**THE IMMUNE SYSTEM & LYMPHOID ORGANS:**

1-The body has a system of cells—the **immune system**—that has the ability to distinguish "self" (the organism's own molecules)from "non-self" (foreign substances). 2-This system has the ability to neutralize or inactivate foreign molecules (such as soluble molecules as well as those present in viruses, bacteria, and parasites) and to destroy microorganisms or other cells (such as virus infected cells, cells of transplanted organs, and cancer cells). 3- The immune system of an individual reacts against its own normal body tissues or molecules, causing **autoimmune diseases.**

**Characteristic features of immune system cells:**

1-The cells of the immune system , ***(i)*** are distributed throughout the body in the blood, lymph, and epithelial and connective tissues;

***(ii)*** are arranged in small spherical nodules called **lymphoid nodules** found in connective tissues and inside several organs; and

***(iii)*** are organized in larger **lymphoid organs**—the lymph nodes, the spleen, the thymus, and the bone marrow. 2- Lymphoid nodules are isolated cells of the immune system found in the mucosa of the digestive system (including the tonsils, Peyer's patches, and appendix), the respiratory system, the reproductive system, and the urinary system are collectively known as **mucosa-associated lymphoid tissue (MALT)** and may be considered a lymphoid organ. 3-The wide distribution of immune system cells and the constant traffic of lymphocytes through the blood, lymph, connective tissues, and lymphoid organs provide the body with an elaborate and efficient system of surveillance and defense.

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| **Thymus:**  1-The thymus is a bilateral organ located in the mediastinum; it attains its peak development during youth. Like bone marrow and B cells, the thymus is considered a central or primary lymphoid organ because T lymphocytes form there. 2-All other lymphoid organs originate exclusively from mesenchyme (mesoderm), the thymus has a dual embryonic origin. 3-Its precursor lymphoblasts originate in the bone marrow, but then move to invade a unique epithelium that developed from the endoderm of the embryo's third and fourth pharyngeal pouches. 4-The thymus has a connective tissue **capsule** that penetrates the parenchyma and divides it into incomplete lobules, with continuity between the cortex and medulla of adjoining lobules. 5-Each lobule has a peripheral darkly stained zone known as the **cortex** and a central light zone called the **medulla.** The cortex is richer in small lymphocytes than the medulla and therefore it stains more darkly. 6-The thymus reaches its maximum development in relation to body weight immediately after birth; it undergoes involution after attaining its greatest size in puberty, but continues to produce lymphocytes until old age. |

**Thymic cortex.**

1-The thymic cortex is composed of an extensive population of T lymphoblasts (also called **thymocytes**) and macrophages in a stroma of **epithelial reticular cells**. 2-The epithelial reticular cells usually have large euchromatic nuclei and are diverse morphologically, but generally either squamous or stellate with long processes. 3-They are typically joined to similar adjacent cells by; ***i)*** **desmosomes** , forming an unusual **cytoreticulum**. Cytoplasmic bundles of intermediate keratin filaments (tonofilaments) give evidence of these cells' epithelial origin. ***ii)*Occluding junctions** between flattened epithelial reticular cells at the boundary between cortex and medulla help to separate these two regions. ***iii)***- **Tight junctions,** Arterioles and capillaries in the thymic cortex are sheathed by flattened epithelial reticular cells with **tight junctions**. 4-The capillary endothelium is continuous and has a thick basal lamina. These features create a **blood-thymus barrier** and prevent most circulating antigens from leaving the microvasculature and entering the thymus cortex.

**Thymic medulla.**

1-The thymic medulla also contains a cytoreticulum of epithelial reticular cells, many less densely packed differentiated T lymphocytes, and structures called **thymic (Hassall's) corpuscles,** which are characteristic of this region . 2-Thymic corpuscles consist of epithelial reticular cells arranged concentrically, filled with keratin filaments, and sometimes calcified. 3- No such a **blood-thymus barrier** is present in the medulla and mature T lymphocytes exit the thymus via venules in this zone.

**Lymph Nodes:**

1-Lymph nodes are bean-shaped, encapsulated structures, generally 2–10 mm in diameter, distributed throughout the body along the course of the lymphatic vessels 2-The nodes are found in the axillae and groin, along the great vessels of the neck, and in large numbers in the thorax and abdomen, especially in mesenteries. 3-Lymph nodes constitute a series of in-line filters that are important in the body's defense against microorganisms and the spread of tumor cells. All this lymph, derived from tissue fluid, is filtered by at least one node before returning to the circulation. 4-These kidney-shaped organs have a convex surface that is the entrance site of lymphatic vessels and a concave depression, the **hilum**, through which arteries and nerves enter and veins and lymphatics leave the organ . A connective tissue **capsule** surrounds the lymph node, sending trabeculae into its interior. 5-The most common cells of lymph nodes are lymphocytes, macrophages and other APCs, plasma cells, and reticular cells; follicular dendritic cells are present within the lymphoid nodules. The different arrangement of the cells and of the reticular fiber stroma supporting the cells creates a **cortex**, a **medulla**, and an intervening **paracortex.**

* **L.N.Cortex:**

The **cortex**, situated under the capsule, consists of the following components:

1-        Many reticular cells, macrophages, APCs, and lymphocytes.

