

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)



HLS Physiology | MID

Leukocytes Pt.1



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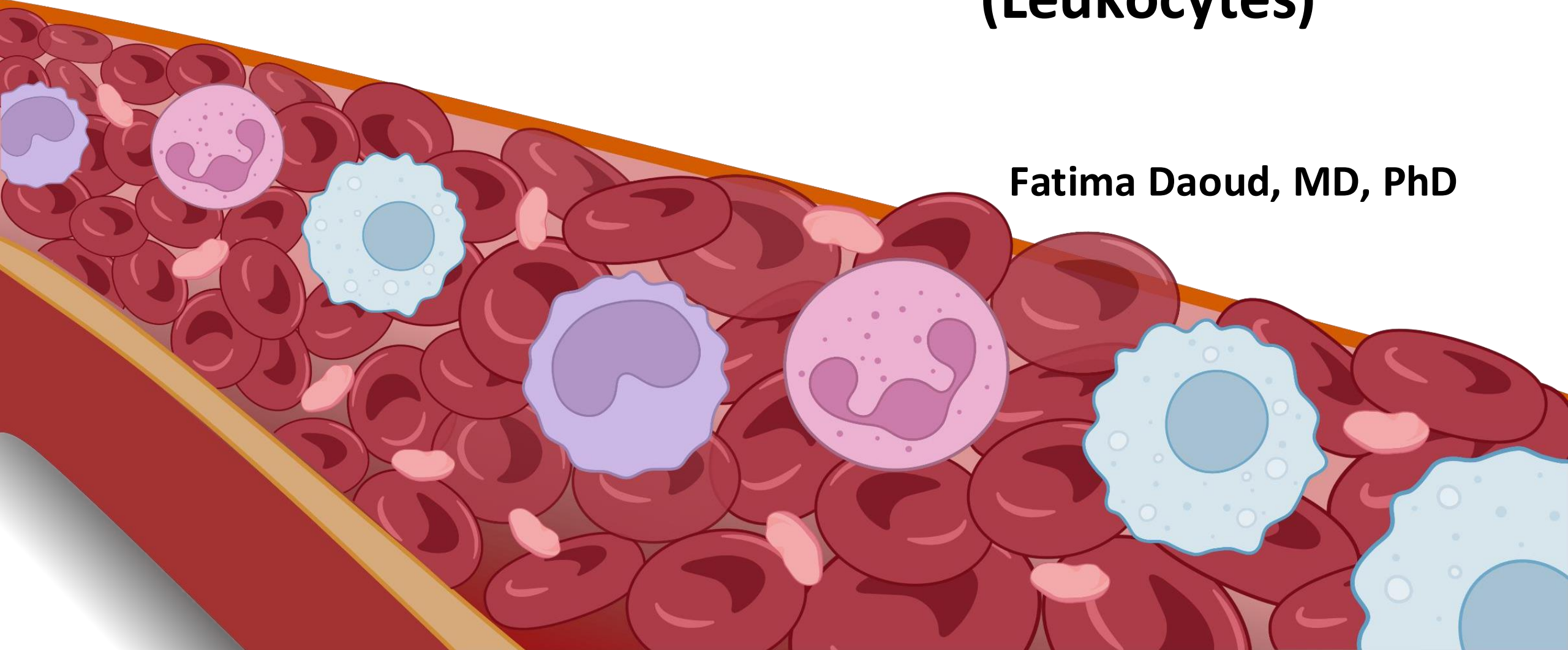
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Hematology

