HLS MODULE
PHYSIOLOGY LECTURE 4
WHITE BLOOD CELLS (WBCs)
BY

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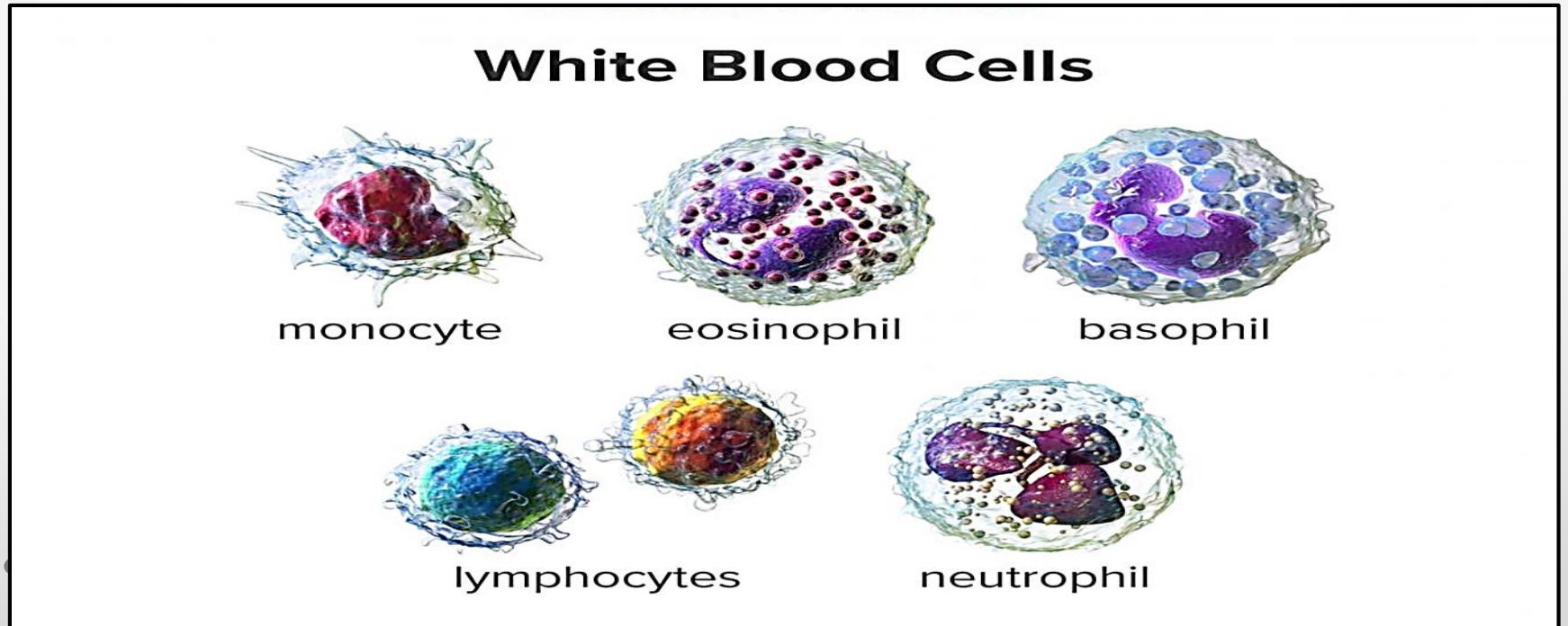


Defensive Mechanisms of the Body

- Our bodies have a special system for protection against the pathogenic organisms.
- This is comprised of blood leukocytes (white blood cells) and tissue cells derived from leukocytes.
- These cells work together in two ways to prevent disease:

(1) by actually destroying invading bacteria or viruses by **phagocytosis**.

(2) by forming **antibodies** and **sensitized lymphocytes**, one or both of which may destroy or inactivate the invader.

White Blood Cells/ Leucocytes

- White blood cells (WBCs) or leucocytes (leukocytes) are nucleated cells.
- leuko is derived from Greek word leukos = white.
- They are the **mobile units of body's protective system** (because they seek out and destroy foreign invaders).
- **Count:** 4,000-11,0000/mm^3 or μl.
- Compared to RBCs, the WBCs are **larger in size** and **lesser in number**. Yet functionally, these cells are important like RBCs because of their role in defense mechanism of body (protect the body from invading organisms by acting like **soldiers**).

CLASSIFICATION of WBCs

Based on the presence or absence of **granules** in the cytoplasm, the leukocytes are classified into **two main groups**:

1. Granulocytes (Granular leucocytes):

Have granules.

Granules contain enzyme **myeloperoxidase enzyme**.

