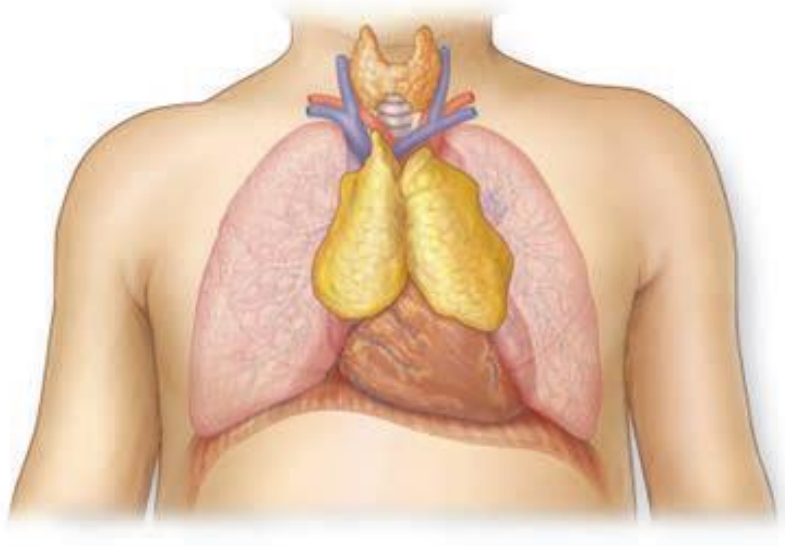
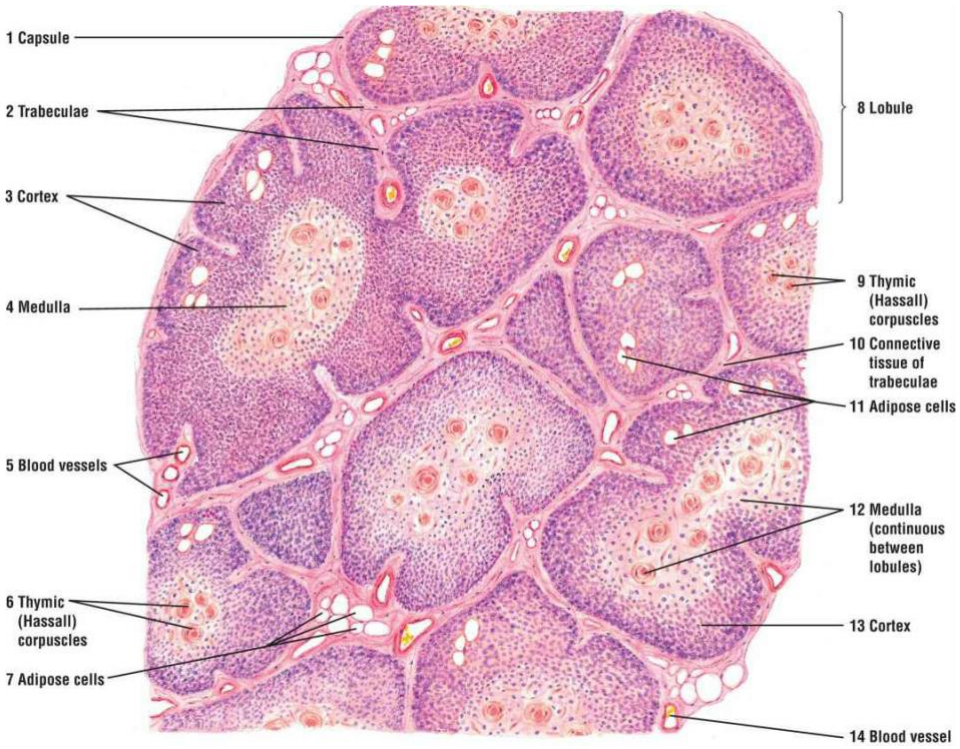
THYMUS GLAND

The thymus gland is a soft, lobulated lymphoepithelial organ located in the upper anterior mediastinum and lower part of the neck.

