Blood is specialized connective tissue.

Composed by:

- **Formed elements**
- **Fluid component**, Plasma (the extracellular matrix)

Formed elements: **cells** and cell fragments (**platelets**)

The cells of blood:

- **Red blood cells** (RBC)
- **White blood cells** (WBCs, leukocytes).
HEMATOPOIEISIS

• Mature blood cells have a relatively short life span
• Must be continuously replaced by stem cells
• Stem cells produce in HEMATOPOIETIC ORGAN
PRENATAL HEMOPOIESIS

• Subdivide into four phases:
  – Mesoblastic:
    • begin after 2 weeks after conception at yolk sac
    • Mesenchymal cells aggregate into blood islands
  – Hepatic
    • Begins at 6 weeks until end of gestation
    • Nucleated erythrocyte
    • Appear of leucocyte (8th week)
  – Splenic
    • Begin at second trimester until end of gestation
  – Myeloid
    • Begin at the end of second trimester
    • Hemopoiesis at bone marrow
POSTNATAL HEMOPOIESIS

• Hemopoiesis almost exclusively in BONE MARROW

• Stem cells undergo
  – multiple cells divisions
  – and differentiation

• Replace the cells that leave the blood stream, die or destroy
## Site of hematopoiesis

<table>
<thead>
<tr>
<th>AGE</th>
<th>SITE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetus: 0-2 months</td>
<td>Yolk sac</td>
</tr>
<tr>
<td>2-7 months</td>
<td>Liver, spleen</td>
</tr>
<tr>
<td>5-9 months</td>
<td>Bone marrow</td>
</tr>
<tr>
<td>Infants</td>
<td>Bone marrow, practically all bones</td>
</tr>
<tr>
<td>Adults</td>
<td>Vertebrae, ribs, sternum, sacrum and pelvis, proximal ends of femur</td>
</tr>
</tbody>
</table>

- Developing cells situated outside of BM sinuses $\rightarrow$ mature cells released into sinus spaces $\rightarrow$ marrow microcirculation $\rightarrow$ general circulation.
- Hematopoiesis starts with pluripotent stem cell
HEMOPOIETIC GROWTH FACTORS

• **REGULATES THE HEMOPOIESIS PROCESS**

• **Induces rapid mitosis or and differentiation**
  – Glycoprotein hormones \( \rightarrow \) regulate proliferation & differentiation

• Produce by specific cells

• Acts on specific stem cells, progenitor cells, and precursor cells

• The route to deliver growth factor:
  – Via blood stream
  – Secrete near the hemopoietic cells
  – Direct cell-cell contact

• Biological effects of HGF mediated through specific receptors on target cells.

• Act:
  – Locally \( \rightarrow \) at the site where they are produce \( \rightarrow \) by **cell-cell contact**.
  – Circulate in plasma
Primary Lymphatic Organs:

- **Lymphatic (lymphoid) organs** contain large numbers of lymphocytes, a type of white blood cell that plays a pivotal role in immunity.

- The *primary lymphatic organs* are
  - The thymus gland.
  - The red bone marrow and

- Lymphocytes originate and/or mature in these organs.
Primary lymphoid organs

The Thymus

- site of maturation of T-lymphocytes
- Secretes hormones (thymopoietin and thymosin)
- critical role in childhood

Studies have identified at least six types of thymic cells. These particular cells PRODUCE interleukin-1 (IL-1), interleukin-4 (IL-4), interleukin-6 (IL-6), thymosin, thymopoietin, and thymulin.

These hormones, secreted by the thymus gland are found to have an effect on T-lymphocyte differentiation and activation. Of these thymic hormones Thymosin, Thymulin and Thymopoietin, may possibly reach the circulation and act on the lymphocytes and tissues at various sites in the human body.
The Thymus is a Primary Lymphoid (Immune) Organ Responsible For the Education of T-Cells

The Young Thymus
Surrounded by a CT capsule; cortex has a lot of lymphocytes, fewer in the medulla

THERE ARE NO GERMINAL CENTERS IN THE THYMUS!

Located over the great vessels of the heart in the area of the mediastinum

Develops from an invagination of EPITHELIUM of the 3rd pharyngeal pouch, so it is called to be an endodermal organ.

