

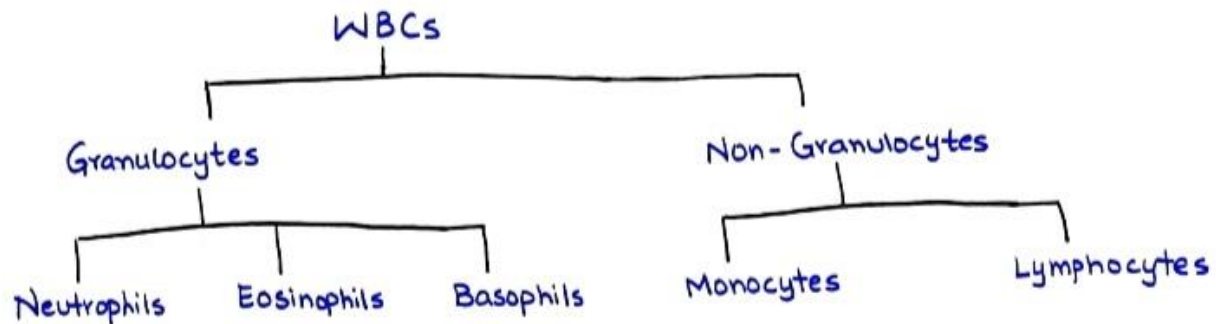
# WHITE BLOOD CELLS (WBCs)

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## TOTAL LEUKOCYTE COUNT (TLC)

Total number of WBCs in 1 ml of blood

Normal range = 4000-11000 WBCs/ml

Less than 4000 → Leukopenia

Greater than 11000 → Leukocytosis

## DIFFERENTIAL LEUKOCYTE COUNT (DLC)

The percentage of different WBCs in total volume.

DLC of neutrophils → 40-75%

Eosinophils → 1-6%

## PRESENCE OF GRANULES

Specific granules are only present in granulocytes (neutrophils, eosinophils, basophils) while non-specific granules are present in all WBCs.

## NEUTROPHILS

- Multi-lobed nucleus (3 or 4 lobes)
- Some granules take acidic dyes (eosinophilic) and some granules take basic dyes
- DLC = 40-75%
- Less than 40% → Neutropenia
- Greater than 75% → Neutrophilia (seen in acute inflammation)
- The classical causes of neutrophilia is pyogenic infections (infections which produce pus)

## EOSINOPHILS

- Bi-lobed nucleus
- Contain Granules stained by acidic dyes (red color)
- DLC = 1-6%
- More than 6% → Eosinophilia  
Eosinophilia is seen in parasitic infections or allergic situations.

## BASOPHILS

- Bi-lobed nucleus
- Contain Granules stained by basic dyes (blue color)
- Least abundant cells in blood
- DLC = 0-2%
- More than 2% → Basophilia  
Basophilia is seen in allergic reaction esp. Type-1 Hypersensitivity reactions.