2. Agranulocytes (Non-Granular leucocytes):

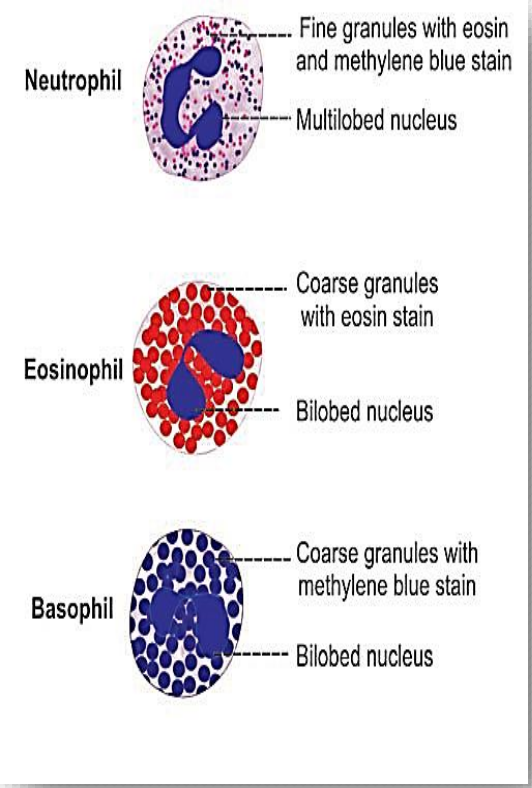
Do not have granules.

No myeloperoxidase enzyme.

1. Granulocytes

Depending upon the staining property of granules, the granulocytes are classified into three types:

1. **Neutrophils**: 50-70%, (the most abundant)
2. **Eosinophils:** 1-4%
3. **Basophils:** 0 -1%



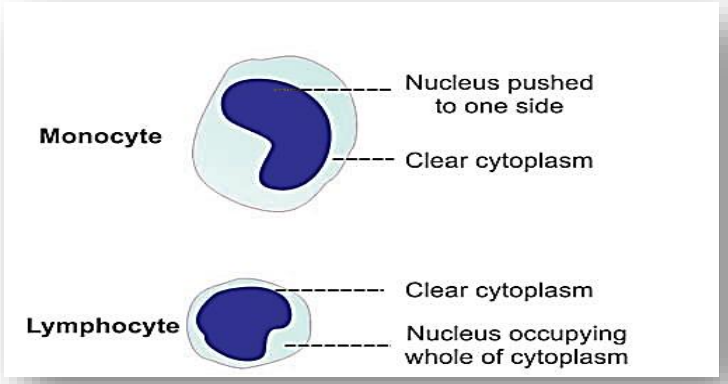
2. Agranulocytes

Non-granulocytes have clear cytoplasm without granules.

They are of two types:

1. Lymphocytes: 20-40 % (30%)

2. Monocytes or macrophages: 2-8 % (5%)



WHITE BLOOD CELLS COUNT (Total - Differential)

1. Total WBC count (TLC): 4,000 to 11,000/mm^3 of blood.
2. Differential WBC count (DC):

Type	Percentage %
Neutrophils	50 - 70
Eosinophils	1 - 4
Basophils	0 - 1
Lymphocytes	20 - 40
Monocytes	2 - 8

Never **L**et **M**onkey **E**at **B**anana

LEUCOPOIESIS

Definition: Process of white blood cells formation.

Site:

Bone marrow is the source of all blood cells

Granulocytes and monocytes are formed only in bone marrow.

Lymphocytes are produced mainly in various lymphoid tissues especially, lymph nodes, thymus and spleen.

