ISSN: 3060-4737 Volume 3, Issue 5 IF(Impact Factor) 10.98 / 2025

HISTOLOGICAL STRUCTURE OF THE IMMUNE SYSTEM ORGANS (THYMUS, LYMPH NODES, SPLEEN) AND AGE-RELATED CHANGES

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Abstract. This article provides a detailed overview of the deep histological structure, cellular and stromal components, functional zones, as well as age-related morphological and functional changes of the main primary and secondary lymphoid organs of the immune system: the thymus, lymph nodes, and spleen. It covers the differentiation of thymocytes in the cortex and medulla of the thymus, types of epithelial cells, Hassall's corpuscles, the blood-thymus barrier, and thymic nurse cells; the follicles, germinal centers, paracortex, high endothelial venules, follicular dendritic cells, and medullary sinuses of the lymph nodes; and the white pulp, periarteriolar lymphoid sheath, marginal zone, macrophage populations, and red pulp of the spleen. Age-related changes, particularly thymic involution associated with adipogenesis, fibrosis, degeneration of epithelial cells, and decreased expression of the FOXN1 gene; fibrosis, lipomatosis, and stromal transdifferentiation in lymph nodes; and de-compartmentalization of the white pulp, disruption of the marginal zone, and increased fibroblasts in the spleen are comprehensively described as key processes of immunosenescence.

Keywords: thymus, lymph nodes, spleen, histological structure, age-related changes, thymic involution, white pulp, red pulp, marginal zone, Hassall's corpuscles, fibrosis, lipomatosis, immunosenescence, epithelial cells, fibroblastic reticular cells.

Introduction. The immune system is a complex, multi-level network that protects the body from external pathogens, internal mutations, and damage to its own cells. Its primary organs include the thymus, which serves as a primary lymphoid organ ensuring the maturation, positive and negative selection of T-lymphocytes, while the lymph

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nodes and spleen, as secondary organs, manage antigen filtration, clonal expansion of lymphocytes, and the generation of effector and memory cells. Changes occurring in the immune system with advancing age are termed immunosenescence. This process leads to decreased resistance to infections in the elderly, a sharp decline in vaccine efficacy, increased incidence of autoimmune diseases, chronic inflammation, and elevated cancer risk. Histological studies have identified early involution in the thymus, fibrosis and stromal changes in lymph nodes, and disruption of the boundaries between white and red pulp in the spleen as the main morphological features. These changes are associated not only with a decrease in cell numbers but also with disruption of stromal architecture, alterations in the cytokine milieu, impaired cell migration, and the emergence of the senescence-associated secretory phenotype (SASP). This article aims to provide an in-depth scientific illumination of the topic, a comprehensive analysis based on existing experimental and clinical studies, a detailed functional linkage of the histological features of the organs, and the derivation of practical conclusions. The purpose is to assist medical students, researchers, clinicians, and gerontologists in fully understanding the age-related dynamics of the immune system and to create a solid scientific foundation for new approaches in regenerative medicine.

Main Part. Histological Structure of the Thymus. The thymus is a primary lymphoid organ located in the upper part of the thoracic cavity, consisting of two lobes and surrounded by a thick connective tissue capsule. The capsule sends septa inward, dividing the organ into lobules. Each lobule is distinguished by subcapsular cortex, cortex, and medulla zones. In the subcapsular cortex, epithelial cells form the blood-thymus barrier and support the initial proliferation of thymocytes. The cortex is a dark zone densely filled with lymphocytes, where positive selection of T-lymphocytes occurs. Cortical thymic epithelial cells play a nurturing and differentiating role for thymocytes; they are also known as thymic nurse cells, with a single epithelial cell enveloping several dozen thymocytes. The medulla is a lighter zone characterized by fewer lymphocytes and more epithelial cells. Hassall's corpuscles are located here; they are concentric aggregates of keratinized epithelial cells. Hassall's corpuscles participate in the negative selection of thymocytes and are formed as a result of terminal differentiation of thymic epithelial cells. The Aire gene is expressed in the medulla, presenting tissue-specific antigens. The stromal structure of the thymus consists of reticular cells, fibroblastic reticular cells, and a network of fibers that support lymphocyte migration. Blood vessels and nerve fibers enter through the septa. In childhood, the thymus has high mass and activity, with clearly demarcated lobules, a wide cortex, and numerous Hassall's corpuscles in the medulla. Electron microscopy studies provide detailed images of the cytoplasmic organelles of epithelial cells,