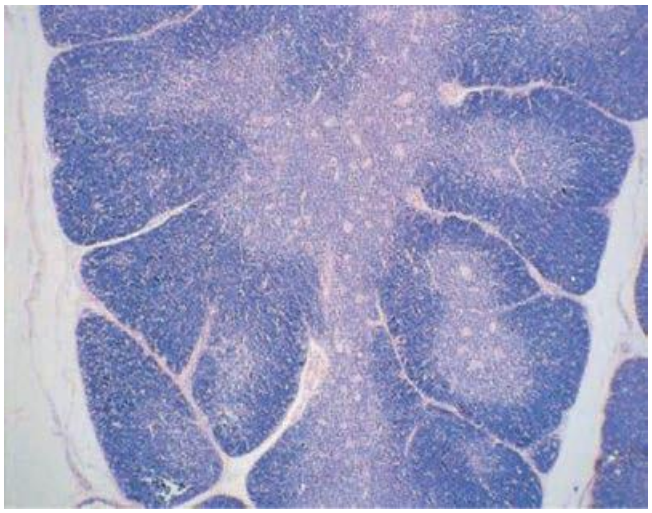


The thymus gland is surrounded by a connective tissue capsule from which arise connective tissue trabeculae that extend into the organ and subdivide the thymus gland into incomplete lobules. Blood vessels pass into the thymus gland via the connective tissue capsule and the trabeculae.
Each lobule consists of a dark-staining outer cortex and a light-staining inner medulla.
The cortex of the thymus appears much darker histologically than does the medulla because of the presence of a large number of T lymphocytes (thymocytes). Immunologically incompetent T cells leave the bone marrow and migrate to the periphery of the thymic cortex, where they undergo extensive proliferation and instruction to become immunocompetent T cells. In addition to the thymocytes, the cortex houses macrophages, dendritic cells, and epithelial reticular cells (thymic epithelial cells).
In the lighter-staining medulla, the epithelial cells form a coarser framework that contains fewer lymphocytes and whorls of epithelial cells that combine to form thymic (Hassall) corpuscles. Because the lobules are incomplete, the medulla shows continuity between the neighboring lobules.

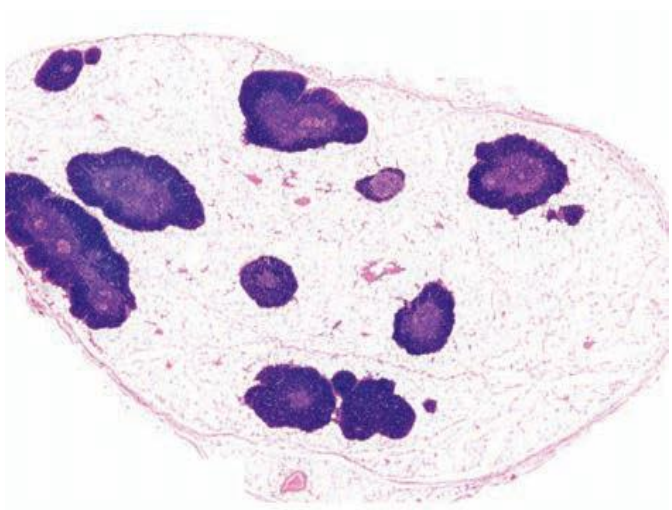
The thymic (Hassall) corpuscles are oval structures consisting of round or spherical aggregations (whorls) of flattened epithelial cells. Thymic (Hassall) corpuscles in the medulla of the gland, which are characteristic features in identifying the thymus gland. It is believed that thymic corpuscles produce cytokine thymic stromal lymphopoietin that induces antigen-presenting cells [APCs] also known as dendritic cells) to promote development of the regulatory T cells.



