Topic 3. Blood

Control questions

1. Connective tissues group. Classification, common features.
2. Main functions of blood and it`s development.
3. Plasma.
4. Classification of blood cells.
5. Erythrocytes. Their structure and functions.
6. Platelets. Their structure and functions.
7. General properties of leukocytes and their classification.
8. Neutrophils. Their structure and functions.
9. Eosinophils. Their structure and functions.
10. Basophils. Their structure and functions.
11. Lymphocytes. T- и B-lymphocytes, their participation in immunological responses.
12. Monocytes. Mononuclear phagocyte system.
13. Hemogramm. Disposal of leukocytes.

Question 1. Connective tissues group. Classification, common features.

Connective tissue is classified into 5 principal subtypes of connective tissues:

I. Connective tissue proper:
   1. Loose connective tissue
   2. Dense connective tissue:
      a) irregular;
      b) regular.

II. Specialized connective tissue:
   1. Adipose tissue;
   2. Reticular tissue;
   3. Elastic tissue.

III. Embryonic connective tissues:
   1. Mesenchymal connective tissue;
   2. Mucous connective tissue.

IV. Supporting connective tissues:
   1. Cartilage tissue;
   2. Bone tissue.

V. Hematopoietic tissues:
   1. Blood;
   2. Bone marrow [3].

Common features (characteristics) of connective tissues:

1. Mesenchymal origin;
2. Extensive intercellular substance called an extracellular matrix (ECM);
3. Participation in support of organism homeostasis.

Question 2. Main functions of blood and it`s development.

Blood is liquid connective tissue. Blood is developed from the mesenchym and performs next functions:

1) delivery of nutrients and oxygen to cells;
2) transport of wastes and carbon dioxide away from cells;
3) delivery of hormones and other regulatory substances to and from cells and tissues;
4) maintenance of homeostasis participating in coagulation and thermoregulation;
5) protection of the body from pathogenic agents, foreign proteins, and transformed cells (i.e., cancer cells).

Question 3. Plasma.

Plasma is the liquid extracellular substance of the blood. The relative volume of the blood cells and plasma in blood is approximately 45% and 55%, respectively. Low hematocrit values often reflect reduced numbers of circulating erythrocytes (a condition called anemia) and may indicate significant blood loss caused by internal or external bleeding.

Most part of the plasma (90%) consists of water. It also contains proteins, gases, electrolytes, nutrients, hormones etc.

The plasma proteins are divided into three major groups designating as the fibrinogens, globulins and albumins. Fibrinogens are made in the liver and their function is blood clotting. Albumins are also made in the liver and have a fundamental role in maintaining the osmotic pressure of the blood. Albumin also acts as a carrier protein; it binds and transports hormones, metabolites, and drugs.

Globulins of plasma include the ά, β and γ globulins. γ globulins are immunoglobulins. The immunoglobulins are antibodies, a class of functional immune-system molecules secreted by plasma cells. ά and β globulins are nonimmune globulins secreting by the liver. They help maintain the osmotic pressure and also serve as carrier proteins for various substances.

Question 4. Classification of blood cells.

Blood's cells and their derivatives are called formed elements. They are cells (leukocytes or white blood cells) and postcellular structures (erythrocytes or red blood cells and platelets or thrombocytes).

Question 5. Erythrocytes. Their structure and functions.

Erythrocytes are the most numerous formed elements of blood. Erythrocytes or red blood cells are anucleate cells devoid of typical organells. They function to bind oxygen for delivery to the tissues and bind carbon dioxide for removal from the tissues. Erythrocytes transport oxygen and carbon dioxide bound to the protein hemoglobin which makes up about 33 per cent of the erythrocyte mass.

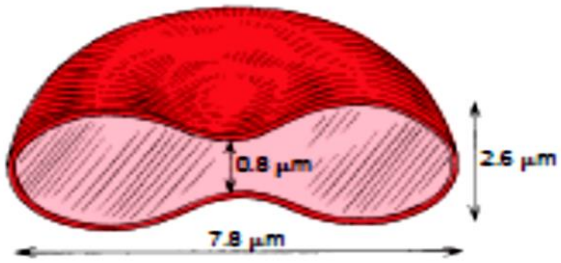

Figure 3.1. Diagram of discocyte [13].

The most numerous erythrocytes (about 80 per cent) have a shape of biconcave disks. They are discocytes. This unusual biconcave shape provides a large surface area relative erythrocyte volume and thus facilitating gas exchange. However, in normal condition about 20% of blood erythrocytes have another shape – spherical, flattened, bell-like, spiny configuration. The condition of blood, when the discocytes become less than 80% is known as poikilocytosis.

