The Lymphatic System

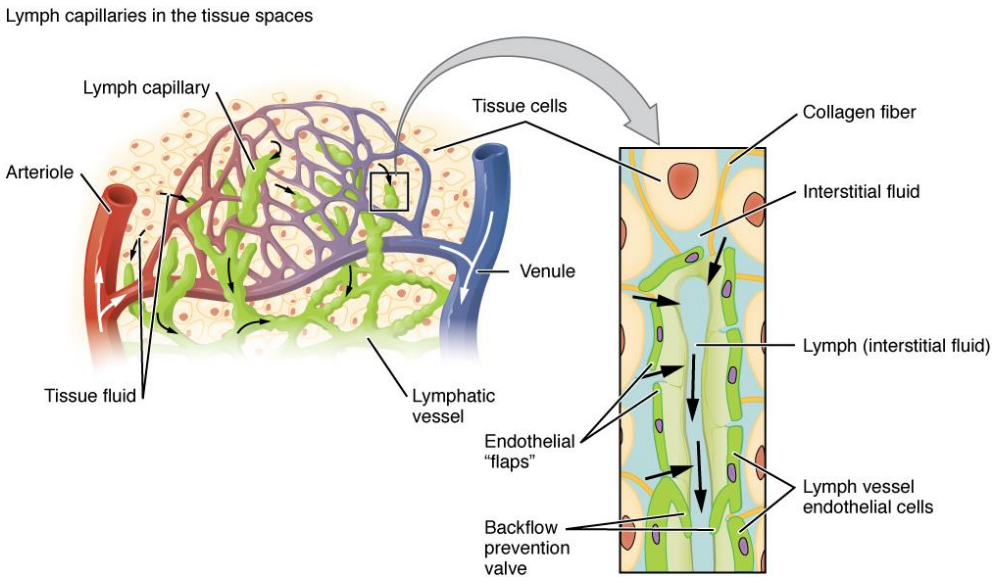
Lymph

Lymph is the name for tissue fluid that enters lymph capillaries. Filtration in capillaries creates tissue fluid, most of which returns almost immediately to the blood in the capillaries by osmosis. Some tissue fluid, however, remains in interstitial spaces and must be returned to the blood by way of the lymphatic vessels. Without this return, blood volume and blood pressure would very soon decrease.

