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Establishment of education "Gomel state medical university"

Department of histology, cytology and embryology

MANUAL
for 1-st year students of faculty of foreign students on gynecology

Topic: 10:
HISTOPHYSIOLOGY OF PERIPHERAL ORGANS OF HEMATOPOIESIS AND IMMUNE DEFENSE

Duration 4 hours

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THE MOTIVATIONAL CHARACTERISTIC OF THE THEME

Blood, lymph and organs where are formed, and also the blood cells which have moved in tissues , make system of blood which participates in maintenance of a constancy of the internal environment of an organism and protection of genetic integrity. Practically any pathological process is reflected in a condition of system of blood that widely use in medicine for diagnostics of diseases.

THE PURPOSE

To define at a microscopic level the tissues of hemopoetic organs, to explain its role in formation of humoral and cellular immunity.

PROBLEMS

The student should know:

1) To state the unitary theory of hematopoiesis.
2) To explain mechanisms cellular and humoral immunity.

The student should be able:

1) To define at a microscopic level a structure of a lymph node and spleens, palatine tonsiLle.
2) To explain a role of hemopoetic organs in formation of humoral and cellular immunity.

REQUIREMENTS TO THE INITIAL LEVEL OF KNOWLEDGE

For full mastering a theme it is necessary for student to repeat from a rate of the general histology and functions of blood cells.

CONTROL QUESTIONS FROM RELATED SUBJECTS

1) The Structure of blood cells
2) Functions of blood cells
3) Properties steam blood cells
4) Concept about cellular immunity

CONTROL QUESTIONS ON THE THEME

1. Antigen dependent differentiation of lymphocytes
2. A role of macrophages in a differentiation of lymphocytes
3. Structure and functions of the lymphatic node.
4. Structure and functions of the spleen.
5. Structure and functions of the palatine tonsils.

THE PRACTICAL PART

1) The Scheme of a structure of the lymphatic node – to enter designations (Exercise № 2 in album)
2) The Scheme of blood supply of a spleen – to enter designations (Exercise № 4 in album)

SLIDES

1. The lymph node

2. The spleen
3. The palatine tonsile

QUESTIONS FOR SELF-CHECKING KNOWLEDGE

1. Structure of lymphatic follicles
2. Structure and functions of lymphatic node:
- cortex;
- paracortical zone;
- medulla;
- lymphatic sinuses.

3. Structure and functions of the spleen:
- features of blood supply;
- white pulp (T – и B – territories);
- red pulp;
- features of structure of the spleen sinuses;
- immune and another functions of the spleen.

4. Structure and functions of the palatine tonsils

HISTOPHYSIOLOGY OF PERIPHERAL ORGANS OF HEMATOPOIESIS AND IMMUNE DEFENSE

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*, comprised of dense connective tissue, which surrounds the node; the *trabeculae,* also comprised of dense connective tissue, which extend from the capsule into the substance of the node forming a framework.

Lymphatic vessels entering the node are designated *afferent. T*hey 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 blood circulatory system. Lymph formed in tissues must cross at least one lymph node before entering the bloodstream. Each node receives lymph from a limited region of the body of which it is said to be a satellite node. Malignant tumors often metastasizc via satellite nodes [1 – 3].

Sinuses of a lymph node are irregular spaces containing lymph that are incompletely lined by reticular cells and numerous macrophages. Reticular cells and their fibers cross the sinuses, and macrophages also span these spaces. The complex architecture of sinuses serves to slow the flow of lymph through the node, thus facilitating uptake and digestion of foreign materials by macrophages.

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

The lymph sinuses in the cortex are arranged in a special manner. Just under the capsule there is a lymph sinus interposed between the capsule and the cortical lymphocytes. This is called the *cortical* or *subcapsular sinus.* Afferent lymphatic vessels drain

lymph into this sinus. Other lymph sinuses extend through the cortex as *trabecular, or peritrabecular, sinuses* and drain into the medullary sinuses. Lymphocytes and macrophages, or their processes, readily pass between lymph sinuses and parenchyma of the lymph node. The sinuses have a lining of endothelium that is continuous where it is directly adjacent to the connective tissue of the capsule or trabeculae, but is discontinuous where it faces the lymphatic parenchyma. Even though a macrophage may be in the lymphatic parenchyma, it often sends pseudopods into the sinus through the endothelial discontinuities. These pseudopods monitor the lymph as it percolates through the sinus.

The *cortex* forms the outer portion of the node. It contains spherical or oval aggregates of lymphocytes called lymph nodules. In an active lymph node, these contain a lighter center called the germinal center [2].

