AN INTRODUCTION TO BLOOD CELLS – FORMATION TO FUNCTION

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Just like every system in our body, the human circulatory system (heart, lungs, blood vessels) also has an important function - it carries nutrients and oxygen to various tissues in our body and removes waste products including carbon dioxide from the tissues. Blood plays a central role in this function of the circulatory system.

- **What is the human blood made of?**

The blood that you see is a deep red coloured fluid and is made of two components:

  - **Cellular** which includes the different types of blood cells [40%]
  - **Non cellular fluid** component which includes a pale yellow or straw colored fluid called as plasma which has various proteins, sugars and important functional components like antibodies.

- **What are the blood cells?**

The human peripheral blood is made of three main types of cells

  - Red blood cells [RBCs, also called erythrocytes]
  - White blood cells [WBCs, also called leucocytes]
  - Platelets [also called thrombocytes]

The WBC in turn has specific subtypes depending on the presence [granulocytes] or absence [agranulocytes] of granules in the cell cytoplasm. [Cytoplasm refers to all the contents of the cell outside the nucleus including various organelles and a gel like fluid called cytosol enveloped by an outer cell membrane]

  - **Granulocytes** include neutrophils, eosinophils and basophils
  - **Agranulocytes** include lymphocytes and monocytes
    - Lymphocyes are further subdivided into T cells, B cells and NK cells.

- **How are the blood cells formed?**

The blood cells are formed in the bone marrow. Bone marrow is the spongy, semi-solid tissue in the central part of bones which has all the blood cells [red marrow] towards the ends of the bones and fat [yellow marrow] in the middle part.

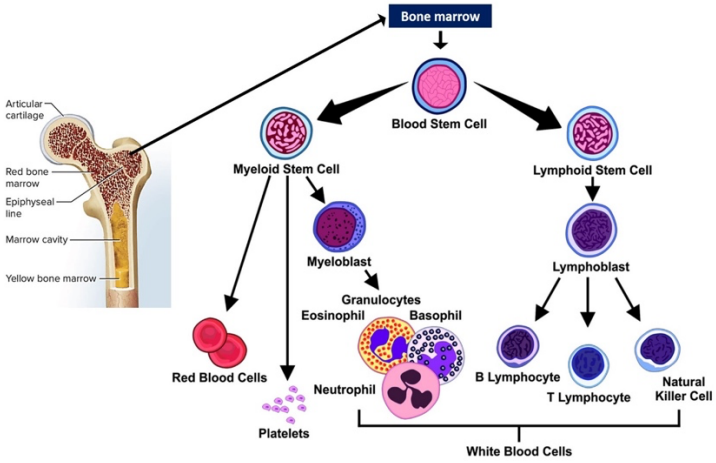
All the human blood cells originate from a precursor referred to as hematopoietic stem cell. These stem cells undergo proliferation and different stages of maturation to finally become a mature cell.

The hematopoietic stem cell forms two intermediate progenitors namely the lymphoid progenitor that forms the lymphocytes and the myeloid progenitor that gives rise to all the other WBCs, RBCs and platelets.

The mature blood cells formed in the marrow then migrate out of the bone marrow to the peripheral circulation.

This formation of mature cells from the primitive stem cell is called as hematopoiesis. The process is tightly regulated by multiple factors so that the production of blood cells in the body can be increased or decreased depending upon the need.

Defects in hematopoiesis forms the basis of various blood diseases including blood cancers.