The histology of the thymus gland varies with age. The thymus gland is highly developed shortly after birth. By puberty, thymus glands begin to involute with gradual regression and degeneration. As a consequence, lymphocyte production declines, and the thymic (Hassall) corpuscles become more prominent. In addition, the parenchyma or cellular portion of the gland is gradually replaced by loose connective tissue and adipose cells.



Micrograph of child's thymus



Micrograph of adult's thymus

VASCULAR SUPPLY

The thymus receives numerous small arteries, which enter the capsule and are distributed throughout the organ via the trabeculae between adjacent lobules. Branches of these vessels do not gain access to the cortex directly; instead, from the trabeculae, they enter the corticomedullary junction, where they form capillary beds that penetrate the cortex.

The capillaries of the cortex are of the continuous type, possess a thick basal lamina and are invested by a sheath of epithelial reticular cells that form a blood–thymus barrier. Thus, the developing T cells of the cortex are protected from contacting blood-borne macromolecules. However, self-macromolecules are permitted to cross the blood–thymus barrier (probably controlled by the epithelial reticular cells), possibly to eliminate those T cells that are programmed against self-antigens. The cortical capillary network drains into small venules in the medulla.

Newly formed, immunologically incompetent T cells arriving from the bone marrow leave the vascular supply at the corticomedullary junction and migrate to the periphery of the cortex. As these cells mature, they move deeper into the cortex and enter the medulla as single positive T cells (I T cells) that are inactive immunocompetent cells. As they leave the thymic medulla via veins draining the thymus, they are referred to as *naïve T cells*.

FUNCTIONAL CORRELATIONS OF THYMUS GLAND

The primary function of thymus gland is to promote the development of cells of the immune system, the T cells (lymphocytes, also called thymocytes), to recognize and respond to antigens.

Undifferentiated lymphocytes are carried from the bone marrow via the bloodstream to the thymus gland. In the thymic cortex, the epithelial reticular cells, also called thymic nurse cells, surround the lymphocytes and promote their differentiation, proliferation, and maturation. Here, the lymphocytes mature into immunocompetent T cells, helper T cells, and cytotoxic T cells, whereby they acquire various surface receptors for the recognition of antigens. After maturation, the T cells leave the thymus gland via the bloodstream and populate the lymph nodes, spleen, and other thymus-dependent lymphatic tissues in the organism.

The maturation and selection of T cells within the thymus gland is a complicated process that includes the positive and negative selection of T cells.

Only a small fraction of lymphocytes generated in the thymus gland reach maturity. As maturation progresses in the cortex, the T cells are presented with self- and foreign antigens by APCs. T cells that are unable to recognize self-antigens or that recognize self-antigens die and are eliminated by macrophages (negative selection), which is about 95% of the total cells.

lymphocytes that recognize the foreign antigens (positive selection) survive, reach maturity, enter the medulla from the cortex, and are then distributed in the bloodstream to other sites in the body.

The macrophages that are close to the perivascular areas and form the blood–thymus barrier are also involved in phagocytosis of apoptotic (dead) lymphocyte that occurred during their differentiation and clonal selection.

the epithelial reticular cells secrete hormones necessary for the proliferation, differentiation, and maturation of T cells and the expression of their surface markers. These hormones are thymulin, thymopoietin, thymosin, thymic humoral factor, interleukins, and interferon.

The thymus gland involutes after puberty and becomes filled with adipose tissue, and the production of T cells decreases. However, because T-lymphocyte progeny has been established, immunity is maintained without new T-cell production. However, if the thymus gland is removed from a newborn, the lymphoid organs will not receive the immunocompetent T cells, and the individual will not acquire the immunologic competence to fight pathogens. Death may occur early in life as a result of complications of an infection and the lack of a functional immune system.

