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BIOGENESIS AND FUNCTIONAL ASPECTS OF LEUCOCYTES (WHITE BLOOD CELLS)

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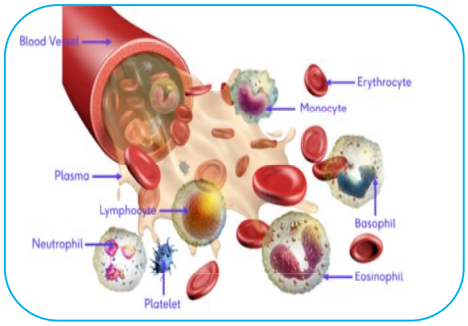
ABSTRACT

The leukocytes are also known as white blood cells. These cells act as the mobile units of the body's protective system. The formation of leukocytes takes place partially in the bone narrow (granulocytes &agranulocytes) and partially in the lymph tissue (lymphocytes and plasma cells). After complete formation, white blood cells are transported in the blood to various parts of the body based on their requirement.

KEYWORDS : *Leukocytes, White blood cells.*



INTRODUCTION

Generally, the transportation of these cells results inmovement of white blood cells to the areas of serious infection and inflammation ,there by arranging a rapid and potent defense against infections agents. Normally the granulocytes and monocytes show a special capability to seek out and destroy a foreign invader.

TYPES OF WHITE BLOOD CELLS

Broadly, six types of white blood cells are observed in mammalian blood . They are polymorphonuclearneutrophils, polymorphonucleareosinophils, polymorpho-nuclear basophils, lymphocytes and monocytes and seldom plasma cells. In additionto this, there are large numbers of thrombocytes, which are fragments of another type of cells just like white blood cells seen in the bone marrow, namelythe megakaryocyte. The cytoplasm of the first three types of cells (neutrophils, eosinophils & basophils) show granular appearance. In clinical terminology, poly-nucleated indicates the presence of multiple nuclei. The granulocytes and monocytes provide the defense to the body against invading organisms primarily by ingesting them (i.e.with the help of phagocytosis). The lymphocytes and plasma cells participate in the immune clearance of foreign antigens in the host body. Finally the function of thrombocytes is to enhancethe blood clotting mechanism.

WHITE BLOOD CELLS (WBC) CONCENTRATION IN THE BLOOD

The adult humans consist of 7,000 white blood cells per micro liter of blood. Of the total white blood cells, the normal percentage of the various types of WBC are approximatelyas follows.

Neutrophils	62%
Eosinophils	2.0%
Basophils	0.2%
Lymphocytes	30.5%
Monocytes	5.3%

The number of thrombocytes in each micro liter of blood is normally 3, 00,000. The thrombocytes are only cell fragmentsderived from megakaryocytes, and do not have nucleus. Thrombocyte population is recycled by 30,000 cells per microliter of blood each day, indicating that the total thrombocyte population is replaced every 10 days.

BIOGENESIS OF WHITE BLOOD CELLS (WBC/ LEUKOCYTES)

Early differentiation of the pleuripotential hematopoietic stem cell (PHSC) results in generation of different types of committedstem cells (**Fig. 1**). Consequently, two main lineages of white blood cells are formed, namely myelocytic and the lymphocytic lineages. The formation of two main lineages of white blood cells takes place such as the myelocytic andlymphocytic lineages. The formation of the granulocytes and monocytes takes place in the bone marrow. The production of lymphocytes and plasma cells happens primarily in the various lymphogenous tissues; specifically the lymph gland,thymus,tonsils,spleen including other secondary lymphoid tissues such as bone marrow and peyer's patches that lie underneath the epithelium of the gut wall. Generally, about three times as many white blood cells are preserved in the marrow as those that circulate in the entire blood. The lymphocytes are preserved in the many lymphoid tissues, except for few that are temporarily being transported in the blood. The formation of megakaryocytes happens in the bone marrow. The fragmentation of these megakaryocytes takes place in the bone marrow resulting in production of platelets (**Fig. 1**).