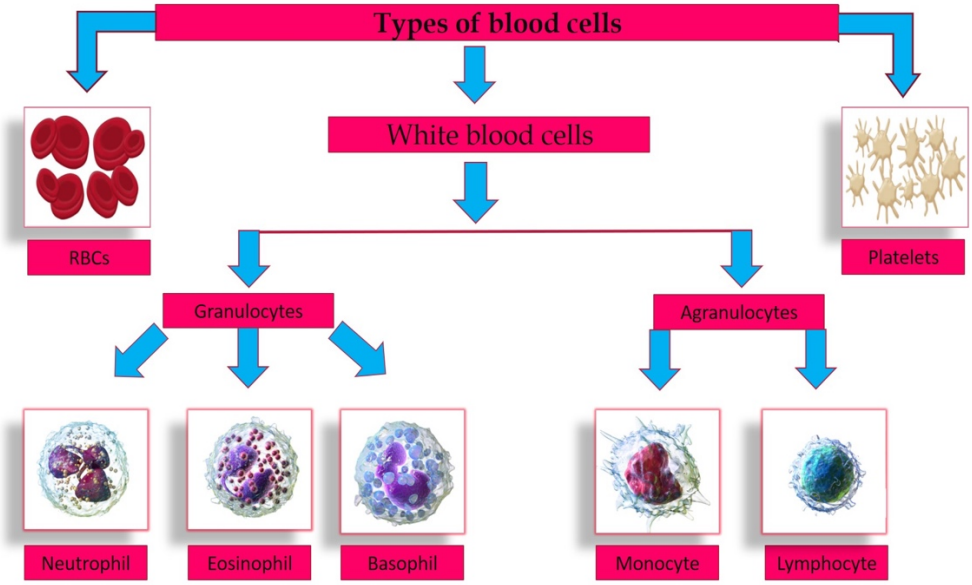


- **How many cells are there in the body?**
  - Blood contributes about 7% of your total body weight. A normal adult has approximately 5 liters of blood in his or her body.
  - One cubic millimeter of your blood has:
    - **4 to 6 million RBCs**
    - **4000 to 11,000 WBCs**
    - **150000 to 400000 platelets.**
  - Every second, 2-3 million RBCs are produced in the bone marrow and released into the circulation

- **Are other organs involved in the formation of blood cells apart from bone marrow?**

Apart from the bone marrow which plays a central role, three other sites are also involved in the process of hematopoiesis – spleen, lymph nodes and thymus. While the spleen and lymph nodes are involved in the terminal stages of B lymphocyte production, most of the stages in the T lymphocyte production and maturation happen in the thymus.

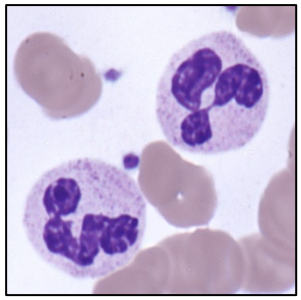
- **Description of individual blood cell types**



Neutrophils = Neutral pink stain. Named according to the staining properties with hematoxylin and eosin staining

- **Cell description:** Neutrophils are characterized by granular cytoplasm and a nucleus which is segmented into multiple interconnected lobes as shown in the image. Hence, they are also called as polymorphonuclear cells

Neutrophils

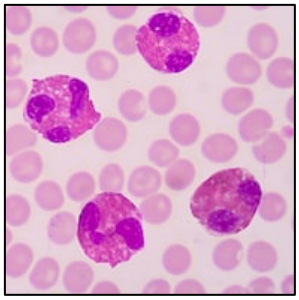


- **Features:** Most common type of WBC seen in the peripheral blood.
- **Size:** 12 to 15 µm
- **Life span in blood:** 2 to 7 days
- **Function:** during infections, neutrophils migrate to the site of infection and perform anti-microbial activity. They are involved in killing and digestion of various bacteria and bacterial toxin products [called as phagocytosis].
- **Clinical significance:** Decrease in neutrophil count can be congenital or acquired due to some secondary causes like infections, drugs and cancer therapy. It can be a manifestation in various hematological diseases like bone marrow failure syndrome and hematological cancers. Increased neutrophil count is usually seen in bacterial infections.

Other causes include inflammatory conditions, some inherited immune deficiency diseases, drugs and blood cancers.

Eosinophil = acid loving. Named based on the presence of large acidophilic granules in the cytoplasm that gives the bright reddish orange colour on hematoxylin and eosin staining

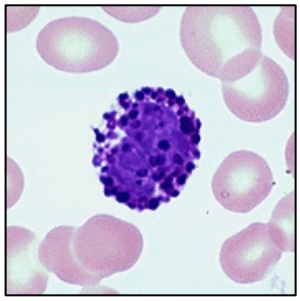
Eosinophils



- **Cell description:** The cell is characterized by the bright reddish orange granules in the cytoplasm and a nucleus which is generally segmented into two interconnected lobes as shown in the image.
- **Features:** The granules in the eosinophils have many chemical mediators of inflammation which actively play a role in both innate and acquired immunity.
- **Size:** 12 to 17 µm
- **Life span in blood:** Eosinophils have a half-life of 12-24 hours in circulation and a tissue life span of 5-7 days
- **Function:** Like neutrophils, eosinophils also migrate to the site of infection and perform anti-microbial activity. Eosinophils are primarily involved in eliciting immune responses to various parasites and worm infestations.
- **Clinical significance:** An increase in eosinophil count is usually seen in parasitic infections. It can also be seen in disease conditions including autoimmune disorders, allergies like asthma and also in some rare forms of blood cancers. Congenital forms of eosinophilia can also be seen with underlying genetic causes.

Basophils= base loving. Named based on the deep bluish stain of large basophilc granules in the cytoplasm.

