Ministry of health Republic of Belarus
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: 9:
HISTOPHYSIOLOGY OF THE CENTRAL ORGANS OF HEMATOPOIESIS AND IMMUNE DEFENSE

Duration 4 hours

Authors:
Associate Professor Ph.D. Kravtsova I.L.
Associate Professor Ph.D. Solodova E.K.

Gomel 2022

THE M0TIVATIONAL 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 central organs of hemopoiesis and immunity, to explain its role in development of T- and B-lymphocytes.

PROBLEMS

The student should know:

1) To state the unitary theory of hematopoiesis.
2) Organization of myeloid and lymphatic tissue.
3) To explain development, structure, tissue and functions of red bone marrow and thymus.

The student should be able:

1) To define at a microscopic level a structure of bone morrow, thymus.
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. Concept about the central and peripheral hemopoetic organs
2. A structure, development and fabric structure of bone marrow
3. Function of bone marrow
4. A structure, development, and structure of thymus.
5. Influence of some hormones on thymus.
6. Antigen dependent differentiation of lymphocytes
7. Antigen independent differentiation of lymphocytes
8. A role of macrophages in a differentiation of lymphocytes

THE PRACTICAL PART

1) The Scheme of a structure of a bone morrow- to enter designations (Exercise №1 in album)

2) Microscopy histological preparations and their sketch in an album (Exercise № 2,3 in album)

3) The Scheme of a structure of blood thymus barrier – to enter designations (Exercise №4 in album)

4) The Scheme of organization of hemopoietic tissue (Exercise 5 in album)

SLIDES

1. Bone marrow
2. Thymus

QUESTIONS FOR SELF-CHECKING KNOWLEDGE

Conception about central and peripheral parts of monogenesis

1. Stages of differentiation of the lymphocytes.
2. Myeloid and lymphoid tissues.
3. Structure, development, tissues and functions of red bone marrow.
4. Structure, development and functions of thymus:

- Lobules of thymus
- Cell structure of the cortex
- Cell structure of the medulla
- Features of blood supply

HISTOPHYSIOLOGY OF THE CENTRAL ORGANS OF HEMATOPOIESIS AND IMMUNE DEFENSE

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, since they have the capacity to distinguish between "self" and "nonself" and to provide for the inactivation or destruction of foreign materials. **Immunity** is this protective response, and the lymphoid system is sometimes called the immune system.

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

Lymphoid organs may be either encapsulated or unencapsulated. Examples of the former include the spleen and lymph nodes. Unencapsulated lymphoid organs s 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 but related systems of immunity. The first is cellular immunity, in which living cells interact with and destroy foreign cells. This category of immunity is mediated 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 pro-

duce 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 this organs lymphoid precursors undergo antigen-independent proliferation and acquire surface antigens that mark them as committed to either the cellular or humoral immune response. The thymus is the organ in which lymphocytes take on the capacity of participating in the cellular immune response. These cells are referred to as T lymphocytes. The progenitor cells for the humoral immune response are called B lymphocytes because they differentiate in the bone marrow.

Lymphocytes leave central lymphoid organs and populate the peripheral lymphoid organs. Peripheral organs include lymph nodes, spleen and lympho-epithelial organs. In these organs lymphocytes undergo antigen-dependent differentiation and form effector cells – T- killers and plasma cells [1].

Thymus

The thymus is a central lymphoid organ. It consists of incomplete lobules partially separated by septa derived from the connective tissue capsule.

While other lymphoid organs originate exclusively from mesenchyme, the thymus has a dual embryologic origin. Its lymphocytes arise from mesenchyme. An epithelial reticular cells takes its origin from the prechordal plate.

The intense lymphocytic proliferation during embryonic and pre-pubertal development pushes apart the epithelial cells. Since these cells are bound together by desmosomes, they remain attached to each other at the ends of their processes, creating an extensive network of stellate epithelial reticular cells.

Each lobule of the thymus consists of a peripheral zone – the cortex – and lightly staining central zone or medulla.

Both the cortical and the medullary zones have the same cellular types, although in different proportions. The most abundant are T lymphocytes and their precursor cells in various stages of differentiation and maturation and the epithelial reticular cells. Besides these cells, the thymus has a few mesenchymal reticular cells and many macrophages. Myoid cells are rarely seen in the postnatal thymus of humans.