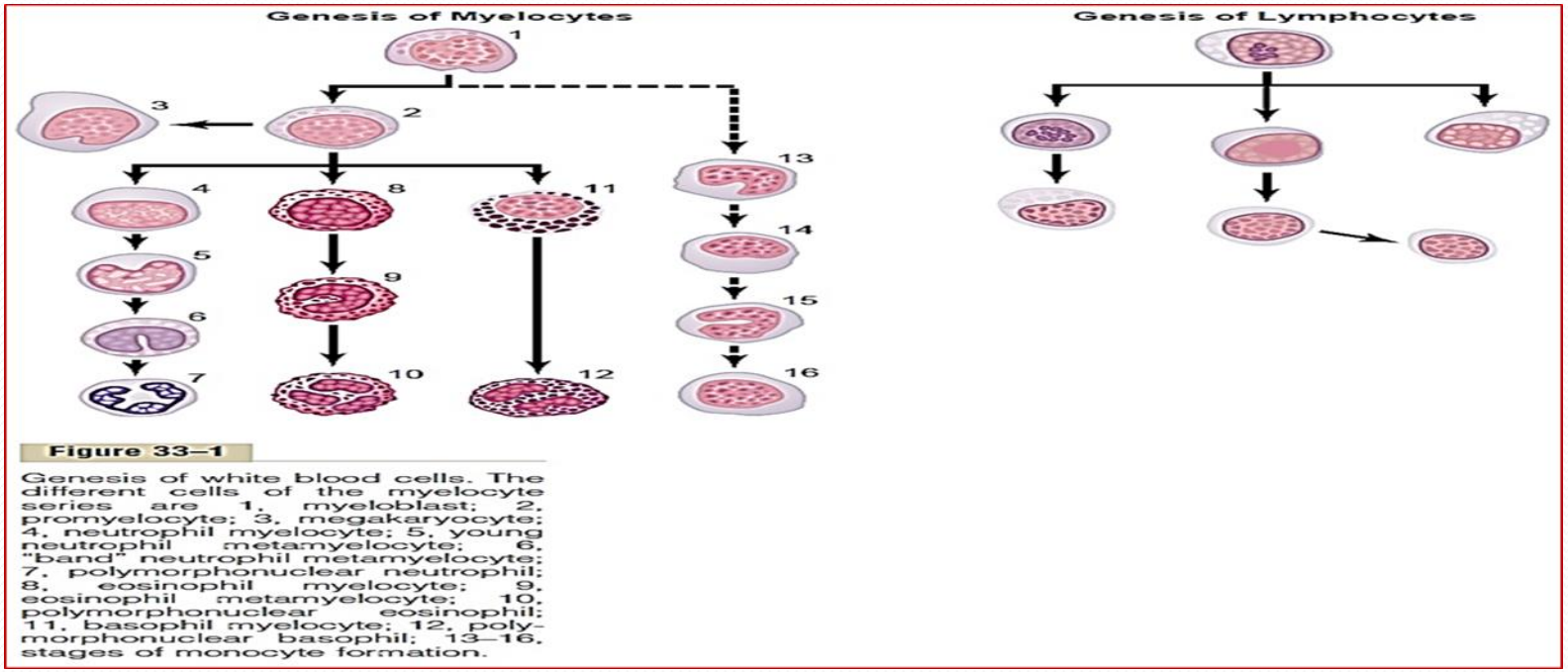


Figure 33–1

Genesis of white blood cells. The different cells of the myelocyte series are 1, myeloblast; 2, promyelocyte; 3, megakaryocyte; 4, neutrophil myelocyte; 5, young neutrophil metamyelocyte; 6, "band" neutrophil metamyelocyte; 7, polymorphonuclear neutrophil; 8, eosinophil myelocyte; 9, eosinophil metamyelocyte; 10, polymorphonuclear eosinophil; 11, basophil myelocyte; 12, polymorphonuclear basophil; 13–16, stages of monocyte formation.

LIFE SPAN & FATE OF WHITE BLOOD CELLS

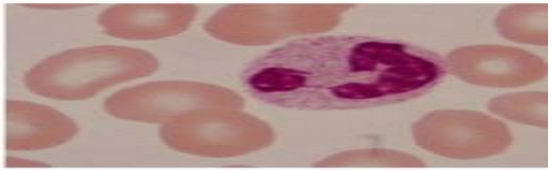
- The life span of **granulocytes in circulation is 4-8 hours**, after which they enter the tissues and stay 4-5 days then they are destroyed by the reticulo-endothelial system (RES) and many are lost from body via the GIT. In infections, their total life span is much shortened because they are attacked and destroyed by the invading organisms (forming **pus cells**).
- The **life span of monocytes in blood is about 72 hours**, after which they **enter the tissues, enlarge and change into the tissue macrophages** which live for **months**.

- Lymphocytes reach the blood stream via the lymphatic vessels. Then, after a few hours in the circulation, they cross the capillary walls by diapedesis to the tissues, from which they re-enter the lymphatic vessels and circulate again. In this way, they live for relatively long periods (weeks or months) ; this life span depends on the body’s need for these cells.

FUNCTIONS OF WHITE BLOOD CELLS

1. Neutrophils (1st Microphages)

- Neutrophils exert a powerful **defense action against bacterial infection**.
- Their main function is **phagocytosis and destruction of the invading bacteria**.
- When an infection occurs, the macrophages already present in tissues immediately start attacking the bacteria, but their numbers are often not very great. However, within the first hour, large numbers of neutrophils begin to invade the inflamed area.
- Thus, **neutrophils are considered the first line of defense against bacterial infections**.
- This is known as **the inflammatory response**. It is initiated by **a marked increase of the number of neutrophils in the blood (neutrophilia)** as a result of **stimulation of the bone marrow to produce and release large numbers of neutrophils by certain products of inflammation that enter the blood stream**.



Mechanism by which neutrophils defend against infection

1. Margination:

The neutrophils are first attracted to the capillary endothelial surface and stick to the capillary walls in the inflamed area.