The most numerous erythrocytes (about 75 per cent) have diameter 7,8 мm. But in H&E-stained smears of blood the erythrocytes are usually 7 to 8 мm in diameter. They are called normocytes. Erythrocytes smaller then 7 мm in diameter are termed microcytes and erythrocytes larger then 8 мm in diameter known as macrocytes. The condition of blood, when the normocytes become less than 75% is known as anisocytosis.

The life span of erythrocytes is 120 days, after most of them are phagocytosed by macrophages in the spleen, bone marrow, and liver. Only about 10% of aged erythrocytes break down intravascularly.

The young erythrocytes are called reticulocytes. Normally they constitute about 1% of the total number of circulating erythrocytes. Reticulocytes have a netlike structure, which is the remnants of organelles, containing ribosomal RNA. Increased numbers of reticulocytes indicate haemorrhage in the organism.

Question 6. Platelets. Their structure and functions.

Platelets or thrombocytes are small, membrane-rounded anucleated cytoplasmic fragments, derived from the giant cells of bone marrow called megakaryocytes. After entry into the vascular system from the bone marrow, the platelets circulate as discoid structures about 2 to 3 мm in diameter. Their life span is about 10 days.

Structurally, platelets may be divided into four zones based on organization and function:

1) The peripheral zone;
2) The structural zone;
3) The organelle zone;
4) The membrane zone [13].

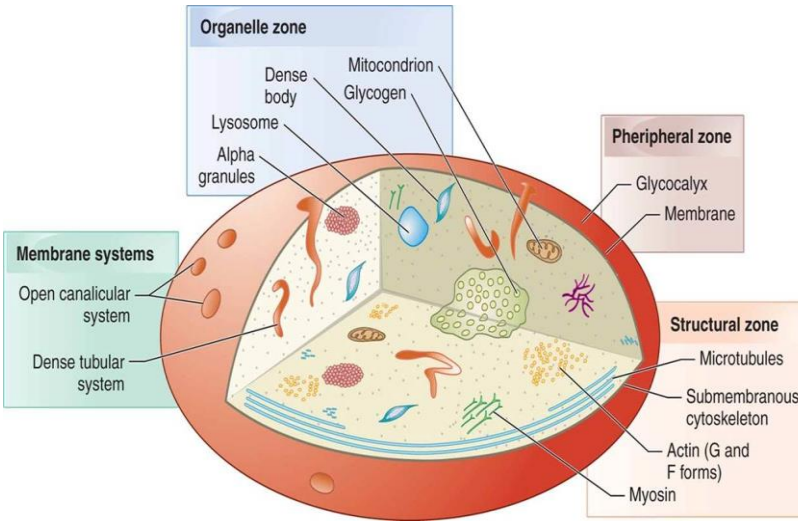

Figure 3.2. Diagram of platelet [11].

The **peripheral zone** consists of plasma membrane and glycocalyx.

The **structural zone** comprises microtubules, actin and myosin filaments that form a network supporting the plasma membrane.

The **organelle zone** occupies the center of the platelet. It consists of mitochondria, peroxisomes, glycogen particles and granules.

The **membrane zone** consists of two types of membrane channels. They are open canalicular system and dense tubular system. Both they are important in regulation of the intraplatelets calcium consentration.

The most numerous granules of platelets are alpha granules that contain fibrinogen, plasminogen, coagulation factor and platelet-derived growth factor. The alpha granules play an important role in the vessels repair, blood coagulation and platelet aggregation [13].

The main functions of the platelet are blood clot formation, and repair of injured tissues.

Question 7. General properties of leukocytes and their classification.

Unlike other formed elements of blood, the leukocytes are white blood cells, because all they contain a nucleus. Leukocytes are involved in defense of the organism against foreign material.

An important property of leukocytes is motility. Leukocytes may leave the capillaries and small venules by passing between endothelial cells and can migrate through the connective tissue where they perform specific functions. The leukocytes in loose connective tissue are normal cellular components. Motility and capability to the phagocytosis are provided by well developed cytoskeleton of leukocytes.

Classification of leukocytes

Leukocytes are classified into 2 groups:

1) Granulocytes that contain specific granules in cytoplasm;
2) Agranulocytes that luck specific granules.