Epithelial reticular cells have large oval nuclei. Thin cytoplasmic processes of adjacent cells are joined by desmosomes. Bundles of tonofilaments in the cytoplasm are evidence of the ectodermal origin of these cells. They have dense granules with thymic hormones (serum thymic factor, thymic humoral factor, thymopoietin, and thymosin), which act to promote the differentiation of pre-T cells to mature T lymphocytes [2, 3].

Cortex

In the cortical zone, small lymphocytes predominate. This area is a very active site of lymphocyte antigen-independent differentiation. The characteristic surface antigens of T lymphocytes are expressed, and maturing T lymphocytes move toward the medulla. They leave the thymus, via venules in the border between the medulla and cortex. These vessels are lined cuboid endothelium.

The thymus releases large numbers of lymphocytes that to populate peripheral lymphoid organs where they colonize thymus-dependent areas and **undergoes** antigen-dependent differentiation.

Epithelial reticular cells envelop groups of lymphocytes multiplying in isolation from circulating antigens. Furthermore, they seem to form a complete covering at the pe-

riphery of the lobules and around the blood and lymphatic vessels. These epithelial cells form a continuous layer that separates the thymic cortical parenchyma from the vessels. Antigenic material has difficulty in passing through this blood-thymus barrier and in coming into contact with the developing T-lymphocytes. The blood-thymus barrier is present only in the cortical zone and is formed by the following layers:

a) the capillary endothelium;
b) its basal lamina;
c) a small amount of connective tissue containing some macrophages;
d) the basal lamina of the epithelial reticular cells;
e) and the cytoplasm of epithelial reticular cells.

This zone is unique in that its blood supply consists only of capillaries and no other types of vessels.

Medulla

The thymic medulla stains lightly because only about 5% of the total number of thymic lymphocytes are found here, but these cells are fully mature T lymphocytes and are generally smaller than the lymphocytes found in the cortex. Recently it has been postulated that the medulla of the thymus is a separate 'compartment*. After thymocytes move into this compartment they probably come into contact with antigens presented to them through dendritic macrophages. Such contact may be a necessary step in making T-tymphocytes competent to distinguish between foreign antigens and proteins of the body itself.

The meduila also contains Hassall's corpuscles, which are a characteristic feature of the thymus. Hassall's corpuscles are 30- 150 mkm diameter and consist of concentric layers of epithelial reticular cells. Some of these cells degenerate and die. The center of a thymic corpuscle may display evidence of keratinization, a not surprising feature since the cells are of epithelial character.

The functional significance of Hassall's corpuscles is unknown [1 – 3].

LYMPHOPOIESIS

Precursors from bone marrow that reach the superficial part of the cortex divide repeatedly to form smaller lymphocytes. During these mitoses the DNA of the lymphocytes undergoes numerous random mutations, as a result of which different lymphocytes acquire the ability to recognize a very large number of different proteins, and to react to them. All lymphocytes that would react against the body's own proteins are destroyed and phagocytized by macrophages and cortical epitheliocytes are also described as *thymic nurse cell*. Deeper lying macrophages are dendritic cells. It is for this reason that 90% of lymphocytes formed In the thymus are destroyed within three to four days.

The remaining lymphocytes are thrown into the circulation as circulating, immunologically competent T-tymphocytes.

True differentiation of T-tymphocytes takes place under the influence of hormones produced by epithelial cells of the thymus. T-lymphocytes are also influenced by direct cell contact with eplthellocytes. Hormones produced by the thymus may also Influence lymphopoiesis in peripheral lymphoid organs [4, 5]**.**

The thymus shows its maximum development immediately after birth and undergoes involution after puberty. Subsequently, much of the organ is replaced by fat. But thymus remains capable of producing great numbers of lymphocytes when stimulated. Involution begins in the cortical zone, which gradually becomes thinner. The medulla begins its process of involution only at puberty. The thymus never disappears completely; it is

still present even in very old people.

The thymus is very sensitive to radiation, glucocorticoids produced by the adrenal cortex, infection, and disease [6].