2-        Lymphoid nodules, with or without germinal centers, formed mainly of B lymphocytes, embedded within the diffuse population of other cells

3-         Areas immediately beneath the capsule, called the **subcapsular sinuses**, where the lymphoid tissue has wide reticular fiber meshes. Lymph containing antigens, lymphocytes, and APCs circulates around the wide spaces of these sinuses after being delivered there by the afferent lymphatic vessels.

4-       **Cortical sinuses**, running between the lymphoid nodules, which arise from and share the structural features of the subcapsular sinuses. They communicate with the subcapsular sinuses through spaces similar to those present in the medulla .

* **Paracortex:**

1-The **paracortex** does not have precise boundaries with the cortex and medulla. It can be distinguished from the outer cortex by its lack of B cell lymphoid nodules and its accumulation of T cells, which can be determined by immunohistochemistry . 2-Venules in the paracortex comprise an important entry point for lymphocytes moving from blood into lymph nodes.

* **The lymph node** **medulla** has two major components:

1- **Medullary cords,** are branched cordlike extensions of lymphoid tissue arising from the paracortex. They contain primarily B lymphocytes and often plasma cells and macrophages .

2-  **medullary sinuses; *i)***Medullary cords are separated by dilated spaces, frequently bridged by reticular cells and fibers, called **medullary sinuses** . They contain lymph, lymphocytes, often many macrophages, and sometimes even granulocytes if the lymph node is draining an infected region. ***ii)***These sinuses are continuous with the cortical sinuses and join at the hilum to deliver lymph to the efferent lymph vessel of the lymph node.

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| * **Spleen:**   1-The spleen is surrounded by a **capsule** of dense connective tissue from which emerge **trabeculae**, which partially subdivide the parenchyma or **splenic pulp**. 2-Large trabeculae originate at the hilum, on the medial surface of the spleen; these trabeculae carry nerves and arteries into the splenic pulp as well as veins that bring blood back into the circulation. 3-Lymphatic vessels that arise in the splenic pulp also leave through the hilum via the trabeculae.  **Function of spleen.** ***1)***The spleen is the largest single accumulation of lymphoid tissue in the body and the only one involved in filtration of blood. ***2)***an important organ in defense against blood-borne antigens. ***3)***It is also the main site of destruction of aged erythrocytes. ***4)***As is true of other secondary lymphoid organs, the spleen is a production site of antibodies and activated lymphocytes, which are delivered to the blood. ***5)***Any inert particles in blood are actively phagocytosed by spleen macrophages. |

**Splenic Pulp****.** The spleen is composed of reticular tissue containing reticular cells, many lymphocytes and other blood cells, macrophages, and APCs. The splenic pulp has two components, the **white pulp** and the **red pulp** .

**I-White pulp:** 1-The small masses of white pulp consist of **lymphoid nodules** and the **periarteriolar lymphoid sheathes**, while the red pulp consists of blood-filled **sinusoids** and **splenic cords** (of Bilroth). 2- The splenic artery divides inside the hilum, branching into small **trabecular arteries** following this connective tissue. 3-They leave the trabeculae and enter the parenchyma as arterioles enveloped by a sheath of T lymphocytes, which is part of the white pulp. Surrounded by the T lymphocytes, these vessels are known as **central arterioles** . 5-Surrounding the lymphoid nodules is a **marginal zone** consisting of many blood sinuses and lymphoid tissue . The marginal zone contains lymphocytes, many macrophages, and an abundance of blood antigens and thus plays an important role in the immunological activities of the spleen.

**II-Red pulp:** 1-The red pulp is composed almost entirely of splenic cords and venous sinusoids . The splenic cords contain a network of reticular cells or reticular fibers that support T and B lymphocytes, macrophages, plasma cells, and many blood cells (erythrocytes, platelets, and granulocytes). 2-The splenic cords are separated by wide, irregularly shaped sinusoids . Unusual elongated endothelial cells, called **stave cells**, line the splenic sinusoids, oriented in parallel with the sinusoid's blood flow. 3-These cells are sparsely wrapped in reticular fibers set in a transverse direction, much like the hoops surrounding the staves of a wooden keg . 4- The highly permeable splenic sinusoids are surrounded by very incomplete basal laminae. The spaces between the endothelial cells of the splenic sinusoids are smaller and only flexible cells are able to pass easily from the red pulp cords into the lumen of the sinusoids. 5-Because the lumen of splenic sinusoids is often blood-filled and very small and because the splenic cords are infiltrated with red blood cells, microscopic distinctions between splenic cords and sinusoids may be difficult.