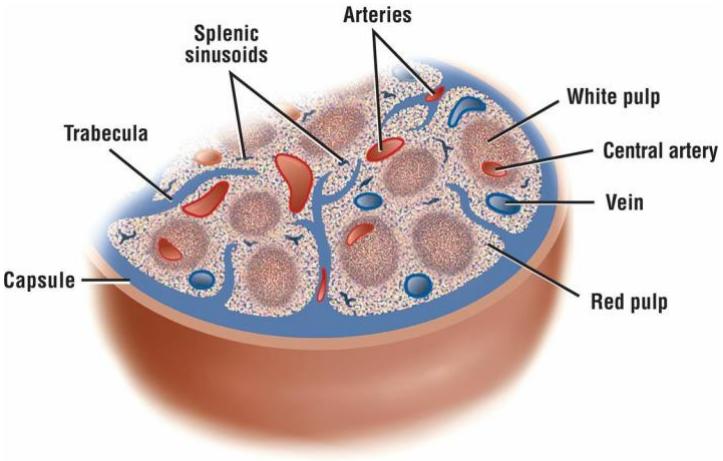
CLINICAL CORRELATIONS

Enlargement of the thymus is often associated with a disease called **myasthenia gravis**. In this condition there is great weakness of skeletal muscle. In many such cases the thymus is enlarged and there may be a tumour in it. Removal of the thymus may result in considerable improvement in some cases.

Myasthenia gravis is now considered to be a disturbance of the immune system. There are some proteins to which acetyl choline released at motor end plates gets attached. In myasthenia gravis antibodies are produced against these proteins rendering them ineffective. Myasthenia gravis is, thus, an example of a condition in which the immune system begins to react against one of the body's own proteins. Such conditions are referred to as **autoimmune diseases**.

SPLEEN

The spleen is a large lymphoid organ with a rich blood supply. It lies in the left upper abdomen. The spleen contains vascular sinusoids supported by a reticulin scaffold.



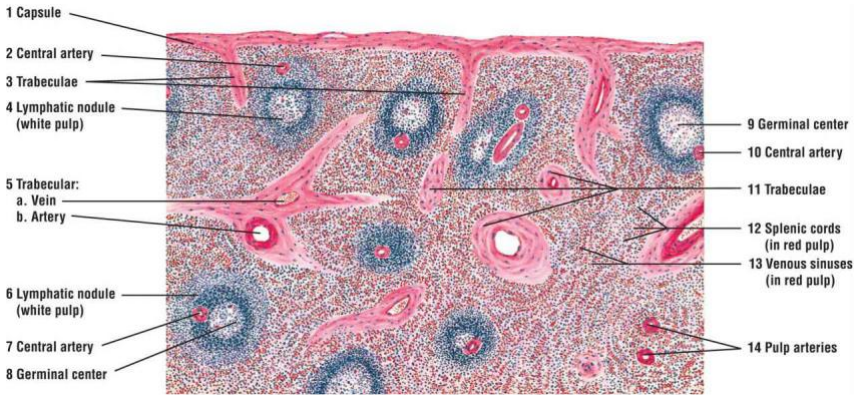
The organ is surrounded by a capsule of dense connective tissue from which emerge trabeculae to penetrate the parenchyma or splenic pulp. The main trabeculae enter the spleen at the hilum and extend throughout the organ. Located within the trabeculae are trabecular arteries and trabecular veins. The trabeculae, arising from the capsule, carry blood vessels into and out of the parenchyma of the spleen.

Splenic pulp has two components: the white pulp (20% of the spleen) and the red pulp. The small masses of white pulp consist of lymphoid nodules and the periarteriolar lymphoid sheaths (PALS), while the red pulp consists of blood-filled sinusoids and splenic cords.

The spleen is characterized by numerous lymphatic nodules that constitute the white pulp. Included in the white pulp are the germinal centers and blood vessels called central arteries located in the peripheries of the lymphatic nodules. Central arteries are branches of trabecular arteries that become ensheathed with lymphatic tissue as they leave the connective tissue trabeculae. These periarterial lymphatic sheaths (PALS) form the lymphatic nodules of the white pulp of the spleen. The central artery in the lymphatic nodule has a peripheral, or an eccentric, position; however, because the artery occupies the center of the periarterial lymphatic sheath, it is called the central artery. The cells in the periarterial lymphatic sheath are mainly T cells. In the more lightly stained germinal center are found B cells, many medium-sized lymphocytes, some small lymphocytes, and lymphoblasts. White pulp is located within the blood-rich red pulp.

