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Modern Views about Structural and Functional Features Spleen

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Abstract: The spleen is a peripheral organ of the immune system, involved in hematopoiesis and is a cemetery for old red blood cells. A brief review presents the latest literature data on the structural and functional areas and cellular components of the organ and the functions they perform.

Keywords: spleen, white pulp, red pulp, reticular cells, lymphocytes.

The rapid development of civilization, an increase in the production, processing and use of hydrocarbons and radioactive substances, entails active anthropogenic pollution of the environment with an increase in background radiation at work and in everyday life. The influence of such unfavorable factors on human health leads to structural changes in tissues, disruption of the activity of individual organs, and in especially severe cases, the entire organism as a whole. All this forces scientist to pay close attention to the organs of immunogenesis, which provide the body's defense mechanisms. The spleen is the largest peripheral lymphoid organ, making a significant contribution to the formation of the immune response, the quantitative and qualitative composition of immunocompetent blood and lymph cells starting from early postnatal ontogenesis, together with the mother's mammary gland and other organs of the infant's immune system, participating in the protection of the newborn's body [1, 4, 11, 13]. Being a blood filter in its function, the spleen quickly reacts to the antigens and damaged cells it contains with changes in microstructure and cytoarchitectonics both in a healthy body and in cases of pathological conditions [10, 11, 14, 23, 24, 25, 26, 27, 28].

It is known that the spleen is the most important peripheral organ of immunity, where processes of further differentiation of a subpopulation of lymphocytes and cells of the mononuclear phagocyte system occur, their cooperative interaction during immune reactions with the subsequent formation of clones of activated immunocompetent cells [2, 3, 6, 7, 15]. Despite numerous studies on the structure and function of the spleen, many questions related to the role of the spleen in various physiological and pathological processes still remain open. This is due to the complexity of the structure of the organ in humans and mammals, the rapid variability of the structure of the spleen depending on the functional state of the body and its biological rhythms [5, 8, 9, 15].

According to modern concepts, the spleen of humans and some other mammals is considered a segmented organ. Each segment includes white pulp, which is divided into lymphoid nodules (follicles) (B-dependent zones) and periarterial lymphoid sheaths (T-dependent zones). The red pulp of the segment consists of venous sinuses (sinusoidal homocapillaries), splenic cords and a marginal zone located at the border of the red and white pulp [2, 5, 8]. A number of researchers also classify the splenic cords and marginal zone as the white pulp of the spleen, since the cell

population of these zones contains almost all types of immunocompetent cells and microenvironment cells that are characteristic of lymphatic follicles [2, 9, 12, 15].

One of the main functions of the spleen, in addition to participating in the processes of hematopoiesis and blood destruction, is its active involvement in the body's immune reactions. An immune response in the spleen develops when antigens enter the blood or lymph [9]. In the periarterial lymphatic follicle (PALF) of the white pulp, there is a central part, which is directly adjacent to the artery wall, and a peripheral part [2, 9]. In the central part, interdigitating cells, characteristic of T-dependent zones, predominate over stromal cells, while in the peripheral part there are more stromal cells. These cells are a special type of reticular cells containing the Forsman glycosphingolipid marker [12].

According to the generally accepted opinion, the reticular tissue of the spleen of most vertebrates is formed by multi-processed reticular cells and reticular fibers. However, to this day, questions of the origin, structural and functional classification of reticular cells in general, and the spleen in particular, remain controversial. According to a number of authors, among reticular cells (RC) of the spleen one can distinguish undifferentiated (poorly differentiated) RK, non-phagocytic RK, as well as differentiated, actively phagocytic RK [12, 38].

Under the name "phagocytic reticular cells" are groups of cells characterized by the presence in the cytoplasm of a large number of diverse lysosomes and phagosomes. These are quite large cells with a diameter of 15-20 microns, irregular in shape due to many cytoplasmic processes. The nucleus is usually irregularly stellate in shape and located eccentrically. Nuclear chromatin is predominantly evenly distributed, with a moderate tendency to aggregate beneath the nuclear membrane. There are numerous mitochondria, the Golgi complex in the form of 2-3 separate groups, the granular endoplasmic reticulum is represented by several, sometimes locally expanded cisterns. Currently, these cells are considered one of the components of the cells of the mononuclear phagocyte system, which differ from macrophages of other organs in their structural and functional characteristics [38].