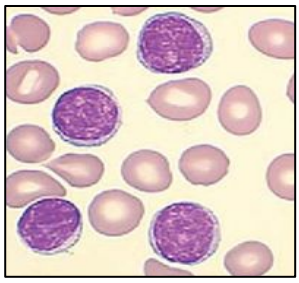
Basophils



- **Cell description:** The cell is characterized by the large bluish granules in the cytoplasm that completely obscure the underlying nucleus when seen under a microscope.
- **Features:** Basophils are present in low numbers and are very rarely seen in the peripheral blood. The granules in the basophils have many chemical mediators of inflammation and clotting.
- **Size:** They are the largest of the granulocytes. Size ranges from 14 to 17 µm
- **Life span in blood:** 2 to 3 days
- **Function:** Like eosinophils they are involved in eliciting immune responses to parasitic infections and allergic responses. They also secrete heparin which prevents the blood from clotting in the circulation and other chemicals like histamine.
- **Clinical significance:** An increase in basophil count is seen in chronic infections and allergic conditions. An increase in basophil count is one of the characteristic features of some hematological cancers like chronic myeloid leukemia and other types of myeloproliferative neoplasms.

Lymphocytes = Lymph + cytes. They are the main cell types found in the lymph and lymph nodes and hence the name

Lymphocytes



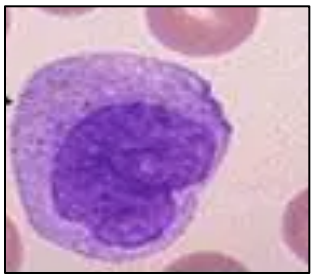
- **Cell description:**The cell is characterized by agranular cytoplasm and an unsegmented oval to round nucleus. There are three classes of lymphocytes – T cells, B cells and NK cells. Unlike B and T cells, NK cells can have some cytoplasmic granules when seen under a microscope.
- **Features:** Second most common type of WBC after neutrophils in peripheral blood. They are also seen in large numbers in lymphoid organs like lymph nodes and spleen.

- **Size:** They are the smallest WBCs seen in the peripheral smear. Size ranges from 7 to 10 µm. Some granular lymphocytes seen in infective and malignant conditions can also be larger in size [large granular lymphocytes].
- **Life span:** Variable. Some lymphocytes [memory cells] can persist for years.
- **Function:** Lymphocytes play a major role in both intrinsic or innate immunity [NK cells] as well as acquired immunity. The acquired immunity can be cell mediated [T cells] or antibody mediated [B cells which secrete antibodies].
- **Clinical significance:** Decrease in lymphocyte count can be congenital which can result in multiple episodes of life-threatening infections or acquired due to secondary causes like viral infections (HIV, corona virus, tuberculosis etc] drugs including cancer therapy. It can be a manifestation in various hematological diseases like bone marrow failure syndrome and hematological cancers. Likewise, an increase in lymphocyte count can also be a manifestation of infections and cancers of blood and lymphatic system.

Monocytes = Mono + cytes. They are the large mononuclear cells found in the peripheral blood

- **Cell description:** The cell is characterized by abundant ground glass cytoplasm and an unsegmented kidney shaped nucleus.

Monocytes



- **Features:** Monocytes form less than 10% of circulating peripheral blood WBCs. Although agranular, the cytoplasm can have vacuoles seen as empty spaces in the ground glass cytoplasm.
- **Size:** Monocytes are the largest cells seen in the peripheral smear. Size ranges from 15 to 20 µm.
- **Life span:** 24 to 48 hours in peripheral blood. Some of the monocytes migrate to different tissues where they persist for months to years.
- **Function:** The monocytes from the peripheral blood migrate to different tissues and are converted to macrophages which engulf the foreign substances, infective microbes and cellular debris and present it to the lymphocytes and granulocytes for initiating immune

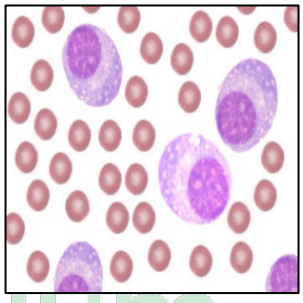
response [macro – large; phages – eaters]. These cells are also referred to as antigen presenting cells

- **Clinical significance:** An increase in monocyte count can be seen in infections like tuberculosis, autoimmune diseases drugs, and some types of blood cancers. Likewise, a decrease in monocyte count can be seen in bone marrow failure, drugs and in some types of blood cancers.

Plasma cells

- **Cell description:** Plasma cells have a bluish cytoplasm with an eccentric nucleus and a characteristic halo around the nucleus as shown in the image.