The arterial system ends in red pulp, which consists of splenic cords (of Billroth) and splenic (blood) sinusoids (Venous sinuses).
The splenic cords are thin aggregations of lymphatic tissue containing small lymphocytes, associated cells, and various blood cells.
splenic sinuses are interconnected blood channels that drain splenic blood into larger sinuses that leave the spleen via the splenic vein. The dilated vessels lined with the modified endothelium of elongated cells that appear cuboidal in transverse sections.

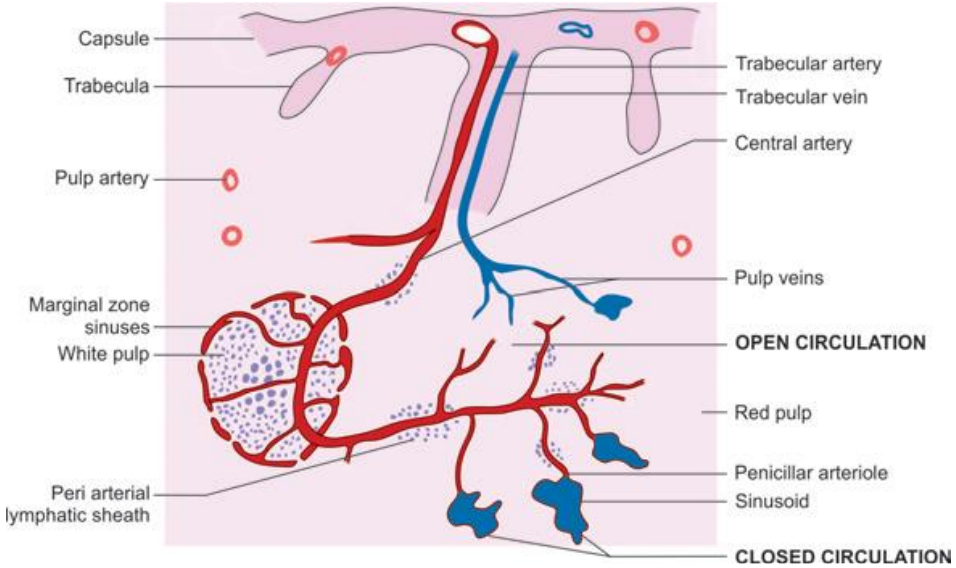
Also present in the red pulp are the pulp arteries (branches of the central artery after it leaves the lymphatic nodule), capillaries and pulp veins (venules).



SPLENIC BLOOD CIRCULATION

Small branches of trabecular arteries are called central arterioles and become enclosed within a sheath of lymphoid cells, the periarteriolar lymphoid sheath (PALS) in white pulp. B cells in these sheaths can form nodules as the largest masses of white pulp, and around these nodules are located the marginal zone sinuses.

Emerging from the white pulp, the central arteriole branches as the penicillar arterioles, which lead to sheathed capillaries. From these, blood flows into either a closed circulation passing directly into splenic sinuses or an open circulation, being dumped from the vasculature into the lymphoid tissue of the red pulp's splenic cords. From there viable blood cells reenter the vasculature through the walls of the sinuses.



FUNCTIONAL CORRELATIONS OF SPLEEN

The spleen filters blood and is the site of immune responses to blood-borne antigens.

The main function of the red pulp is to filter the blood. It removes antigens, microorganisms, platelets, and aged or abnormal erythrocytes from the blood.

The white pulp is the immune component of and consists of accumulated lymphocytes primarily T cells, macrophages, and antigenpresenting cells (APCs). The lymphatic nodules contain mainly B cells. As a result, T cells and B cells interact, become activated, proliferate, and perform their immune response.