2. Diapedesis:

Diapedesis is the process by which the neutrophils squeeze through the pores of blood capillaries. Neutrophils bind firmly to special adhesion molecules, then they insulate themselves through capillary walls between the endothelial cells.

The Inflammatory Response [HD Animation].mp4

3. Amoeboid Movement:

Neutrophils show amebic movement, characterized by protrusion of the cytoplasm and change in the shape. Ameboid motion is helped by their actin & myosin content.

4. Chemotaxis:

Chemotaxis is the attraction of neutrophils towards the injured tissues by the **chemical substances** released at the site of injury.

The most important chemotactic substances include:

- bacterial toxins, the degenerative products of inflamed tissues and complement (positive chemotaxis).

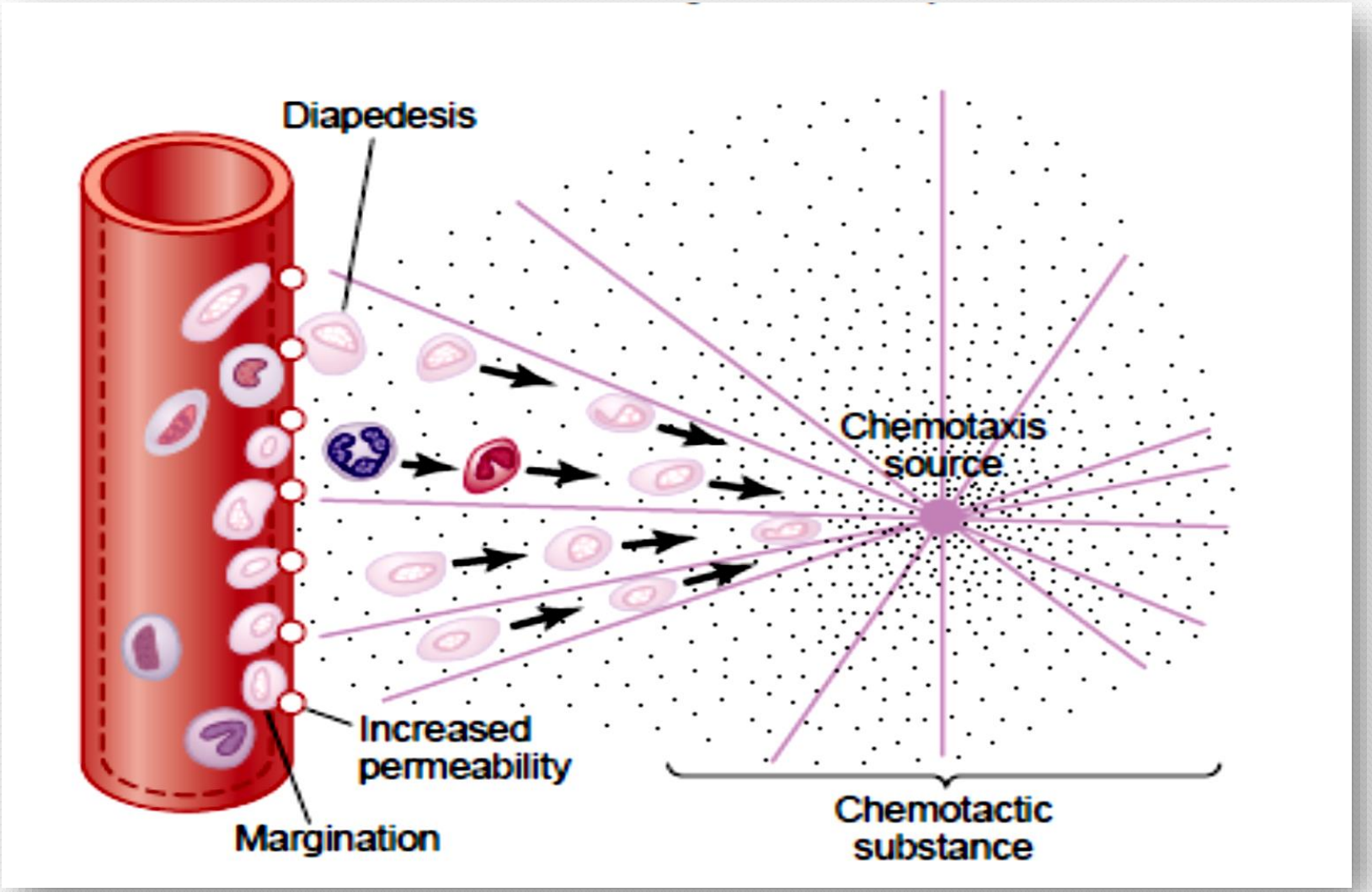
Neutrophil Chemotaxis Chasing a Bacterium.mp4

5. Phagocytosis:

The most important function of the neutrophils and macrophages is phagocytosis.

