THE BLOOD:

Blood is a specialized connective tissue in which cells are suspended in fluid extracellular material called **plasma**. The **elements** circulating in the plasma are **erythrocytes** (red blood cells), **leukocytes** (white blood cells) and **platelets**.

Serum:

1-When blood leaves the circulatory system, either in a test tube or in the ECM surrounding blood vessels, plasma proteins react with one another to produce a clot,which includes formed elements and a yellowish liquid called **serum**.

2-Serum contains growth factors and other proteins released from platelets during clot formation,which confer biological properties very different from those of plasma.

Function of the blood:

1-Blood is a distributing vehicle, transporting O2 , CO2, nutrients, metabolites, hormones, and other substances to cells throughout the body. O2 is bound mainly to hemoglobin in erythrocytes, while CO2 is carried in solution as CO2 or HCO3.

2-Blood important in heat distribution, the regulation of body temperature, and the maintenance of acid-base and osmotic balance.

3-Leukocytes are one of the body's chief defenses against infection. These cells are generally spherical and inactive while suspended in circulating blood, but when called to sites of infection or inflammation they cross the wall of venules, migrate into the tissues, and display their defensive capabilities.

The major plasma proteins include the following:

***i)*Albumin**, the most abundant plasma protein, is made in the liver and serves primarily in maintaining the osmotic pressure of the blood.

***ii)*globulins**, made by liver and other cells, include transferrin and other transport factors; fibronectin; prothrombin and other coagulation factors;lipoproteins and other proteins entering blood from tissues.**globulins**, which are immunoglobulins (antibodies) secreted by lymphocytes in many locations.

***iii)*Complement proteins**, a system of factors important in inflammation and destruction of microorganisms.

***iv)*Fibrinogen**, the largest plasma protein, also made in the liver, which during clotting polymerizes as insoluble, cross-linked fibers which block blood loss from small vessels.

BLOOD CELLS:

1-Erythrocytes:

A-Erythrocytes (red blood cells) are terminally differentiated, lack nuclei, and are packed with the O2-carrying protein hemoglobin.
B-Erythrocyte differentiation includes loss of the nucleus and all organelles shortly before the cells are released by bone marrow into the circulation. Lacking mitochondria, mature erythrocytes rely on anaerobic glycolysis for their minimal energy needs. Lacking nuclei, they cannot replace defective proteins.
C-Human erythrocytes normally survive in the circulation for about 120 days. By this time defects in the membrane's cytoskeletal lattice or ion transport systems begin to produce swelling or other shape abnormalities.

Leukocytes:

1-Leukocytes(white blood cells) migrate to the tissues where they become functional. According to the type of cytoplasmic granules and the shape of their nuclei, leukocytes are divided into two groups: polymorphonuclear **granulocytes** and mononuclear **agranulocytes.**
2-Both types are spherical while suspended in blood plasma, but become amoeboid and motile after leaving the blood vessels and invading the tissues.

Granulocytes:

1-possess two types of granules: the **specific granules** that bind neutral, basic, or acidic stains and have specific functions and the **azurophilic granules**, which are specialized lysosomes, stain darkly, and are present at some level in all leukocytes.
2-Granulocytes have **polymorphic nuclei** with two or more lobes and include the **neutrophils, eosinophils,** and **basophils**.
3-All granulocytes are terminally differentiated cells with a life span of only a few days.
4- Their Golgi complexes and rough ER are poorly developed. They have few mitochondria and depend largely on glycolysis for their low energy needs, containing glycogen that allows them to function in tissue with little O2, such as inflamed areas.

Function of granulocytes:

1-When the cells phagocytose microorganisms, several azurophilic granule proteins act collectively to kill and then digest them.
2-The bactericidal proteins include **myeloperoxidase**,which bind and produce holes in cell membranes of microorganisms; and **lysozyme**, which dissolves bacterial cell wall components.

Agranulocytes:

1- do not have specific granules, but they do contain azurophilic granules (lysosomes). The nucleus is round or indented.
2-This group includes**lymphocytes** and **monocytes .**

NEUTROPHILS (POLYMORPHONUCLEAR LEUKOCYTES):

1-Neutrophils constitute 60–70% of circulating leukocytes. with nuclei having two to five lobes linked by thin nuclear extensions .
2-Neutrophils are inactive and spherical while circulating but become actively amoeboid during diapedesis and upon adhering to solid substrates such as collagen in the ECM.
3-The cytoplasm of the neutrophil contains two main types of granules: the more abundant **specific granules,** which are very small and near the limit of light microscope resolution , and **azurophilic granules,** which are specialized lysosomes with components to kill ingested bacteria .
4-Neutrophils are short-lived cells with a half-life of 6–7 hours in blood and a life span of 1–4 days in connective tissues before dying by apoptosis.

Function of Neutrophils:

1-Neutrophils are active phagocytes of bacteria and other small particles and are usually the first leukocytes to arrive at sites of infection, where they actively pursue bacterial cells using chemotaxis.
2-Neutrophils also contain glycogen, which is broken down into glucose to yield energy via the glycolytic pathway.
3- The ability of neutrophils to survive in an anaerobic environment is highly advantageous, since they can kill bacteria and help clean up debris in poorly oxygenated regions, eg, inflamed or necrotic tissue.