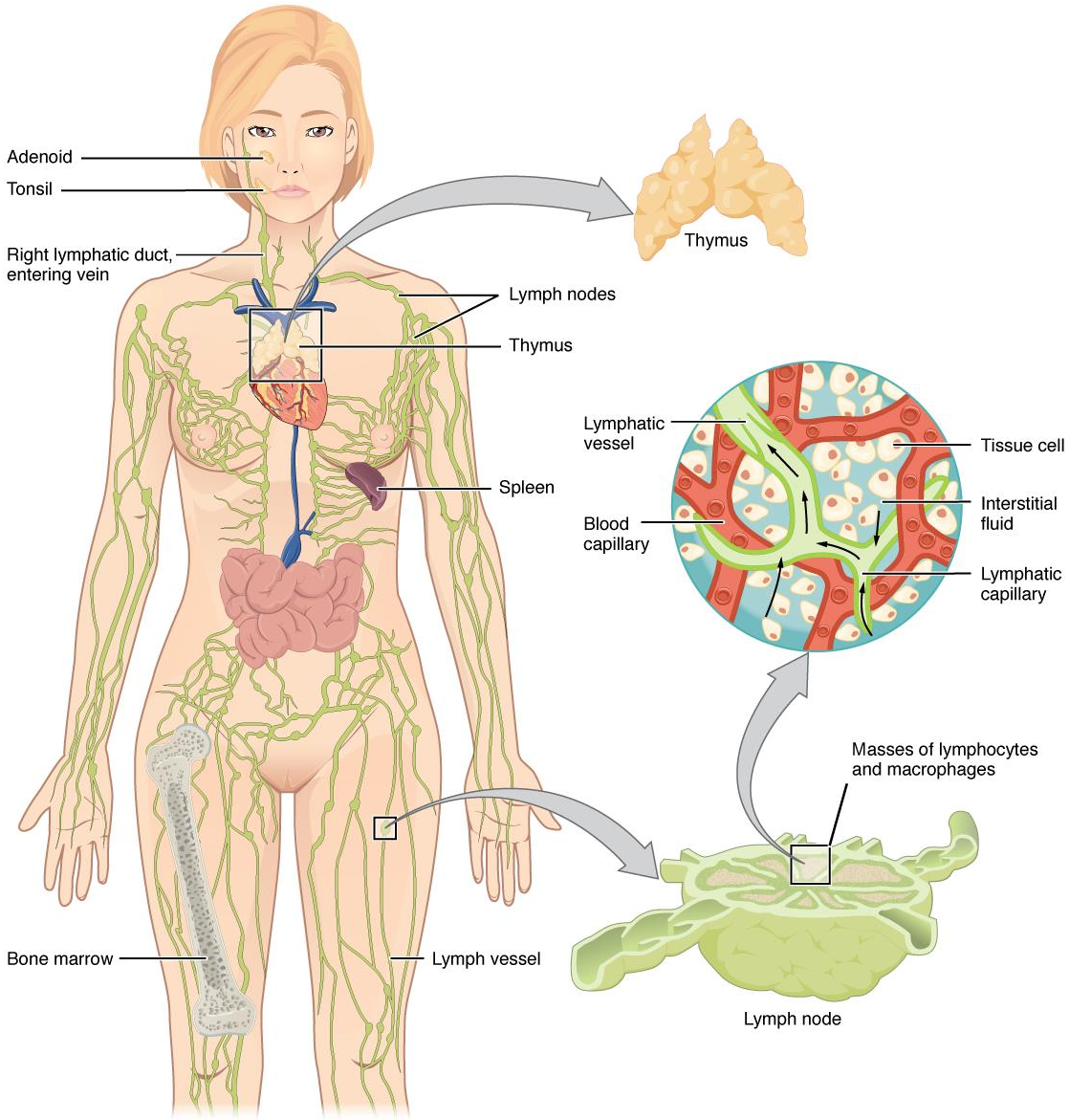
Lymph vessels

The system of lymph vessels begins as dead-end **lymph capillaries** found in most tissue spaces. Lymph capillaries are very permeable and collect tissue fluid and proteins. Lymphatic capillaries are interlaced with the arterioles and venules of the cardiovascular system. Collagen fibers anchor a lymphatic capillary in the tissue. Interstitial fluid slips through spaces between the overlapping endothelial cells that compose the lymphatic capillary. The overlapping ends are termed 'flaps'. Lymph vessels are located in almost every tissue in the body except the central nervous system, bone marrow, bones, teeth, and the cornea of the eye, which do not contain lymph vessels.

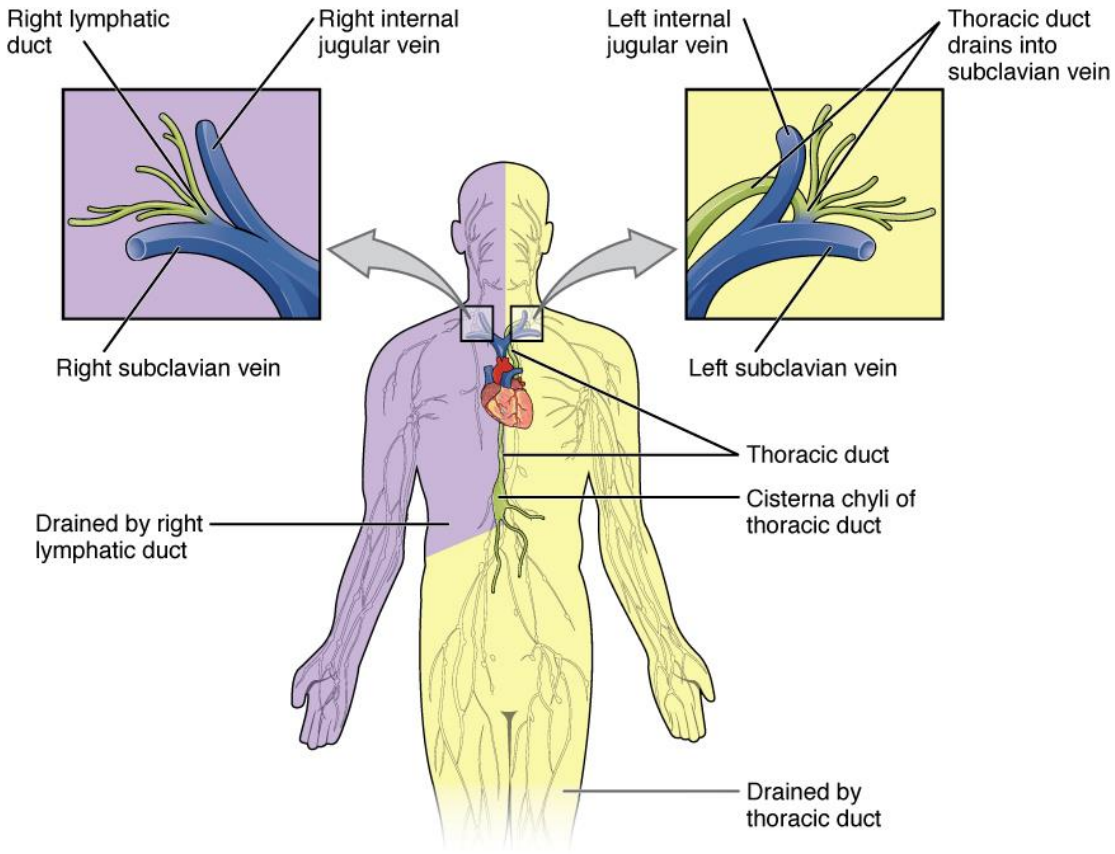
Lacteals are specialized lymph capillaries in the villi of the small intestine; they absorb the fat-soluble end products of digestion, such as fatty acids and vitamin A.



