White Blood Cells (leukocytes)
Introduction

- Our bodies are continually exposed to various microorganisms
- Our bodies have a special system for combating the different infections and toxic agents.
- This is composed of blood leukocytes & tissue cells derived from the leukocytes.
- These cells work in 2 ways to prevent disease:
  - i) by actually destroying the invading bacteria or viruses by phagocytosis and
  - ii) by forming antibodies & sensitized lymphocytes, one or both of which may destroy or inactivate the invader.
Leukocytes: mobile units of body’s immune system.

Immunity is the body’s ability to resist or eliminate potentially harmful foreign materials or abnormal cells.

Leukocytes primarily function as defense agents outside the blood, to carry out their function, leukocytes use “seek out & attack” strategy. (i.e. they go to sites of invasion or tissue damage.)

Leukocytes are formed partially in the bone marrow & in the lymph tissue.

The main reason WBCs are present in blood is to rapidly transported from their sites of production or storage to wherever they are needed: areas of serious infection & inflammation. Thus Providing rapid and potent defense.
There are five types of leukocytes, they lack Hb so they are colourless (i.e. white) unless specifically stained for microscopic visibility. Unlike erythrocytes, (which are of uniform structure, identical function, & constant no.) leukocytes vary in structure, function & no.

According to staining properties of WBCs, WBCs are divided into

**Leukocytes**

<table>
<thead>
<tr>
<th>Granulocytes</th>
<th>Agranulocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymorphnuclear</td>
<td>Unlobed nucleus</td>
</tr>
<tr>
<td>Neutrophil 62%</td>
<td>Lymphocyte 30%</td>
</tr>
<tr>
<td>Eosinophil 2.3%</td>
<td>Large lymphocyte</td>
</tr>
<tr>
<td>Basophil 0.4%</td>
<td>Monocyte 5.3%</td>
</tr>
<tr>
<td></td>
<td>Small lymphocyte</td>
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</tbody>
</table>
WHITE BLOOD CELLS

- Neutrophils (50–70%)
- Eosinophils (2–4%)
- Basophils (<1%)
- Lymphocytes (20–30%)
- Monocytes (2–8%)
Total count: 4,000 – 11,000 WBCs/µL or mm3 of blood

Concept of pool: There are 3 different areas in our body where different WBCs reside

1. Marrow pool: 90% neutrophils
2. Blood pool: 3% Marginal pool
3. Tissue pool: 7%

Genesis of WBCs: Leukopoiesis

In bone marrow → PHSC (Pluripotential hemopoietic stem cells) differentiates → committed stem cells → CFU-GM

- Granulocytes & monocytes are formed only in bone marrow, lymphocytes & plasma cells are produced in various lymphogenous tissues
- WBCs formed in the bone marrow are stored in the marrow & lymphocytes are stored in lymphoid tissue & small no. circulate in the blood.
Genesis of WBCs (*Leukopoiesis*):

- **Second level**
  - proerythroblast
  - basophilic erythroblast
  - erythroblast
  - normoblast
  - reticulocyte

- **Third level**
  - myeloblast
  - lymphoblast

- **Fourth level**
  - promyelocyte

- **Fifth level**

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Row [a] represents the myelocytes showing neutrophilic, basophilic and eosinophilic from left to right. Row [b] represents the metamyelocyte cells again starting with neutrophilic on the left.
Life span of WBCs

Granulocytes:

after released from bone marrow, 4-8 hours circulate in blood

& another 4-5 days in the tissues.

Survive only for few hours in serious infection

Monocytes:

10-20 hrs in blood.

Once in tissue they swell up to much larger size to become tissue macrophage → in this form they can live for month.

Lymphocytes:

Life span for week or months depending on body’s need.

They continually circulate in blood & move from blood to tissues & from tissues to blood and again
Neutrophils:

- **Size**: 10-14 \( \mu \text{m} \) in diam.
- **Nucleus**:
  1. Multilobed (1-6 lobes) therefore called polymorphnuclear leucocytes.
  2. Young cell have single horse shoe shaped nucleus.
  3. As the cells grow older nucleus becomes multilobed. Lobes are connected with one another by chromatin threads.
  4. Arneth count: More the no. of lobes, the more mature is the neutrophil. More the no. of mature cells, Arneth count shifts to right (Vit. B12 or folate deficiency).

