ Stimulate the formation of clot-dissolving enzymes to remove clots; because clots are not permanent, after repair, the clots are removed by platelets action