

MODULE HLS (HEMO & LYMPH)

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LEUKOCYTES



LEUKOCYTES

The Total Leukocytic Count is <mark>4,000–11,000/mm³ of blood Functions of Leukocytes</mark>

Leukocytes are responsible for the body's defense against pathogenic organisms and their toxins.

The matured cells are released into circulation and remain in circulation for a few hours before they enter the tissues (circulation pool): At rest, many leucocytes, especially neutrophils, adhere to the endothelial lining of blood vessels, which is called the Margination Pool of Leucocytes. In addition, Leucocytes circulate in the blood (the Active Circulation Pool).





LEUKOCYTES

Functions of Leukocytes

Disruption of Margination causes Leukocytosis: Leucocytes adhere to the inner lining of the blood vessel, called Margination. In exercise and other conditions of increased hemodynamics, leukocytosis occurs mainly due to the disruption of the margination of leucocytes





A. Granular Leukocytes :

- 1. Neutrophils: (60-70% of WBCs)
- They represent the First Line of Defense against invading organisms.
- They perform their function by:
 - a. Margination: Neutrophils attach to the walls of capillaries.
 - b. **Diapedesis:** Neutrophils squeeze themselves through the pores of capillaries and pass into tissue spaces.
 - c. Amoeboid movement: This movement allows neutrophils to reach invading organisms.
 - d. Chemotaxis: Breakdown products of inflamed tissues and bacterial toxins attract neutrophils to the infected area.
 - e. Phagocytosis: This is the most important property of neutrophils. They can ingest invading bacteria and necrotic tissue by engulfing them (endocytosis). It results in the formation of a phagocytic vacuole. The neutrophil granules release their contents into the phagocytic vacuoles, killing the bacteria.
- In more severe infections, pus is formed. It consists of necrotic tissue, dead neutrophils, and dead macrophages.



A. Granular Leukocytes :



A. Granular Leukocytes :



Figs. 17.10A to D: Details of diapedesis of neutrophils. It occurs in three phases: margination and pavementing, rolling and adhesion, and emigration and diapedesis.

TYPES OF LEUKOCYTES A. Granular Leukocytes: Phagosome forming Damage and digest on Lysosome **Neutrophils: Phagocytosis:** 5 Phagocytosis Lysosome Release of microbial products fusion

- a. Ingestion through phagocytosis, a food vacuole is formed.
- b. The fusion of lysosomes with the food vacuole; the pathogen is broken down by enzymes
- c. Waste material is expelled or assimilated

Parts:

- 1. Pathogens
- 2. food vacuole
- 3. Lysosomes

- 4. Waste material
- 5. Cytoplasm
 - 6. Cell membrane

A. Granular Leukocytes :

2. Eosinophils: (2-6% of WBCs) Eosinophils increase in parasitic infestations. They kill too large parasites to be engulfed by releasing toxic substances.

- They also increase during allergic conditions.
- Eosinophils are weakly phagocytic and show chemotaxis.

3. Basophils: (0-1% of WBCs)

Basophils are similar to mast cells. They contain histamine (increases capillary permeability) and Heparin (naturally occurring anticoagulant).

B. Agranular Leukocytes:

- 1. Monocytes: (2-8% of WBCs)
 - They are the largest type of leukocytes.
 - They enter the blood from the bone marrow and circulate for 72 hours. Then they enter the tissues & become tissue macrophages. The tissue macrophage system was earlier known as the reticuloendothelial system.
 - Monocytes migrate by amoeboid movement in response to chemotactic stimuli to the sites of inflammation soon after neutrophils.
 - They phagocytose bacteria, dead neutrophils, and remnants of destroyed tissues. Few monocytes are transformed into highly specialized mononuclear cells called dendritic cells: They play an important role in antigen processing and presentation to the T cells.



