



Data From Foreign Literature on The Morphofunctional Properties of Lymphoid Cells Of The Spleen

Saidov Akmal Abdulloyevich¹, Ochilov Komil Rahimovich², Xatamova Sarvinoz Muyidinovna³, Haydarova Nargizaxon Axtamjon qizi⁴, Mirahmedova Nargiza Rizayevna⁵, Sharafi Tamina Floridovna⁶

^{1,2,3,4,5,6}Bukhara State Medical Institute named after Abu Ali ibn Sino, Uzbekistan.

*Corresponding author's E-mail: Saidov Akmal Abdulloyevich

| Article History | Abstract |
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| Received: 06 June 2023 Revised: 05 Sept 2023 Accepted: 12 Dec 2023 | <p><i>The spleen is an excellent lymphoid organ that harmoniously combines innate and adaptive immunity, helping to strictly remove blood-borne microorganisms and old erythrocytes from circulation. The functions of the spleen are focused on systemic circulation. Thus, it does not have afferent lymphatic vessels. It consists of two functionally and morphologically distinct sections: red pulp and white pulp. Red pulp is a blood filter that removes foreign substances and damaged and effete erythrocytes. It is also a storage site for iron, erythrocytes and platelets. As an example, it is the site of hematopoiesis in rodents, especially in the fetus and neonatal animals. The spleen is also the largest secondary lymphoid organ containing a quarter of the body's lymphocytes, initiating immune reactions against blood-borne antigens. This function is loaded into the white pulp that surrounds the central arterioles. The white pulp consists of three lower parts: the periarteriolar lymphoid shell (PALS), the follicles and the marginal zone.</i></p> |
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1. Introduction

The spleen is surrounded by a capsule consisting of dense fibrous tissue, elastic fibers and smooth muscles. The outermost layer of the spleen capsule consists of mesothelial cells, which may be indistinct in the histological section. - From the capsule, irregularly located trabeculae of smooth muscle and fibroelastic tissue come out to the spleen parenchyma. These trabeculae also have blood and lymphatic vessels and nerves. Lymph vessels are efferent vessels through which lymphocytes pass to the spleen lymph nodes. (157)

Since it is a blood filter, the spleen is a high vascular organ. Blood flow through the spleen is a much more complex but important and sometimes controversial concept. Blood enters the spleen in the hilus through the spleen artery. (10. 67. 89. 109) the spleen artery divides into trabecular arteries located within the trabeculae entering the spleen parenchyma. The small arterioles branch from the trabecular arteries, entering the red pulp and becoming central arterioles surrounded by lymphoid tissue. The small arterioles diverge from the central arterioles and feed the capillary divisions of the white pulp (22-23. 46. 89). Some of them end in the marginal sinus at the junction of the white pulp and the marginal zone, others end in the marginal zone, and a few extend beyond the white pulp and end in the red pulp (23. 78. 90. 112). The Marginal sinus and blood entering the marginal zone pass through the marginal zone in the direction of the red pulp. Blood passes through the marginal zone and flows directly into the adjacent venous sinuses, the open ends of which are continuous with the marginal zone called the "expressway", or enters the reticular network of the red pulp, the "slow path" (93). About 90% of the total spleen blood flow bypasses the reticular network of the red pulp and passes through the adjacent venous sinuses (45. 78). As the central arterioles continue, the white pulp subsides and they develop into penicillary arteries surrounded by red pulp. They cause arterial capillaries ending in the reticular branch of the red pulp in rodents (44. 90. 99). Blood from the red pulp accumulates in the venous sinuses, which penetrate the trabecula and merge into the trabecular veins. The trabecular veins then fuse in the hilus to form the spleen vein, which flows into the hepatic portal system.

Red pulp. The red pulp consists of a three-dimensional network of spleen cords and venous sinuses. The spleen cords consist of reticular fibers, reticular cells, and the spleen cords connected by them are made up of reticular fibers, reticular cells, and macrophages connected by them (28. 180). Reticular cells are considered myofibroblasts and may play a role in spleen contraction (28). As can be seen with electron microscopy, reticular fibers are actually covered by reticular cells and their processes (28). Reticular fibers consist of collagen and elastic fibers, microfibrils, basal layers of the reticular cell, and adrenergic nerve fibers without myelene (58).

Within the spaces between the phalanges are blood cells, including erythrocytes, granulocytes and circulating mononuclear cells. Also associated with spleen follicular pulps are lymphocytes and hematopoietic cells, as well as plasma cells and plasmablasts where follicles and the outer periarteriolar lymphoid shell migrate after antigen-specific differentiation (13. 78. 147. 178). Red pulp macrophages are actively phagocytic, removing old and damaged erythrocytes and blood particles. Additional medullary hematopoiesis is common in the red pulp of rodents, especially in fetuses and newborns. Any combination of erythroite, myeloid and megacaryocyte cells can be obvious.

The venous sinuses can be found along the red pulp, including being directly connected to the marginal zone as described above (8. 12. 88). They are covered by a network of loose endothelial cells located in the basal membrane between the endothelial cells and the reticular fibers of the red pulp (Saito et al., 2018). The penicillary arteries and arteriolar capillaries are also located in the red pulp, but are more difficult to detect by microscopic light.

The spleen can contain various pigments. A typical finding is the accumulation of hemosiderin in the cytoplasm of macrophages in red pulp, sometimes also in white pulp (19). In fact, Iron pigments (i.e., hemosiderin and ferritin) are the most abundant pigments in the macrophages of the red pulp (22). The iron in the hemoglobin of phagocytosed erythrocytes is converted into hemosiderin for storage in the spleen. According to historical control data from the National Toxicology Program (NTP), hemosiderin pigmentation is more common in women than in men (Ward et al., 1999). Ceroid and lipofuscin from the oxidation of lipids are usually also found in the spleen, but they are less common than hemosiderin (Ward et al., 1999). Melanocytes containing Melanin may be located in the spleen, especially in black mice, usually in the trabecula, or in the red pulp (Ward et al., 1999).

White pulp. The white pulp is divided into a periarteriolar lymphoid shell (PALS), follicles and a marginal zone (3.4-5). It consists of lymphocytes, macrophages, dendritic cells, plasma cells, arterioles and capillaries, and is located in a reticular circle similar to that found in the red pulp (88). When the central arterioles enter the red pulp, they are surrounded by pals made up of concentric layers of lymphocytes and reticular fibers and flattened reticular cells (112. 145. 156. 178). The PALS is divided into internal and external pals (6). The T-cell-dependent internal PALS may be slightly darker staining than the external pals due to their cellular arrangement, which is mainly composed of small lymphocytes (9. 13. 34. 67). However, the difference does not exist uniformly and is usually very thin and difficult to detect with a light microscope (Stefanski et al., 2020). Internal PALS cells are primarily CD4 + T-cells, but a smaller number of CD8 + T-cells, as well as interdigitating dendritic cells and migrating B-cells (Van Rees et al., 1996). External PALS are small to medium lymphocytes (both B - and T-cells), macrophages, and plasma cells caused by antigenic stimulation (1-16. 17). It is an important site of lymphocyte movement, where the formation of plasma cells takes place (34. 56. 58). The follicles are continuous with the PALS and are usually located at the bifurcation sites of the central arterioles (99). They consist mainly of B-cells with fewer follicular dendritic cells and CD4 + T-cells, but usually do not contain CD8 + T-cells (96). Follicles have larger lymphocytes in the follicular Center, which are surrounded by a mantle zone or a crown made up of small and medium lymphocytes (99). Follicles may have germinal centers produced by antigen stimulation, which stain less due to the presence of fewer cells, and include macrophages and apoptotic B-cells in the body.

Recent studies have shown that pathological changes in the spleen are characteristic signs of various infectious diseases. However, many researchers have begun to study the standard structural and histological composition of the spleen in various laboratory animals, such as the White bats *Rattus norvegicus* (Maynard and Downes, 2019), albino mice *Mus musculus* (Cesta), after an extremely dangerous disease. But the lack of available information about the anatomical, histological and histochemical properties of the spleen under the influence of the virus means a significant gap in our understanding of the structure of this organ and its function of this type. The study of morphological parameters of the spleen under the influence of lymphocyte activity is important in clinical,

pathological and functional studies, providing valuable insights for ongoing medical and biological research.

Mesenchyma cells are the source of origin of the spleen, which is located between the dorsal mesogastrium layers as early as the fifth and sixth weeks of fetal development. The characteristic shape of the spleen is what happened at the beginning of the fetal period. During embryonic development, the circulation of the stomach leads to the fusion of the surface of the left mesogastrium with the peritoneum above the left kidney and, as a result, the dorsal attachment of the lienorenal ligament. Near the Yellow Sac wall and dorsal aorta are sources of cells necessary for the hematopoietic function of the spleen. In the second trimester, the production of spleen red blood cells and white blood cells begins.(102,. 120. 121)

Through light and electron microscopy, studies have studied the differentiation of the vascular Tree of the spleen tissue of human fetuses up to 14-24 weeks of gestation. These studies focus specifically on the differentiation of auxiliary (stationary) cells responsible for T-cell - and B-cell maturation and their specific maturation in Zamiri.(123. 156)

Here, the initial stage, which is called the " primary vascular network", lasts until the 14th week of pregnancy). Mesenchyma cells and a network of argyrophilic fibers include many erythrocytes, normoblasts, and macrophages.(120)

The characteristic organ structure is established at the next stage of transformation of the fetal spleen, starting from 15 - gw. Spleen lumps begin to form at the age of 15-17. They consist of a central artery surrounded by a shell of lightly dyed stationary cells similar to myofibroblasts. On the edge of these lumps will be located red pulp. Initially, mobile cells are distributed throughout the reticulum. Soon they develop from the lacuna between the reticular network and begin to accumulate in the venous sinuses, which come into contact with the venous system. The endothelial wall of these sinuses remains continuous, confirming the theory of "open" vascularization of the spleen. The development of large vessels is associated with the differentiation of spleen trabecules.(90)

The development of white pulp is associated with the stage of lymphoid colonization inside the spleen, starting from about 18 weeks. The accumulation of lymphocytes around the central arteries develops within 19 and 20 weeks. These lymphoid cells show morphological and immunogystochemical characteristics of T-precursor cells. Several precursors of interdigitating cells (IDCs) are recognized within the currently folding periarterial lymphoid shell (PALS), confirming the differentiation of the T-cell region.(122. 129)

Around the 23rd week, the set of primary follicles is felt at the edge of the pals. Precursors of the follicular dendritic reticulum cell (fdrc), a distinctive stationary cell of the B - cell region, are recognized. This observation leads to the conclusion that small primary follicles represent the initial formation of the B-cell region .

The main contribution of Stroma cells to the organogenesis of lymphoid tissue is recognized during embryonic development. The formation of lymph nodes and Peyer plaques is largely due to the early interaction between stromal VCAM-1 + ICAM-1 + MAdCAM-1 + lymphoid tissue (LTO) cells and hematopoietic CD3 - CD4 + IL-7ra + lymphoid tissue inducer. It is also an important molecule for the development of lymphoid tissue, and without a functional lymphotoxin signaling pathway, both the formation of lymph nodes and Peyer's plaques are canceled. Interestingly, the embryonic spleen develops without lymphotoxin signaling. Lymphoid tissue inducer cells can also be similarly secreted because the loss of the RORg gene, which is important for the development of LTi, causes the embryonic lymph node to stop, but not spleen organogenesis.

Recent advances have identified cellular components and molecular signaling events that guide postnatal spleen regeneration. How do these findings combine with the paradigm for secondary lymphoid organogenesis? Regulation of spleen organogenesis is considered specific because compared to other secondary lymphoid organs, the embryo develops without spleen lymphotoxin signaling. (11. 14) at the same time, the spleen is also structurally and functionally unique, performing double functions in filtering red blood cells carried out in the red pulp and in adaptive immune responses generated in the white pulp. (23) unlike embryonic spleen organogenesis, the maturation of the marginal zone of both MAdCAM-1 +T and B lymphocytes and the cleavage of white pulp occur in the postpartum period, and in mouse models lacking lymphotoxin, both structures are severely disrupted. (109) therefore, spleen organogenesis can be divided into two distinct stages. The initial stage of the formation of red pulp begins in the development of the embryonic spleen. This

occurs independently of lymphotoxin signaling and instead depends on the expression of “homeobox” transcription factors such as Tlx1 and Pbx1 . Subsequently, complete white pulp and marginal zone formation and lymph node organogenesis-like, lymphotoxin-dependent, occur during postnatal spleen development.(109)

Thus, there may be individual spleen stroma cells that independently regulate the embryonic and postnatal development of the spleen.(81) in the interval between late embryonic and early postnatal development, lymphotoxin becomes necessary for the renewal of spleen tissue and the organization of white pulp compartments. Nuclear factor kappa B (NFkB) signaling is critical to the maturation and function of the cell by specific lymphoid tissue factors. (167)

After the rise of lymphotoxin symptoms in the spleen, the formation of the marginal zone becomes an important stage in the formation of white pulp, eventually establishing immunity. There is no clear relationship between the early development of the spleen and the formation of the marginal zone in adults around the phenomena that lead to the maturation of the marginal zone. (156)

In conclusion, it can be said: immunogistological analysis of the spleen from the 11th week of pregnancy to the early postpartum period has shown that the development of fetal organs can be divided into four stages in advance. In Stage 0, classical organ structures will contain erythrocyte precursors, several macrophages, and nearly lymphocytes. At stage I, the fetal spleen develops interstitial arterial vessels and began to colonize lymphocytes.

2. Conclusion

In Phase II, B and T lymphocytes form periarteriolar clusters. Clusters of B cells dominated because B cells were clustered around more peripheral branches of the spleen arterioles, while T cells occupied the centrally located parts of the vessels. The vascular lobules of stage I and II consist of Central arterioles surrounded by B cells, capillaries and peripheral venules. (12. 13. 89. 109) interestingly, the accumulation of B cells around peripheral arterioles does not represent precursors of follicles, but apparently remains in the adult spleen red pulp as periarteriolar B cell clusters, while follicles containing FDC develop in late phase II from B cells in direct contact with the T cell. In Stage III before birth, lobular architecture changes completely. Chemokine CXCL13 is riveted in vascular smooth muscle and adjacent stroma cells in the I stem and is involved in blood rhyology.

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