Made of: Specialized epithelial cells (called epithio-reticular cells) that are joined to one another by long processes with desmosomes on the extremities of the cells (like starfish joined together at the tips) make up the bag-like support for:
The Thymus undergoes a process called THYMIC INVOLUTION, as T cells leave the thymus to populate other Lymphoid effector organs, the organ shrinks, leaving only the epithelioreticular cells

NOTE: There are generally NO B – lymphocytes cells in the Thymus.
The thymus with two tissue components

- Parenchyma and Stroma.
- The parenchyma is composed mostly of T lymphocytes in various stages of development into mature T cells.
- The stroma is composed of special thymic epithelial cells. Consists of sparse, delicate epithelial cells obscured by all of the lymphocytes. These epithelial cells form the support structure for the developing T cells but also play an important role in isolating the T cells from foreign antigens during their development.
- It has two distinct but identical lobes that are each surrounded by a tough, fibrous capsule. Within each lobe is a superficial region of tissue called the cortex and a histologically distinct deep region called the medulla.
- Epithelial tissues and lymphatic tissues containing dendritic cells and macrophages make up the majority of both regions of the thymus.
epithelial reticular cells
- support thymic parenchyma
- secrete thymosin
- participate in T cell maturation
- contribute to blood-thymus barrier in cortex...
Each lobule has an outer, darker staining cortex and an inner, paler staining medulla.

In the cortex, (the parenchyma), consists mostly of the developing T lymphocytes and reticular cells. Epithelial cells are called Thymic nurse cells in the cortex contain maturing lymphocytes.
In the medulla

- **The stroma** consists of prominent **Epithelial Reticular Cells** that have large, pale-staining nuclei and substantial amounts of eosinophilic (pink-staining) cytoplasm.

- There many T cells because most of them have entered the bloodstream via vessels at the cortico-medullary junction.

- Thymic corpuscles or Hassal corpuscles

- Antigen presenting cells (APC) are also found in the medulla where they are called **Thymic interdigitating cells**.

- T cells that recognize these self-antigens Cells and are removed by a process called apoptosis.
T-cells that survive selection process allowed to cross venule endothelium to enter circulation.
Primary Lymphatic Organs :-

• **Red Bone Marrow**

• It is the site of stem cells that are ever capable of dividing and producing blood cells.

• Some of these cells become the various types of white blood cells: neutrophils, eosinophils, basophils, lymphocytes, and monocytes.

• In a child, most of the bones have red bone marrow, but in an adult it is limited to the sternum, vertebrae, ribs, part of the pelvic girdle, and the proximal heads of the humerus and femur.
bone marrow

• Two types of bone marrow:
  – *Red Marrow* - consisting mainly of hematopoietic tissue
  – *Yellow Marrow* - consisting mainly of fat cells

• **At birth**, all bone marrow is red.

• With age, more and more of it is converted to the yellow type; only around half of adult bone marrow is red

• **In Adults** Red marrow is found mainly in the Flat bones and in the epiphyseal ends of long bones such as the femur and humerus

• Yellow marrow is found in the medullary cavity, the hollow interior of the middle portion of long bones
Bone Marrow

• Bone marrow is specially designed to support the proliferation, differentiation, and maintenance of hematopoietic cells

• The stroma of the bone marrow is all tissue not directly involved in the primary function of hematopoiesis.

• Cells that constitute the bone marrow stroma are:
  • fibroblasts (reticular connective tissue)
  • macrophages
  • adipocytes
  • osteoblasts
  • osteoclasts
  • endothelial cells, which form the sinusoids.
BONE MARROW

A gelatinous, vascular connective tissue located in medulary cavity of long bones

**Responsible for hemopoiesis**

**Structure**:

**Vascular compartment**

- Extensive network of sinusoids, arteries and veins form the

**Hemopoietic compartment**

- Islands of hematopoietic cells
- Hemopoietic cells in various stage of maturation
Red Bone Marrow :-

• The red bone marrow consists of a network of reticular tissue fibers, which support the stem cells.
• They are packed around thin-walled sinuses filled with venous blood. Differentiated blood cells enter the bloodstream at these sinuses.
• Lymphocytes differentiate into the B lymphocytes.
• Bone marrow is not only the source of B lymphocytes, but also the place where B lymphocytes mature.