According to the staining of their specific granules, all granulocytes are divided into neutrophils, eosinophils, and basophils. The nuclei of granulocytes have 2 or several lobes or segments.

Agranulocytes includes lymphocytes and monocytes. Their nuclei are round or bean shaped.

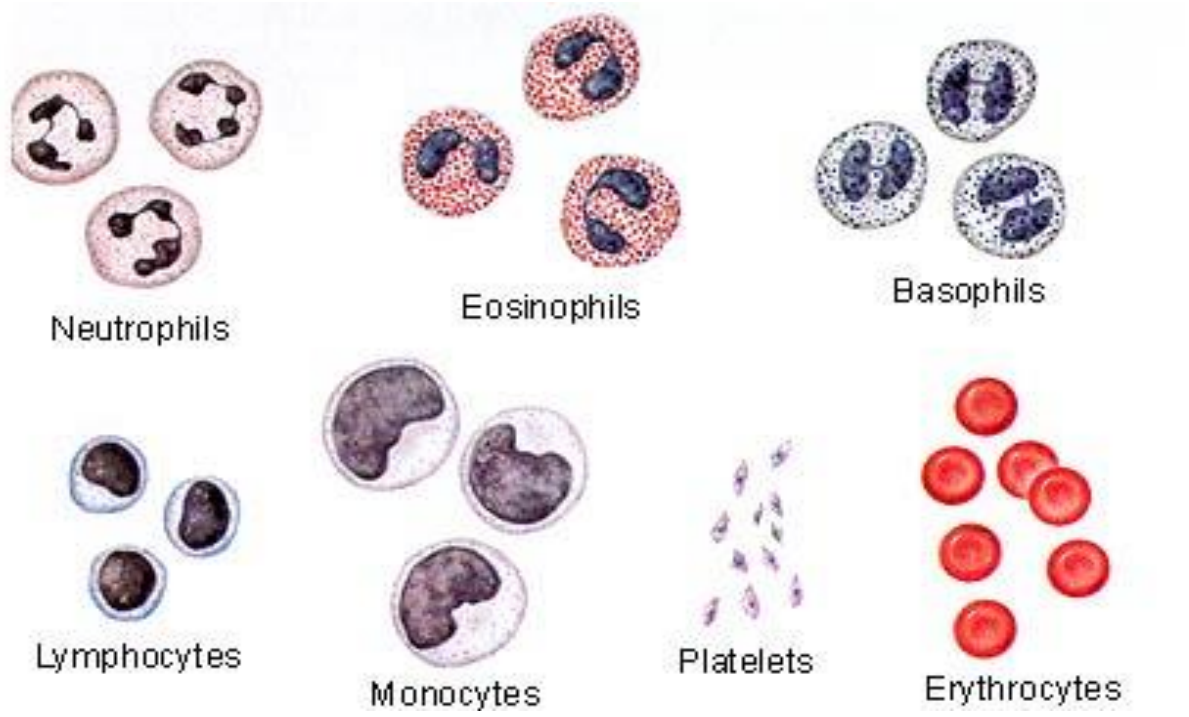

Figure 3.3. Diagram of peripheral blood cell types.

Question 8. Neutrophils. Their structure and functions.

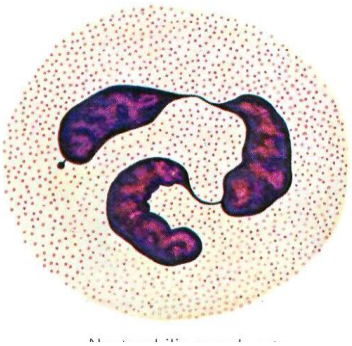

Figure 3.4. Diagram of neutrophil [7].

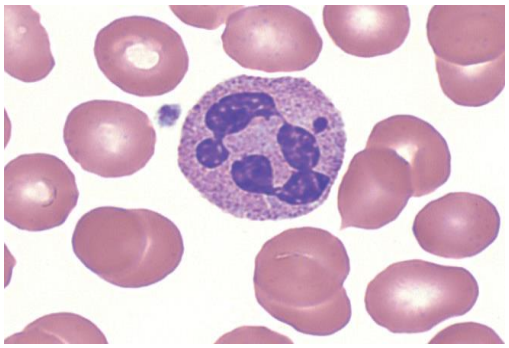

Figure 3.5. Photomicrograph of a human blood smear [14].