Lymph capillaries unite to form larger lymph vessels, whose structure is very much like that of veins. There is no pump for lymph (as the heart is the pump for blood), but the lymph is kept moving within lymph vessels by the same mechanisms that promote venous return. The smooth muscle layer of the larger lymph vessels constricts, and the one-way valves (just like those of veins) prevent backflow of lymph. Lymph vessels in the extremities are compressed by the skeletal muscles that surround them; this is the **skeletal muscle pump**. The **respiratory pump** (inflation of lungs) alternately expands and compresses the lymph vessels in the chest cavity and keeps the lymph moving.



Where is the lymph going? Back to the blood to become plasma again. The lymph vessels from the lower body unite in front of the lumbar vertebrae to form a vessel called **cisterna chyli**, which continues upward in front of the backbone as the **thoracic duct**. Lymph vessels from the upper left quadrant of the body join the thoracic duct, which empties lymph into the left subclavian vein. Lymph vessels from the upper right quadrant of the body unite to form the right lymphatic duct, which empties lymph into the right subclavian vein. Flaps in both subclavian veins permit the entry of lymph but prevent blood from flowing into the lymph vessels.



Lymphoid organs

The lymphoid organs are where lymphocytes mature, proliferate, and are selected, which enables them to attack pathogens without harming the cells of the body. Primary lymphatic organs are where lymphocytes are formed and mature. They provide an environment for stem cells to divide and mature into B- and T- cells. There are two primary lymphatic organs: the **red bone marrow**

and the **thymus gland**. Both T-cell and B-cells are 'born' in the bone marrow. However, whereas B cells also mature in the bone marrow, T-cells have to migrate to the thymus, which is where they mature in the thymus.

Secondary lymphoid tissues are arranged as a series of filters monitoring the contents of the extracellular fluids, i.e. lymph, tissue fluid and blood. The lymphoid tissue filtering each of these fluids is arranged in different ways. Secondary lymphoid tissues are also where lymphocytes are activated.

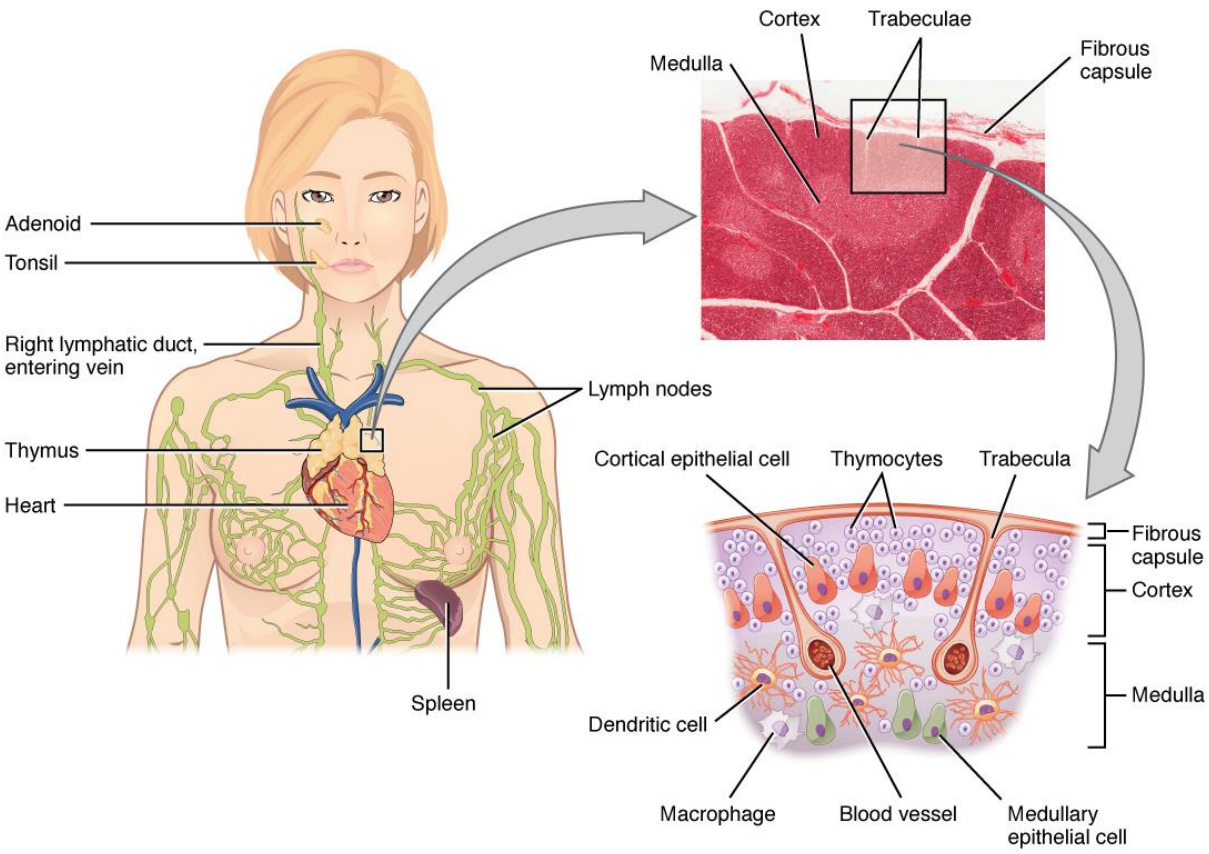
Therefore, lymphocytes develop and mature in the primary lymphoid organs, but they mount immune responses from the secondary lymphoid organs. A naïve lymphocyte is one that has left the primary organ and entered a secondary lymphoid organ. Naïve lymphocytes are fully functional immunologically, but have yet to encounter an antigen to respond to. In addition to circulating in the blood and lymph, lymphocytes concentrate in secondary lymphoid organs.