The portion of the cortex adjacent to the medulla is free of nodules; it is called the *deep cortex.* Other names applied to the deep cortex are the paracortical zone. Nodules are the territory of B-lyrnphocytes; the deep cortex is the territory of the T-lymphocytes. Both B- and T-lymphocytes are present where the deep and nodular cortex meet.

Antigen-presenting cells, here called dendritic cells or interdigitating tells, are found in the paracortical areas of lymph nodes. Also found are the high-endothelial venules, which are described below [1].

The **medulla** consists of medullary cords, composed of closely packed lymphocytes and numerous plasma cells, and the intervening medullary sinuses, which receive and circulate the lymph from cortical sinuses. Medullary sinuses communicate with efferent lymphatic vessels through which lymph leaves the lymph node [3].

Histophysiology of Lymph Nodes

As lymph flows through the sinuses, 99% or more of the antigens and other debris are removed by the phagocytic activity of macrophages that span the sinuses.

As lymph filters through the nodules, the bulk of the antigenic material is destroyed by macrophages. Some antigen, however, is trapped on the surface of specialized cells known as follicular dendritic cells. This bound antigen is not phagocytized but is exposed on the dendritic cell surface where it may be recognized and acted upon by immunologically competent lymphocytes. If a B cell recognizes the antigen, under appropriate conditions the B lymphocyte may be activated. Activated B lymphocytes migrate to the germinal center and undergo a series of cell divisions and transformations that lead to the production of immature immunoblasts. These in turn divide and give rise to plasma tells and memory B lymphocytes. Plasma cells leave the germinal center and migrate into the medullary cords. Here, these cells actively synthesize specific antibodies and release them into the lymph flowing through the medullary sinuses. Memory B cells, which can secrete some antibody and also bind some to their surface, leave the nodule and flow with the lymph to reenter the blood circulatory system. The presence of memory cells provides for a more rapid and more persistent immunologic response when an antigen is next encountered. This is called a secondary immune response [1 – 3].

As a consequence of infection and antigenic stimulation, affected lymph nodes enlarge, reflecting the blood-borne lymphocytes, which are predominantly T cells, can repopulate the lymph nodes by leaving through specific venules in the paracortical zone of the lymph node. These vessels, post-capillary, or high-endothelial, venules, have an unusual endothelial lining consisting of tall cuboidal cells. Lymphocytes are capable of traveling between the endothelial cells of this vessel. Other lymphoid tissues, such as Peyer's

patches of the ileum, also possess high-endothelial venules. It has been shown that certain lymphocytes preferentially recirculate through different lymphoid tissues. Thus, peripheral lymph nodes have more T lymphocytes than B lymphocytes, whereas the reverse is true of Peyer's patches. This "homing" behavior is due to complementary molecules on the lymphocytes and the endothelial cells of postcapillary venules. Each type of lymphocyte has a different integral membrane glycoprotein at its surface that binds to carbohydrates on endothelial cells. The carbohydrates present on endothelial cells vary according to anatomic site. This receptor-ligand interaction results in the differential localization of B and T lymphocytes. Lymphocytes that pass between the endothelial cells of the venules penetrate the paracortical zone and medullary sinuses and leave the node via efferent lymphatics together with newly formed lymphocytes. In this way, most T lymphocytes recirculate many times. Recirculation of lymphocytes also occurs through venules found in the spleen, tonsils, and Peyer's patches of the ileum [4 – 6].

Function

1. They are centers 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 particulate matter are removed from lymph through phagocytosis by macrophages. Antigens thus carried into these cells are 'presented' 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 T-lymphocytes attack cells that are foreign to the host body [5, 6].

Infection In any part of the body can lead to enlargement and Inflammation of lymph nodes draining the area. Inflammation of lymph nodes is called lymphadenitis [3].

Carcinoma (cancer) usually spreads from its primary site either by growth of malignant cells along lymph vessels, or by 'loose' cancer cells passing through lymph to nodes into which the area drains. This leads to enlargement of the lymph nodes of the region. Examination of lymph nodes gives valuable information about the spread of cancer. In surgical excision of cancer lymph nodes draining the region are usually removed [1].

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 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 which sends out trabeculae. They contain some smooth muscle 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 certain other mammals (cat, dog, horse) they are quite abundant, and 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. This, in turn, is divided into *white pulp* and *red pulp.* In a fresh section of the spleen one can observe white spots. These are lymphatic nodules. Mainly the white pulp is a complex of lymphatic nodules. These nodules are called *Malpighian bodies. Each* nodule has a germinal centre and a surrounding cuff of densely packed lymphocytes.