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desmosomal connections, and the complex structure of the blood-thymus barrier. Histological Structure of the Lymph Nodes. Lymph nodes are secondary lymphoid organs of round or bean shape that perform the function of filtering lymph flow and initiating immune responses. Each node is surrounded by a thick capsule from which trabeculae extend inward. The outer part is called the cortex and contains B-cell follicles. Secondary follicles develop germinal centers, where B-lymphocyte proliferation, class switching, affinity maturation, and memory cell formation occur. Mantle and marginal zones are present around the follicles. Follicular dendritic cells retain antigens for long periods in the germinal centers. The paracortex is the T-cell zone, enriched with high endothelial venules. These venules ensure the selective passage of lymphocytes from blood into the lymph node. The medulla consists of medullary cords and sinuses, where plasma cells, macrophages, and lymph flow filtration occur. Reticular cells form the supportive skeleton throughout the node. The histological structure of lymph nodes changes dynamically depending on antigen stimulation: during an immune response, follicles enlarge, germinal centers increase, high endothelial venules become activated, and lymphocyte flow intensifies. Histological Structure of the Spleen. The spleen is the largest lymphoid organ located in the abdominal cavity; it performs blood filtration, erythrocyte breakdown, and immune response functions. The organ is enclosed by a capsule and trabeculae. The spleen is divided into white pulp and red pulp. The white pulp is lymphoid tissue consisting of the periarteriolar lymphoid sheath and lymphoid follicles around central arteries. Germinal centers are located in the center of the follicles, surrounded by a mantle and marginal zone. The marginal zone is the transitional zone between the white and red pulp, enriched with marginal zone macrophages, marginal metallophilic macrophages, and specialized B-cells. This zone rapidly recognizes blood-borne antigens and initiates T-independent immune responses. The red pulp is filled with blood vessel sinuses and Billroth's cords; it performs blood filtration, removal of erythrocytes, and storage of platelets. Reticular fibers, fibroblasts, and fibroblastic reticular cells maintain the structural integrity of the spleen. A distinctive histological feature of the spleen is its direct connection with the bloodstream: central arteries supply the white pulp and then pass into the marginal zone and red pulp. This structure combines immune and hematological functions. Electron microscopy clearly shows the fenestrated endothelium of the sinusoids and the high phagocytic activity of macrophages in the cords.

Research Results. Numerous histological, morphometric, immunohistochemical, and molecular studies have thoroughly investigated the age-related changes in the thymus, lymph nodes, and spleen. In the thymus, the involution process begins at

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puberty and gradually intensifies. With age, the cortex-to-medulla ratio decreases sharply, the number of cortical thymocytes significantly declines, and degeneration of epithelial cells is observed. Functional lymphoid tissue is replaced by fat and connective tissue. For example, after the age of 25, the thymus remains only as islands; after 40, adipose tissue predominates and the perivascular space expands. The number and size of Hassall's corpuscles change, and Aire gene expression decreases. Studies show that although the overall volume of the thymus may not change significantly, the functional parenchyma decreases by approximately 3% per year. These changes reduce naïve T-cell production, narrow the TCR repertoire, and lead to diminished immunity. In mouse models, involution is clearly observed from 4 to 12 months; in humans, almost complete adipose replacement occurs after the age of 50. Decreased FOXN1 gene expression and signs of epithelial-to-mesenchymal transition have been confirmed as key molecular mechanisms of involution. Age-related changes in lymph nodes begin somewhat later but are significant. The total number and size of nodes decrease, while the capsule and trabeculae thicken. In the cortex, the number of follicles and germinal centers declines, and T-cell density in the paracortex decreases. Fibrosis intensifies, the reticular network is disrupted, and the number and activity of high endothelial venules decrease. Sinuses in the medulla undergo fibrosis, and macrophage activity declines. Studies have identified lipomatosis and reduced cellularity in head and neck lymph nodes; fibrosis reaches two points between 61 and 75 years, while lipomatosis can reach 50%. These changes hinder antigen recognition and clonal expansion of lymphocytes. Stromal transdifferentiation and vascular remodeling play an important role in the age-related changes of lymph nodes. In the spleen, age-related changes are clearly manifested in the de-compartmentalization of the white pulp. The volume of white pulp decreases, the boundaries of the periarteriolar lymphoid sheath and follicles become blurred, and the number of marginal zone macrophages significantly declines. The proportion of red pulp increases, and fibrosis and pigmentation intensify. The overall mass and diameter of the spleen decrease, and the boundaries between white and red pulp become indistinct. Studies in mouse and human spleens have confirmed the loss of clear demarcation between T- and B-cell zones with age, an increase in fibroblasts, and delayed immune responses. In human spleens, atrophy of the white pulp, decreased follicle numbers, and predominance of red pulp are observed after the fourth decade. These changes impair the spleen's blood filtration, antigen presentation, and marginal zone functions. Overall, the research results indicate that the general mechanism of age-related changes involves a decrease in lymphoid cells, stromal fibrosis, adipogenesis, degeneration of epithelial cells, and alteration of the cytokine environment. These processes weaken both the adaptive and