Neutrophils are the most of circulating leukocytes. Typically, 54% to 62% of leukocytes are mature neutrophils with a nucleus consisting of 2 to 5 lobes. However, 3% to 5% of leukocytes are immature neutrophils with a band like nucleus. Increase in number of immature leukocytes in blood is called shift to the left. Absence of immature leukocytes in blood is called shift to the right [14].

Diameter of neutrophils is 10-12 μm.

In women, on one of the nuclear neutrophil lobes there is Barr body. Barr body is condensed, single, inactive X chromosome [17].

The neutrophil is an active phagocyte and its cytoplasm contains numerous granules providing this function. The cytoplasm of the neutrophil contains 2 types of granules - specific and nonspecific granules. The presence of specific granules is indicated by the salmon-pink color of the cytoplasm. Specific granules contain alkaline phosphatase and bacteriostatic agents or antimicrobial peptides (lactoferrin, lysozyme etc).

Nonspecific or azurophilic granules are primary lysosomes containing enzymes: acid phosphatase, myeloperoxidase, cationic antibacterial proteins called defensins [13]. Nonspecific granules are identical in all types of leukocytes.

Neutrophils are the most numerous first cells to enter the inflammatory site. They constitute the first line of defense against invasion by microorganisms, especially bacteria. Neutrophils are active phagocytes of small particles and have sometimes been called microphages. Phagocytosis begins with recognition and attachment of foreign material (bacterium), mainly by Fc receptors that interact with the Fc region of antibodies that coat bacterial surfaces. C3b receptors of neutrophils facilitate binding C3b-coated bacterium [13].

Main neutrophils functions are:

1. Antibacterial defense;
2. Regulatory function (neutrophils release the cytokines).

Neutrophils are short-lived cells. Duration of neutrophils in blood sirculation is a few hours, life span is about 8 days. Neutrophils die soon after they have phagocyted materials.

Question 9. Eosinophils. Their structure and functions.

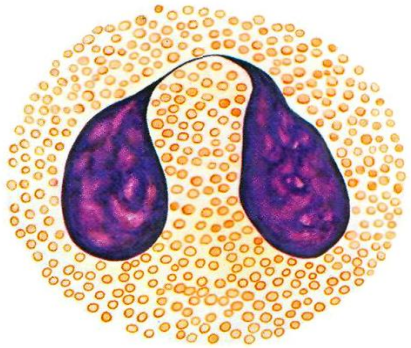

Figure 3.6. Diagram of eosinophil [7].

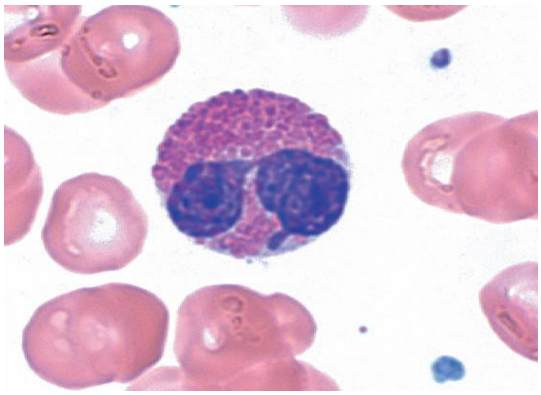

Figure 3.7. Photomicrograph of a human blood smear [14].

Eosinophils amount is 1-3% of circulating leukocytes. Diameter of eosinophils is 9-14 μм. Life span is a few days. A nucleus of eosinophils consists of 2 to 3 lobes.

Eosinophils contain both nonspecific (azurophilic granules) and large specific granules in their cytoplasm. Specific granules of eosinophils are stained with acidic dyes. Specific granules of eosinophils have elongated shape. The center of these granules contains a crystalline body that is seen with the electron microscope. Specific granules of eosinophils contain the major basic protein (MBP), eosinophil cationic protein (ECP) and enzymes: eosinophil peroxidase (EPO), histaminase, arylsulfatase, and so on. MBP, ECP, and EPO have a cytotoxic effect on protozoans and helminthic parasites. Histaminase neutralizes the activity of histamine, arylsulfatase neutralizes the action of SRS-A [13].

Eosinophils release arylsulfatase and histaminase at condition of allergic reaction, thereby limiting effects of vasoactive agents. Thus, the amount of eosinophils in blood increases at allergies and parasitic infections.

Main neutrophil functions are:

1) Antiparasitic defence;
2) Moderation of inflammation in allergic reaction [3].

Question 10. Basophils. Their structure and functions.

Figure 3.8. Diagram of basophil [7].

