WBCs characteristics and functions

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Objectives:

1. Discuss how to recognize different WBCs types and describe their site of production, life span and function.
2. Differentiate between marginating and circulating pools of WBCs.
3. Understand the principle behind the total, relative and absolute WBCs count.
4. Describe the properties of phagocytic WBCs and physiological leukocytosis.
5. Describe the tissue macrophages and the reticulo-endothelial system.
6. Understand how to apply this knowledge in clinical practice.
Introduction:

Our bodies are exposed to bacteria, viruses, fungi, and parasites, which occur normally in the skin, the mouth, the respiratory passageways, the GIT, the lining membranes of the eyes, and even the urinary tract.

WBCs (leukocytes) and tissue cells derived from leukocytes work together in two ways to prevent disease:

1. By destroying invading bacteria or viruses by phagocytosis. Phagocytes is a selective process.
2. By forming antibodies and sensitized lymphocytes, one or both of which may destroy or inactivate the invader.
Leukocytes (White Blood Cells):

- Are the *mobile units* of the body’s defense system.
- Some are formed partially in the bone marrow (*granulocytes* and *monocytes* and a few *lymphocytes*)
- Some are partially formed in the lymph tissue (*lymphocytes* and *plasma cells*).
- Most of them are specifically transported to areas of serious infection and inflammation, thereby providing a rapid and potent defense against infectious agents.
- There are six types of white blood cells that are normally present in the blood:
  1. Polymorphonuclear neutrophils
  2. Polymorphonuclear eosinophils
  3. Polymorphonuclear basophils
  4. Monocytes
  5. Lymphocytes
  6. Plasma cells (occasional)
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
Leukocytes (White Blood Cells) cont.:  

- The granulocytes and monocytes protect the body against invading organisms mainly by **phagocytosis**.  
- Both the granulocytes and monocytes are formed only in the **bone marrow**. About three times as many white blood cells are stored in the marrow as circulate in the entire blood.  
- The lymphocytes and plasma cells function mainly in connection with the immune system.  
- 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 and in so-called **Peyer’s patches** underneath the epithelium in the gut wall.
The lymphocytes are mostly stored in the various lymphoid tissues, except for a small number that are being transported in the blood. The adult human being has about 7000 white blood cells per microliter of blood (range 4000-11000). The normal percentages of the different types are approximately the following:

- Polymorphonuclear neutrophils: 62.0% (2.5-7.5 X10³)
- Polymorphonuclear eosinophils: 2.3% (0.04-0.4 X10³)
- Polymorphonuclear basophils: 0.4% (0.01-0.1 X10³)
- Monocytes: 5.3% (0.2-0.8 X10³)
- Lymphocytes: 30.0% (1.5-3.5 X10³)
Life Span of the White Blood Cells

- In the blood, the life of the granulocytes is normally 4 to 8 hours and another 4 to 5 days in tissues where they are needed.
- **Margination** is the temporarily sequestration of leukocytes in microcirculation from the circulating blood, but can be rapidly mobilized in times of need.
- Margination can be found within the spleen, liver, bone marrow and the lung (some authors believe that the lung harbors more leukocytes within its microvascular network than any other organ).
- The monocytes live **10 to 20 hours** in the blood, before wandering through the capillary membranes into the tissues, where they swell to much larger sizes to become *tissue macrophages* that can live for months.
Along with lymph drainage, lymphocytes enter the circulatory system continually. After a few hours, they pass out of the blood back into the tissues by **diapedesis**. Then they re-enter the lymph and return to the blood again and again.

The lymphocytes have life spans of weeks or months.

**Diapedesis** is the process by which WBCs can squeeze through the pores of the blood capillaries. The portion sliding through is momentarily constricted to the size of the pore.

Both neutrophils and macrophages can move through the tissues by **ameboid motion**.
Increased permeability  
Margination  
Diapedesis  

Chemotaxis source  

Chemotactic substance
The physiological function of WBCs

- In the **tissues**, it is mainly the neutrophils and tissue macrophages that attack and destroy invading bacteria, viruses, and other injurious agents. However, in the **blood**, only the neutrophils which are the mature cells that can attack and destroy bacteria.

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

- **Chemotaxis** is effective up to 100 micrometers away from an inflamed tissue.

- Agents that cause chemotaxis include:
  1. Some of the bacterial or viral toxins.
  2. Degenerative products of the inflamed tissues themselves.
  3. Several reaction products of the “complement complex” activated in inflamed tissues.
  4. Several reaction products caused by plasma clotting in the inflamed area, as well as other substances.
The physiological function of WBCs (cont.)

- Phagocytosis is a selective process. The smooth protein coated surfaces of natural structure makes them immune from phagocytosis. Conversely, most dead tissues and foreign particles have no protective coats, which makes them subject to phagocytosis.