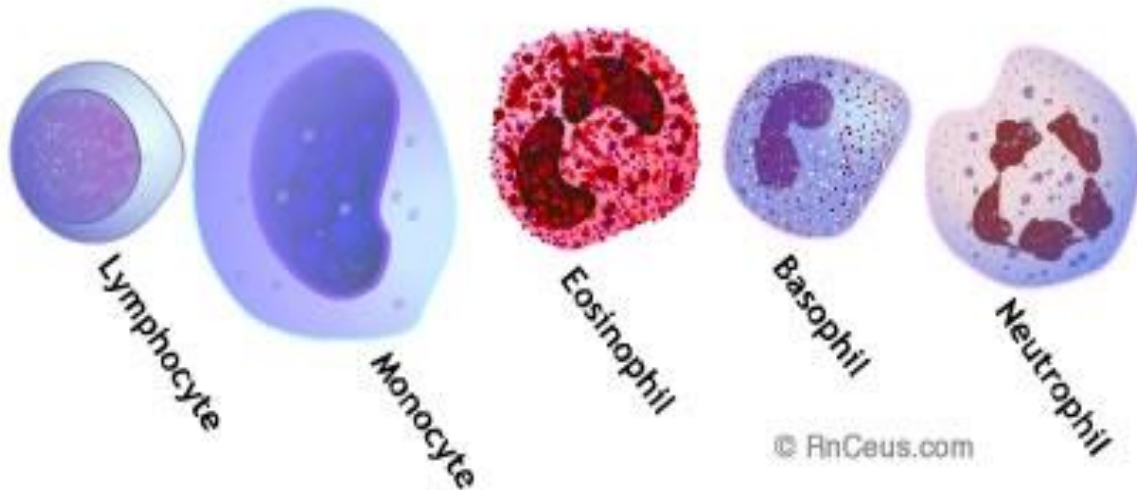
## MONOCYTES

- Contain Non-specific granules
- DLC = 2-10%
- More than 10% → Monocytosis  
Monocytosis is classically seen in chronic infections such as tuberculosis.

## LYMPHOCYTES

- Large nucleus
- Very little cytoplasm

- DLC = 15-40%
  - More than 40% → Lymphocytosis
- Lymphocytosis is classically seen in viral infections and chronic infections.



## GRANULOPOIESIS

**Granulopoiesis** is the process by which committed hemopoietic progenitor cells develop into granulocytes under the influence of various growth factors and cytokines. The first recognizable granulocytic precursor is the myeloblast.

## NEUTROPHIL PRODUCTION

Granulocyte → Myeloblast → Promyelocyte → Myelocyte → Metamyelocyte → Stab cells/  
Band cells → Neutrophils

### 1. MYELOBLAST

- Rapidly multiplying cell
- Large nucleus with euchromatin (loose chromatin)
- Some basophilic cytoplasm
- Multiple nucleoli

### 2. PRO-MYELOCYTE

- Nucleoli number reduces
- Non-specific granules appear. These granules are also called lysosomes or primary granules or azurophilic granules.
- Maximum primary granules are seen in this stage.

### 3. MYELOCYTE

- Nucleus starts condensing
- Specific granules appear
- Myelocyte is destined to become either neutrophil, basophil or eosinophil

Upto development of myelocyte, mitotic divisions take place. After myelocyte stage, the cells do not proliferate.

### 4. META-MYELOCYTE

- Nucleus becomes indented and heterochromatin forms

### 5. STAB CELLS/ BAND CELLS

- Nucleus becomes horse-shoe shaped

### 6. NEUTROPHILS

- The final product i.e. neutrophil is formed.

Granulopoiesis takes about 1-2 weeks.

Life of neutrophil in blood is about 8-12 hours while in tissues is 1-2 days.

Some of the neutrophils are circulating while others are loosely attached with endothelial cells. The circulating neutrophils are called **circulating pool of neutrophils**. The attached neutrophils are called **marginated pools**. The neutrophils present in bone marrow which are five times more abundant than those present in blood, are called **bone marrow pool**.

During acute inflammations, a lot of neutrophils from bone marrow pool and marginated pool enter into circulation to be moved to tissues. Hence in acute inflammation, the blood sample from a patient may contain a large number of neutrophils.

Neutrophils survive in tissues for 1-2 days and eventually undergo apoptosis.

Many neutrophils also move to *GIT* from circulation and appear in feces. A significant amount of fecal matter is neutrophils.

## NEUTROPHILS

- Most abundant WBCs
- Fastest to reach the site of inflammation and hence are said to be cells of acute inflammation.
- Size about **12 microns**
- Multi-lobed nucleus

- Neutrophils are cells related with innate immunity (non-specific).
- Neutrophils have a lot of **glycogen granules**. If needed, this glycogen can be converted into glucose and anaerobic glycolysis can take place even in absence of oxygen.
- **Primary granules** full of acid hydrolases and myeloperoxidases which helps in producing HOCl. HOCl is highly toxic for bacteria and other microbes. Primary granules have some protein molecules called defensins which work functionally like immunoglobulins.
- Neutrophils also have **secondary granules**. These granules have:
  1. Lysozymes - for killing bacterial cell wall
  2. Lactoferrins - extract iron from microbe. In absence of iron, microbial enzymes don't work and microbial metabolism fails
  3. Alkaline phosphatase
  4. Bacteriostatic products - stops bacterial growth
  5. Bactericidal products - kills bacteria
- All neutrophils have **tertiary granules**, which have certain enzymes that help the neutrophil to digest connective tissue so neutrophils can make path for moving towards the inflammation. These enzymes include collagenases, gelatinases, hyaluronidases etc.
- When neutrophils are fighting against microbes, they produce highly-reactive **oxygen-derived radicals**. Myeloperoxidases and membrane oxidases work on molecular oxygen and convert it into super oxide radicals ( $O_2^-$ ),  $H_2O_2$  radicals, hydroxide ( $OH^-$ ) radicals and HOCl radicals.

