Chapter 6
Blood Tissue

6.1. Basic Composition of Blood

Blood is a connective tissue composed of free cells in a fluid matrix. Unlike other types of connective tissues, blood lacks fibers except during the clotting response. Blood can be looked at in terms of the extracellular material, the Plasma, and the cellular component, the Formed Elements.

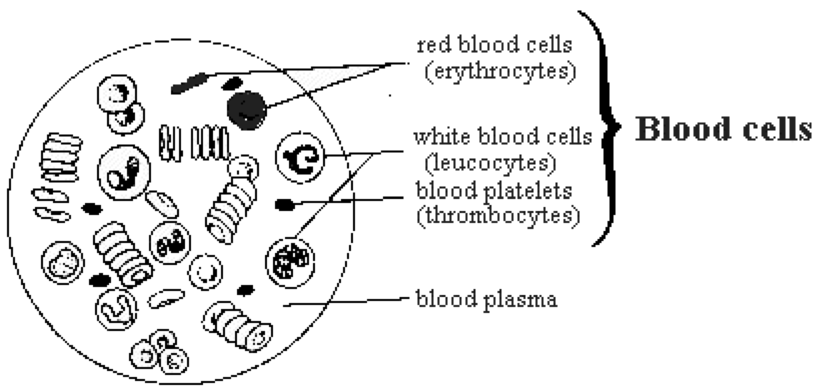

Fig.6.1. Composition of Blood

6.2. Plasma

The plasma acts as a medium for the circulation of cells and metabolic substances. The primary components of plasma are: water, inorganic salts, and the plasma proteins.

Plasma Proteins - are special proteins unique to the blood. They include:

1. Albumins - the most abundant class. They serve primarily to maintain blood viscosity and volume.
2. Fibrinogens - serve primarily in clot formation.
3. Globulins - a class of plasma proteins of diverse size and function. They include: Gamma Globulins such as the antibodies and Beta Globulins - used in the transport of hormones, lipids, and metal ions.

Plasma also contains certain microscopic particles such as Chylomicra - fatty bodies Chylomicra increase in number after a fat-rich meal. Hemoconia - small particles of diverse origin, possibly the fragments of cells.

6.3. The Formed Elements

The formed elements are the blood cells. There are three distinct classes: erythrocytes, leucocytes, and thrombocytes. All of the formed elements arise from hemopoietic tissue. In the embryos, fetus, and even the neonate there are a number of hemopoietic organs: spleen, liver, bone marrow, and yolk sac. In the adult hemopoiesis is restricted only to the red marrow. All of the various formed elements begin there. However, one class of leucocytes complete their maturation outside of the red marrow. All of the various formed elements arise from a multipotent stem cell called the Hemocytoblast. The hemocytoblast is derived from mesenchymal cells. The hemocytoblast will give rise to five lineages of stem cells producing all of the various formed elements.

6.3.1. Erythrocytes

The erythrocytes are the red blood cells and are the most numerous of the formed elements. Erythrocytes are anucleated, red colored cells shaped like biconcave discs. They are 8 um by 2 um in dimension. Their shape increase surface area for gas exchange. The mature erythrocyte lacks most of the typical organelles to allow it to hold more Hemoglobin. Hemoglobin is a complex protein composed of four globular polypeptide chains, each bearing a Heme Group.The heme group contains iron. Iron binds to oxygen allowing for it's transport through the blood stream. It will also bind to carbon dioxide. The iron of the heme group gives the red color to erythrocytes. Since erythrocytes are by far the most abundant of the formed elements, they give the red color to blood. Erythrocytes are flexible cells which allows them to travel through the smaller capillaries. This flexibility is due to a subplasmalemmal framework of microfilments made up of the protein Spectrin.

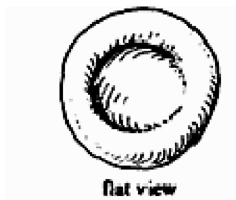

Fig.6.2. Erythrocyte (Red blood Cell, Biconcave in shape)

1) The Life Cycle of the Erythrocyte

Erythrocytes are short lived cells typically having a life span of approximately 120 days. The steps of hemopoiesis which gives rise to erythrocytes is termed Erythropoiesis and occurs in the red marrow. Erythropoiesis is stimulated by the hormone Erythropoietin . Erythropoietin is produced by the kidneys in response to a decrease in erythrocyte numbers.

The multipotent stem cell the hemocytoblast differentiates into a Proerythroblast in the red marrow. The proerythroblasts will differentiate Basophilic Erythroblasts. Basophilic erythroblasts have smaller nuclei and an increased number of ribosomes. This increase in ribosome number allows for the synthesis of hemoglobin and is responsible for the basophilic nature of these cells. The basophilic erythroblasts develop into Polychromatophilic Erythroblasts.