- The antibodies synthesized by the immune system adhere to the bacterial membranes and thereby make the bacteria especially susceptible to phagocytosis.

- The antibody molecule also combines with the C3 product of the complement cascade. The C3 molecules, in turn, attach to receptors on the phagocyte membrane, thus initiating phagocytosis. This process by which a pathogen is selected for phagocytosis and destruction is called opsonization.

- A single neutrophil can usually phagocytize 3 to 20 bacteria before the neutrophil itself becomes inactivated and dies.
Macrophages are much more powerful phagocytes than neutrophils, often capable of phagocytizing as many as 100 bacteria.

They also have the ability to engulf much larger particles, even whole red blood cells or, occasionally, malarial parasites. After digesting particles, they can survive and function for many more months.

Both neutrophils and macrophages contain bactericidal agents that kill most bacteria even when the lysosomal enzymes fail to digest them.

Fixed tissue macrophages are present in all potential routes by which invading organisms frequently enter the body such as the subcutaneous tissues, lymph nodes, alveolar walls, and liver sinusoids (Kupffer Cells) → future first line of defense.

The total combination of monocytes, mobile macrophages, fixed tissue macrophages, and a few specialized endothelial cells in the bone marrow, spleen, and lymph nodes is called the reticuloendothelial system.
Kupffer cells lining the liver sinusoids, showing phagocytosis of India ink particles into the cytoplasm of the Kupffer cells.
The physiological function of WBCs (cont.)

- Within a few hours after the onset of acute, severe inflammation, the number of neutrophils in the blood sometimes increases fourfold to fivefold—from a normal of 4000 to 5000 to 15,000 to 25,000 neutrophils per microliter (i.e. neutrophilia).

- Neutrophilia is caused by products of inflammation that enter the bloodstream, are transported to the bone marrow, and there act on the stored neutrophils of the marrow to mobilize these into the circulating blood.

- Mainly five factors are believed to play dominant roles in feedback control of the macrophage response to inflammation. They are:
  1. Tumor necrosis factor (TNF).
  2. Interleukin-1 (IL-1).
  4. Granulocyte colony-stimulating factor (G-CSF).
INFLAMMATION

Activated macrophage

- TNF
- IL-1
- GM-CSF
- G-CSF
- M-CSF

Endothelial cells, fibroblasts, lymphocytes

- GM-CSF
- G-CSF
- M-CSF

Bone marrow

- Granulocytes
- Monocytes/macrophages
**Pus:**

Is an exudates typically white-yellow in color. It is the end product of inflammation that contains varying portions of necrotic tissue, dead neutrophils, dead macrophages, and tissue fluid.

Pus from anaerobic infections can more often have a foul odor.
Eosinophils

- Eosinophils are weak phagocytes.
- Are often produced in large numbers in people with parasitic infections, and they migrate in large numbers into tissues diseased by parasites.
- 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 tendency to collect in tissues in which allergic reactions occur.
- The eosinophils are believed to detoxify some of the inflammation-inducing substances and probably also to phagocytize and destroy allergen-antibody complexes, thus preventing excess spread of the local inflammatory process.
The basophils in the circulating blood are similar to the large tissue **mast cells** located immediately outside many of the capillaries in the body. Both liberate **heparin** into the blood.

The mast cells and basophils also release **histamine**, as well as smaller quantities of **bradykinin** and **serotonin**. It is mainly the mast cells in inflamed tissues that release these substances during inflammation.

The antibody **IgE** has a special tendency to become attached to mast cells and basophils. Therefore, when reacting with the specific antigen causes the mast cell or basophil to rupture and release large quantities of **histamine**, **bradykinin**, **serotonin**, **heparin**, **slow-reacting substance of anaphylaxis**, and a number of **lysosomal enzymes** → allergic manifestations.
Leukopenia

- A clinical condition occurs in which the bone marrow produces very few white blood cells. This will allow invasion of adjacent tissues by bacteria that are already present.
- Within 2 days after the bone marrow stops producing white blood cells, ulcers may appear in the mouth and colon, or the person might develop some form of severe respiratory infection.

The Leukemias

- Lymphocytic leukemias: usually begin in a lymph node or other lymphocytic tissue.
- Myelogenous leukemias: begin by cancerous production of young myelogenous cells in the bone marrow. Usually, the more undifferentiated the cell, the more acute is the leukemia.
Q. Regarding Opsonization?

• A. It involves breakdown of antibodies
• B. It means neutralization of antigen by antibody
• C. Antigen gets attached directly to the phagocyte receptor
• D. Antibody makes a bridge between antigen and receptor
• E. The antigen is surrounded by edges of cell membrane