    More the younger cells → shift to left (infection).
Cytoplasm: contains neutrally stained granules

2 types of granules are present

1. **Primary/ lysosomal granules**: less in number. Contain various enzymes like acid hydrolases, myeloperoxidase (produces HCl for killing bacteria). These granules are lysosomal granules containing acid hydrolases, which can digest bacteria. After a bacterium is phagocytosed by the neutrophil, primary granules release their enzymes which remain within the neutrophil & kill the bacterium, thus no harm to innocent cells. In addition, primary granules also contain powerful broad spectrum antimicrobial polypeptide defensin

2. **Secondary granules**: more numerous. Contain
   i. Lactoferin,   ii. Vit B12 binding protein &
Functions:

1. Phagocytosis: Whenever the body gets invaded by bacteria, neutrophils are the 1st line of defence to seek out, ingest & kill the bacteria.

2. Pyrogen: They contain fever producing substance: endogenous pyrogen which is an important mediator of febrile response to bacteria.

Variation in count:

Neutrophilia: ↑ in neutrophils. Causes are:

- A. Physiological 1) Exercise, 2) After injection of epinephrine, 3) Pregnancy, menstruation & lactation, 4) Newborn, 5) After meals, 6) Mental or emotional stress.

- B. Pathological 1) Acute pyogenic (pus forming) infections, 2) Following tissue destruction, e.g. i) Burns ii) After hemorrhage, iii) Myocardial infarction, iv) After surgery v) Poisoning by lead, mercury, insect venom

Neutropenia: ↓ in neutrophils:

- 1) In children, 2) Typhoid, paratyphoid fever, 3) Viral infection, 4) Malaria, 5) Aplasia of bone marrow,
Eosinophils:

- Size: 10-14 µm in diam. (2%)
  - Nucleus:
    1. Usually (85%) cells ‘bilobed’.
    2. Lobes are connected with one another by chromatin threads thus producing spectacle appearance.
    3. Remaining 15% cells have trilobed nucleus.
  - Cytoplasm:
    1. Acidophilic, appears light pink in colour after staining
    2. Granular
      - Coarse, stain bright brick red with acidic (eosin) dye.
      - Granules do not cover the nucleus.
      - They contain very high peroxidase content (histaminase), lysozymes & Major Basic Protein (MBP)
Functions:
1. Mild phagocytosis: because less motile than neutrophils
2. Eosinophils collect at the sites of allergic reactions & detoxify inflammation inducing substances by degrading the mediators (e.g. histamine, bradikinin)
3. They enter the tissues & are specially abundant in the mucosa of respiratory tracts, GIT, urinary tract, where they provide mucosal immunity
4. Eosinophils attack parasites that are too large to be engulfed by phagocytosis. Eosinophil granules release chemicals (peroxidase) which are toxic to larvae of parasites
Variation in count:

Eosinophilia: \( \uparrow \) in eosinophils

- Causes are:- 1) Allergic conditions e.g. bronchial asthma, hay fever, filariasis 2) Parasitic infestation, trichinosis & schistosomiasis e.g. worms (hookworm, roundworm & tapeworm), 3) Skin disease like urticaria.

Eosinopenia: \( \downarrow \) in eosinophils

- Causes are:- 1) ACTH & steroid therapy, 2) Stressful conditions, & 3) Acute pyogenic infections
**Basophils:**

**Nucleus:**
1. irregular bilobed, often ‘S’ shaped & its boundary is not clear because of overcrowding with coarse granules.

**Cytoplasm:**
1. Is slightly basophilic & appear blue, it is full of granules.

**Granules:**
1. Contain heparin, histamine & 5HT.
Functions:

1. Mild phagocytosis
2. Role in allergic reaction:

   Basophils release histamine, bradykinin, no. of lysosomal enzymes, slow reacting substance of anaphylaxis (SRS-A) & serotonin (5HT). These substances cause local vascular & tissue reactions that cause many allergic manifestations.