At this point in erythropoiesis the cells begin to show two patterns of staining: basophilic staining due to the presence of ribosomes and eosinophilic staining due to the presence of hemoglobin. The nucleus of these cells is even smaller, having been further reduced and it's functions have been terminated. The polychromatophilic erythroblasts develop into Normoblasts.

During the normoblast stage the nucleus is very reduced and will be eventually extruded form the cell. The normoblasts will differentiate into Reticulocytes. Due to the dual nature of their staining reticulocytes are also known as "polychromatophilic erythrocytes". Typically the reticulocyte will mature into a erythrocyte and then leave the red marrow to enter into circulation. However, about 1% to 2% of the erythrocytes in circulation are really reticulocytes which are still completing maturation (unless there is a disorder). When erythrocytes become Senescent they have used up all of their enzymes necessary to maintain ATP and can not replace them. The cells become fragile. These senescent cells are trapped, engulfed, and degraded by phagocytic cells of the liver, spleen, and bone marrow. Hemoglobin is degraded into Bilirubin. Iron is released from the degrading hemoglobin and is complexed with protein to be stored as Ferritin or as Hemosiderin which will be available for erythropoiesis.

6.2.2. Leucocytes

Leucocytes are the white blood cells. They are the only complete cells of the formed elements. Leucocytes can be described as connective tissue cells which utilize the blood stream for transport from the hemopoietic red marrow to areas where they are required. Leucocytes are a variety of motile, nucleated cells which serve in the defense of the body from disease causing organisms (i.e.; the immune system). Leucocytes care divided into two large groups based on their appearance under light microscopy:

1) Granular Leucocytes or Granulocytes -leucocytes having prominent cytoplasmic granules and a lobulated nucleus. They are basophils, eosinophils, and neutrophils.

2) Agranular Leucocytes or Agranulocytes -leucocytes lacking prominent cytoplasmic granules and having a spherical nucleus. They are lymphocytes and monocytes. The steps of hemopoiesis which give rise to the leucocytes are broadly called Myelopoiesis and occur, at least initially, in the red marrow. In myelopoiesis the hemocytoblast can follow three distinct pathways giving rise to different leucocytes: The hemocytoblast can differentiate into a Myeloblast which can ultimately develop into any of the three granulocytes. The hemocytoblast can differentiate into a Monoblast which will eventually develop into the monocyte.

The hemocytoblast can differentiate into a Lymphoblast which will eventually develop into the lymphocytes.

2) Granulocytes - leucocytes having prominent cytoplasmic granules and a lobulated nucleus. They derive from myeloblasts and develop and mature in red marrow.

a) Neutrophils

Neutrophils are the most abundant of the granulocytes and the most numerous type of leucocyte in the blood stream. Neutrophils are chemotatically attracted to areas in which bacteria and other foreign substances are concentrated such as sites of inflammation/infection. They are attracted there by substances known as Chemotactic Factors generated at the inflammation site and diffusing into the surrounding tissues. Chemotactic factors may be chemicals released by phagocytized bacteria or by a wide range of host factors (e.g.; complement activation). In the mature neutrophil the nucleus has a highly lobulated appearance. On average the nucleus will have three to five lobes. This is why neutrophils are also called "polymorphonuclear leucocytes". The lobulated nucleus allows the neutrophil to be used in gender determination since the Barr Body is visible in the neutrophils of women.

Neutrophils demonstrate two populations of cytoplasmic granules: 80% of the granules appear as tiny pink granules containing antibacterial substances such as lactoferrin, lysozyme, and cobalamin-binding protein. 20% of the granules are larger and blue in color. These granules are primarily lysosmes containing peroxidase, acid hydrolase, acid phosphatase, and other enzymes involved in antibacterial digestive actions. These granules will also contain lysozyme.

b] <u>Eosinophils</u>

Eosinophils usually have bilobed nucleus and an abundance of orange-red granules. The granules will obscure portions of the nucleus. In some respects, these granules are like the typical lysosome in that they contain hydrolytic compounds. In other ways though they are different form the typical lysosome since they contain a number of substances that moderate the inflammation response and aid in the rejection of parasites by the body. They contain <u>histaminase</u>, <u>arylsulphatase</u>, and the hormone <u>hydrocortisone</u> to depress the allergic and immune reactions. They also contain <u>MBP</u> (Major Basic Protein) which is released onto the surfaces of a parasite to promote antibody mediated immune response. Eosinophils are rare cells. They are found in low numbers in chronic inflammatory reactions. They phagocytize antigen-antibody complexes (such as antibody coated bacteria). Eosinophils occur in the connective tissues of the respiratory tract and the digestive tract. They are chemotactically attracted to areas where allergic reactions are occurring.

c] <u>Basophils</u>

Basophils are rare leucocytes having a distinctive appearance. They have a bilobed or "U-shaped" nucleus and prominent basophilically staining granules. They also have metachromatically staining granules. The granules of basophils contain a number of pharmacologically active substances which promote inflammation and some GAGs. Basophils in many ways resemble mast cells but they are unrelated. Basophil functions include: i} increasing vascular permeability in the inflammation response ii} binding to the immunoglobulin IgE which is produced by the plasma cells.