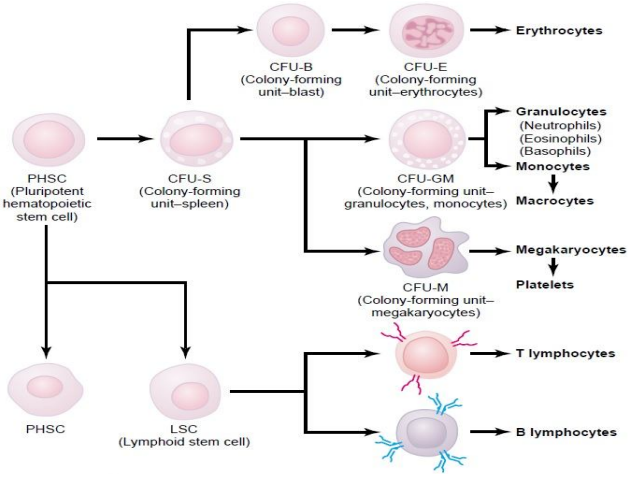


Figure 1: Biogenesis of Leucocytes. White blood cells are derived from pleuripotential hematopoietic stem cells.

LIFE SPAN OF THE WHITE BLOOD CELLS

Granulocytes are short lived with a typical life span of 4 to 8 hours. During serious tissue infection,this total life span is shortened to only a few hours because the granulocytes proceed even more rapidly to the infected area. The monocytes also exhibit only 10-20 hours of transmit time in the blood, before passing through the blood vesselmembranes into the tissues.Once in the tissues, monocytes bulge into larger cells to become tissue macrophages, and in this form monocytes can survive for months unless killed while performing phagocytic infections. These tissue macrophages are the basis of the tissue phagocytosis which provides continuous defense against infections. The entry of lymphocytes takes place into the circulatory system continuously along with drainage of lymph from the lymph nodes and other lymphoid tissue. After a few hour,they move out of the blood back into the tissues by diapedesis. Then theyreenter the lymph and later into theblood, and this process repeats

several times and a continuous circulation of lymphocytes is guaranteed throughout the body. The lymphocytes exhibit life span of weeks or months, based on the body's need for these cells.

NEUTROPHILS & MACROPHAGES DEFEND AGAINST INFECTIONS

Neutrophils and tissue macrophages attack and destroy invading bacteria, viruses and other injurious bacteria. The tissue macrophages start life as blood monocytes which act as immature cells even in the blood and exhibit very low capability to fight infections agents at that time. After entering into the tissues,monocytes start to swell & sometimes enhancing their diameters as much as fivefold to as great as 60 to 80 micrometers. These cells are now termed as macrophages and they are able to combat disease agents in the tissues.

MOVEMENT OF BLOOD CELLS INTO TISSUE SPACES BY DIAPEDESIS

Neutrophils and monocytes squeeze through the pores of the blood capillaries with the help of diapedesis (**Fig. 2**). Even though a pore is much smaller than a cell,a smallportion of the cell slides through the pores of blood capillaries at a time, and thereby large number of these cells enters the tissues from circulating blood by a chemotactic mechanism (**Fig. 2**).

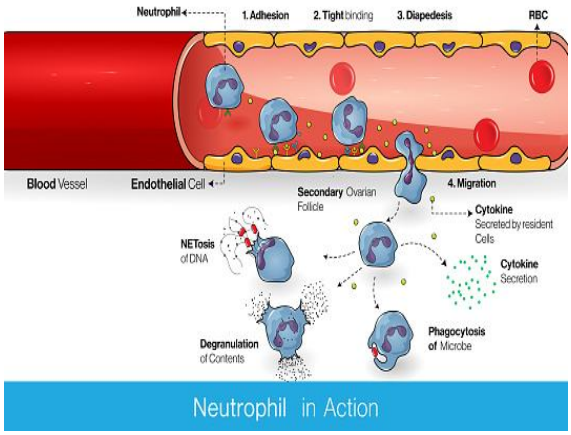


Figure 2: Diapedesis of neutrophil through the capillary pore into surrounding tissues spaces by squeezing through the capillary membrane.

AMOEBOID MOVEMENT OF WHITE BLOOD CELLS THROUGH TISSUE SPACES

The movement of neutrophils and macrophages takes place through the tissues with the help of amoeboid movement (**Fig. 2**). The movement of some cells at velocities as great as 40μm/min,a distance as great as their own length, each minute.

CHEMOTAXIS OF WHITE BLOOD CELLS TOWARDS THE INFLAMED TISSUE AREAS

Many different chemical substances in the tissues are responsible for the movement of both neutrophils and macrophages toward the source of chemical, a process termed 'chemotaxis'. Because of the inflammation of the tissue, at least a dozen different products are responsible for causing chemotaxis toward the inflamed area. For example ; a)Degenerative reaction products of the inflamed tissues, b) Activation of several reaction products of the complement complex in inflamedtissues, c) few of the bacterial or viral toxins and d) plasma clotting in the inflamed area that leads to formation of several reaction products. Chemotaxis is based on the concentration gradient of the chemotactic substance. The concentration is maximum at the source and decreases away from the source that leads to unidirectional movement of white cells towards the source of the chemical. Chemotaxis is very effective upto 100 μm away from an inflamed tissue. Any tissue area is not more than 50 micrometers

away from a capillary and the chemotactic signal is capable of moving hordes of white cells from the capillaries into the inflamed area.