3. Liberates heparin which
5. Activates the enzyme lipoprotein lipase: removes fat particles from the blood after fatty meal.
Variation in count:

Basophilia: ↑ in basophil count
  - Causes are:- 1) Viral infections, e.g. influenza, small pox & chicken pox 2) Allergic diseases & chronic myeloid leukemia.

Basopenia: ↓ in basophil count
  - Causes are:- 1) Corticosteroid therapy, 2) Drug induced reactions & 3) Acute pyogenic infections

Mast Cells:

Large tissue cells resembling basophils. Present in bone marrow & immediately outside the capillaries in the skin.
  - These do not enter the blood circulation.
  - Functions: Mast cells play role in allergic reactions similar to the basophils.
Monocytes:

- **Size:** Largest WBC 18-20 µm.
- **Nucleus:**
  1. Is large single unlobed, eccentric in position (present on one side of the cell).
  2. It is notched/ indented (kidney Shaped)
  3. It has reticulated chromatin network.
- **Cytoplasm:**
  1. Is abundant, pale blue & usually clear with no granules.

Granules:

1. Sometimes contain fine purple dust like granules called Azur granules
Functions:

1. Role in phagocytosis: These are powerful phagocytes & capable of phagocytosing as many as 100 bacteria. They also have ability to engulf large particles such as RBCs & malarial parasites.

2. Precursor of tissue macrophages: The mature monocyte stay in blood only for few hours & then they leave blood and enter extravascular tissue, to become tissue macrophages.

3. Role in tumor immunity: kill tumor cells after sensitization by lymphocytes
4. Synthesis of biological substances:
Monocytes synthesize complement &
other imp. substances like prostaglandin
E & clot promoting factors. They
secrete: i) IL1 Interleukin1 ii)
Hemopoietic factors, iii) TNF-α, iv)
Binding proteins like transferrin, v)
lysosomes, vi) Proteases vii) Acid
hydrolases

5. Macrophages play a key role in the
lymphocyte – mediated immunity.
Monocyte- macrophage appear not before
24 hours & called 2nd line of defence.
Variation in count:

**Monocytosis: ↑ in monocyte count**

- Causes are:- 1) Certain bacterial infections, e.g. tuberculosis, syphilis & subacute bacterial endocarditis
- Viral infections
- Protozoal & rickettsial infections, e.g. malaria, kala azar
- Some leukemias

**Monocytopenia: ↓ in monocyte count**

- Causes are:- It is rare, may be seen in hypoplastic bone marrow.
Lymphocytes:

2 types of lymphocytes

Morphologically: small & large

Functionally: T & B lymphocytes

- Small lymphocytes: 7-10 µm
  
  Nucleus rounded, cytoplasm: just rim is seen. Older cells.

- Large lymphocytes: 10-14 µm
  
  Nucleus is big with indentation, definite cytoplasm is seen. Precursor of small lymphocytes.
Functional subtypes: small lymphocytes are broadly classified into

1. B lymphocyte: processed in the bone marrow, concerned with the humoral immunity.
2. T lymphocyte: processed in thymus, concerned with the cellular immunity.

Functions of B lymphocytes: B lymphocytes & their derivatives, plasma cells are responsible for humoral (antigen mediated) immunity. They produce antibodies (gamma globulins). This is a major mechanism against the invading organisms:
   - by direct action
   - by making them inactive by agglutination, precipitation, neutralization or lysis and
   - through complement system
Functions of T lymphocytes: T lymphocytes are responsible cellular (Cell mediated/T cell) immunity. T cell immunity play imp defensive role against:

- viral & bacterial infections
- tumor cells

Variation in count:

Lymphocytosis: ↑ in lymphocyte count

- Causes are:- Physiological 1) In healthy & young children 2) In female during menstruation
- and Pathological: 3) Chronic infections like tuberculosis, hepatitis & whooping cough
- 4) Lymphatic leukemia 5) Viral infections like chicken pox 6) Autoimmune disease like thyrotoxicosis

Lymphocytopenia: ↓ in lymphocyte count

- Causes are:- 1) Patients on corticosteroid & immunosuppressive therapy 2) Hypoplastic bone marrow 3) Widespread irradiation 4) Acquired Immune Deficiency syndrome (AIDS)