EOSINOPHILS:

1-Eosinophils are less numerous than neutrophils, constituting only 2–4% of leukocytes in normal blood. this cell is about the same size as a neutrophil, but with a characteristic bilobed nucleus .
2-The main identifying characteristic is the abundance of large, red specific granules(about 200 per cell) that are stained by eosin.

Function of eosinophils:
1-The major basic protein,along with eosinophilic peroxidase, other enzymes and toxins, have cytotoxic effects on parasites such as helminthic worms and protozoa.
2-Eosinophils also phagocytose antigen-antibody complexes and modulate inflammatory responses in many ways.
3-They are an important source of the factors mediating allergic reactions and asthma.

BASOPHILS:
1-Basophils are less than 1% of blood leukocytes and are therefore difficult to find in smears of normal blood. The nucleus is divided into two or more irregular lobes, but the large specific granules overlying the nucleus usuallydark its shape.
2-The azurophilic specific granules stain dark blue or metachromatically with the basic dye of blood smear stains and are fewer and more irregular in size and shape than the granules of the other granulocytes .
3-The metachromasia is due to the presence of heparin and other sulfated glycosaminoglycans (GAGs) in the granules.

Function of basophils:
1-Basophilic specific granules also contain much histamine and various mediators of inflammation, including platelet activating factor, eosinophil chemotactic factor, and phospholipase A which produces low molecular weight factors called **leukotrienes**.
2-By migrating into connective tissues, basophils may supplement the functions of mast cells, with which they share a common progenitor cell origin.
3-Both basophils and mast cells have metachromatic granules containing heparin and histamine, have IgE bound to surface receptors, and secrete their granular components in response to certain antigens.

LYMPHOCYTES:
1-Lymphocytes constitute a family of leukocytes with spherical nuclei. They can be subdivided into functional groups according to distinctive surface molecules , notably **T lymphocytes**, **B lymphocytes**, and **natural killer (NK) cells**.
2-Lymphocytes have diverse functional roles related to immune defense against invading microorganisms, foreign or abnormal antigens, and cancer cells.
3-Most lymphocytes in the blood are small , medium and large lymphocytes.

Small lymphocytes:
1- The small lymphocytes that predominate in the blood are characterized by

spherical nuclei, sometimes indented, and condensed, very basophilic chromatin, making them easily distinguishable from granulocytes.
2-The cytoplasm of the small lymphocyte is scanty, and in blood smears it appears as only a thin rim around the nucleus. It is slightly basophilic and may contain a few azurophilic granules, along with a few mitochondria and a small Golgi apparatus; it contains free polyribosomes .

MONOCYTES:
1-Monocytes are bone marrow–derived agranulocytes. The nucleus is large, off-center, and may be oval, kidney-shaped, or distinctly U-shaped .
2-The chromatin is less condensed than in lymphocytes and stains lighter than that of large lymphocytes.
3-The cytoplasm of the monocyte is basophilic and contains very small azurophilic granules (lysosomes),These granules are distributed through the cytoplasm, giving it a bluish-gray color in stained smears.
4-Circulating monocytes are precursor cells of the mononuclear phagocyte system. After crossing the walls of postcapillary venules, monocytes differentiate into **macrophages** in connective tissues, microglia in the CNS, osteoclasts in bone.

PLATELETS:
1-Blood platelets (**thrombocytes**) are nonnucleated, disklike cell fragments . Platelets originate by fragmentation at the ends of cytoplasmic processes extending from giant polyploid cells called **megakaryocytes** in the bone marrow .
2- Platelets promote blood clotting and help repair minor tears or leaks in the walls of blood vessels, preventing loss of blood. Platelets have a life span of about 10 days.platelets often appear in clumps.
3- Each platelet has a lightly stained peripheral zone, the **hyalomere,** and a central zone containing darker staining granules, called the **granulomere** .

Function of platelets:
The role of platelets in controlling hemorrhage can be summarized as follows:
1-Primary aggregation. platelet aggregation to collagen via collagen-binding protein in the platelet membrane. Thus, a **platelet plug** is formed as a first step to stop bleeding.
2-Secondary aggregation. Platelets in the plug release an adhesive glycoprotein and ADP, both of which are potent inducers of platelet aggregation,increasing the size of the platelet plug.
3-Blood coagulation. During platelet aggregation, **fibrinogen** from plasma, and others from damaged endothelium, and various factors from platelets promote the sequential interaction of plasma proteins, giving rise to a **fibrin** polymer that forms

a three-dimensional network of fibers trapping red blood cells and more platelets to form a **blood clot,** or **thrombus** .
4-Clot retraction. The clot that initially bulges into the blood vessel lumen contracts slightly because of the interaction of platelet actin and myosin.
5-Clot removal. Protected by the clot, the vessel wall is restored by new tissue, and the clot is then removed, mainly by the proteolytic enzyme **plasmin,**formed continuously through the local action of **plasminogen activators** from the endothelium on **plasminogen** from plasma. Enzymes released from platelet lambda granules also contribute to clot removal.

Lymph :

1-Is the fluid which accumulates from the tissues and return to the blood circulation through lymphatic system .

2- it takes lymphocytes and antibodies when it pass through the lymph nodes .

3-the lymph infiltrated from small intestinal wall has milky appearance due to fatty corpuscles . lymph coagulates slower than blood .