Mammalian stem cells differentiate into several kinds of blood cell within the bone marrow. This process is called haematopoiesis. All lymphocytes originate, during this process, from a common lymphoid progenitor before differentiating into their distinct lymphocyte types. The differentiation of lymphocytes follows various pathways in a hierarchical fashion as well as in a more plastic fashion. The formation of lymphocytes is known as lymphopoiesis. B cells mature into B lymphocytes in the bursa equivalent, which in humans is the GALT, which is thought to be located in the Peyer's patches of the intestine, while T cells migrate to and mature in a distinct organ, called the thymus.
THYMUS

- Thymic hormones
- Production and differentiation of T cells
- Mature T cell
- Transported by circulatory system

Migrate to thymus

Pluripotent stem cell

Lymphoid stem cells
- Interleukin-7
- Mature T cell
- B cells
- Natural killer cells

RED BONE MARROW

- Lymphoid stem cells
- Interleukin-7

PERIPHERAL TISSUES

- Cell-mediated immunity
- Antibody-mediated immunity
- Immunological surveillance
Blood Composition.

• Blood is a fluid connective tissue constituting about 7% of our total body weight (about 5 liters in the human). The primary components are:

  – A. Plasma:

    The liquid in which peripheral blood cells are suspended. Composed of water, electrolytes such as Na+ and Cl, (0.9%), 7% plasma proteins (such as albumin, fibrinogen, globulins), hormones, fats, amino acids, vitamins carbohydrates, lipoproteins as well as other substances. The normal plasma volume is 40 ml/kg of body weight.

  – B. Formed Elements (blood cells):

    • 1. Erythrocytes (red blood cells or rbc): occupy about 40-45% of the total blood volume or 30 ml/kg body weight.
    • 2. Leukocytes (white blood cells or wbc) and Platelets: together make up about 1-2% of the total blood volume.
Pluripotent(ial) Hematopoietic Stem Cell

- Give rise to the separate cell lineage
- Exact phenotype unknown → immunological testing: CD34+, CD38-
- Appearance ~ small/medium size lymphocyte
- Cell differentiation occurs from the stem cell down the erythroid, granulocytic and other lineages via the committed hematopoietic progenitors cells → restricted in their developmental potential.
HEMATOPOIESIS - Growth factors

Pluripotent Stem Cell (PSC) → Committed Stem Cell 
- SCF, IL-1

Myeloid Progenitor Cell (MPC) 
- IL-3, GM-CSF

CFU-GM → 
- CFU-M, CFU-N, CFU-Eo, CFU-B

- M-CSF, G-CSF, IL-6

Megakaryocyte (CFU-Meg) → Platelets
- TPO, EPO

Lymphoid Progenitor Cell (LPC) 

T Lymphocyte 
- M-CSF

B Lymphocyte 
- M-CSF

RBC 
- EPO

Monocyte 
- M-CSF

Neutrophil 
- IL-3

Eosinophil 
- IL-3

Basophil 
- IL-3

Colony-forming Unit - granulo-monocyte (CFU-GM)

IL-3, GM-CSF
Megakaryoblasts are the precursors of the megakaryocytes.

They may show cytoplasmic expansion.
Megakaryoblasts

The marrow cavity is filled with red bone marrow. A few of the numerous named types or broader groups can actually be recognized.

Precursors of platelets are the haemopoietic cells easiest to find in red bone marrow. The very dark and large megakaryoblast and the even larger but light megakaryocytes are clearly visible even at low magnifications. Adipocytes are present also in the red bone marrow.
Platelets

Platelets, also called thrombocytes (thromb- + -cyte, "blood clot cell), are a component of blood whose function (along with the coagulation factors) is to stop bleeding by clumping and clotting blood vessel injuries.

Platelets have no cell nucleus: they are fragments of cytoplasm that are derived from the megakaryocytes of the bone marrow, and then enter the circulation.

These unactivated platelets are biconvex discoid (lens-shaped) structures, 2–3 µm in greatest diameter.
PLATELETS

250,000-400,000 platelets/mm³
2 to 4 µm in diameter
Display peripheral clear region (hyalomere) and central darker region (granulomere)
receptor molecules (glycocalyx) on plasmalemma
Function: Blood clott
Agranulocytes

**Lymphocytes**: common in the lymph system and of three types: B cells, T cells and natural killer cells.

**Monocytes**: they present pieces of pathogens to T cells so that the pathogens may be recognized again and killed. Monocytes eventually leave the bloodstream to become tissue macrophages.
LYMPHOID LINAGE:

- Lymphocytes constitute 20%–40% of the body’s white blood cells and 99% of the cells in the lymph.
- These lymphocytes continually circulate in the blood and lymph and are capable of migrating into the tissue spaces and lymphoid organs,
- Two morphological distinct lymphocytes can be observed in the blood the first type is the small agranular lymphocyte having high nuclear-to-cytoplasm ratio. These lymphocytes are further divided into two types they are T and B lymphocytes
- The second type is a large cell, which is granulated, and posses low nuclear-to-cytoplasmic ratio. They are called as large granulated lymphocytes. Lymphocytes normally possess specific receptors for antigens and thus mediate specific immunity.
Development of lymphocytes

1. Lymphocytes destined to become T cells migrate to the thymus and develop immunocompetence there. B cells develop immunocompetence in the bone marrow.

2. After leaving the thymus or bone marrow as naive immunocompetent cells, lymphocytes “seed” secondary lymphoid organs (especially lymphoid tissue in the lymph nodes), where the antigen challenge occurs and the lymphocytes become fully activated.

3. Mature immunocompetent lymphocytes recirculate continuously in the bloodstream and lymph and throughout the lymphoid organs of the body.

Key:
- Site of lymphocyte origin
- Primary lymphoid organs; site of development of immunocompetence as B or T cells
- Secondary lymphoid organs; site of antigen challenge and final differentiation to mature B and T cells

(a)
Lymphocytes

- The main functional cells of the immune system
- 30% total blood leukocytes
- Recirculating immunocompetent cells
- Small, medium, large (6-30mm)
- Slightly indented, spherical nucleus
- Thin cytoplasm (small lymphocytes)

**T lymphocytes** – cell-mediated immunity

**B lymphocytes** – production of circulating Ab

**Natural killer cells (NK cells)** – programmed to kill virus-infected cells and some tumor cells

are primarily responsible for **humoral immunity**
• **T lymphocytes (T cells).** These are so-named because they develop for a time in the thymus and later depend on thymic hormones. There are several subclasses of T cells.

  - The immature lymphocytes only differentiate in the cortex.
  - The T-cell progenitors proliferate in the outer cortex.

  - However, only 5% of the T-cells formed survive. The survivors are the ones that can recognize self-MHC encoded surface glycoproteins, (i.e will be immunotolerant to antigen presenting cells from the same person).

• Make up 70% of all body lymphocytes

• Differentiating T-cells accumulate between epithelial reticular cells.

• They can then pass into the venules and efferent lymphatics along the border between the cortex and the medulla. Or they pass into the medulla, where they are further selected by thymic dendritic cells and matured before passing out of the medullary venules and efferent lymphatics.
T lymphocytes

• The T lymphocytes are found in the bone marrow as Pre-T lymphocytes. Then they enter the thymus to become Matured T lymphocytes. Most of the circulating lymphocytes are T lymphocytes and contribute to about 80% of the lymphocyte population.

• The T cells play two important functions - effector and regulatory.

• The effector function includes cytolysis of cell infected with microbes and tumour cells and lymphokine production.

• The regulatory functions are either to increase or to suppress other lymphocytes and accessory cells.

• T cells are two types:
  - T helper cells
  - T cytotoxic cells
**T Helper lymphocytes** that help B lymphocytes to produce antibodies and help phagocytes to destroy ingested microbes.

**T Cytotoxic lymphocytes** that kill cells harbouring intracellular microbes.

These two types of T cells shows differences in their surface markers. The T helper cells express CD4 marker on their cell surface, whereas the T cytotoxic cells express CD8 marker on their cell surface. Thus T h cells will be referred to as CD4 cells and Tc cells as CD8 cell.
T-LYMPHOCYTES

• Do not produce antibodies.

• Function in “cell-mediated immunity.”

• “NATURAL KILLER” cells destroy viruses.
  • Secrete “lymphokines” which attract phagocytic cells.
  • Secrete “perforin” which eats holes in the cells membrane or viral coat of invaders.

• “Helper T cells”:
  • Induce macrophages to destroy other antigens
  • STIMULATE B-LYMPHOCYTES TO PRODUCE ANTIBODIES.
    (Can help hundreds of B-lymphocytes mature by releasing “B-cell growth factor.”)