Secondary lymphoid organs include: **spleen, lymph nodes, lymph nodules, Peyer's patches** and **mucosa associated lymphoid tissue (MALT**). All of these tissues have many features in common, including the following:

- The presence of lymphoid follicles, the sites of the formation of lymphocytes, with specific B cell-rich and T cell-rich areas
- An internal structure of reticular fibers with associated fixed macrophages
- Germinal centers, which are the sites of rapidly dividing B lymphocytes and plasma cells
- Specialized post-capillary vessels known as high endothelial venules; the cells lining these venules are thicker and more columnar than normal endothelial cells, which allow cells from the blood to directly enter these tissues

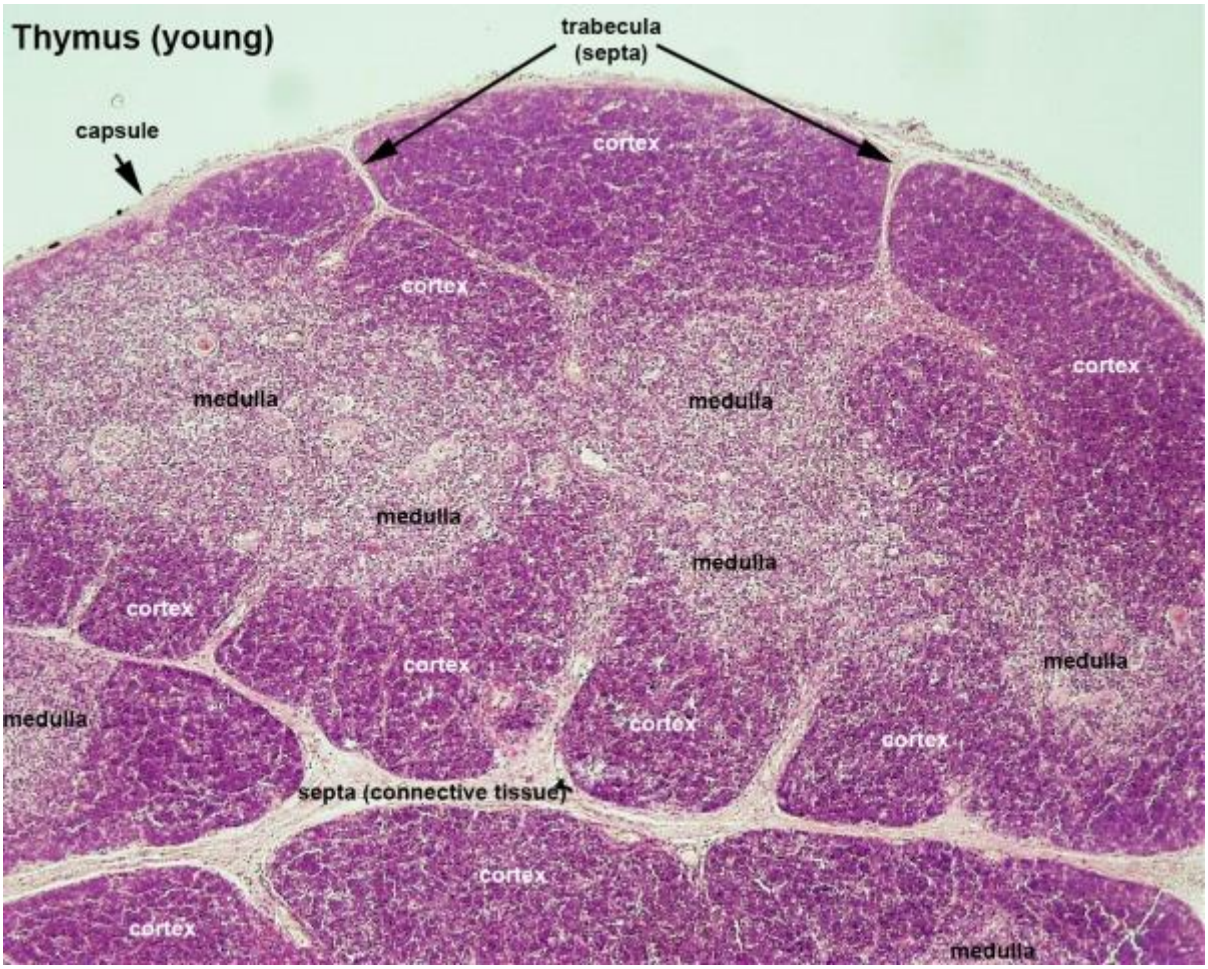
Thymus

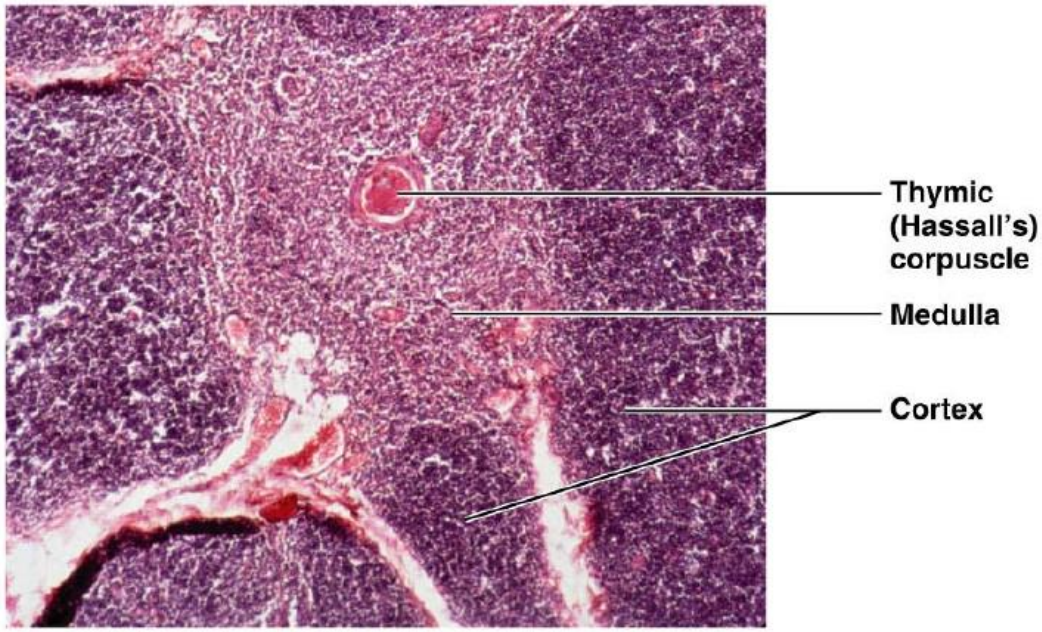
The **thymus** is a bilobed organ found in the space between the sternum and the aorta of the heart, located inferior to the thyroid gland. In the fetus and infant, the thymus is large and extends under the sternum. With increasing age, the thymus shrinks, and relatively little thymus tissue is found in adults (involuted thymus).