Peripheral lymphoid organs include lymph nodes, spleen and lympho-epithelial organs. **Their main function is antigen-depending differentiation.**

Structural and functional unit of peripheral immune organ is lymphatic nodules. Also lymphatic nodules – or lymphatic follicles – 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. The cells are mainly B lymphocytes, although some T lymphocytes are present, as are reticular cells and fibers, macrophages, and antigen-presenting cells (follicular dendritic cells). In histologic sections, nodules are strongly stained by hematoxylin as a consequence of the presence of a dense population of small lymphocytes that possess a basophilic nucleus with condensed chromatin and a narrow rim of cytoplasm. The interior 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 of activated lymphocytes (immunoblasts) that have large, euchromatic nuclei as well as a larger amount of cytoplasm. Many cells in a germinal center are in mitosis. Germinal centers appear in a nodule when an antigen is present to which some of the lymphocytes can respond. The response consists of enlargement, mitosis, and differentiation into plasma cells. Some of the products of mitosis do not differentiate into plasma cells but remain as small lymphocytes known as memory tells. These cells are found mainly in the mantle zone of secondary nodules. The mantle zone is composed of those small lymphocytes which surround the germinal centers of secondary nodules. Nodules that contain germinal centers are termed secondary nodules, whereas those lacking germinal centers are called primary nodules.

Follicular dendritic cells are nonphagocytic cells with extensive, sheetlike cytoplasmic extensions. Their nuclei are irregular in shape, and few organelles indicative of secretion or phagocytosis (ie, rough en-doplasmic reticulum orlysosomes) are present in their cytoplasm. These cells can trap antigens on their surfaces and "present" these antigens to B and T lymphocytes to produce an appropriate immunologic response [5, 6].

REFERENCES

1. Singh, I. Textbook of Human Histology : with Colour Atlas and Practical Guide / I. Singh ; revised and edit. by N. Vasudeva, S. Mishra. – 8th edition. – New Delhi : Jaypee Brothers, 2016. – 300 p. – Mode of access: https://docs.google.com/file/d/0BxvjJ4mG_bfYV2ZjSTZzZ3VmVUU/edit?resourcekey=0-l0rcPJlIPE-C8jNx7fsOiA – Date of access: 25.01.2022.

2. Lowe, J. S. Stevens & Lowe's human histology [Electronic resource] / J. S. Lowe, P. G. Anderson, S. I. Anderson. – 5th ed. – China : Elsevier, 2020. – VIII, [I], 426 c. : color. ill. + Student Consult online. – Mode of access: https://www.sciencedirect.com/book/9780723435020/stevens-and-lowes-human-histo logy-fourth-edition – Date of access: 25.01.2022.

3. Кузнецова, Т. Г. Гистология, цитология и эмбриология : учеб.-метод. пособие для студентов 2 курса фак-та по подготовке специалистов для заруб. стран, обуч. на англ. языке = Histology, cytology and embryology in English for 2-nd year students of Faculty on preparation of experts for foreign countries, studying on speciality of “General Medicine» of medical higher educational institutions / Т.Г.Кузнецова, Е. К. Солодова ; пер. Т.Г.Кузнецова, – Гомель : ГомГМУ, 2016. – Ч. 2. – 64 с.

4. Солодова, Е. К. Тестовые задания по гистологии: учеб.-метод. пособие для студентов 1 курса факультета по подготовке специалистов для зарубежных стран медицинских вузов: в 2 ч. = Histology tests: teaching workbook for 1st year students of Faculty on preparation of experts for foreign countries of medical higher educational institutions: in 2 parts / Е. К. Солодова; ред. англ. текста А. Ф. Максименко. – Гомель: ГомГМУ, 2015. – Ч. 1. – 44 с. – Mode of access: https://elib.gsmu.by/handle/GomSMU/2466 – Date of access: 25.01.2022.

5. Солодова, Е. К. Тестовые задания по гистологии: учеб.-метод. пособие для студентов 2 курса факультета по подготовке специалистов для зарубежных стран медицинских вузов: в 2 ч. = Histology tests: teaching workbook for 1st year students of Faculty on preparation of experts for foreign countries of medical higher educational institutions: in 2 parts / Е. К. Солодова; ред. англ. текста А. Ф. Максименко. – Гомель: ГомГМУ, 2014. – Ч. 2. – 44 с. – Mode of access: https://elib.gsmu.by/handle/GomSMU/2467 – Date of access: 25.01.2022 [5 – 7].