• “Suppressor T Cells” prevent overreaction of the system. (Inhibit B-lymphocyte production.)
Most of the lymphocytes are small; a bit bigger than red blood cells, at about 6-9µm in diameter, The rest (around 10%) are larger, about 10-14µm in diameter. These larger cells have more cytoplasm, more free ribosomes and mitochondria. Lymphocytes can look like monocytes, except that lymphocytes do not have a kidney-bean shaped nucleus, and lymphocytes are usually smaller. Larger lymphocytes are commonly activated lymphocytes. The nucleus is round small spherical and has abundant dark staining condensed chromatin. It is surrounded by a narrow rim of basophilic cytoplasm (pale blue/purple staining)
B lymphocytes

• Bone marrow is its major site of maturation
• A single B cell has an identical binding site for antigen.
• They are very important in antibody-mediated immunity as they secrete specific immunoglobulins in response to antigenic stimulus.
• The B cells are of two subunits.
• **T-cell-independent cell**: which do not require the help of T cells for the production of immunoglobulins.
• **T-cell-dependent cell**: which require the help of T cells for the production of immunoglobulins.
PRIMARY IMMUNE RESPONSE

- B-lymphocyte – antigen contact induces mitosis (plasma cells) for more antibody carrying cells. Antibodies released to circulatory systems.

SECONDARY IMMUNE RESPONSE

- Some “activated B-lymphocytes” become plasma cells.
- Some remain smaller, but retain antigen-recognition ability. (B memory cells)

- Next time similar antigen is encountered, response is MUCH FASTER due to resident and waiting memory cells.
Plasma cells:

Are derived from B lymphocytes that left the blood stream in connective tissue.

Usually the round to oval nucleus is eccentrically located in the cell due to the presence of a large Golgi apparatus. The predominant staining pattern of the cytoplasm is bluish to purple (basophilic) due to the large amount of rough endoplasmic reticulum, ribosomes. And packed with rough ER.

The nucleus has the appearance of being "spoked" or having a "clock face".
Agranulocytes

Lymphocytes: common in the lymph system and of three types: B cells, T cells and natural killer cells.

Monocytes: they present pieces of pathogens to T cells so that the pathogens may be recognized again and killed. Monocytes eventually leave the bloodstream to become tissue macrophages.
MYLOID LINEAGE:

Myeloblast (myelomonoblast) → Promyelocyte → Myelocyte → Metamyelocyte → Band neutrophil → Neutrophil

Marrow

Tissues

Blood

Monocyte → Immature macrophage → Mature macrophage → Neutrophil
MYLOID LINEAGE:

Mononuclear Phagocytes:

Myeloblast: The stem cell of the leucocytic series with lightly basophilic cytoplasm. The nuclei are large and rounded. The chromatin is in the form of moderately coarse interconnected strands. They constitute 0.3 to 0.5 per cent of marrow cells. Myeloblasts increase in leukemia.

- The mononuclear phagocytic system consists of monocytes circulating in the blood and macrophages in the tissues.
- During hematopoiesis in the bone marrow, granulocyte-monocyte progenitor cells differentiate into promonocytes, which leave the bone marrow and enter the blood, where they further differentiate into mature monocytes.
- Monocytes circulate in the bloodstream for about 8 h, during which they enlarge; they then migrate into the tissues and differentiate into specific tissue macrophages or into dendritic cells.
- The cell enlarges five- to tenfold; its intracellular organelles increase in both number and complexity; and it acquires increased phagocytic ability, produces higher levels of hydrolytic enzymes, and begins to secrete a variety of soluble factors.
Monocytes

They are normally referred to as the mononuclear phagocytic cells. Found as free circulating cells in the blood stream. They constitute approximately 4-10% of the nucleated cells in the blood. The monocyte has a diameter of 12-17mM with a characteristic Horseshoe-shaped nucleus and cytoplasmic granules. The monocytes are the precursors of the tissue-bound macrophages. They migrate to the tissues and becomes macrophages.
Monocytes

- The C-shaped nucleus of a textbook monocyte may not be easy to find. The nuclei will vary from a peanut- to a "fat" S-shape in smears. Whatever the shape of the nucleus, it is usually not lobed and not round. The nucleus is bound, at least on its concave side, by a wide rim of non-granular cytoplasm. Note also the light area of monocyte cytoplasm, which is often visible close to the concave surface of the nucleus. A large Golgi apparatus is located in the area.
Macrophages

- After the monocytes become macrophages most importantly the phagocytic property of the cell increased.
- It contains azurophilic lysosomal granules that contains myeloperoxidase, lysozyme, acid hydrolases such as beta glucuronidase, phosphate etc.
- They are elongated, with finely granular, pale eosinophilic (pink) cytoplasm and central, ovoid nucleus (oval or elongate), which is less dense than that of a lymphocyte.
- They have indistinct shape contour, often appear to merge into one another and can form aggregates known as giant cells. Macrophages express certain characteristic molecules on their cell surface, which can be identified by specific monoclonal antibodies.
GRANULOCYTOPOIESIS

- Formation of the granulocytes (neutrophil, eosinophil, and basophil)
GRANULOCYTOPOIESIS
Granulocytic Cells

Neutrophils from the major part of the white blood corpuscles (40-75%) they are motile short lived cells with multilobed nucleus, the cytoplasm contains granules which do not take up acidic or basic stains strongly and hence named neutrophils.

The major function of the neutrophils is phagocytosis which is similar to macrophages.

Neutrophils can attack and destroy bacteria and viruses even in the circulating blood, when a tissue is damaged or inflamed, the neutrophils reach that area along with macrophages destroy the unwanted tissues by phagocytosis.
Neutrophil

1. **Progranulocyte:** Also called promyelocyte. It arises and differentiates from myeloblasts. It has large cells; its nuclei are rounded with coarse chromatin. Cytoplasm is basophilic with some azurophilic granules. This cell type constitutes about 4 per cent of marrow cells.

2. **Neutrophilic myelocyte:** This arises from progranulocytes. It is smaller, has less basophilic cytoplasm containing differentiated granules and a nucleus with more compact chromatin.

3. **Neutrophilic bands:** These are immature neutrophils. The nuclei are horseshoe- or drumstick-shaped.

4. **Neutrophilic metamyelocyte:** It has a kidney-shaped nucleus and is not capable of division. It differentiates into mature neutrophilic myelocytes.

5. **Neutrophil (segmented):** This is a mature cell. Its nucleus is markedly lobulated. The lobules may be connected with a thin chromatin thread. Chromatin is compact, and there is abundant cytoplasm. Granules in the cytoplasm are small and may be inconspicuous.
Neutrophil

- 60-70% of total leucocytes
- 9-12 µm in diameter
- **Multilobe nucleus** (2 and 5 lobes)

**Three types of Granules:**
- Small specific granules
- Azurophilic granules (Lysosomes)
- Tertiary granules (gelatine and cathepsins)

**Function:**
- Phagocytes
Neutrophil

Function:
Neutrophils are born in the bone marrow. They circulate in the blood for 6-10 hours, and then enter the tissues. They are motile, and phagocytic and will destroy damaged tissue and bacteria. They self destruct after one burst of activity. They are important in inflammatory reactions.

mature neutrophil with a drumstick chromosomal appendage
Eosinophils

These are acidophilic leucocytes and are called eosinophils because, eosin, an acidic dye stains the granules of the cytoplasm of these cells intensely.
The granules are rich in hydrolytic enzymes. The nucleus is usually bilobed or ellipsoidal. They are about 2-5% of the leucocytes in healthy individuals.
Increase in number of eosinophils (eosinophilia) is observed in Allergic reaction especially during infection with intestinal parasites. At the time of parasitic infection, degranulation of eosinophils occurs and hydrolytic components of the granules are released, which kill the parasites.
EOSINOPHILS

4% of total leucocyte
10 - 14 µm in diameter

**Bilobed nucleus**

Many large specific granules stained by eosin

Function:

- Eliminate antibody-antigen complexes
- Destroy parasitic worms
Basophils

These cells are named so, because of their cytoplasm containing granules that stains with basic dye. Basophils constitute about 0.4% of white cells. The basophils granules are believed to contain heparin, histamine, serotonin, platelet activating factor and other vasoactive amines that may be released at the site of inflammation or regions of immediate hypersensitivity reaction.
BASOPHILS

<1% of total leucocyte

8-10 µm in diameter

**S-shape nucleus** *(irregular lobes)*

**Large specific granules** obscured the nucleus

**Granules (dark blue)** contain heparin & histamin

Surface receptor *(Ig E receptors)*

Function:

As initiator of inflammatory process
ERYTHROPOIESIS

- Formation of red blood cells
- Generates $2.5 \times 10^{11}$ erythrocytes /day
- By two types of unipotential progenitor cell
  - BFU-E
  - CFU-E
- Regulate by : erythropoietin
Red blood cells are the most numerous type of cell found in blood. One microlitre of blood contains around 5 million cells. They are essential for transport of carbon dioxide and oxygen around the body. They are 'born' and mature in the bone marrow. When they mature, they make haemoglobin, the protein that binds oxygen. Haemoglobin can also bind carbon dioxide, but at a different site to that for oxygen. Eventually around 90% of the dry weight of the cell is made up of this protein. The nucleus is lost from the cell, phagocytosed by macrophages, and the DNA broken down. The red blood cells can then enter the circulation. These cells only live for about 120 days. However, the iron in the haemoglobin is extracted from the erythrocytes by the liver and spleen, and the remaining heme is excreted by the liver as bile pigments. Around 3 million RBCs die and are scavenged by the liver each second.
Erythropoiesis

- This occurs entirely in the red bone marrow. Red marrow can be found in vertebrae, ribs, skull, sternum, scapula, and proximal ends of the limb bones (known as the trabecular area).
- Red marrow is also known as myeloid tissue. It is not generally found in other areas of the long limb bones; which are instead filled with fatty yellow marrow. During childhood, red marrow is far more extensive.
The haemocytoblast, in the presence of Multi-CSF, will develop into a Progenitor cell. These cells will go on to form all types of blood cell, except Lymphocytes. In the presence of EPO, the progenitor cell will become a proerythroblast.

In the presence of more EPO, this will develop into a polychromatophilic erythroblast, then a normoblast, which will then eject its nucleus, and become a reticulocyte, before finally becoming a fully formed RBC.
**ERYTHROPOIESIS**

15-20µm- basophilic cytoplasm, nucleus with nucleoli.

14-17µm-mitosis, basophilic cytoplasm, nucleoli disappears.

10-15µm- 'POLYCHROMASIA'
Hb appears, nucleus condenses.

7-10µm- **PYKNOTIC** Nucleus.
Extrusion, Hb is maximum.

7.3µm- Reticulum of basophilic material in the cytoplasm.

7.2µm- Mature red cell with Hb.
RETICULOCYTE
ERYTHROCYTE

- Biconcave-shape disk
- Without nuclei and organelles
- Have soluble enzymes
- Filled with Hemoglobin (Hb)
- Average life span of erythrocyte: 120 days
DENDRITIC CELLS

- The dendritic cell (DC) acquired its name because it is covered with long membrane extensions that resemble the dendrites of nerve cells.
- The same major function, the presentation of antigen to TH cells.
- The dendritic cell descend from the myeloid cell lineage. They circulate in blood as immature cells and mature as complete dendritic cell in the tissue.
- The dendritic cell express high level of both class I and class II MHC molecules. They are potent antigen-presenting cells. Most dendritic cells process the antigen and present it to T h cells.
- There are different types of dendritic cells
  - Langerhans’ cells
  - Interdigitating dendritic cells
  - Interstitial dendritic cells
  - Veiled cells
Natural killer cells

- NK cells were subsequently shown to play an important role in host defense both against tumor cells and against cells infected with some, though not all, viruses.
- These cells, which constitute 5%–10% of lymphocytes in human peripheral blood,
- they can recognize potential target cells in two different ways.
- NK cells express CD16, a membrane receptor for the carboxyl-terminal end of the IgG molecule, called the Fc region, they can attach to these antibodies and subsequently destroy the targeted cells.
Erythroid series

* Proerythroblast
** Early erythroblast (Basophilic )
*** Intermediate erythroblast (Polychromatic)
**** Late erythroblast (Orthochromatic )
Erythroid precursors

- Normal red cells are produced in the bone marrow from erythroid precursors or erythroblasts.
- The earliest morphologically recognisable red cell precursor is derived from an erythroid progenitor cell which in turn is derived from a multipotent haemopoietic progenitor cell.
proerythroblast

- Normal proerythroblast [dark red arrow] in the bone marrow. This is a large cell with a round nucleus and a finely stippled chromatin pattern. Nucleoli are sometimes apparent.
- The cytoplasm is moderately to strongly basophilic.
Basophilic erythroblast

- Spherical nucleus, nucleoli not visible, basophilic cytoplasm
Polychromatophilic erythroblast

- smaller nucleus — condensed chromatin, baso- and eosinophilia in the cytoplasm
Orthochromatophilic erythroblast

- small nucleus with highly condensed chromatin,
  nucleus extruded,
  eosinophilic cytoplasm
Normal erythroblasts in the BM