B. Agranular Leukocytes:

1. Monocytes-Macrophage system :



B. Agranular Leukocytes:

- 2. Lymphocytes: (20-30% of WBCs)
- They are formed in lymphoid tissues and enter the circulation via the lymphatic vessels.
- Lymphocytes play an important role in the body's defense through the immune system.



- The body can resist almost all types of organisms and toxins that tend to damage tissues and organs.
- Immunity refers to all physiological mechanisms that enable an organism to recognize and defend against infectious agents. Immunity The body can resist almost all types of organisms and toxins that tend to damage tissues and organs.
- These body defenses can be grouped in two categories:
 - Non-Specific immunity
 - Specific immunity





Antigens:

- These are <u>Substances that can induce an immune response and</u> react specifically with its products.
- Foreign organisms or toxins possess certain chemical structures that are specific to them and different from all other compounds. Such chemical structures are known as "Antigenic Determinants".
- Their molecular weight is more than 10,000.
- Antigens usually have many antigenic determinants, which may differ from each other or be repeated molecular structures.
- Antigenic determinants may be present on cell membranes or may be free, e.g., bacterial toxins.

Antigens:

Immune responses broadly involve two steps:

- 1. Recognition of pathogen or the foreign material
- 2. Reactions or responses to eliminate it. The responses are called Immune Responses.

Largely, immune responses are of two types:

- 1. Innate or Nonadaptive Response (Innate immunity).
- 2. Acquired or Adaptive Response (Acquired immunity).
- There are two types of immunity: Innate (non-specific) and Acquired (specific) immunity

The Immune System

Acquired

Humoral

Cell

Mediated

Innate

- Physical Barriers
- Natural killer Cells
- Macrophages

Antigens : Types of Immunity: I. INNATE IMMUNITY = NON-SPECIFIC IMMUNITY

Innate immunity is composed of non-specific mechanisms which defend the body against invasion by most organisms. It is neither specific for particular infectious agents nor improved by repeated encounters with the same agent. It includes the following mechanisms:

- 1. Resistance of the skin to invasion by organisms.
- 2. Destruction of organisms swallowed by HCl and digestive enzymes in the stomach.
- 3. Phagocytosis of the bacteria by granulocytes and tissue macrophages.



Antigens : Types of Immunity:

I. AQUIRED IMMUNITY = SPECIFIC IMMUNITY

The body can recognize the invading agent and develop a powerful specific immune response against it. It is carried out in 2 ways:

- A. Cellular Immunity (Cell-Mediated Immunity)
- B. Humoral Immunity

Antigens : Types of Immunity:

IMMUNITY



I. AQUIRED IMMUNITY = SPECIFIC IMMUNITY

A. Cellular Immunity (Cell-Mediated Immunity)

- Formation of Activated Cytotoxic T-Lymphocytes, which can <u>circulate in the</u> <u>blood</u>, <u>detect</u> and <u>attack the antigen specifically</u>.
- This type of immunity is produced by the Activated Cytotoxic T-Lymphocytes.
- It occurs when the body is exposed to Viruses, Fungi, a Few Bacteria (e.g., the tubercle bacillus), Cells from other individuals (tissue transplants), or Tumor Cells.
- Cytotoxic T cells cannot recognize free antigens. They are activated when their T cell receptor "sees" the antigen to which they are specific in association with the MHC class I protein:
- 1. The antigen may be ingested by an antigen-presenting cell (macrophages, dendritic cells, and B cells), partially digested, and presented on its cell membrane coupled with the MHC class I protein. In addition, the antigen-presenting cells also release interleukin-1 (IL-1), which activates T-lymphocytes.
- 2. T-helper cells are activated when they recognize the antigen in association with MHC class II proteins on the surface of antigen-presenting cells. The T-helper cells secrete interleukins that activate T cytotoxic cells.

