

The lymphoid system consists of cells, tissues, and organs that protect the internal environment against invasion and damage by foreign substances. Certain cells of this system are known as immunocompetent cells. They have the capacity to distinguish различать between "self" and "nonself" and to provide the inactivation or destruction of foreign materials. Immunity is this protective response, and the lymphoid system is called the immune system.

In general, lymphoid tissues and organs consist of a framework of reticular fibers secreted by "reticular cells," which have mesenchymal origin. The "epithelial reticular cells" of the thymus are an exception исключение to this generalization общего правила. Lymphocytes, macrophages, antigen-presenting cells, and plasma cells situated in spaces between the reticular cells and fibers.

Lymphoid organs may be encapsulated or unencapsulated. Encapsulated lymphoid organs are the spleen and lymph nodes. Unencapsulated lymphoid organs include tonsils, Peyer's patches in the ileum, and lymphoid nodules found in the mucosa of the alimentary, respiratory, urinary, and reproductive tracts.

There are 2 different systems of immunity. The first is cellular immunity, in which living cells interact with and destroy foreign cells. This category of immunity is provided by T-lymphocytes. The other class is called humoral immunity because specific circulating immunoglobulins (antibodies) interact with foreign substances and promote their inactivation or destruction. B-lymphocytes differentiate into plasma cells after encountering a foreign substance. Plasma cells then synthesize and secrete the immunoglobulins. In most cases, B lymphocytes require the cooperation of T lymphocytes to produce antibodies. The cellular and humoral immune systems also require accessory cells, such as macrophages and antigen-presenting cells, for an optimal response to occur.

There are central and peripheral lymphoid organs. A central are bone marrow and the thymus. In these organs the lymphoid precursors undergo antigen-independent proliferation and acquire surface receptors that mark them as committed to the cellular or humoral immune response.

The thymus is the organ in which the lymphocytes take on the capacity of

participating участия in the cellular immune response. These cells belong to category of T lymphocytes.

The progenitor cells for the humoral immune response are called B lymphocytes because they are differentiate in the bone marrow.

After the lymphocytes leave central lymphoid organs and populate the peripheral lymphoid organs. Peripheral organs include lymph nodes, spleen and mucosa-associated lymphatic tissue organs. In these organs, the lymphocytes undergo antigen-dependent differentiation to produce the effector cells – T- killers and plasma cells.

Bone marrow

In our organism, the bone marrow is located in intercommunicating spaces of sponge bones that are covered by loose connective tissue. Thin connective tissue septa containing large amount of sinusoidal capillaries penetrate into bone spaces. Sinusoids of bone marrow have large diameter and discontinued basal membrane and endothelium in their walls. They provide the exit of mature blood cells from bone marrow into bloodstream.

The bone marrow is represented by myeloid tissue. Myeloid tissue consists of stroma, blood vessels and cords of hemopoietic cells at different stages of their development. Stromal component of bone marrow myeloid tissue is represented by reticular tissue forming a framework. Reticular tissue consists of reticular cells and reticular fibers. Reticular cells have stellate shape and form the intercellular contacts by their processes. Reticular network performs the supportive and regulatory functions for developing blood cells of bone marrow. Reticular network performs a supportive function for developing blood cells. Also, phagocytic reticular cells regulate the processes of blood cells development in bone marrow.

Fat cells are scattered singly within the stroma of red bone marrow unlike yellow bone marrow where they produce the large concentrations.

Cells lying free within the meshes of the bone marrow represent all stages of red and white blood cells development. Maturing erythrocytes often surround the macrophage, forming erythroblastic islets. In these islets, the macrophages accumulate and then transmit the iron to the developing erythrocytes of bone marrow for

biosynthesis of hemoglobin.

The largest cells of bone marrow are called megakaryocytes. Bone marrow megakaryocytes lie along sinusoidal capillaries and extend their cytoplasmic processes through sinusoidal walls. The bits of megakaryocytes cytoplasm, known as platelets segregate from these cells into bloodstream.

THYMUS

The thymus is a bilobed lymphoepithelial organ located in the superior mediastinum, anterior to the heart and great vessels. The thymus is a central lymphoid organ. The lymphatic tissue of this organ consists of stromal component, presenting by epithelial reticular cells and T-lymphocytes.