Neutrophils (microphages) and monocytes (macrophages) engulf the foreign bodies by the process of phagocytosis.

The Process Of Phagocytosis.mp4


Diapedesis
Chemotaxis source
Increased permeability
Margination
Chemotactic substance

Course of phagocytosis:

1. The phagocytes move towards the sites of bacteria, destructed cells and foreign cells by positive chemotaxis.
2. The phagocytic cells adhere to the foreign particles.
3. The phagocytic cells surround and engulf the foreign particles.
4. The membranes fuse and form vacuole surrounds the foreign particles (phagosome).
5. Fusion of the vacuole with lysosome.
6. The hydrolytic enzymes in the lysosome digest and engulf the foreign particles.
7. A single neutrophil can usually phagocytize 3 to 20 bacteria before the neutrophil itself becomes inactivated and dies.

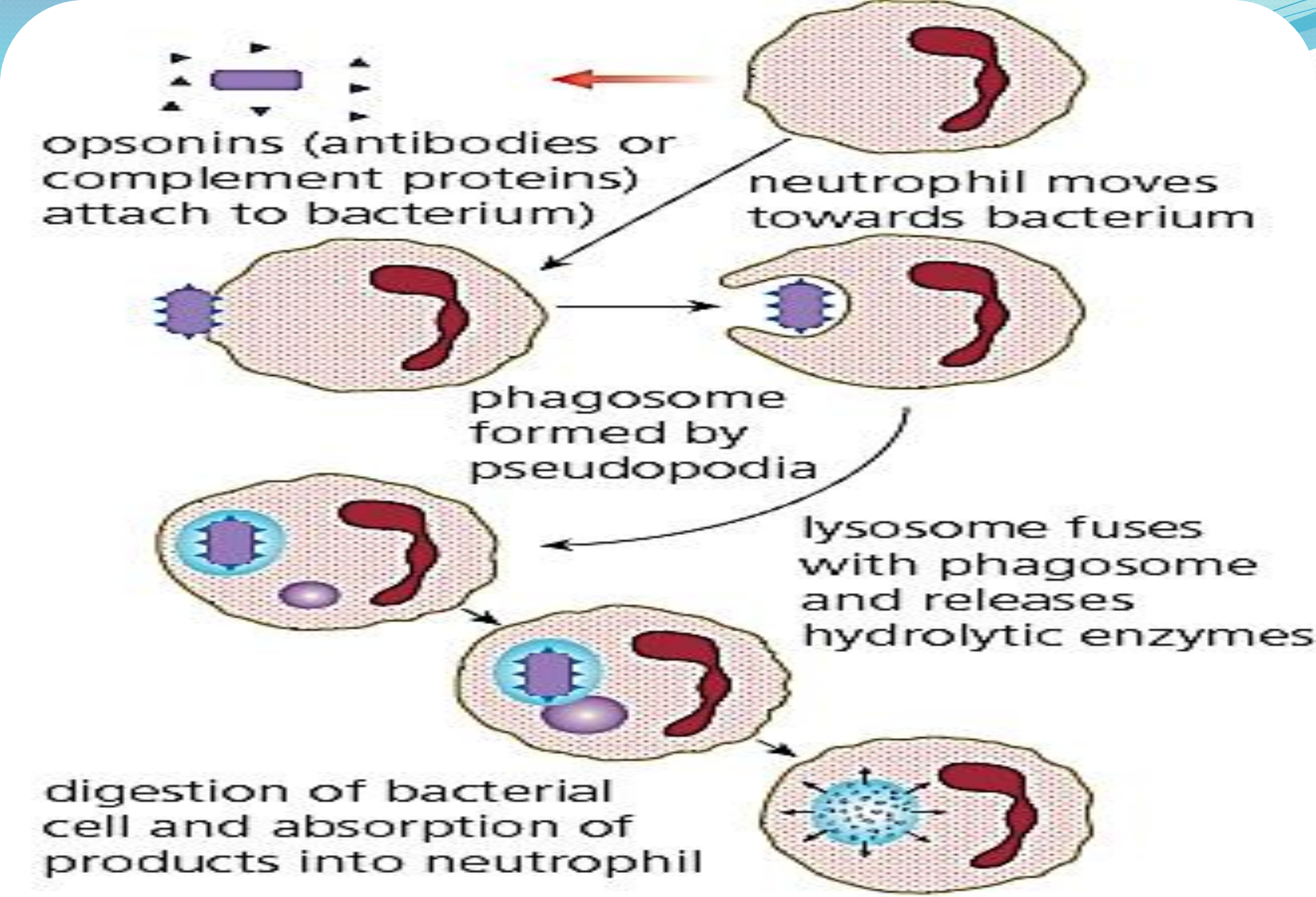


Figure 11.2 Phagocytosis by a white cell — a eutrophil

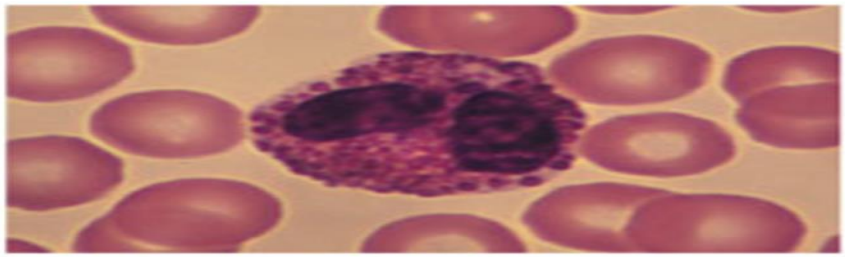
Mechanism of action of neutrophils

- Certain plasma factors coat the bacteria making them **tasty to the phagocytes**. This process is called **opsonization** and the main **opsonins include certain complement proteins as well as immunoglobulin G (IgG)**.
- The **coated bacteria bind to receptors on the neutrophil cell membranes**. This markedly increases the motor activity of these cells leading to ingestion of the bacteria by the active process of **phagocytosis** (forming phagocytic vacuoles in their cytoplasm called **phagosomes**).
- The **lysosomes** and other **cytoplasmic granules** then come in **contact** with the **phagosomes** in which they discharge their contents. The latter include:
  - Various **proteases (proteolytic enzymes)** that **digest bacteria**.
  - The **myeloperoxidase enzyme**: This enzyme catalyzes the reaction between H_2O_2 and Cl^- to form **hypochlorite which is a powerful bactericidal substance**.