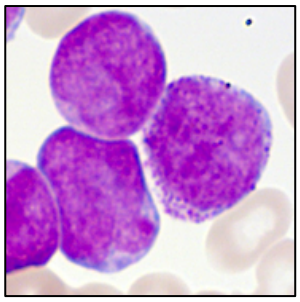
Plasma cells



- **Features:** Plasma cells are the terminally differentiated B cells. After leaving the marrow, some B cells are activated when they encounter specific antigens in the presence of T cell subsets called Helper T cells in the spleen or lymph nodes and differentiate further into plasma cells.
- **Size:** They are large cells ranging from 14 to 20 µm.
- **Life span:** variable.
- **Function:** Plasma cellssecretes antibodies [immunoglobulins] which play an important role in adaptive immune response.
- **Clinical significance:** Cancers arising from the plasma cells are called as plasma cell dyscrasias which includes multiple myeloma.

Blasts

Blasts



- **Cell description:** Blasts are immature cells with large nucleus and bluish cytoplasm. The shape and other features vary depending upon the lineage and morphological subtypes.
- **Features:** Blasts are the precursors in the marrow which give rise to all the peripheral blood WBCs [myeloblasts, lymphoblasts and monoblasts], RBCs [erythroblasts] and platelets

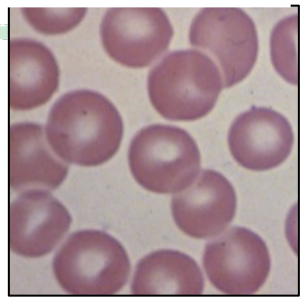
[megakaryoblasts]. Except erythroblasts which are common, blasts are present in low numbers in bone marrow and are not present in peripheral blood normally.

- **Size:** Variable
- **Function:** In normal hematopoiesis blasts undergo differentiation to form intermediate precursors which eventually gives rise to the mature WBCs.
- **Clinical significance: Blasts are the defining cells of a type of blood cancer called as acute leukemias.** Based on the blast lineage, acute leukemias are classified as acute myeloid leukemia and acute lymphoblastic leukemia. Unlike normal blasts, the cancer blasts proliferate very rapidly and at the same time cannot undergo maturation. Hence there is accumulation of immature blasts which eventually replaces all the normal cells in the marrow resulting in peripheral blood cytopenia in the patient. These blasts can also be seen in the peripheral blood.

Red Blood Cells (RBCs)

- **Cell description:** They are biconcave, or disc shaped with a central pallor. The cells are devoid of many organelles including nucleus and the cytoplasm is filled with hemoglobin which is the protein involved in transport and exchange of oxygen and carbon di oxide between lungs and tissues.

RBCs



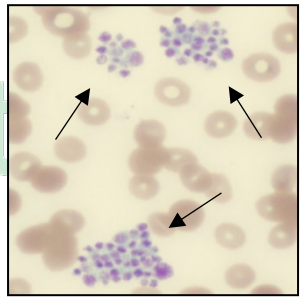
- **Features:** RBCs are the most abundant cells in the peripheral blood. The red colour of the blood is because of the heme iron present in the hemoglobin of RBCs. The formation of RBCs, termed erythropoiesis, can be increased or decreased based on the tissue oxygen levels.
- **Size:** These are smaller than the WBCS measuring around 6 to 8 µm.
- **Life span:** 100 to 120 days.
- **Function:** The main job of red blood cells is to transport oxygen from the lungs to different tissues in the body and to remove carbon dioxide from the tissues and transport it back to the lungs for release.

- **Clinical significance:** A decrease in RBC and/or hemoglobin results in anemia. It is one of the commonest clinical presentation and can be a result of decreased production or increased destruction of RBCs. The various causes include nutritional [iron, vitamin B12, folic acid], hereditary causes like sickle cell anemia and thalassemia, blood loss, infections like malaria, drugs, bone marrow disorders and various blood cancers. An increase in RBC count termed polycythemia can be a secondary manifestation of various respiratory diseases or can be a primary manifestation of certain blood cancers.

Platelets

- **Cell description:** In a peripheral blood smear, platelets are seen as small circular dots usually in clusters as shown in the image.
- **Features:** Platelets are small cytoplasmic fragments arising from megakaryocytes in the bone marrow. Each megakaryocyte gives rise to about 3000 to 5000 platelets in the marrow which migrates to the peripheral blood.

Platelets



- **Size:** These are the smallest cells in the peripheral blood measuring 2 to 3 µm.
- **Life span:** 8 to 12 days.
- **Function:** The main job of platelets is to prevent blood loss during injuries. Platelets initiate the entire clotting mechanism by forming platelet clumps and constricting the blood vessels. Apart from hemostasis, platelets also have inflammatory role as it secretes various chemical mediators of inflammation.
- **Clinical significance:** A decrease in platelet count is called as thrombocytopenia which can be immune mediated or result from infections, marrow disorders or blood cancers. Functional defects of platelets where there is a defect in platelet mediated blood clotting can also be seen with normal or decreased platelet counts. An increase in peripheral blood platelet count can be seen in iron deficiency, infections, blood loss and some types of blood cancers.