Most lymphoid organs originate exclusively from mesenchyme, but the thymus has a dual embryologic origin. Its lymphocytes arise from mesenchyme, but epithelial reticular cells originate from the prechordal plate.

The thymus is fully formed at birth and functionally active until about the time of puberty. After puberty, this organ undergoes the process of involution, when T-cell differentiation and proliferation reduce and most of the lymphatic tissue is replaced by adipose tissue.

The thymus is surrounded by a thin connective tissue capsule. Connective tissue trabeculae extend from capsule into the parenchyma of the organ dividing it into multiple lobules. Each lobule is composed of a dark staining basophilic cortex and a lighter-staining eosinophilic medulla. Different staining of the cortex and medulla depends on the amount of T-lymphocytes in these two regions of the thymic lobules. The cortex contains numerous densely packed T-lymphocytes, whereas the medulla contains fewer T-lymphocytes.

Cortex

In thymic cortex T lymphocytes, also called thymocytes, occupy all spaces within an extensive meshwork of epithelial reticular cells. They are small lymphocytes.

Epithelial reticular cells have features of both epithelial and reticular cells. Stellate shape epithelial reticular cells are bound together by their processes, that produce an extensive network for the developing T lymphocytes. Desmosomes situate at the

communicating processes of epithelial reticular cells.

Epithelialreticular cells have large oval nuclei. Bundles of tonofilaments in the cytoplasm are evidence *доказательство* of the ectodermal origin of these cells. They have dense granules with thymic hormones (serum thymic factor, thymic humoral factor, thymopoietin, and thymosin). These hormones act to promote the antigen-independent differentiation of pre-T cells into mature T lymphocytes.

Macrophages reside within the thymic cortex also and they are responsible for phagocytosis of T lymphocytes that do not fulfill thymic education. These T lymphocytes are programmed to die before leaving the cortex. Approximately 98% of the T cells undergo this death by apoptosis and are then phagocytosed by the macrophages.

Medulla

The thymic medulla as the cortex, contains a large number of epithelial reticular cells and cloosely packed by T lymphocytes. However, the medulla stains less intensely because it contains mostly large T-lymphocytes. They are less numerous then in cortex.

The most characteristic feature of the thymic medulla is the thymic (Hassall's) corpuscles, that stain with eosin. Thymic corpuscles are isolated masses of closely packed, concentrically arranged epithelial reticular cells that exhibit flattened nuclei. The more central mass of the corpuscle contains fully keratinized epithelial reticular cells. Functionally the thymic corpuscles produce interleukins (IL-4 and IL-7) that function in thymic differentiation and education of T lymphocytes.

Blood–thymus barrier and T-cell education

T-lymphocytes reaching the thymic cortex via postcapillary venules are prevented from contact with antigen by a physical barrier called the blood–thymus barrier. The blood–thymus barrier there is between the T cells and the lumen of cortical blood vessels and it is formed by the following layers:

1. the capillary endothelium;
2. its basal lamina;
3. perivascular connective tissue containing macrophages;
4. the basal lamina of the epithelial reticular cells;

5. the cytoplasm of epithelial reticular cells.

Macrophages residing in the surrounding perivascular connective tissue may phagocytose antigenic molecules that escape from the capillary lumen into the cortical parenchyma.

The thymus is populated by T-prelymphocytes that originate from the bone marrow and are destined to develop into immunocompetent T cells. Maturation and differentiation of T-prelymphocytes into immunocompetent T cells is called thymic cell education. This process is characterized by the expression of specific surface CD molecules (antigens).

For antigen-independent differentiation in thymic cortex T lymphocytes express TCRs, and both CD4 and CD8 molecules on their surfaces. These cells are then presented with self- and foreign antigens by epithelioreticular cells. If the lymphocyte recognizes self- or foreign antigen, it will survive, a process called positive selection. If not, the cell will die in cortex. Cells that pass the positive-selection leave the cortex and enter the medulla. Here, they undergo another selection process in which cells that recognize self antigen displayed by self-MHC are eliminated, a process called negative selection. Cells that survive after selection are now ready for the immune response; they leave the thymus from the medulla and pass in peripheral lymphoid organs where become either cytotoxic CD8 T- lymphocytes or helper CD4 T- lymphocytes.

Hormonal substances secreted by epithelioreticular cells within the thymic (Hassall's) corpuscle promote the process of thymic cell education.

Peripheral lymphoid organs

Peripheral lymphoid organs include lymph nodes, spleen and mucosa-associated lymphatic tissue organs. Their main function is antigen-dependent differentiation.

Structural and functional unit of peripheral immune organs is lymphatic nodule or lymphatic follicle. Also, the lymphatic nodules can be found isolated in the loose connective tissue of several organs, mainly in the lamina propria of the digestive tract, upper respiratory tract, and urinary passages. They are composed of densely packed B lymphocytes that differentiate into plasma cells upon appropriate

antigenic stimulation.

Primary nodules or follicles are spherical or ellipsoid aggregations of cells, 0.2- 1 mm in diameter. In histologic sections, nodules are strongly stained basophilically by hematoxylin because consist of mainly B-lymphocytes which infiltrate the stromal component of follicles. The center of the nodule often shows a less densely stained region called the germinal center. This difference in staining of the central region is due to the presence here of activated B lymphocytes and B immunoblasts that have large, euchromatic nuclei. Many B immunoblasts in a germinal center are in mitosis. In response of antigen presenting in organ the B- lymphocytes differentiate into plasma cells and B memory cells. Both these cells are found mainly in the peripheral or mantle zone of secondary nodules. The mantle zone is composed of those small B lymphocytes which surround the germinal centers of secondary nodules. Nodules that contain germinal centers are called secondary nodules, whereas those lacking for не имеющие germinal centers are called primary nodules.

Except B lymphocytes and stromal component, the follicles contain macrophages and follicular dendritic cells. Follicular dendritic cells are nonphagocytic cells with multiple, thin, hairlike branching cytoplasmic processes that interdigitate between B lymphocytes in the germinal centers. Antigen–antibody complexes adhere to the dendritic cytoplasmic processes by means of the antibody’s Fc receptors, and the cell can retain antigen on its surface for weeks, months, or years. Follicular dendritic cells are not antigen-presenting cells because they lack MHC II molecules.

LYMPH NODES

Lymph nodes are encapsulated spheroid or kidney-shaped organs composed of lymphoid tissue. They are distributed throughout the body, always along the course of the lymphatic vessels.

The supporting elements of the lymph node are the capsule and the trabeculae. The capsule comprised of dense connective tissue, which surrounds the node. The trabeculae extend from the capsule into the substance of the node forming a framework.

Lymph node contains the lymphoid tissue. Lymphoid tissue of the lymph node

consists of 2 components. They are stromal component and developing T- and B-lymphocytes in stage of antigen-depending differentiation.

The stromal component is represented by reticular cells, that develop from mesenchyme.

Lymphatic vessels entering the node are designated afferent. They enter the node at various points on the convex surface of the capsule and percolates through the subcapsular sinuses, passes to the peritrabecular and medullary sinuses, and leaves the lymph nodes by the efferent lymphatic vessels.

Lymph nodes can be compared to filters through which lymph flows and is cleared of foreign particles before its return to the bloodstream.

Sinuses of a lymph node are irregular spaces incompletely lined by endothelium and containing a network of reticular tissue. Reticular cells and reticular fibers cross the sinuses, and macrophages also span in these spaces. The reticular tissue of sinuses provides more slow the flow of lymph through the node, thus facilitating содействуя take over захвату and digestion of foreign materials by macrophages.

The parenchyma of the lymph node is divided into cortex and medulla.

The cortex forms the outer portion of the node. It contains lymph nodules which are represented by reticular framework and infiltrating it lymphocytes, dendritic cells, follicular dendritic cells, macrophages and plasma cells.

The portion of the cortex adjacent to the medulla is free of nodules; it is called the deep cortex or the paracortical zone. This region contains most of the T lymphocytes and the deep cortex is also called the thymus-dependent cortex.

The medulla is the inner part of the lymph node. The medulla contains the cords of lymphatic tissue called medullary cords, separating by medullary sinuses.

The medullary cords contain lymphocytes (mostly B lymphocytes), macrophages, dendritic, and plasma cells, infiltrating the reticular tissue.

Thus, in lymph nodes the lymphatic nodules of cortex and medullary cords of medulla are the territories of B-lymphocytes; but paracortex is the territory of T-lymphocytes. Both B- and T-lymphocytes are present where the deep and nodular cortex meet.