Antigens : Types of Immunity:

I. AQUIRED IMMUNITY = SPECIFIC IMMUNITY A. Cellular Immunity (Cell-Mediated Immunity)

MHC Antigens

Major histocompatibility complex or MHC antigens are self-antigens that help in identifying and rejecting the foreign antigens:

- They are also called HLA antigens (human leucocyte associated antigens), as they were first identified on the membrane of leucocytes. However, afterward they were found to be present on the surface of all the body cells except in red cells (remember, red cells contain blood group antigens).
- 2. Like blood group antigens they are chemically glycoproteins. They are made up of α and β subunits.

Mechanism of Action of MHC Antigens

The proteins in the cells are continuously broken down to their peptide fragments. MHC I molecules pick up the peptide fragments containing 8–10 amino acids, whereas MHC II molecules pick up peptides containing 13–17 amino acids:

- When a peptide fragment of a self protein is picked up by the MHC antigen and expressed on the surface of the APC along with MHC proteins, T cells ignore it.
- However, when the peptide fragment is of a foreign protein, T cells recognize it and get activated that induce cell- mediated immunological responses.

Antigens : Types of Immunity:

- I. AQUIRED IMMUNITY = SPECIFIC IMMUNITY
 - A. Cellular Immunity (Cell-Mediated Immunity)



Antigens : Types of Immunity:

- I. AQUIRED IMMUNITY = SPECIFIC IMMUNITY
 - A. Cellular Immunity (Cell-Mediated Immunity)
 - When cytotoxic T cells are activated, they proliferate and differentiate into clones of :
 - 1. Activated Cytotoxic T Cells:
 - They destroy the antigen by:
 - Directly attacking the cell expressing the antigen by inserting pore-forming molecules (perforins) into the membrane, causing cell lysis.
 - Secreting substances that attract macrophages to the site of the antigen so that it is phagocytosed and killed.
 - 2. Memory T Cells

Remain dormant inside the body, and on second exposure to the same antigen, these cells proliferate more rapidly and powerfully than T lymphocytes.

Antigens : Types of Immunity:

I. AQUIRED IMMUNITY = SPECIFIC IMMUNITY

B. Humoral Immunity

- B-lymphocytes are responsible for humoral immunity.
- Humoral immunity mainly acts against bacterial infections.
- B-lymphocytes are activated by the antigen when they come into direct contact with it.

B-lymphocytes have membrane-bound antibodies on their surface, which act as receptors for antigen recognition.



Antigens : Types of Immunity:

IMMUNITY



I. AQUIRED IMMUNITY = SPECIFIC IMMUNITY

B. Humoral Immunity

 Activated B-lymphocytes proliferate, forming a clone of B-lymphocytes specific to this antigen.

These cells differentiate into:

1. Plasma Cells, which contain a well-developed endoplasmic reticulum. The plasma cells secrete antibodies specific to the antigen. Secreted antibodies circulate in the blood. When they encounter the antigen, they combine with it and destroy it. There are Five Types of antibodies: IgG, IgA, IgM, IgD and IgE



2. Memory B cells, which remain dormant until the antigen reenters the body. Then they launch a more rapid and more powerful secondary immune response



Antigens : Types of Immunity:

I. AQUIRED IMMUNITY = SPECIFIC IMMUNITY

B. Humoral Immunity

Mechanism of Action of Antibodies:

A. Direct Attack of the Antigen: Binding of antigen to its antibody causes :

- 1. Agglutination of Bacteria, i.e., the antigens clumps together.
- 2. Precipitation of the Antigens, i.e., when soluble antigens are bound to antibodies, they become insoluble and precipitate.
- 3. Lysis: Antibodies directly attack the cell membrane of bacteria, causing their rupture.
- 4. **Opsonization:** Some antibodies coat the microorganisms and make them "tasty" for Phagocytosis by neutrophils and macrophages.
- **B.** Activation of the Complement System:

There is a group of plasma proteins designated as complement proteins as they complement the effects of antibodies in destroying antigens.



The Complement System:





