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MORPHOFUNCTIONAL FEATURES OF THE SPLEEN - A PERIPHERAL ORGAN OF IMMUNITY

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Abstract: The article provides an overview of the latest data on the structural and functional characteristics of the spleen, a peripheral organ of the immune system. Data on the stromal-lymphoid relationships of the organ, on its capsular-trabecular formations are presented, and the latest data on the T- and B-cell zones and structural and functional features of the spleen during the life of young mammals are also described.

Key words: vascular system, fibroblastic reticular cells, lymph node, secondary lymphoid organ, stromal cell, immune system.

Relevance. The spleen is a mysterious organ. Even the ancient Greeks and Romans removed the spleens of runners to increase running speed. The functions of the spleen are still not fully understood. For a long time it was considered an endocrine (without excretory ducts) gland. Since there is no reliable data on the secretory activity of the spleen, this theory had to be abandoned, although recently it has to some extent received a second life. The spleen is now credited with hormonal regulation of bone marrow function. According to [42], bone marrow mesenchymal stem cells (BMSCs) are considered important regulators of immune function. Specific markers of BMSCs were identified using flow cytometry and successful induction of these cells into steatoblasts and osteoblasts was observed. Compared with the aging model, the index of the spleen and thymus was significantly increased, and the histological changes in the tissues of the spleen and thymus were improved. BMSCs significantly reduce tissue damage in the aging spleen and thymus, and they may improve organ aging through their effects on cytokines, oxidative stress, and P21 / PCNA.

The spleen is the primary filter for blood-borne pathogens and antigens and a key organ for iron metabolism and red blood cell homeostasis. [43] However, along with them, it also performs immune and hematopoietic functions in mice, which indicates an additional role for this secondary lymphoid organ. The spleen contains all major types of mononuclear phagocytes, including macrophages, dendritic cells (DCs), and monocytes. [40] These cells are key defenders of the body as they identify pathogens and cellular stress, remove dying cells and foreign materials, regulate tissue homeostasis and inflammatory responses, and shape adaptive immunity [22]. Research has shown that the immune system performs more than just controlling pathogens. Even without infection, the immune system can produce sterile inflammatory responses. This non-canonical function is currently the subject of much debate. These discussions assume that the classical role of the immune system in killing pathogens is only part of the overall function of the immune system. In this direction, efforts are being made to comprehensively, from the point of view of physiological homeostasis, study the role of the immune system [Medzhitov R. _ 2021]. This organ is now believed to play a central role in the regulation of the immune system, being a metabolically active organ, and is involved in endocrine function in relation to non-alcoholic fatty liver disease. In recent years, after in-depth studies of the organization and structure of the spleen, cell function, secretion and innervation, a better understanding of the function of the spleen has been achieved. It was originally believed that the spleen not only filters the blood, but is also an important center for regulating the body's immune, metabolic and endocrine systems. However, a number of questions have arisen: is the spleen a player or a bystander and what is the role of certain cytokines, adipokines/growth factors and neurotransmitters in this complex mechanism? Adipokines have pro- and anti-inflammatory properties and play a critical role in the integration of systemic metabolism with immune function [35]. In other words, what is the

contribution of the spleen to the development of non-alcoholic fatty liver disease, and is it a further manifestation of metabolic syndrome [40].