Connective tissue holds the lobes closely together but also separates them and forms a capsule. The connective tissue capsule further divides the thymus into lobules via extensions called trabeculae. The outer region of the organ is known as the cortex and contains large numbers of thymocytes (immature T cells), cortical epithelial cells and some macrophages and dendritic cells. The cortex is densely packed so it stains more intensely than the rest of the thymus. The medulla, where thymocytes migrate before leaving the thymus as naïve T cells, contains a less dense collection of thymocytes, medullary epithelial cells and dendritic cells, in addition to thymic (Hassall's) corpuscles.

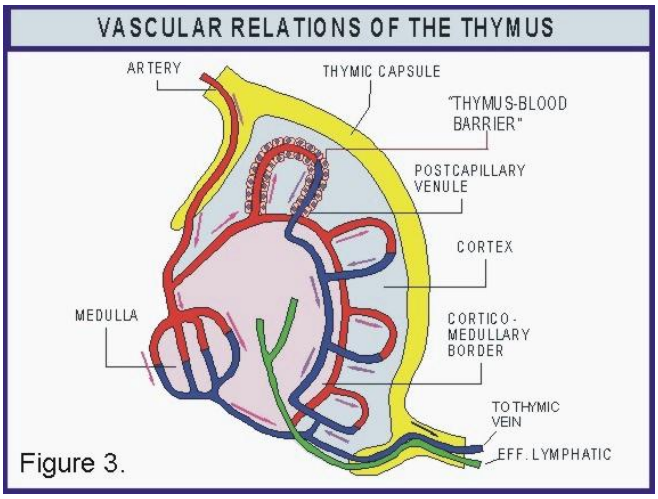
Hassall's corpuscles are degenerated epithelial cells that do not produce any thymic hormones. They contain some T cells and macrophages.