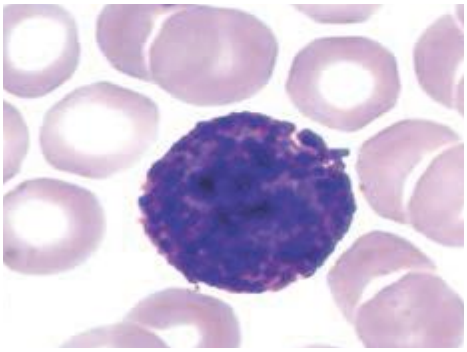

Figure 3.9. Photomicrograph of a human blood smear [14].

Basophils are the least numerous blood leukocytes – 0-1%. Diameter of them is 8-10 μм. Life span is a few days. A nucleus of basophils consists of 2 to 3 lobes.

Basophils contain both nonspecific or azurophilic granules and large specific granules in their cytoplasm.

Specific granules of basophils are stained with basic dyes. Specific granules of basophils contain heparin, histamine, slow reacting substance of anaphylaxis (SRS-A).

Heparin (a sulfated glycosaminoglycan) is an anticoagulant. Histamine is vasoactive agent, which brings on the dilation of small blood vessels and increases the permeability of capillaries and small venules. SRS-A causes the slow contraction of smooth muscles in the pulmonary airways.

Basophils are related, but not identical, to mast cells of the connective tissue. Both the mast cells and the basophiles bind an immunoglobulin E (IgE), which is produced by lymphocytes in the presence of the allergen in organism. It leads to degranulation to release the basophiles specific granules agents into surrounding tissue. Histamine and another vasoactive agents cause the vascular disturbances associated with immediate hypersensitivity reactions and anaphylaxis [13].

Main basophils functions are:

1) Regulation of permeability of the blood vessels;
2) Participation in the inflammatory response;
3) Participation in immune (allergic) response.

Question 11. Lymphocytes. T- and B-lymphocytes, their participation in immunological responses.

Figure 3.10. Diagram of lymphocyte.

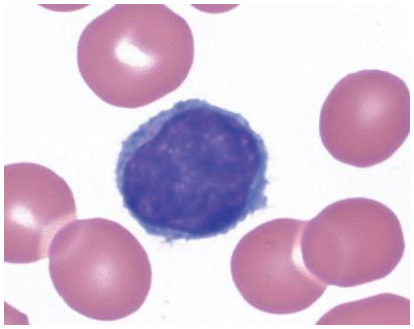

Figure 3.11. Photomicrograph of a human blood smear [14].

Lymphocytes are the main functional cells of the immune system. Lymphocytes amount is 25-33% of circulating leukocytes. Three groups of lymphocytes can be identified according to size: small (5-6 μm in diameter), medium and large (> 10 μm in diameter). In the bloodstream more than

90% - are small lymphocytes. Life span of lymphocytes is a few days to a few years.

The lymphocyte has an intensely staining, spherical nucleus surrounding by a thin rim of pale blue cytoplasm. The cytoplasm contains free ribosomes, a few mitochondria and other organelles.

According their differentiation and functions lymphocytes can be subdivied to three functional categories:

1) T lymphocytes (T cells) differentiating in the thymus. T-cells have a long life-span and are involved in cell-mediated immunity (70-80%);

2) B lymphocytes (B cells) differentiating in the bursa of Fabricius in birds or in the bursa-equivalent organs (bone marrow) in mammals. B-cells have variable life-span and are involved in the humoral immunity, producing antibodies (10-20%);

3) Natural killer cells (NK) are differentiated in bone marrow and are programmed to kill certain types of virus-infected cells and some types of tumor cells (5-10 %) [13].

Several different types of T lymphocytes have been identified:

1) cytotoxic T lymphocytes (T-killer cells);

2) helper T lymphocytes;

3) suppressor T lymphocytes.

Main events of T lymphocytes differentiation in thymus and B lymphocytes differentiation in bone marrow are expression of membrane surface receptors. Receptors of the lymphocytes can be divided into two main groups:

1) Specific receptors of lymphocytes for recognizing and binding with the antigens;

2) Marker receptors or CD receptors providing interaction and cooperation of lymphocyte with other immune cells.

Specific receptors of T lymphocytes are called T-cell receptors (TCRs). Specific receptors of B lymphocytes are called B-cell receptors (BCRs). BCRs are represented by IgM and IgD.

Marker receptors are cluster of differentiation (CD) molecules. They are specific markers designated by numbers according to an international system.