## MOVEMENT OF NEUTROPHILS

When cells are injured they produce chemical-mediators of inflammation.

During inflammation process:

1. Arterioles dilate to increase blood flow.
2. Chemical-mediators of inflammation work on nearby endothelial cells due to which endothelial cells shrink and produce inter-endothelial gaps. From these gaps, a lot of protein-rich fluid move towards inflammation.
3. The endothelial cells start expressing certain molecules called **adhesion molecules**, which hook the WBCs. The neutrophils under influence of chemical mediators also express corresponding adhesion molecules. The neutrophils attach to the endothelial cells and then moves out through endothelial gaps towards the inflamed area.
4. Once the neutrophils are out of circulation, they are attracted towards inflamed tissue by chemo-attractants released from inflamed tissue.

If bacteria is coated with **opsonins such as C3b or IgG**, neutrophils can phagocytose these easily because neutrophils have opsonin receptors on their surface.

Cells of acute inflammation are neutrophils and macrophages.

Cells of chronic inflammation are macrophages and lymphocytes.

## EOSINOPHILS

- Bi-lobed nucleus
- Acidophilic granules
- 1-6% of WBCs
- **Eosinophilic granules** contain:
  1. Eosinophilic basic proteins
  2. Eosinophilic cationic proteins
  3. Eosinophilic peroxidases
  4. Eosinophil-derived neurotoxins

The first three are cytotoxic to protozoans and helminthes.

The eosinophil-derived neurotoxins produce dysfunction in helminthes nervous system.
- Eosinophil produce **histaminases**, which break down histamine, hence inflammatory response decreases.
- Eosinophils produce **aryl sulfatases**, which break down **leukotrienes** (products produced at site of injury). Hence inflammatory response decrease.
- Circumstances in which **eosinophilia** is produced (NAAPCAN)
  - N - Neoplasia
  - A - Allergy
  - A - Asthma
  - P - Parasites
  - C - Collagen Vascular Diseases
  - A - Allergy (repeated)
  - N - Neoplasia (repeated)

## BASOPHILS

- **0-2%**
- Basophils are coated with receptors for IgE
- **Basophilic granules** secrete:
  1. Heparin and heparan sulfate which acts as anti-coagulant
  2. Histamine
  3. Leukotrienes which are powerful chemical mediators for inducing inflammation

- **Basophilic stippling**, also known as punctate basophilia, is the presence of numerous basophilic granules that are dispersed through the cytoplasm of erythrocytes in a peripheral blood smear.

Basophilic stippling is indicative of disturbed erythropoiesis. Stippling is seen in:

T - Thalassemia

A - Anemia of chronic diseases

I - Iron deficiency anemia

L - Lead poisoning

## MONOCYTES

- 2-10%
- In blood, monocytes survive about 2-10 days. Then they move to tissues and are called macrophages where they can live for long periods.
- **Macrophages present in:**
  1. CNS - as microglia
  2. Alveoli - as alveolar macrophages
  3. Liver - as Kupfer cells
  4. Lymph nodes and spleen - as histiocytes
  5. Lymph node sinuses - as sinus macrophages
  6. Skin dermis - as Langerhann cells
  7. Kidney - as mesangial cells
  8. Bone - as osteoclasts
  9. Inflamed tissue
- **Macrophage functions:**
  1. Phagocytosis - phagocytize microbes, old cells, injured cell debris
  2. Antigen-presenting cells i.e. coated with MHC-II along with MHC-I

## LYMPHOCYTES

Three types of lymphocytes

1. B-lymphocytes
2. T-lymphocytes
3. NK cells