3) <u>Agranulocytes</u> - leucocytes lacking prominent cytoplasmic granules and having a spherical nucleus. They initially develop in red marrow but migrate elsewhere to mature.

a] <u>Monocyte</u>

Monocytes could be considered to be immature macrophages that are in transit to the connective tissues. Even at this time, however, they are still highly phagocytic. After having been in circulation for 1 to 2 days, they enter into the connective tissues and differentiate into macrophages. They may undergo further division and enzyme synthesis. As macrophages they are highly mobile moving about by diapedesis.

Monocytes have a pale basophilic cytoplasm, lacking granules easily discernible under light microscopy, and a large, kidney-shaped nucleus. They do possess numerous small granules but again these can not be seen under the typical light microscope.

b] <u>Lymphocytes</u>

Lymphocytes look quite a bit like monocytes. They also have a pale basophilic cytoplasm, lacking granules easily discernible under light microscopy, and a large, indented nucleus. The nucleus is not as strongly indented, kidney shaped, in lymphocytes. They also possess numerous small granules but again these can not be seen under the typical light microscope. Lymphocytes can be identified according to size. They range from 6 to 18 um in diameter. Based on size they are termed: <u>small</u>, <u>medium</u>, and <u>large</u>. Only small and medium sized lymphocytes are found in blood circulation. Most of the lymphocytes in the blood or lymph are actually <u>recirculating immunocompetent cells</u>.

These cells have developed the capacity to recognize and respond to foreign invaders and antigens. There are two types of lymphocytes. The two types are:

1. <u>T Lymphocytes</u> - long living cells which mature in the thymus and are involved in cell-mediated immunity.

2. B Lymphocytes - are cells having a varying longevity which mature in some still undetermined area ("bursa-equivalent") and are involved in antibody-mediated immunity.

Both types are involved in the memory of the immune system and will develop to respond to specific antigens. Some B cells and some T cells will develop into Effector Cells. A B cell that has become exposed to an antigen will undergo mitosis producing more B cells. Some of these will become Plasma Cells which will secrete antibodies specific to the antigen. T cells can also undergo mitosis producing a number of T.

T cell varieties involved in cell-mediated immunity:

(1) Cytotoxic T Cells (aka; Killer T Cells) - recognize other cells with foreign antigens on their cell membranes and destroy them (by lysis).

(2) Helper T Cells - assist B cells and T cells in the immune response. They secrete factors in response to antigens which will stimulate B cells and other leucocytes to destroy the invader.

(3) Suppressor T Cells - suppress the immune response. Some cells become Memory Cells. Memory cells are long lived cells that allow the immune system to respond more swiftly and more efficiently when exposed to the same pathogen again.

6.2.3. Thrombocytes

Thrombocytes, also called "platelets", function to arrest bleeding and to cause thrombosis, clot formation. Thrombocytes are the smallest of the formed elements. They are 2 to 4 um long and shaped like flattened discs. They are actually fragments of the cytoplasm of large Megakaryocytes which explains their lack of organelles. Each of these large, multilobed cells will give rise to between 1,000 and 5,000 thrombocytes. Under the light microscope they show two regions:

1. Granulomere - the central portion of the thrombocyte.It stains purple.
2. Hyalomere - the peripheral portion of the thrombocyte, it is peripheral to the granulomere. It stains pale blue.

About a third of the body's thrombocytes are located in the spleen.

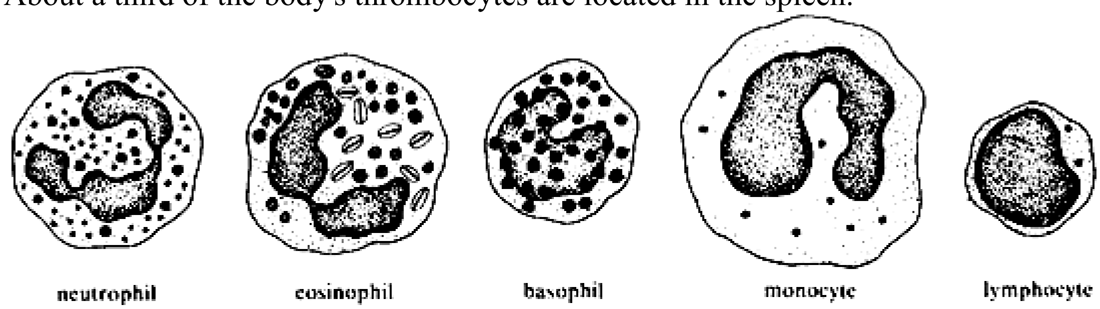

Fig.6.3. While Blood Cells