Dendritic cells

Dendritic cells (DCs) or interdigitating cells are bone marrow–derived APCs. DCs monitor the local environment for foreign substances that they then process and present to antigen-specific T cells. They are much more efficient (i'ficz(ə)nt) in эффективны antigen presentation than other APCs. They express high level of MHC II and costimulatory molecules necessary for activation of T cells. In the lymph node, DCs are usually localized in T lymphocyte–rich areas.

Functions of lymph nodes

1. They are centres of lymphocyte production. Both B-lymphocytes and T-lymphocytes are produced here by multiplication of preexisting lymphocytes. These lymphocytes (which have been activated) pass into lymph and thus reach the blood stream.

2. Bacteria and other foreign matters are removed from lymph through phagocytosis by macrophages. Antigens thus carried into these cells that then 'presented' it's to lymphocytes stimulating their proliferation. In this way lymph nodes play an important role in the immune response to antigens.

3. Plasma cells (representing fully mature B-lymphocytes) produce antibodies against invading antigens, while в то время как T-lymphocytes are attack) the cells that are foreign to the our organism.

THE SPLEEN

In humans the spleen is the largest lymphatic organ and an important antibody-forming organ. It represents an important defense against microorganisms that penetrate the circulation. While lymph nodes serve служит as immunologic filters of the lymph, the spleen is the immunologic filter of the blood.

General Structure

The spleen is surrounded by a capsule of dense connective tissue from which trabeculae extend into the parenchyma of the organ. Capsule and trabeculae contain some amount of contractile cells myofibroblasts. These cells are not only contractile,

but they also produce the extracellular connective tissue fibers. In humans, these cells are not numerous. In mammals their contraction causes the expulsion of accumulated blood from the spleen, which serves to store blood cells.

Splenic Pulp

The parenchyma of the spleen consists of splenic pulp. Splenic pulp is divided into white pulp and red pulp.

The red pulp of the spleen consists of venous sinuses and pulp or splenic cords (Billroth's cords). Splenic cords consist of reticular tissue and blood cells.

The white pulp of the spleen is lymphoid tissue. Lymphoid tissue of the spleen also consists of 2 components. They are stromal component and developing T- and B-lymphocytes in stage of antigen-dependent differentiation.

The stromal component is represented by reticular cells, which are developed from mesenchym.

The white pulp of the spleen is represented by lymph nodules or Malpighian bodies and periarterial lymphoid sheaths. Lymph nodules are the territory (territory) of B-1. Periarterial lymphoid sheaths are the territory of T-1. The lymph nodules also have germinal center. The zone of red pulp surrounding lymph nodules is called marginal zone. The marginal zone contains numerous antigen presenting cells and in lymph nodules surrounded by sinusoids. Therefore in marginal zone the immune reactions are begun.

Blood Circulation

The splenic artery divides into trabecular arteries. When they enter the parenchyma are called the pulp arteries.

The pulp arteries are surrounded by a dense sheath of T-lymphocytes, called the periarterial lymphatic sheath (PALS). The part of pulp artery surrounded by PALS are known as the central artery or white pulp artery. The PALS has a cylindrical configuration. Along its course, the lymphocytic sheath surrounded by a dense of B-lymphocytes forming a lymphatic nodule in which the vessel occupies an eccentric position, although it is still called the central artery.

After leaving the white pulp, the central artery divides into a number straight **прямых** penicillar arterioles. Near their termination, the penicillar arterioles are surrounded by ellipsoid. The ellipsoid is a sheath of phagocytic cells whose function is to digest blood-borne particles.

The penidlli then continue as arterial capillaries, that continue into the splenic sinuses

There are two routes of blood circulation in spleen. In one, called the closed route, arterial capillaries open directly into the splenic sinuses and then drain into branches of the splenic vein. These branches enter the trabeculae veins, that continue into the splenic vein leaving the spleen.

In the open route, the arterial capillaries open and discharge blood into the splenic cords. As a result, blood passes through the spaces between the red pulp cord cells, coming into direct contact with lymphocytes and reticular cells there. Blood cells would then enter the sinuses by passing between the endothelial cells that constitute the wall of the sinus.

Splenic Functions

Splenic functions are:

- (1) Immune defense: lymphocyte production and antibody production.
- (2) phagocytosis of particulate matter in the blood,
- (3) the destruction of damaged and aged red blood cells,
- (4) blood cell formation during early fetal development.