These nodules appear within the dark red tissue, rich in blood, called the red pulp. The red pulp is like a sponge. It is composed of elongated structures, the splenic cords (Billroth's cords), which lie between the *venous* sinusoids. The cords form a network. The splenic cords consist of a framework of reticular cells and reticular fibers containing large numbers of erythrocytes, macrophages, lymphocytes, plasma cells, and granulocytes [3].

Blood Circulation

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

For some distance each arteriole is surrounded by a dense sheath of lymphocytes. These parts of the vessels are known as the central arteries or white pulp arteries. The aggregated population of lymphocytes around the central artery are designated as the periarterial lymphatic sheath (PALS). The PALS has a roughly cylindrical configuration**.** Along its course, the lymphocytic sheath may thicken to form a lymphatic nodule in which the vessel occupies an eccentric position, although it is still called the central artery.

Nodules are the territory of B-lymphocytes; lymphocytes of the PALS are chiefly T-lymphocytes, The nodules usually contain germinal centers and, as in other lymphatic organs, the germinal center is a reaction center that forms in response to antigen, In the human, the germinal centers may become extremely large and visible with the naked eye.

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

Distal to the ellipsoid the vessel dilates to form an *ampulla.* The penidlli then continue as arterial capillaries.

The exact route whereby blood moves from the arterial capillaries into the splenic sinuses is not yet clear. Two routes have been proposed and both may in fact be operational. 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, ultimately converge into larger veins, and leave the spleen as the splenic vein [4 – 6].

In the proposed route, 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 [3].

The *sinusoids* of the spleen, or venous sinuses are lined by unusually cells. *The endothellal cells* here are elongated and are shaped like bananas. *They* are arranged with their longitudinal axis parallel to the direction of the vessel *and are referred to as stave cells. T*he splenic sinuses are surrounded by thick, ring-like fornications of basal lamina material. The endothelial cells have not tightly adherent to their neighbors and they allow blood cells to pass into and out of the sinuses quite readily. The fibrils in their cytoplasm may help to alter the shape of the endothellal cells thus opening or closing gaps between ad-

joining cells.

Also, the processes of macrophages extend between the endothelial cells and into the lumen of the sinuses to monitor the passing blood.

The zone of red pulp immediately surrounding white pulp is the ***marginal zone,*** This zone has a rich network of sinusoids. Numerous antigen presenting cells are found close to the sinusoids. This region seems to be specialized for bringing antigens confined to circulating blood (eg., some bacteria) Into contact with lymphocytes in the spleen so that an appropriate Immune response can be started against the antigens [1 – 4].

Splenic Functions

Splenic functions are:

– immune defense: lymphocyte production and antibody production;

– in phagocytosis of particulate matter in the blood;

– the destruction of damaged and aged red blood cells;

– blood cell formation during early fetal development.

Despite this variety of functions the spleen is not essential to life and can be surgically removed if necessary. Surgical removal of the spleen (splenectomy) reduces the ability of the body to deal with blood borne infections.

Since it contains both B and T lymphocytes and macrophages, the spleen is important in body defense. In the same way that lymph nodes "filter" the lymph, the spleen is considered as a "filter" for the blood.

Under the stimulus of antigens, splenic B lymphocytes proliferate and give rise to antibody-producing plasma cells.

Of all the phagocytic cells of the organism, those of the spleen are most active in the phagocytosis of living particles (bacteria and viruses) and inert particles that find their way into the bloodstream [3].

When there is an excess of lipids in the blood plasma (hyperlipidemia), the macrophages of the spleen accumulate considerable quantities of these substances. In diabetes, hyperlipidemia is frequent, and for this reason large macrophages, their cytoplasm containing numerous lipid droplets, are common in the spleens of diabetics.

The spleen acts as a filter for worn out red blood cells. Normal erythrocytes can change shape and pass easily through narrow passages in penicilli and ellipsoids. However, cells that are aged are unable to change shape and are trapped in the spleen where they are destroyed by macrophages.

The macrophages of the red pulp cords engulf entire pieces of the erythrocytes that frequently fragment in the extracellular spaces. The engulfed erythrocytes are digested by lysosomes of the macrophages. The hemoglobin is broken down. The protein part, globin, is hydrolyzed to amino acids that are reutilized for protein synthesis. Iron is released from heme and is transported in blood, in combination with transferrin, to the bone marrow, where it is reused in erythropoiesis. Iron-free heme is metabolized to bilirubin, which is excreted by liver cells in the bile.

In fetal life the spleen is a centre for production of *all* blood cells. In later life only lymphocytes are produced here [1, 4, 6].

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