WBC

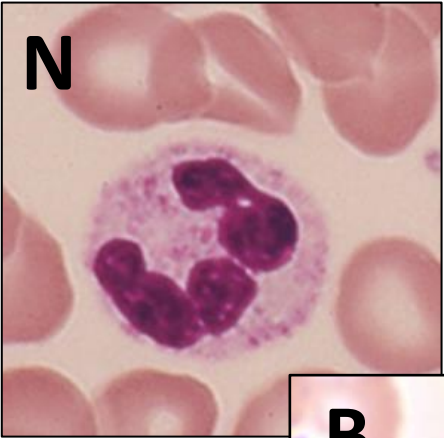
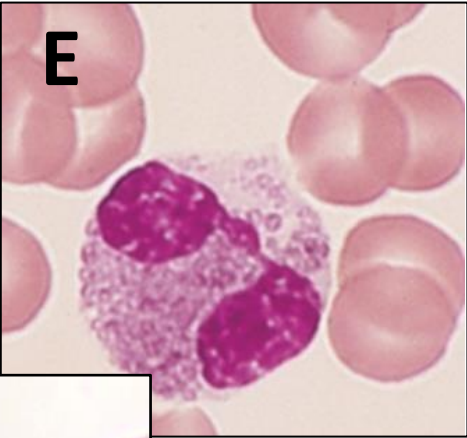
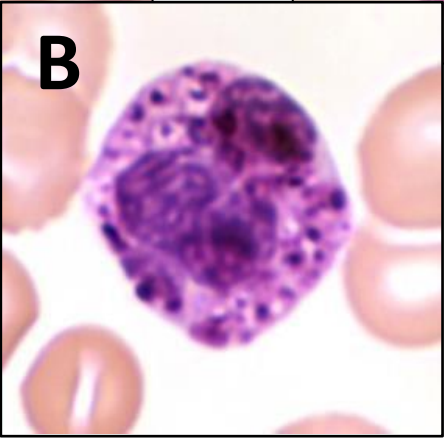
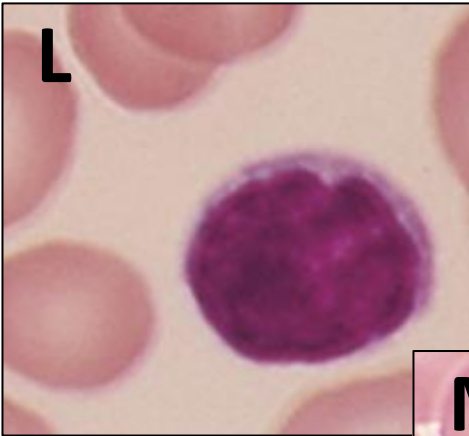
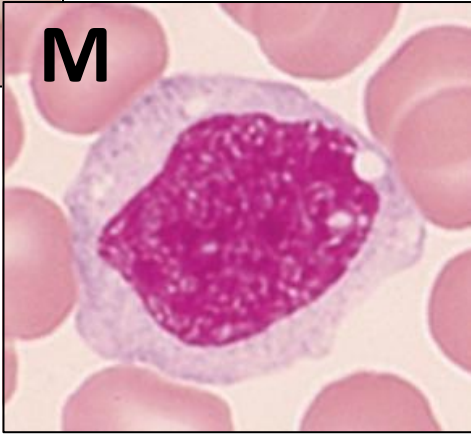
White Blood Cells (Leukocytes)