Non-phagocytic RKs are oval, spindle-shaped or stellate in shape, contain an oval or elongated nucleus with a diffuse distribution of chromatin. In their cytoplasm, well-developed endoplasmic reticulum and lamellar Golgi complex are revealed. They are in close contact with the fibrous structures of the intercellular substance and participate in their production [34]. Some authors call these cells the own stromal elements of the reticular tissue of lymphatic follicles or fibroblasts of the reticular tissue [35].

Undifferentiated or inactive RKs are difficult to identify due to the lack of clear structural features and poor development of subcellular organelles. The results of histochemical and immunocytochemical studies showed that among them, at least two subpopulations are distinguished: dendritic and interdigitating RKs [29]. Dendritic reticular cells [DCs] play an important role in a variety of immune responses and perform some of the functions of macrophages. On the plasmalemma they have receptors for the Gc fragment of immunoglobulins and retain immune complexes on their surface [29, 30].

Depending on the location, several types of DCs are distinguished: lymphoid, follicular and intertwining, which form weaves and close contacts with lymphocytes and with each other DCs are considered mainly components of the stroma of the B-dependent zones of the spleen [29].

Interdigitating reticular cells (IDCs) also have numerous processes that contact each other and with lymphocytes [31, 32]. They are mainly localized in thymus-dependent areas of the organ and form a microenvironment for lymphocytes of the periarterial zones [36]. It has been established that IDCs are very close in morphological characteristics to Langerhans cells of the skin epidermis, containing special Birbeck granules in the cytoplasm [41]. These cells are morphologically closest to the cells of the mononuclear phagocyte system. In extreme situations, the phagocytic activity of IDCs can increase many times, which is accompanied by a change in their subcellular organization towards macrophages [37, 41].

Spleen fibroblasts are stellate in shape with extremely long cytoplasmic processes. Signs characteristic of these cells are a dark, electron-dense cytoplasmic matrix and significantly dilated cisterns of the granular endoplasmic reticulum containing flocculent material. At the periphery of the cell, an apparent fusion of the tubules and vacuoles of the smooth endoplasmic reticulum with the adjacent reticular fibers is observed. The cytoplasm of fibroblasts, more often in the cortical zone, contains a significant amount of microfibrils [30].

The germinal center (reproduction center) of the white pulp consists of B lymphocytes at different stages of proliferation and differentiation, T helper cells, macrophages and dendritic reticular cells. Single plasma cells can also be found in it. The germinal center makes up about 40% of the entire white pulp of the human spleen [31]. The function of the reproduction centers is the production of activated B-lymphocytes of immunological memory.

Macrophages play a huge role in performing various functions of the spleen, from the elimination of old blood cells to active participation in the body's immune reactions. They differ from other phagocytes in origin and functional characteristics and belong to the mononuclear phagocyte system. Common features characteristic of cells of the mononuclear phagocyte system are their development from bone marrow monocytes, the ability to phagocytosis and pinocytosis and present antigens to T- and B-lymphocytes. In addition, they can produce a number of biologically active substances that have a regulatory effect on the functional activity of lymphocytes and other cells [39]. The presence on the surface of these cells of receptors for the Pc fragment of immunoglobulin and C3 complement ensures the ability of macrophages of lymphoid organs, unlike other phagocytes, for immune phagocytosis [32]. The participation of macrophages in the immune response is multifaceted. They, eliminating and destroying the antigen up to 90% of it, bring the remaining part to the surface in a more immunogenic form - in the form of a superantigen. The cooperative interaction of macrophages with activated T and B lymphocytes is a necessary condition for the development of most immune reactions [31, 42]. Macrophages create a microenvironment for lymphocytes. The size and shape of macrophages are variable and depend on the functional state of the cell, organ and organism as a whole. The nuclei are large, contain a nucleolus, and a small amount of chromatin is condensed near the nuclear membrane. Macrophages with a more developed lysosomal apparatus belong to the phagocytic type, with a more developed endoplasmic reticulum - to secreting macrophages of the periarterial zones, and macrophages of the third group are dendritic cells located in the germinal centers of the lymphatic follicles of the spleen [41, 42].