Macrophages in the spleen also break down the hemoglobin of worn-out erythrocytes, recycle the iron from hemoglobin, and return it to the bone marrow, where it is reused for synthesis of new hemoglobin by developing erythrocytes. The heme from the hemoglobin is further degraded and excreted into bile by the liver cells.

During fetal life, the spleen is a hematopoietic organ, producing granulocytes and erythrocytes. This hematopoietic capability, however, ceases after birth.

The spleen serves as an important reservoir for blood. Because it has a spongelike microstructure, much blood can be stored in its interior. When needed, the stored blood is returned from the spleen to the general circulation.

CLINICAL CORRELATIONS

Enlargement of the spleen, splenomegaly, can occur from a variety of causes, including lymphoma or other malignant growth, infections such as mononucleosis, or sickle cell disease and other types of anemia. The splenic capsule is relatively thin, and an enlarged spleen is susceptible to traumatic rupture, a potentially life-threatening occurrence due to loss of blood into the abdominal cavity. Such rupture may require prompt surgical removal of the spleen, splenectomy, after which most functions of the organ are carried out by other lymphoid organs, with erythrocyte removal occurring in the liver and bone marrow.

MUCOSA-ASSOCIATED LYMPHOID TISSUE

The mucosa-associated lymphoid tissue (MALT) is composed of a nonencapsulated, localized lymphocyte infiltration and lymphoid nodules in the mucosa of the gastrointestinal, respiratory, and urinary tracts. it provides immunological protection against invasion by pathogens via vulnerable exposed absorptive surfaces.

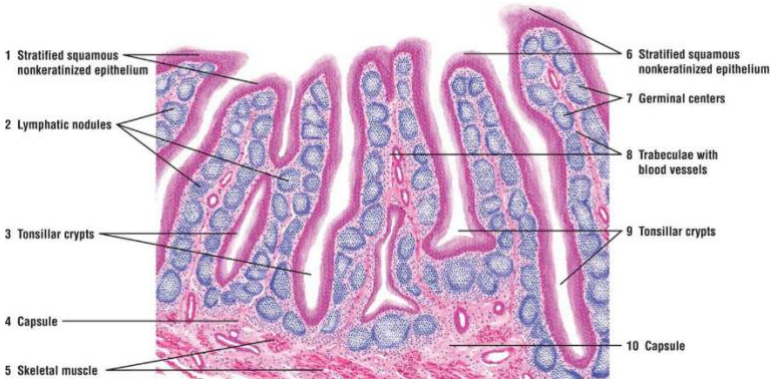
The best examples of these accumulations are those associated with the mucosa of the gut: gut-associated lymphoid tissue (GALT), the bronchus-associated lymphatic tissue (BALT), and the tonsils (palatine, pharyngeal, and lingual).

PALATINE TONSILS are located in the posterior lateral walls of the oral cavity The paired palatine tonsils consist of aggregates of lymphatic nodules located in the oral cavity. The surface of the palatine tonsil is covered by a stratified squamous nonkeratinized epithelium that also covers the rest of the oral cavity.

Each tonsil is invaginated by deep grooves called tonsillar crypts that are also lined by stratified squamous nonkeratinized epithelium.

lymphatic nodules distributed along the lengths of the tonsillar crypts in the connective tissue Below the epithelium. The lymphatic nodules frequently merge with each other and usually exhibit lighter-staining germinal centers, indicative of B-cell formation.

A dense connective tissue underlies the palatine tonsil and forms its capsule. Arise from the capsule, connective tissue trabeculae, some with blood vessels, and pass toward the surface of the tonsil between the lymphatic nodules. Below the connective tissue capsule are sections of skeletal muscle fibers.



CLINICAL CORRELATIONS

Inflammation of the tonsils, tonsillitis, is more common in children than adults. Chronic inflammation of the pharyngeal lymphoid tissue and tonsils of children often produces hyperplasia and enlargement of the tonsils to form "adenoids," which can obstruct the eustachian tube and lead to middle ear infections.