Fatima Daoud, MD, PhD

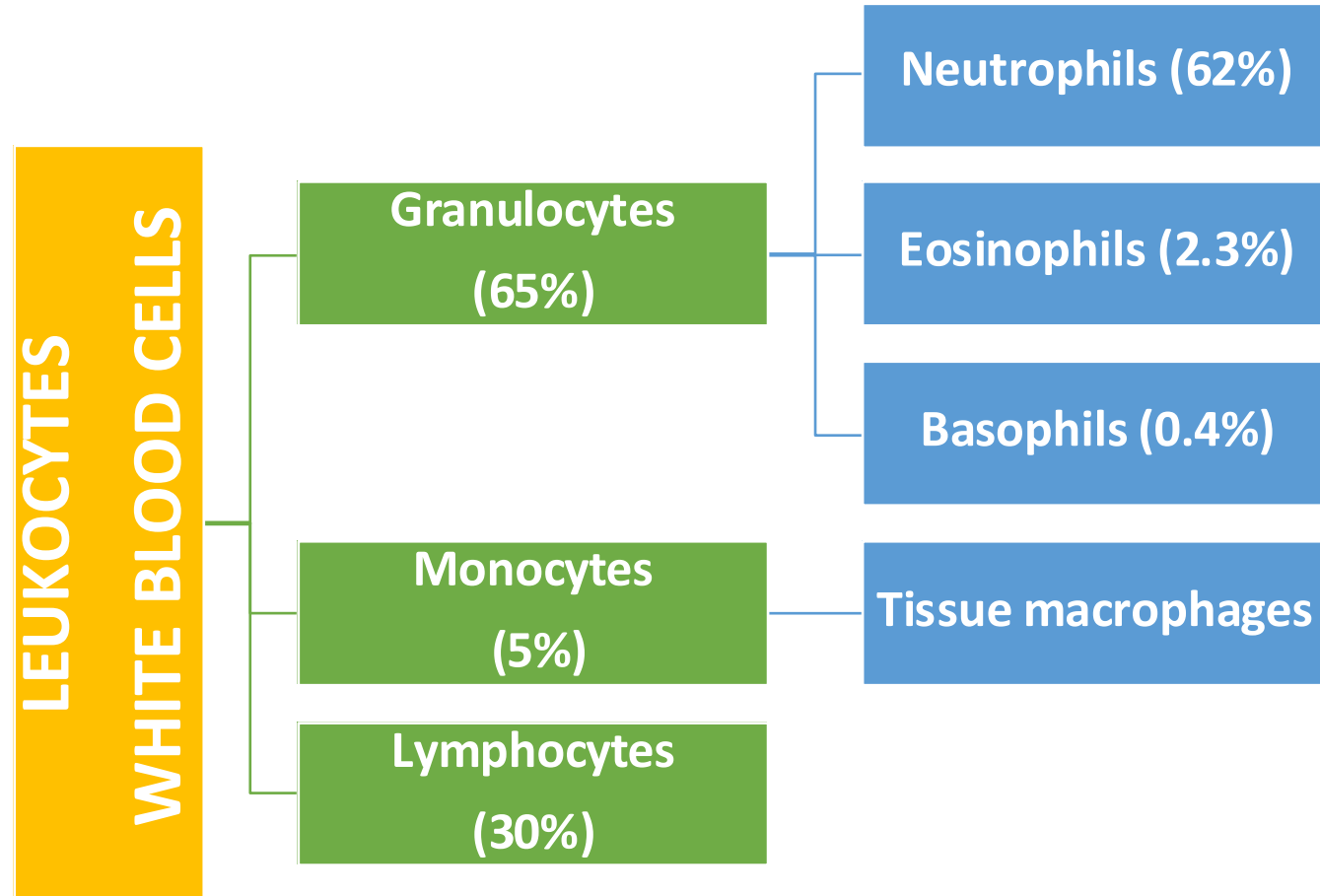


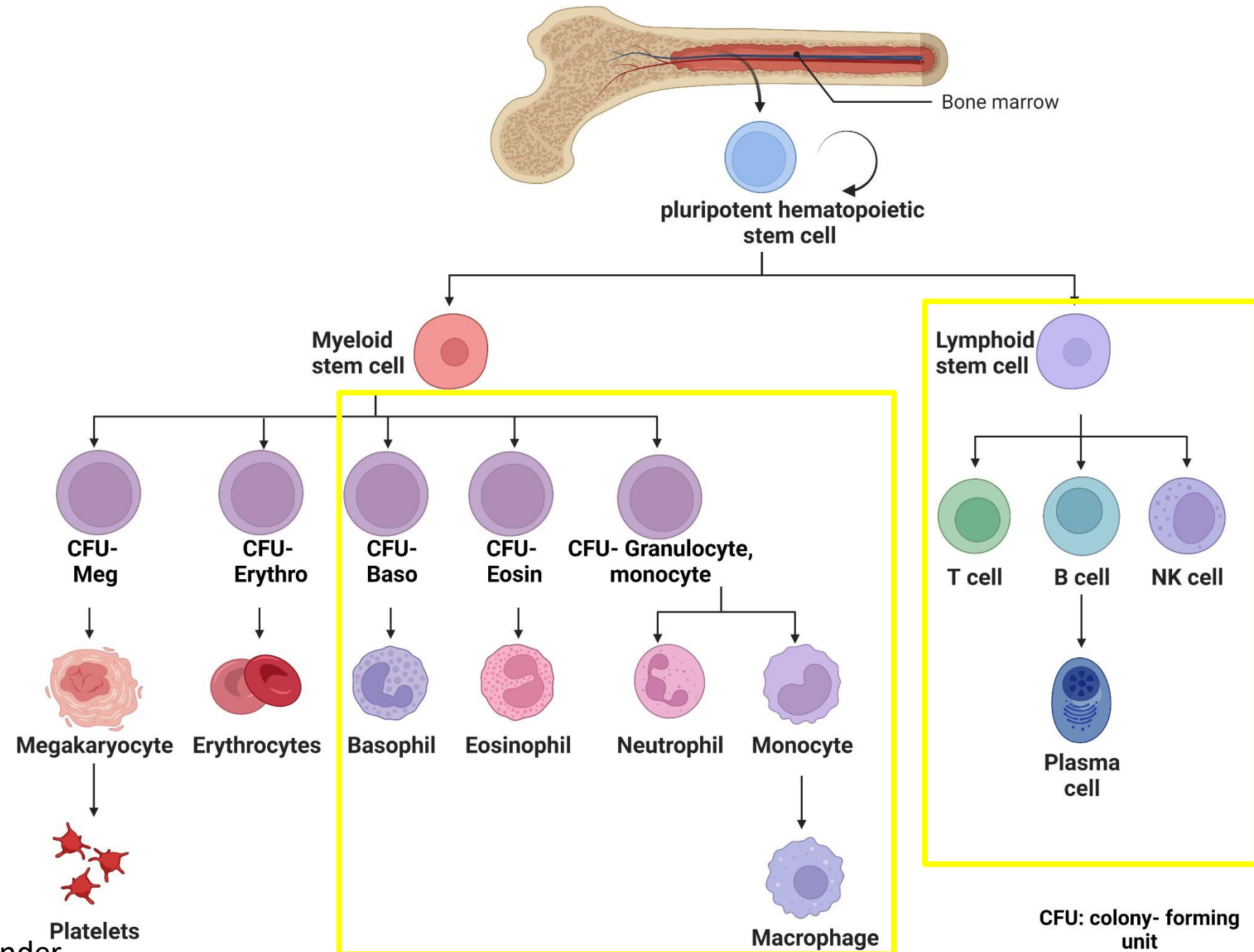
First, white blood cells are classified into two types based on the presence of specific granules in their cytoplasm: granulocytes and agranulocytes.

Granulocytes	Non- Granulocytes
Neutrophils	Monocytes
Eosinophils	Lymphocytes
Basophils	



The adult human has about 7,000 white blood cells per microliter of blood.
The normal percentages of the different types of white blood cells are approximately as follows.





****The granulocytes and monocytes are formed only in the bone marrow.**

****Lymphocytes and plasma cells are produced mainly in the various lymphogenous tissues—especially the lymph glands, spleen, thymus, tonsils, and various pockets of lymphoid tissue elsewhere in the body, such as in the bone marrow.**

****The white blood cells formed in the bone marrow are stored within the marrow until they are needed in the circulatory system. when the need arises, various factors cause them to be released.**

****Normally, about three times as many white blood cells are stored in the marrow as circulate in the entire blood. This represents about a 6-day supply of these cells**

****The life of the granulocytes after being released from the bone marrow is normally 4 to 8 hours circulating in the blood and another 4 to 5 days in tissues where they are needed**

White blood cells are derived from two distinct stem-cell lines in the bone marrow::

- Lymphocytes and natural killer cells are derived from lymphoid stem cells.
- The remaining white blood cells are produced by myeloid stem cells.

Granulocytes and monocytes are formed only in the bone marrow. Lymphocytes are mostly produced in lymphogenous tissues.

Granulocytes are generated in the bone marrow and kept there until they are required in the circulatory system. This stored amount is equivalent to about a six-day supply of these cells.

However, lymphocytes are largely retained in lymphoid tissues, with only a small number temporarily transported through the blood.

This scheme reveals two cell types that require further differentiation before becoming completely functional::

- First, monocytes in the circulation must differentiate into macrophages once they reach tissues.
- Second, B lymphocytes mature into plasma cells capable of producing antibodies.