The spleen, being the largest secondary lymphoid organ in the body, performs a wide range of immunological functions along with its role in hematopoiesis and red blood cell clearance. [36] The physical organization of the spleen allows it to filter the blood from pathogens and abnormal cells and facilitate unlikely interactions between antigen-presenting cells (APCs) and related lymphocytes. A spleen-specific PCs regulate the response of T and B cells to these antigenic targets in the blood. There are cell types, cellular organizations, and immunological functions that are specific only to the spleen, influencing the initiation of adaptive immunity and to systemic blood-borne antigens. It has been shown [12] that fibroblastic reticular cells (FRCs) are found in the spleen, which are an important part of the infrastructure of stromal cells and secondary lymphoid organs (SLO). With their help, fibroblasts of lymphoid organs are formed, specialized niches for the interaction of immune cells and thereby control the activation and differentiation of lymphocytes. Moreover, PRKs create and cover a network of extracellular matrix (ECM) microfibers called the channel system. Channels generated by PRK promote fluid and immune cell control by funneling fluids containing antigens and inflammatory mediators through the VLO. Functions and interactions of immune cells, the complex relationships between cellular KFR and fibrillar conduction networks that together provide the basis for efficient communication between immune cells and tissues. The physical organization of the spleen allows it to filter the blood from pathogens and abnormal cells and facilitate interactions between antigen-presenting cells and related lymphocytes. APCs are unique to the spleen because they regulate T and B cell responses to these antigenic targets in the blood. The spleen is the first of the immune lymphoid organs to arise in association with adaptive immunity in early jawed vertebrates. The spleen, especially its lymphoid compartment, the white pulp (WP), has undergone numerous modifications during evolution. The spleen also contains about one-quarter of the body's lymphocytes and initiate an immune response to blood antigens [P Kubes 2018]. This function is assigned to the white pulp surrounding the central arterioles. The white pulp consists of three subcompartments: the periarteriolar lymphoid membrane (PALM), follicles and marginal zone. [24] Histocytometric studies have shown [13, 28] that the spleen is surrounded by a capsule consisting of dense fibrous tissue, elastic fibers and smooth muscle, as well as the outer layer of the capsule. The spleen consists of mesothelial cells covering it, unevenly located trabeculae of smooth and elastic tissue fibers emerging from the capsule into the spleen parenchyma [34, 40]. Other authors [39] have shown that these trabeculae also contain blood vessels, lymphatic vessels and nerves.

The spleen is a peripheral immune organ surrounded by a capsule consisting of dense fibrous tissue, elastic fibers and smooth muscles - that’s what the spleen is, it is a large lymphoid organ without the structure of the cortex-medullary layer, the capsule surrounding it extends inward, passing through connective tissue trabeculae [27].

The outer layer of the spleen capsule consists of mesothelial cells, which may not be visible on histological sections. Irregularly distributed trabeculae of smooth muscle and fibroelastic tissue extend from the capsule into the splenic parenchyma. The complex vascular system of the spleen plays a central role in the successful filtration of blood and recycling of red blood cells. Blood enters the spleen in the hilum area and flows sequentially as follows: splenic artery → trabecular arteries → small arterioles → red pulp → central arterioles → small arterioles → capillary bed of various sections of the red pulp and white pulp. [41] The red pulp is a blood filter that removes foreign material, damaged and dying red blood cells. The spleen is the primary filter of blood-borne pathogens and antigens and a key organ for iron metabolism and red blood cell homeostasis. Along with this, immune and hematopoietic functions of the mouse spleen were also discovered, indicating additional functions of this secondary lymphoid organ. [16]

White pulp: ALS and lymphoid follicles. The lymphoid compartments of the white pulp include the periarteriolar lymphoid membranes [PLM], primary and secondary follicles, marginal zone and mantle, which vary among species [25]. Identification and characterization of each splenic compartment, including assessment of the relative size and cellularity of the periarteriolar lymphoid

sheaths (PLM), the size and maturation of lymphoid follicles, the presence or absence of marginal zone cells, and the relative abundance of smaller lymphoid aggregates, are key to accurately assessing the immunological impact on the spleen.

Trabeculae also contain blood and lymphatic vessels and nerves. Lymphatic vessels are efferent vessels through which lymphocytes migrate to the splenic lymph nodes. It follows that the spleen is a blood filter and is a highly vascular organ [41]. Blood flow through the spleen is a rather complex but important and sometimes controversial concept. Blood enters the spleen at the hilum through the splenic artery. The splenic artery is divided into trabecular arteries, located inside the trabeculae, which flow into the splenic parenchyma. Small arterioles arise from the trabecular arteries and enter the red pulp, where they become central arterioles surrounded by lymphoid tissue, characterizing the closed circulatory system of the spleen [14]. Along with this, the sinusoids of the red pulp of the spleen form the basis of the open type of blood circulation of the spleen, thanks to which it received the name of the red blood cell cemetery.

Thus, our study established that the spleen represents an important site for the clearance of exosomes and nanoparticles and can direct the resulting immune responses. In addition, it must be pointed out that the spleen, this small, forgotten organ, continues to surprise us with unexpected physiological functions: after recently linking the spleen to the pathophysiology of non-alcoholic fatty liver disease, the manifestation of hematopoietic function contributes to the fact that this small, forgotten organ, certainly deserves even closer attention from scientists in the future. It should also be pointed out that many issues of the structural and functional development of the spleen, and other organs of the immune system, both in the dynamics of early postnatal ontogenesis and in the case of extragenital pathology of the mother, require further and in-depth analysis [1-11, 17-23, 29-33] .

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