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innate components of the immune system, increasing disease risk in the elderly. Morphometric analyses and immunohistochemical methods have quantitatively assessed these changes, confirming their functional significance. For example, epithelial cell clusters appear in the thymus, limiting its regenerative capacity; fibrosis in lymph nodes restricts T-cell movement; and disruption of the marginal zone in the spleen impairs antigen presentation.

Conclusion: The histological structure of the immune system organs is a key factor determining their functional efficiency. Age-related changes in the thymus, lymph nodes, and spleen—such as involution, fibrosis, and restructuring of lymphoid tissues—are among the main causes of immunosenescence. These changes weaken the maturation of T- and B-cells, antigen recognition, and immune responses, resulting in diminished protective mechanisms of the body. The research results indicate that new therapeutic approaches are necessary to understand and slow down these processes. Future studies should focus on deeper investigation of molecular mechanisms and their application in clinical practice. This article serves as an important step in illuminating the age-related dynamics of the immune system.

References

1. Liang Z, et al. Age-related thymic involution: Mechanisms and functional impact. Aging Cell. 2022;21(8):e13671.

2. Hale LP, et al. Histologic and molecular assessment of human thymus. Ann Diagn Pathol. 2004;8(1):50-60.

3. Rezzani R, et al. Thymus and aging: morphological, radiological, and functional overview. Age. 2014;36(1):685-713.

4. Kousa AI, et al. Age-related epithelial defects limit thymic function and regeneration. Nat Immunol. 2024;25:1234-1250.

5. Hadamitzky C, et al. Age-dependent histoarchitectural changes in human lymph nodes. J Anat. 2010;216(5):556-562.

6. Deng Y, et al. Comprehensive characterisation of age-related changes in secondary lymphoid organs. Cell Death Dis. 2025;16:1-15.

7. Turner VM, Mabbott NA. Influence of ageing on the microarchitecture of the spleen and lymph nodes. Biogerontology. 2017;18(5):723-738.

8. Alex L, et al. Microscopic study of human spleen in different age groups. Int J Res Med Sci. 2015;3(7):1701-1706.

ISSN: 3060-4737 Volume 3, Issue 5 IF(Impact Factor) 10.98 / 2025

9. Flores KG, et al. Analysis of the human thymic perivascular space during aging. J Clin Invest. 1999;104(8):1031-1039.

10. Srinivasan J, et al. Age-Related Changes in Thymic Central Tolerance. Front Immunol. 2021;12:676236.

11. Li YR, et al. Thymus aging and immune reconstitution, progresses and challenges. Semin Immunol. 2023;70:101-115.

12. Steinmann GG. The involution of the ageing human thymic epithelium is independent of puberty. Scand J Immunol. 1985;22(5):563-575.

13. Bekkhus T, et al. Stromal transdifferentiation drives lipomatosis and induces extensive vascular remodeling in the aging human lymph node. J Pathol. 2022;258:264-277.

14. Elmore SA. Enhanced histopathology of the spleen. Toxicol Pathol. 2006;34(5):648-655.

15. Cakala-Jakimowicz M, et al. Aging-Related Cellular, Structural and Functional Changes in the Lymph Nodes. Cells. 2021;10(11):3148.

16. Budamagunta V, et al. Cellular senescence in lymphoid organs and immunosenescence. Aging. 2021;13(15):19966-19985.

17. Kwok T, et al. Age-Associated Changes to Lymph Node Fibroblastic Reticular Cells. J Immunol. 2022;208(1):219.16.

18. Yamada D, et al. Review of clinical and diagnostic imaging of the thymus: from age-related changes to thymic tumors. Jpn J Radiol. 2024;42(5):456-470.