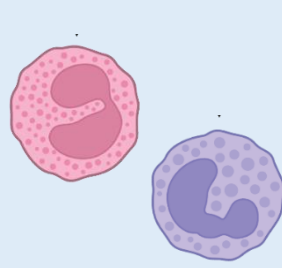
Blood function: Protection

Our bodies are exposed to bacteria, viruses, fungi, and parasites. However, we have an immune system that works continuously to protect us against them.

This system is mostly constituted of white blood cells, which collaborate to prevent disease in two ways:

White blood cells work together in two ways to prevent disease:

- (1) by actually destroying invading bacteria or viruses by **phagocytosis**.
(Neutrophils and macrophages)
- (2) by forming antibodies and sensitized lymphocytes, which may destroy or inactivate the invader.



Granulocyte



- The granulocytes are formed only in the bone marrow.
- They stored within the marrow until they are needed in the circulatory system.
- The life of the granulocytes after being released from the bone marrow is normally 4 to 8 hours circulating in the blood and another 4 to 5 days in tissues where they are needed.
- In times of serious tissue infection, this total life span is often shortened.
- **In times of serious tissue infection, this total life span is often shortened to only a few hours because the granulocytes proceed even more rapidly to the infected area, perform their functions, and, in the process, are themselves destroyed.

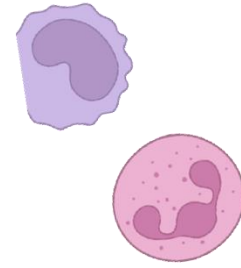
Monocyte/macrophage



- The monocytes are formed only in the bone marrow.
- The monocytes also have a short transit time, 10 to 20 hours in the blood.
- Once in the tissues, they swell to much larger sizes to become tissue macrophages (can live for months).

Tissue macrophages begin life as blood monocytes. While still in the blood, monocytes are immature cells and have little ability to fight infectious agents. However, once they enter tissues, they begin to enlarge. These cells are then called macrophages, and they are extremely capable of combating disease agents in the tissues.

Actions of Phagocytic Cells



- 1. Margination**
- 2. Tight binding**
- 3. Diapedesis**
- 4. Chemotaxis**
- 5. Ameboid Motion (pseudopodia)**
- 6. Phagocytosis**

Neutrophils and macrophages undergo several processes before they can phagocytose an infection: margination, tight binding (adhesion), diapedesis, chemotaxis, amoeboid motion (pseudopodia formation), and phagocytosis.

**The neutrophils are mature cells that can attack and destroy bacteria even in the circulating blood. Conversely, the tissue macrophages begin life as blood monocytes, which are immature cells while still in the blood and have little ability to fight infectious agents at that time. However, once they enter the tissues, they begin to swell—sometimes increasing their diameters as much as fivefold—to as great as 60 to 80 micrometers, a size that can barely be seen with the naked eye. These cells are now called *macrophages*, and they are extremely capable of combating disease agents in the tissues.

In the bloodstream, formed elements typically pass through the middle of the vessel. When a pathogen invades nearby tissue, the endothelium begins to express certain proteins on its surface in order to capture circulating neutrophils and monocytes.

This attachment is **weak at first**, and the cells continue to roll toward the sides of the blood vessels. This is also known as **margination**, because the cells are now at the margins of the blood vessels rather than in the middle. White blood cells and the endothelium interact more and more until the binding becomes **increasingly tight**.

The goal is to attract neutrophils and monocytes to the site of infection, so they must cross endothelial cells to reach the interstitium.

