



- When a microorganism enters the human body, it will face three type of defenses:

• **Physical barriers:**

✓ Most of the infectious agents that an individual encounters do not penetrate the body surface, but are prevented from entering by a variety of biochemical and physical barriers:

- ❖ Lysozyme in tears and other secretions.
- ❖ Removal of particles by rapid passage of air over turbinate bones.
- ❖ Mucus and cilia in bronchi.
- ❖ Skin.
- ❖ Acid in the gut.
- ❖ Flushing of urinary tract.
- ❖ Low pH of vagina in females.

• **Innate (natural) immunity:**

✓ It is represented by:

- ❖ *Cells*: which include phagocytes (macrophages and neutrophils) and natural killer cells (against viruses and tumors).
- ❖ *Soluble proteins*: which include the complement system, cytokines and interferons (against viruses).

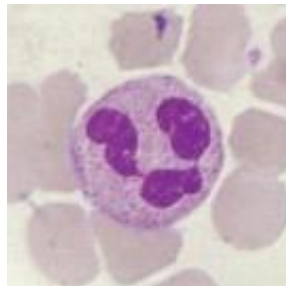
• **Acquired (adaptive) immunity:**

✓ It is represented by:

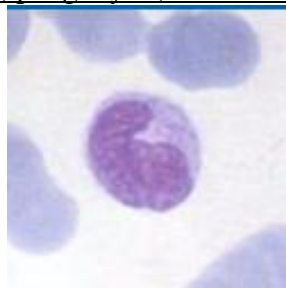
- ❖ *B-Lymphocytes*: which can be converted to plasma cells that will produce different types of immunoglobulins (antibodies).
- ❖ *T-lymphocytes*: which are divided mainly into (CD4+) helper T-cells and (CD8+) cytotoxic T-cells.

- White Blood Cells (WBCs):

• **Phagocytes:**



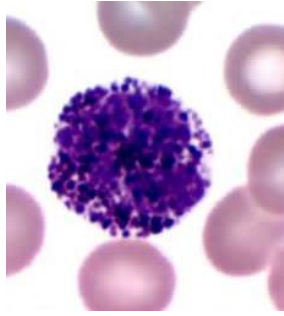
Neutrophils (PMNs): acute inflammatory response cells; Increased in bacterial infections; phagocytic; multilobed nucleus.



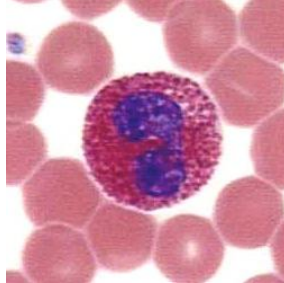
Monocytes/Macrophages (when they migrate to tissues): Phagocytose bacteria, cellular debris, old RBCs and scavenges damaged cells and tissues; Macrophages differentiate from circulating blood monocytes; macrophages are activated by  $\gamma$ -interferon; macrophages can function as antigen-presenting cells via MHC-II and they are important in granuloma formation



- **Granulocytes:**



Basophils: they mediate allergic reaction; they have granules which contain: heparin, histamine and leukotrienes.



Eosinophils: defend against helminthic infections (via major basic protein); highly phagocytic for antigen-antibody complexes; produce histamine.



Lymphocytes: they are divided into B-cells, T-cells and natural killer cells; B-cells and T-cells mediate adaptive immunity; natural killer cells are part of the innate immune response.

- **The process of phagocytosis (engulfment of a microorganism by a phagocyte to be killed):**

1. The microorganism will attach to the phagocyte by non-specific receptors.
2. Pseudopodia will be wrapped around the microorganism to form a phagosome.
3. The Phagosome will fuse with proteolytic enzymes present inside the cell and known as lysosomes.
4. The microorganism will be killed and microbial products will be released.

- **Phagocyte killing mechanisms:**

- ✓ Oxygen-dependent: represented by
  - ❖ *Reactive Oxygen Species (ROS):*  $O_2^-$ ,  $H_2O_2$ ,  $OH^-$  and  $HOCl$  (chloramines).
  - ❖ *Nitric Oxide (NO):* which is synthesized from arginine.
- ✓ Oxygen-independent: represented by
  - ❖ *Lysozyme:* splitting mucopeptides in bacterial cell wall.
  - ❖ *Lactoferrin:* complex with iron.
  - ❖ *Proteolytic enzymes and other hydrolytic enzymes:* digestion of killed organisms.


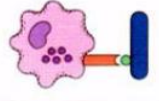
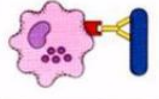
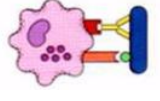
- **Natural Killer cells (NK-cells):**

- They are large granular lymphocytes which develop in the bone marrow.
- They have no antigen-specific receptors and they kill target cells by direct contact and release of perforin and granzymes.
- They can kill viral infected cells and some tumor cells.



- **Complement system:**

- A group of about 20 proteins found in the plasma.
- They react in a cascade fashion (like clotting factors).
- Complement system belongs to the innate (natural) immunity.
- **The major activation pathways are:**
  - ✓ Classical pathway: activated by antigen-antibody complexes.
  - ✓ Alternative pathway: activated by bacterial and viral surfaces.
- At the end of the cascade, Membrane Attack Complex (MAC) will be formed which will result in Cell lysis.
- **Biological effects of complement activation:**
  - ✓ Cell lysis: C5b, C6, C7, C8 and C9
  - ✓ Chemotaxis (attraction of WBCs to the site of invasion): C5a (neutrophil chemotaxis).
  - ✓ Opsonization (the process by which is pathogen is marked for ingestion by a phagocyte): C3b

	phagocyte	opsonin	binding
1		-	±
2		complement C3b	++
3		antibody	++
4		antibody and complement C3b	++++

- **Interferons:**

- A family of proteins which can be made by different cells following a viral infection.
- **There are three types of interferons:**
  - ✓ IFN- $\alpha$
  - ✓ IFN- $\beta$
  - ✓ IFN- $\gamma$

- **Acute phase proteins:**

- They are made by the liver early after infection.
- The stimulus for increased production is macrophage.
- **C-reactive protein:**
  - ✓ Promotes phagocytosis.
  - ✓ Binds to bacterial phospholipids.
  - ✓ Activates complement.