- In addition, the enzyme **NADPH oxidase** is activated. This enzyme is present in the **phagosomal membranes** and is also formed by the organelles called **peroxisomes**. It **catalyzes formation of several toxic O_2 metabolites (powerful oxidizing agents) particularly superoxide and hydrogen peroxide**, which are also effective **bactericidal agents**.

2. EOSINOPHILS

These are also **weak phagocytic cells (2nd microphages)** that show chemotaxis, but they are **less motile and weaker than neutrophils**. **They are produced in large numbers in:**

1. Parasitic infections (e.g. bilharziasis), in which the eosinophils attack the parasites (specially the juvenile forms) and kill many of them by (1) hydrolytic enzymes, (2) highly reactive forms of O_2 that especially lethal to parasites; and (3) by releasing from the granules a highly larvacidal polypeptide called major basic protein.



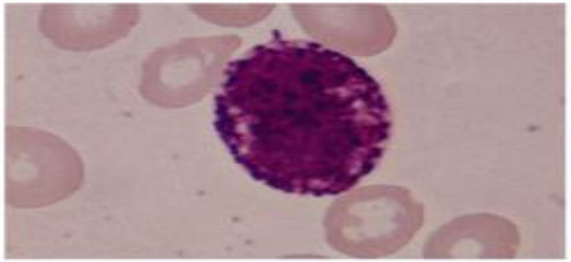
2. Allergic diseases (e.g. bronchial asthma) in which eosinophils are attracted to the site of allergic reactions (by a special chemotactic factor released from the basophils and mast cells) where they **decrease and prevent spread of allergic inflammatory process by** :

a. **Detoxification** of some inflammation-inducing substances released by the basophils and mast cells.

b. **Phagocytosis** and destruction of the **allergen-antibody complexes**.

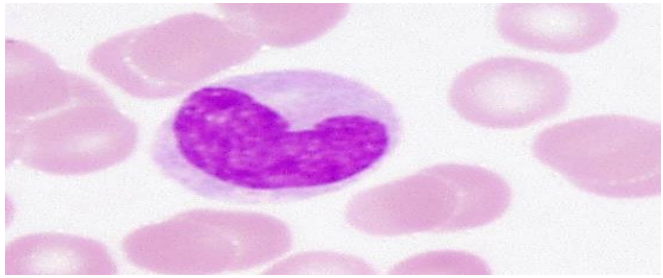
3. BASOPHILS

- These are **non-phagocytic cells.**
- **They resemble the mast cells**.
- **Both form :**
  - **Heparin (**essential to prevent the intravascular blood clotting).
  - **Histamine** and other V.D. mediators (specially **leukotriens**) ae well as small amounts of **bradykinin and serotonin**. These substances **produce the local vascular and tissue reactions that occur in allergic conditions**.
  - The immunoglobulin E (IgE), is attached to mast cells and basophils. When the specific antigen for the specific IgE antibody subsequently reacts with the antibody, the resulting attachment of antigen to antibody causes the mast cell or basophil to rupture and release large quantities of histamine and other allergic mediators to mediate allergic manifestation.



4.MONOCYTES (Macrophages)

- Monocytes are the **largest cells** among the leukocytes.
- Like neutrophils, monocytes also are **phagocytic** in nature and **motile** (but at much slower rate than neutrophils), so they are considered the **second line of defense against bacterial infection**.
- Monocytes can phagocytize large quantities of bacteria, necrotic tissues or other foreign particles in the tissues.
- **Monocytes** are the **precursors of the tissue macrophages** which are the main constituent of **Monocyte-Macrophage cell system (**reticuloendothelial system (REM)).
- Monocytes stay in the blood only for few hours (72 hour). Afterwards, these cells enter the tissues from the blood and become tissue macrophages.
- Examples of tissue macrophages are: Von-Kupffer cells in liver, alveolar macrophages in lungs and macrophages in spleen.
- Macrophages play an important role in immunity.



Monocyte-Macrophage cell system (reticuloendothelial system; RES) :

This system consists mainly of the **tissue macrophages** (which are originally monocytes that have entered from blood) and **few specialized endothelial cells** in the bone marrow, spleen and lymph nodes.

Its main function is :

Defense:

The tissue macrophages attack and phagocytose the invading organisms in the:

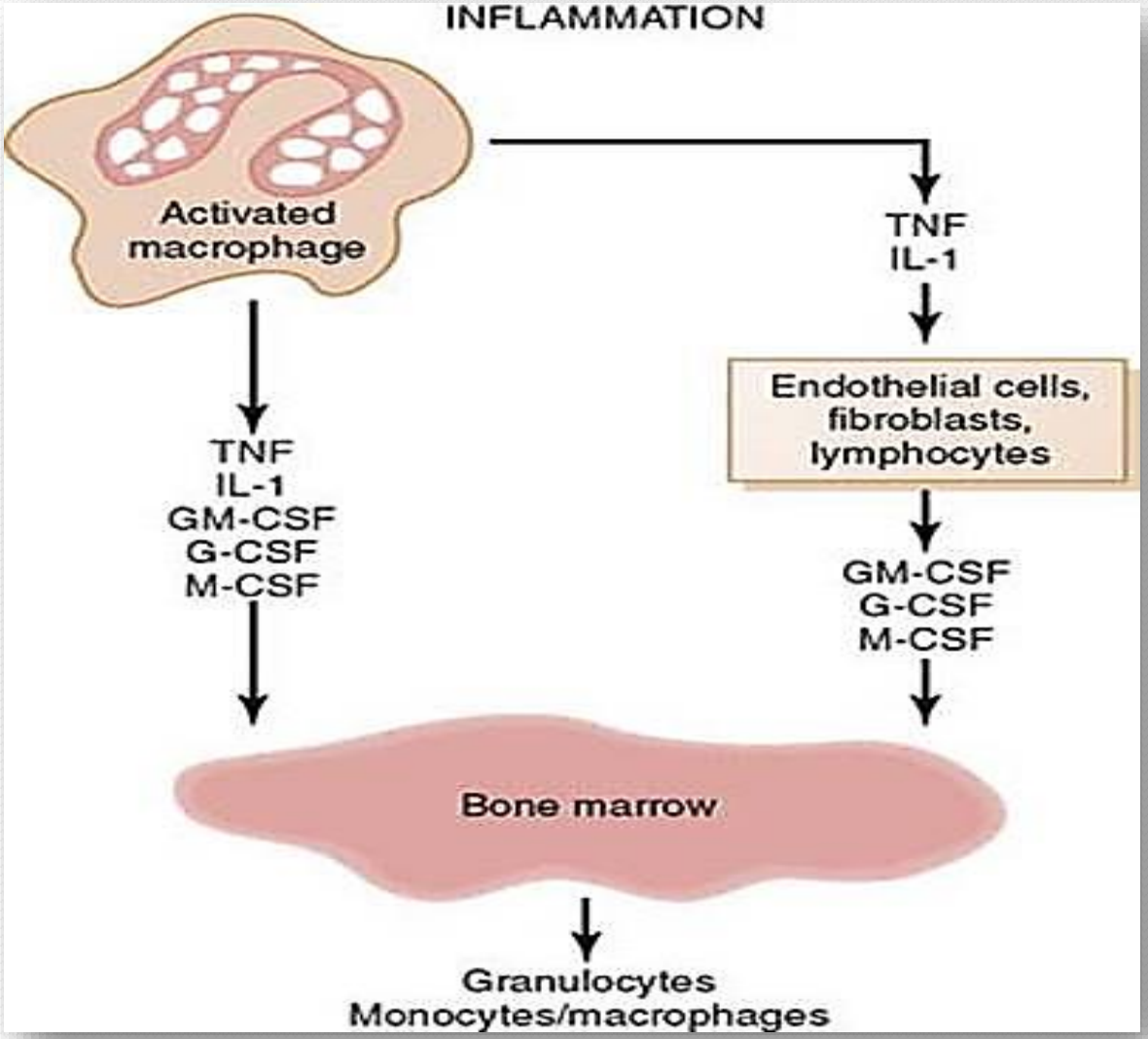
Skin & subcutaneous tissue (by macrophages called histiocytes).

Lungs (in which bacteria and foreign particles e.g. dust are engulfed by the pulmonary alveolar macrophages).

Liver (in which Kupffer cells attack bacteria that continuously pass from GIT).

Lymph nodes (in which macrophages attack bacteria transmitted from tissues).

Bone marrow & spleen (in which macrophages attack the bacteria that enter blood stream).


INFLAMMATION
Activated macrophage
TNF
IL-1
GM-CSF
G-CSF
M-CSF
TNF
IL-1
Endothelial cells, fibroblasts, lymphocytes
GM-CSF
G-CSF
M-CSF
Bone marrow
Granulocytes
Monocytes/macrophages

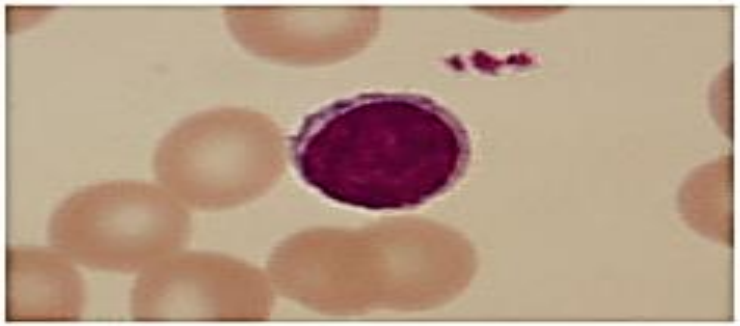
5.LYMPHOCYTES

Lymphocytes play an important role in immunity.

The lymphocytes are classified into two categories, **T lymphocytes** and **B lymphocytes**.

T lymphocytes are responsible for the development of cellular (cell-mediated) immunity.

B lymphocytes are responsible for the development of humoral (antibody-mediated) immunity.



Variations of leucocytic count

Physiological variations: In infants, WBCs count is about 20,000 / mm^3 (and lymphocytes constitute about 50% of total count).

In children: 10,000 to 15,000 / mm^3.

In adults, it ranges between 4,000 and 11,000 / mm^3 of blood.

1. Leucocytosis: It is the increase in total WBCs count more than 20,000/mm^3 (mature functioning cells).

Leukocytosis occurs in both physiological and pathological conditions.

A. PHYSIOLOGICAL LEUCOCYTOSIS

1. Exercise.
2. Following meals.
3. Menstruation.
4. Pregnancy.
5. Parturition.

B. Pathological leucocytosis

All types of leukocytes do not share equally in the increase of total leukocyte count.

Neutrophilia: occurs in cases of tissue damage (e.g. myocardial infarction) and pyogenic infections (e.g. tonsillitis)

Eosinophilia: occurs in allergic and parasitic diseases.

Basophilia: occurs in allergic conditions.

Lymphocytosis: occurs in tuberculosis and lymphocytic leukemia.

Monocytosis: occurs in myelogenous leukemia.

2. Leukopenia

Definition: A clinical condition in which the bone marrow produces **very few white blood cells**, leaving the body unprotected against many bacteria and other agents that might invade the tissues. The term leukopenia is generally used for **pathological** conditions only.

Causes:

- Irradiation of the body by x-rays or gamma rays
- Exposure to drugs and chemicals that contain benzene or anthracene nuclei, is likely to cause aplasia of the bone marrow.
- Some common drugs, such as chloramphenicol (an antibiotic) and thiouracil (used to treat thyrotoxicosis).
- It also might occur in infections (e.g. typhoid fever) as a result of bone marrow depression.

3. Leukemia

A malignant disease of **bone marrow** in which there is uncontrolled production of **abnormal white blood cells** that can be caused by cancerous mutation of a myelogenous or lymphogenous cell. So that, the leucocytic count may increase up to 500,000/mm^3 or more.

It causes:

- Bone pain and easy fractures (in the myelogenous type).
- Spread of leukemic cells in the body causing extensive tissue destruction everywhere.
- Infection, severe anemia and bleeding tendency (due to replacement of red cells and platelets forming cells in the bone marrow by the nonfunctional abnormal leukemic cells).
- Excessive use of the body metabolic substrates by the growing cancerous cells, which depletes the energy of the patient and leads to death.

THANK YOU