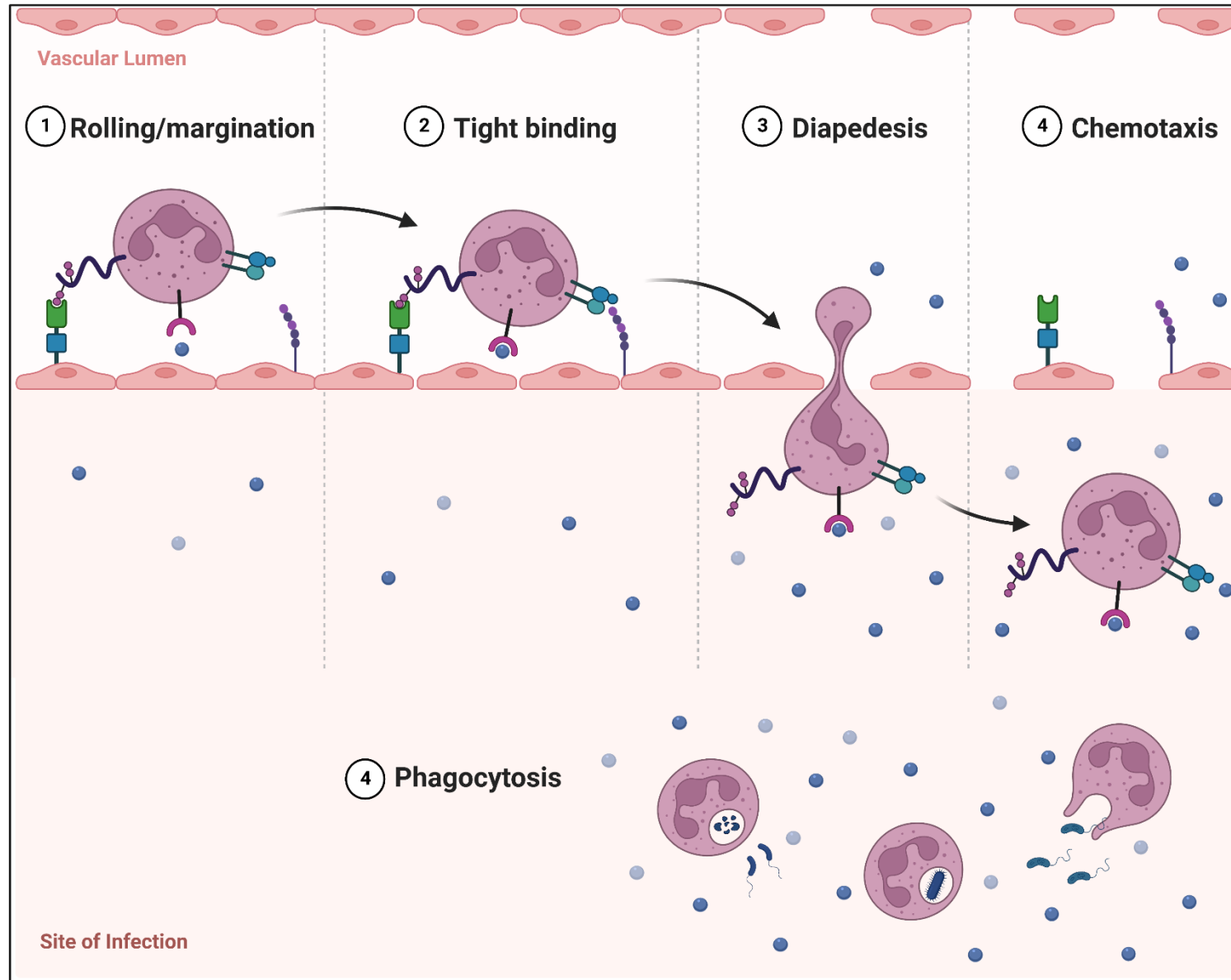
As a result, neutrophils and monocytes squeeze themselves through gaps between endothelial cells in a process known as **diapedesis**.

Once in the interstitial space, neutrophils and monocytes attempt to locate the source of the infection. Because they move with **pseudopodia**, monocytes and neutrophils display what is called **amoeboid motion**.

Several substances are released by inflamed tissue to direct neutrophils and macrophages to the site of infection. These substances are most **concentrated at the source of infection**. As a result, neutrophils and macrophages track these molecules in a process known as **chemotaxis**.

These chemicals may include bacterial or viral toxins, degradation products of inflamed tissues, and several products of the complement system.