Mature plasma cells, or plasmacytes, are characterized by a relatively small nuclear size, therefore their nuclear-cytoplasmic ratio is significantly lower than that of proplasmacytes and plasmablasts. The plasmacyte nucleus is located eccentrically and contains dark clumps of chromatin, which in their localization resemble spokes in a wheel. The nucleolus is usually absent in mature plasma cells. The cytoplasm occupies a relatively large area and usually expands towards the pole opposite the nucleus. Plasma cells originate from B lymphocytes and are the main sources of various classes of immunoglobulins or antibodies. Cellular elements of the plasma series constantly proliferate in the immune organs, and under pathological conditions, and due to an increase in the intensity of the immune system, their number and degree of maturity increases significantly [32, 35, 37].

Lymphoid and stromal cells in the white pulp of the spleen are localized, forming structural and functional zones that have a heterogeneous functional orientation [31]. The main function of germinal centers is the production of activated B-lymphocytes of immunological memory; it is also possible that processes of further proliferation and differentiation of cells of the mononuclear phagocyte system occur in them [32]. The periarterial and marginal zones are the main site of cooperative interaction of T- and B-lymphocytes with microphages, as a result of which the corresponding clones of antibody-producing plasma cells are formed [30]. The mantle zone is formed by small lymphocytes surrounding the proliferation center of lymphoid follicles [33].

The marginal zone is localized around the entire follicle and surrounds the T- and B-dependent zones. Opi is a transitional area between the white and red pulp. Marginal zone lymphocytes are characterized by high alkaline phosphatase activity [19–22, 35].

The red pulp makes up about 75% of the volume of the human spleen and includes venous sinuses with terminal hemocapillaries and non-filtering zones [42]. The stroma of the red pulp is represented by reticular cells and fibers. The reticular fibers of the red and white pulp are represented by different types of collagen. Near the trabeculae in the red pulp and in the marginal zone, a group of activated fibroblasts was found that perform a barrier function and are therefore called barrier cells. They are characterized by dense cytoplasm and have an elongated shape with processes. The number of such cells increases significantly with infectious influences and the appearance of defective blood cells. The source of the development of barrier cells can be fibroblasts located near the trabeculae. The main role of these cells is to delimit the source of infection [17–19, 37].

A significant part of the red pulp does not contain terminal capillaries and does not perform a filtering function. Such zones are aggregates of B- and T-lymphocytes. as well as mononuclear phagocytes. In place of these aggregates, lymphatic follicles may subsequently form [29, 30].

Blood circulation in the spleen, and especially its hemomicrocirculatory bed, is closely related to the main function of the organ to eliminate old red blood cells and blood platelets, as well as foreign particles [39, 40, 42, 44– 46].

M. Kashimura and A. Shibatta [40], using a scanning electron microscope, identified 3 types of hemomicrocirculation in the human spleen:

- open circulation in the red pulp, ensuring highly efficient removal of foreign material;
- closed circulation in the red pulp, represented by the arteriolar labyrinth, facilitating the communication of blood flow with the smallest number of macrophages;
- microcirculation of the white pulp and marginal zone is characterized by phagocytosis of foreign substances and delivery of their antigens to the lymphocytes of the white pulp.

The spleen of rats, similar to the human spleen, is equipped with a special circulatory structure. With an open circulatory system, blood from the arteriolar terminals opens directly into the red pulp. From the red pulp, blood passes through the wall of the sinuses, which acts as a filtration barrier, then enters the lumen of the sinuses, and then into the venous circulation. Unlike the human spleen, this organ of rats has more pronounced marginal sinuses and canal systems connected to the marginal zone. Through these channels, lymphocytes are recirculated between the red and white pulp. The endothelial cells covering the wall of the sinuses are connected to each other using tight junctions. The cytoplasm of cells forms tubular invaginations with extensions and peculiar niches, the meaning of which remains not entirely clear [32, 35, 39, 42, 44–49].

Thus, a significant amount of data has now been accumulated on the structure and function of the spleen in humans and other mammals. However, many issues related to the participation of the spleen in the body's immune responses under physiological and pathological conditions have not yet been fully elucidated. The problem of interorgan and intersystem relationships between the spleen and organs of both the immune and other systems remains poorly understood.

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