PHAGOCYTOSIS

Phagocytosis is predominantly caused by neutrophils and macrophages.

PHAGOCYTOSIS BY NEUTROPHILS

The neutrophils entering the tissues are already maturedand can quick start phagocytosis. A single neutrophil can generally phagocytize up to 3 to 20 bacteria.

PHAGOCYTOSIS BY MACROPHAGES

Macrophages are the end-stage derivatives of monocytes that gain entry into the tissues from the blood. Each macrophage destroy approximately 100 bacteria. Macrophages show the capability to ingest much larger particles including whole erythrocytes or rarely malarial parasites. The life span of macro phages is many months long.

MOST PHAGOCYTIZED PARTICLES ARE DIGESTED BY INTRACELLULAR ENZYMES

Neutrophils and macrophagescontain abundant lysosomes filled with proteolytic enzymes and digest bacteria and other foreign protein material. The lysosomes of only macrophages consist of more amounts of lipases,which are capable of digesting the thick lipid membranes possessed by some bacteria including tubercle bacillus.

NEUTROPHILS AND MACROPHAGES CAN DESTROY BACTERIA

Neutrophils and macrophages consist of bactericidal agents that destroy most of the bacteria even if the lysosomal enzymes are not able to digest them. Much of the killing effect results from many powerful oxidizing agents formed by enzymes in the membrane of the phagosome or by a special organelle known as the peroxisome. The examples for oxidizing agents are more quantities ofsuperoxide (o_2^-) ,hydroxyl ions (OH^-) and hydrogen peroxide (H_2O_2),and these oxidizing agents are lethal to most bacteria even in small quantities. Myeloperoxidase i.e.one of the lysosomal enzymes, catalyzes the reaction between H_2O_2 and chloride ions to form hypochlorite which is a powerful bactericidal agent. Some bacteria especially tuberculosis bacillus consist of coats that are resistant to lysosomal digestion and also produce some compounds that partially show the resistance to the killing effects of the neutrophils as well as macrophages. These bacteria are responsible for the occurrence of chronic diseases namely tuberculosis.

MONOCYTE – MACROPHAGE SYSTEM

The macrophages act as mobile cells that wander through the tissues. The mobile macrophages phagocytize large quantities of bacteria, necrotic tissue,viruses and other foreign particles in the tissue.Monocyte – macrophage system is present in almost all tissues of the body. The entire combination of monocytes,fixed tissue macrophages,mobile macrophages and a small number ofendothelial cells in the lymphatic tissue is termed as the reticulo-endothelial system.A generalized phagocytic system is seen in more abundance in those tissue areas where large quantities of toxins,particles and other unwanted compounds must be killed.

MACROPHAGES IN THE SKIN ANDSUBCUTANEOUS TISSUES(HISTIOCYTES)

If infection starts in a subcutaneous tissue, local inflammation sets in leading to the in situ division of skin tissue macrophages. Histiocyteseventually attack and kill the infections agentsin the skin.

MACROPHAGES IN THE LYMPHATIC TISSUE

If the particles are not killed locally in the tissues, they can enter the lymph and flow to the lymph nodes situated intermittently along the course of the lymph flow. The trapping of the foreign particles takes place in these lymph nodesin a meshwork of sinuses lined by tissue macrophages.

MACROPHAGES IN THE LIVER SINUSOIDS (KUPFFER CELLS)

Large number of bacteria from ingested food constantly pass through the digestive tract mucosa into the portal blood. Before entry of this blood into the general circulation, it passes through the liver sinusoids which are lined with tissue macrophages termed as 'kupffer cells'. Almost none of the bacteria from GIT passes from portal blood into general circulation.

ALVEOLAR MACROPHAGES IN THE LUNGS

More number of tissue macrophages are integral to the alveolar walls. Once the particles are trapped in the alveoli, only then alveolar macrophages execute phagocytosis. If the particle is not digested due to large size, the macrophages create a giant cell capsule around the particle and this large sized particle is dissolved slowly.

MACROPHAGES OF THE SPLEEN AND BONE MARROW

If an invading organism by chance enters the general circulation, the other lines of defense of tissue macrophage system is present in the spleen and bone marrow.In these tissue, the trapping of macrophages happens with the help of reticular meshwork of the two organs.

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