Actions of Phagocytic Cells



****Neutrophils and monocytes can squeeze through the pores of the blood capillaries by *diapedesis*.**

****Both neutrophils and macrophages can move through the tissues by ameboid motion.**

****Many different chemical substances in the tissues cause both neutrophils and macrophages to move toward the source of the chemical. This phenomenon is called *chemotaxis*.**

*****phagocytosis*, which means cellular ingestion of the offending agent.**

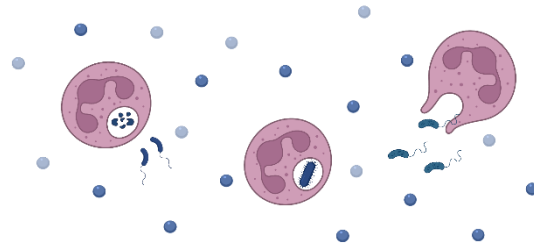
A 3D medical illustration showing a cross-section of a blood vessel. The vessel wall is composed of reddish-brown, textured cells. Inside the vessel, there are several red blood cells, which are biconcave and reddish. A large neutrophil is prominently featured in the center, characterized by its multi-lobed, purple nucleus and light blue, granular cytoplasm. Other smaller neutrophils are visible further back in the vessel. The overall scene is set against a dark red background, representing the interior of the blood vessel.

Neutrophil

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Phagocytosis



Phagocytes must be **selective** and likelihood of phagocytosis is increased when :

1. If the surface is rough, the likelihood of phagocytosis is increased.

First, normal cells have smooth surfaces; therefore, surface roughening can make a cell more susceptible to phagocytosis.

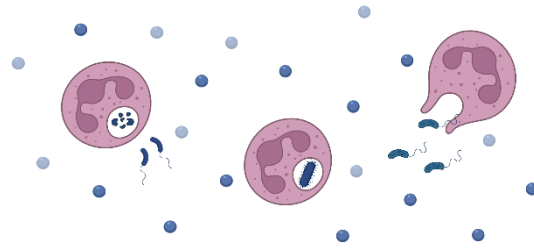
2. Most dead tissues and foreign particles have no protective protein coats.

Second, our cells have protective protein coatings, which most dead cells lack, making dead cells more vulnerable to phagocytosis.

3. The antibodies adhere to the bacterial membranes and thereby make the bacteria especially susceptible to phagocytosis (opsonization).

Finally, antibodies can safeguard our bodies by marking or tagging cells that must be phagocytosed, with the help of the complement system. This process is called opsonization.

Phagocytosis



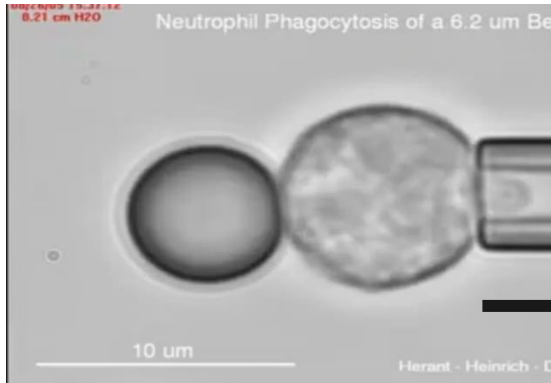
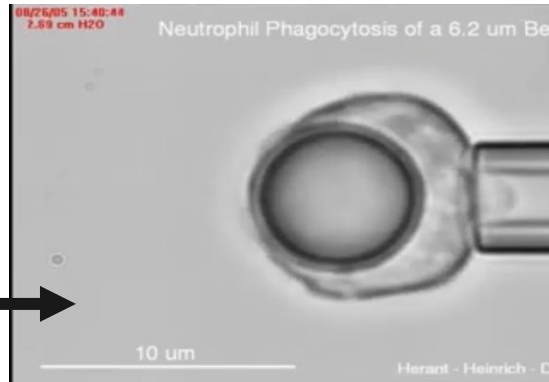
How does a phagocytic cell kill a microorganism?

- Enzymatic digestion
- Hypochlorite (myeloperoxidase)
- Reactive oxygen metabolites
 - superoxide anion
 - hydrogen peroxide
 - hydroxyl radicals

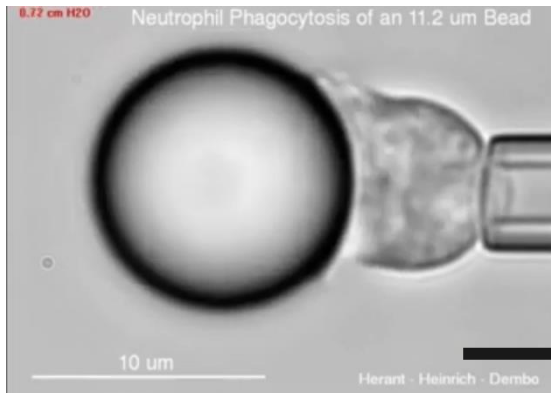
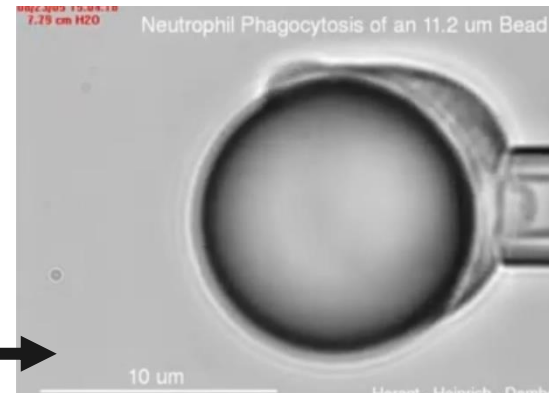
How Phagocytic Cells Kill Microorganisms

- Lysosomes and other cytoplasmic granules of the neutrophil or macrophage quickly come into contact with the phagocytic vesicle, discharging many digestive enzymes and bactericidal substances into the vesicle.
- Lipases are enzymes found in macrophages that break down the thick lipid walls found in some bacteria.
- Myeloperoxidase, a lysosomal enzyme, also catalyzes a process that produces hypochlorite, which is particularly bactericidal.
- Furthermore, peroxisomes produce potent oxidizing agents such as superoxide, hydrogen peroxide, and hydroxyl ions, which are toxic to most bacteria even in small amounts.

The lecture also describes an experiment in which a neutrophil is attached to a pipette. The goal is to examine neutrophil phagocytic activity toward particles of varying sizes. It can be observed that, beyond a certain size, the neutrophil is unable to phagocytose the particle.



Successful
Phagocytosis



Unsuccessful
Phagocytosis

Neutrophil



- Mature cells that can attack and destroy bacteria even in the circulating blood.
- Not capable of phagocytizing particles much larger than bacteria.

Monocyte/macrophage



- Monocyte are immature cells while still in the blood and have little ability to fight infectious agents at that time.
- They have the ability to engulf much larger particles (RBC).
- Macrophages are much more powerful phagocytes.
- Can extrude the residual products and often survive and function for many more months.

Eosinophils



- They form about 2 percent of all the blood leukocytes.
- Eosinophils are weak phagocytes.
- They are often produced in large numbers in people with parasitic infections.
- The parasites are too large to be phagocytosed by eosinophils or atherosclerosis phagocytic cells; Eosinophils attach themselves to the parasites by way of special surface molecules and release substances that kill many of the parasites.
- Eosinophils also have a special propensity to collect and accumulate in tissues in where allergic reactions occur. Mast cells and basophils recruit them because they produce eosinophil chemotactic factor.
- Eosinophils are thought to detoxify some of the inflammatory chemicals generated by mast cells and basophils. They also phagocytose and destroy allergen–antibody complexes, thus helping prevent excessive spread of the local inflammatory process.

Basophils



- ~ 0.5% of total white blood cells
- Similar to the large tissue mast cells located immediately outside many of the capillaries in the body.
- They express IgE antibody on the surface and antigen binding causes rupture of basophil and release large quantities of intracellular granules.
- The mast cells and basophils release *histamine*, *heparin*, as well as smaller quantities of *bradykinin* and *serotonin*.

رسالة من الفريق العلمي:

قال رسول الله ﷺ:
"مَنْ صَلَّى عَلَيَّ صَلَاةً صَلَّى اللَّهُ عَلَيْهِ بِهَا عَشْرًا"
اللهم صل وسلم على نبينا محمد



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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
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