Cytotoxic T lymphocytes specific markers are CD8. Helper T lymphocytes specific markers are CD4. B lymphocytes specific markers are CD9, CD19, CD20, and CD24. NK cells have not specific receptors as in T- and B- lymphocytes. Their specific markers include CD16, CD56, and CD94 [13].

NK cells are larger than B and T cells (about 15 μm in diameter) and have a kidney-shaped nucleus. Because NK cells have several large azurophillic cytoplasmic granules they are also called large granular lymphocytes (LGLs).

Cytotoxic T lymphocytes are effector cells in cellular immunity. They attack and destroy other foreign cells (fungi, virus infected cells, tumor cells or cells of another individual) to the host body.

Helper T lymphocytes are cells inducing the reactions of immunity;

Suppressor T lymphocytes have a role opposite to that of helper T lymphocytes. They suppress the activities of B lymphocytes and of other T lymphocytes.

B lymphocytes are cells differentiating into plasma cells that are effector cells in humoral immunity.

Long-living lymphocytes are called memory T- cells and memory B-cells. The memory cells do not participate in primary immune response to a specific antigen. Particles, which are foreign for our organism (foreign cells or substances) are called antigens.

Memory T- cells and memory B-cells are programmed to be ready to differentiation into effector cells when the same antigen should appear in organism again. Its secondary immune response that is more rapid and more intense than primary [13].

Question 12. Monocytes. Mononuclear phagocyte system.

Figure 3.12. Diagram of monocyte.

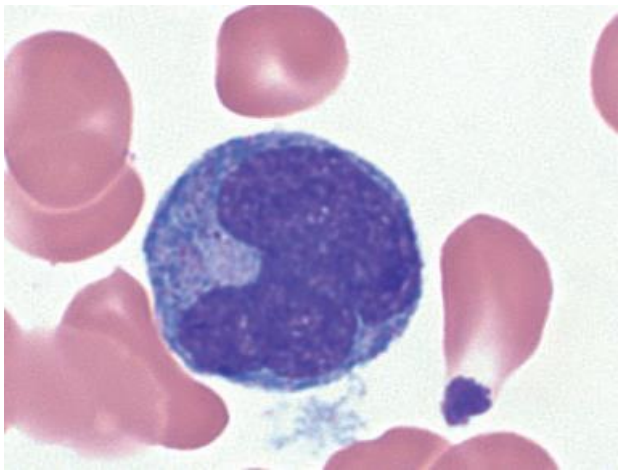

Figure 3.13. Photomicrograph of a human blood smear [14].

Monocytes are the largest leukocytes. Diameter of monocytes is 12-15 μm. Monocytes amount is 3-7% of circulating leukocytes. Life span is a few hours to a few days before differentiating of monocytes into macrohpages. A large amount of rough endoplasmic reticulum and azurophilic granules or primary lysosomes is present in monocytes cytoplasm. The nucleus of the monocyte is typically indented and often has a bean shape.

Blood monocytes are the precursors of the all tissues phagocytes or macrophages that belong to the mononuclear phagocytotic system of organism.

Mononuclear phagocyte system includes:

1. Monocytes of blood;
2. Histiocytes of connective tissue;
3. Kupffer cells of the liver;
4. Microglial cells of the central nervous system;
5. Macrophages of lungs alveoli;
6. Spleen, lymph nodes, bone marrow macrophages;
7. Macrophages pleural, peritoneal, and synovilal fluids;
8. Dendritic cells of the epidermis [13].

Functions of monocytes are:

1) Nonspecific protection against microbes, tumor and virus-infected cells;
2) Participation in immune responses in the role of antigen-presenting cells;
3) Phagocytosis of old and dead cells;
4) Regulatory function.

Question 13. Hemogramm. Disposal of leukocytes.

Hemogramm

Erythrocytes (per 1 l)	Hemoglobin (Hb) (g/l)	Reticulocytes (%)	ESR mm/hr	Platelets (per 1 l)	Leukocytes (per1 l)	Hematocrit (%)
4 - 5,5 $x10^{12}$	130-160	1-2	5-9	150-450 $x10^{9}$	4-9 x 10^{9}	35-50

ESR – erythrocyte sedimentation rate

Disposal of leukocytes (Leukocyte formula (%))

Neutrophils (%)			Eosinophils (%)	Basophils (%)	Lymphocytes (%)	Monocytes (%)
primary	band	mature				
0	3-5	54-62	1-3	0-1	25-33	3-7