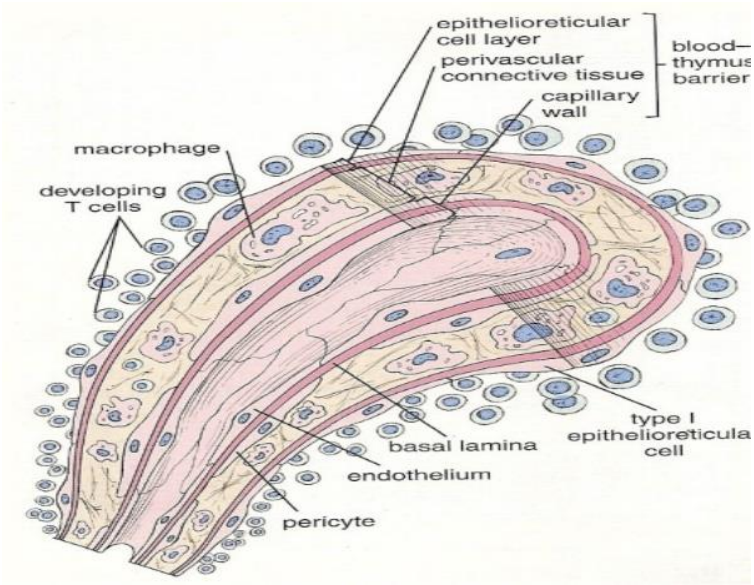




Thymocytes proliferate and mature in the thymus but only 1-3% survive the selection process that allows mature T cells to enter the circulation. In the thymus, APCs scan for T cells that may self-react; these cells are killed so as to

prevent autoimmunity (negative selection). This 'education' of T cells must occur in a very controlled environment. To ensure that no foreign antigens, there is a very tight blood-thymus barrier (note that thymocytes can only enter the thymus via bloodstream; there are no afferent lymph vessels).





Thymic hormones (thymosin and thymopoietin) are necessary for what may be called "immunological competence". To be competent means to be able to do something well. Thymic hormones enable the T cells to participate in the recognition of foreign antigens and to provide immunity. This capability of T cells is established early in life and then is perpetuated by the lymphocytes themselves. The newborn's immune system is not yet fully mature, and infants are more susceptible to certain infections than are older children and adults. Usually by the age of 2 years, the immune system matures and becomes fully

functional. This is why some vaccines, such as measles vaccine, are not recommended for infants younger than 15 to 18 months of age. Their immune systems are not mature enough to respond strongly to the vaccine, and the protection provided by the vaccine may be incomplete.

Spleen

The **spleen** is located in the upper left quadrant of the abdominal cavity, just below the diaphragm, behind the stomach. The lower rib cage protects the spleen from physical trauma. It is a major secondary lymphoid organ.

It is about 12 cm (5 in) long and is attached to the lateral border of the stomach via the gastrosplenic ligament. The spleen is a fragile organ although it has a connective tissue capsule, and is dark red due to its extensive vascularization. The spleen is sometimes called the filter of the blood because of its extensive vascularization and the presence of macrophages and dendritic cells that remove microbes and other materials from the blood, including dying red blood cells.

The functions of the spleen are centered on the systemic circulation. As such, it lacks afferent lymphatic vessels. It is comprised of 2 functionally and morphologically distinct compartments, the red pulp and the white pulp. The red pulp is a blood filter that removes foreign material and damaged erythrocytes. It is also a storage site for iron, erythrocytes, and platelets. The spleen is also the largest secondary lymphoid organ containing about one-fourth of the body's lymphocytes and initiates immune responses to blood-borne antigens. This function is charged to the white pulp which surrounds the central arterioles.

In the fetus, the spleen produces red blood cells, a function assumed by the red bone marrow after birth.

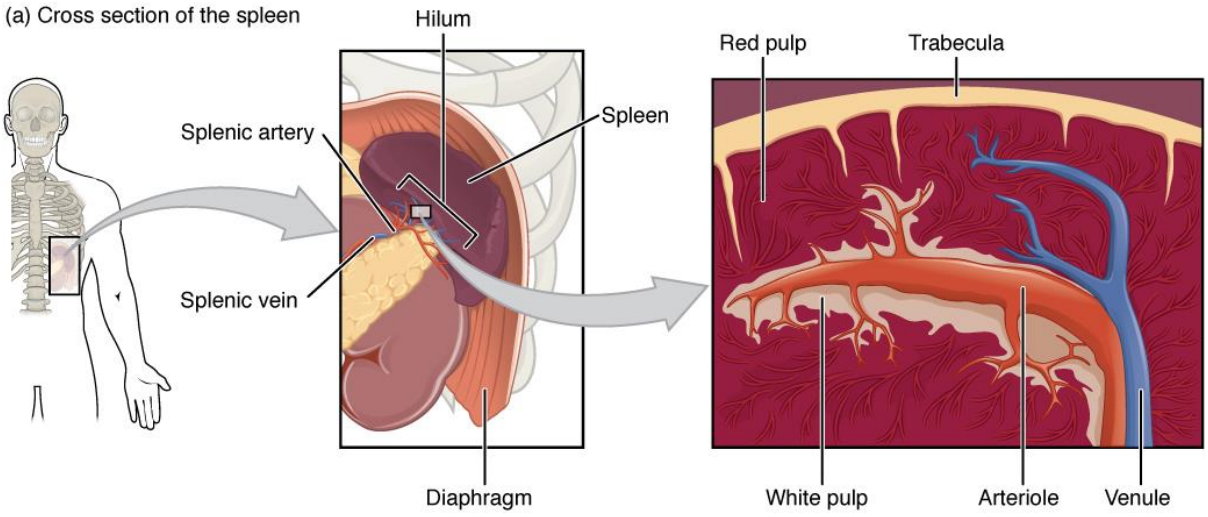
The functions of the spleen after birth are:

1. Produces lymphoid cells in response to antigens. The newly-formed lymphocytes then enter the blood stream.
2. Contains some fixed plasma cells that produce antibodies to foreign antigens.
3. Contains fixed macrophages (RE cells) that phagocytize pathogens or other foreign materials in the blood. The macrophages of the spleen also

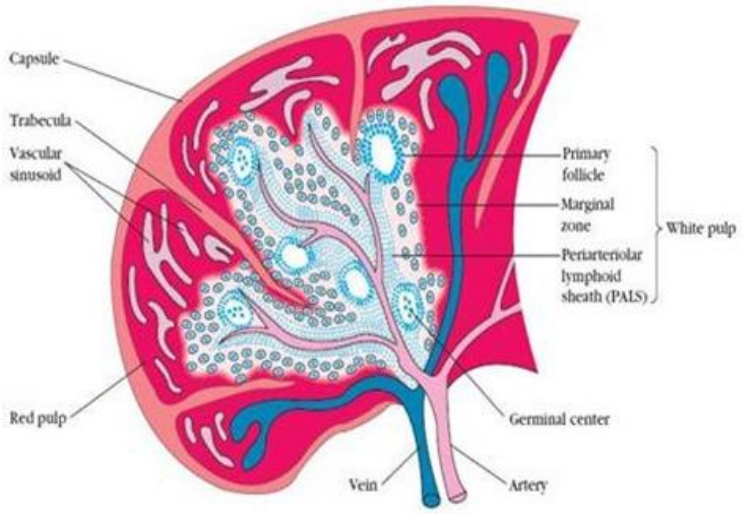
phagocytize old and damaged red blood cells and form bilirubin. By way of portal circulation, the bilirubin is sent to the liver for excretion in bile.

4. Acts as a reservoir of blood in times of shock or hemorrhage.

The spleen is not considered a vital organ, because other organs compensate for its functions if the spleen must be removed. The liver and red bone marrow will remove old red blood cells from circulation, and the many lymph nodes and nodules will produce lymphocytes and monocytes and phagocytize pathogens (as will the liver). Despite this redundancy, a person without a spleen is somewhat more susceptible to certain bacterial infections such as pneumonia and meningitis.

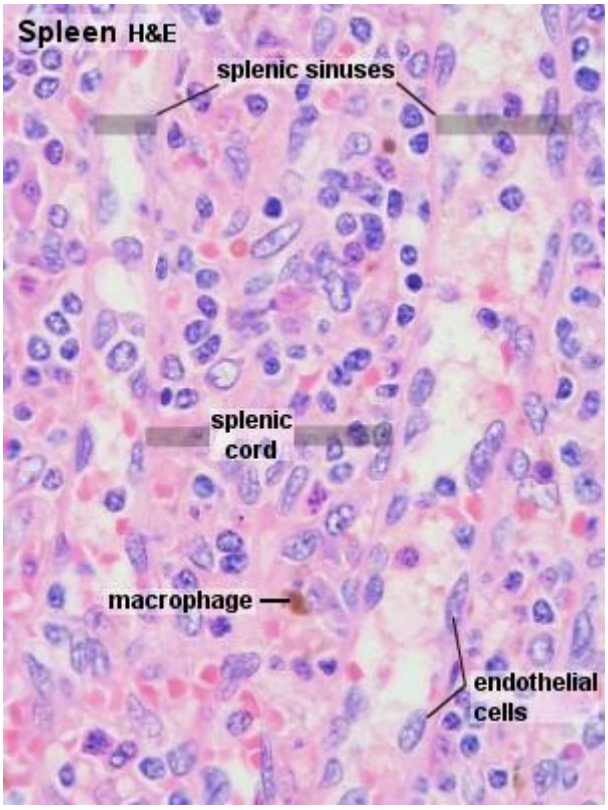


The spleen is surrounded by a capsule composed of dense fibrous tissue, elastic fibers, and smooth muscle. The spleen is also divided by extensions of the capsule called trabeculae, and within each splenic nodule is an area of red pulp, consisting of mostly red blood cells, and white pulp, which is composed of three sub-compartments: the periarteriolar lymphoid sheath (PALS), the follicles, and the marginal zone.

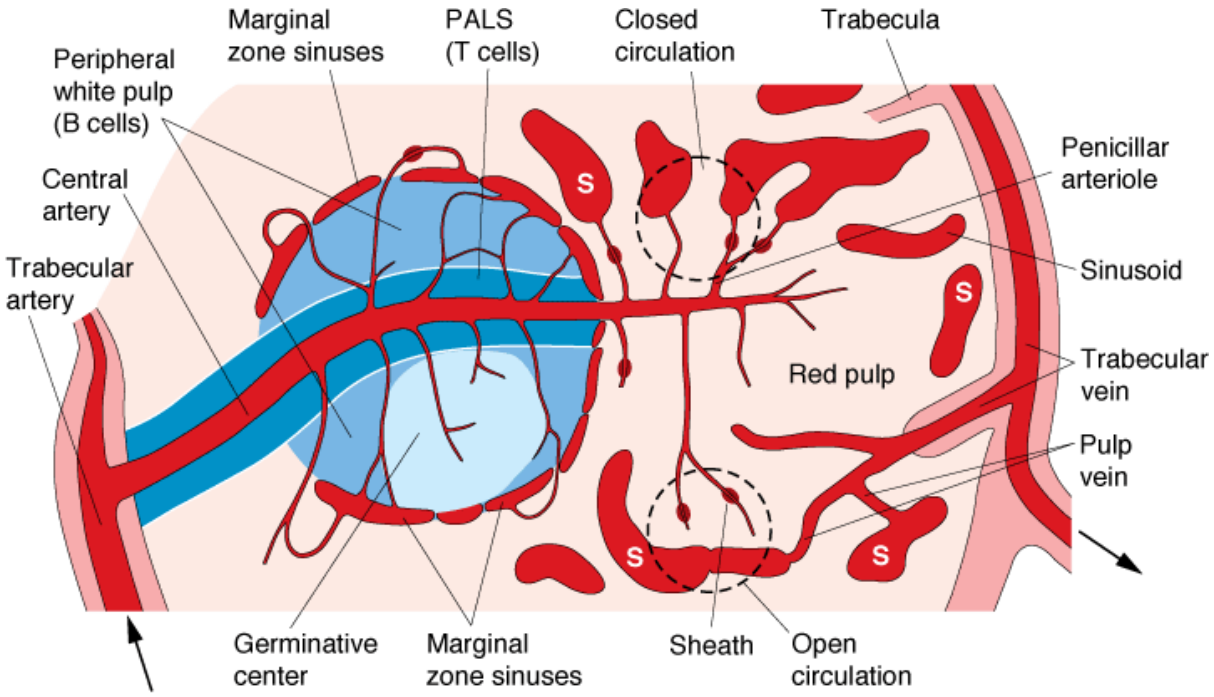


Upon entering the spleen through the hilum, the splenic artery splits into trabecular arteries. Trabecular arteries divide into central arteries (surrounded by white pulp), then into several arterioles and eventually into sinusoids. Blood from the capillaries subsequently collects in the venous sinuses and leaves via the splenic vein.

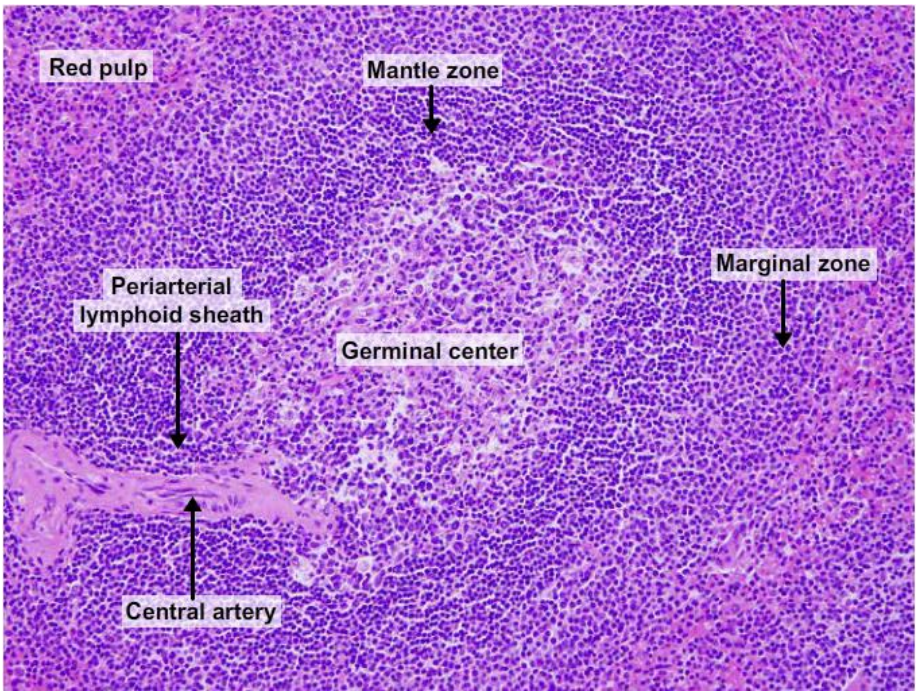
The red pulp has reticular fibers with fixed macrophages attached, free macrophages, and all of the other cells typical of the blood, including some lymphocytes. The red pulp is composed of a three dimensional meshwork of splenic cords and venous sinuses.



The white pulp surrounds a central arteriole. It is subdivided into the PALS, the follicles, and the marginal zone. The PALS have the structure of diffuse lymphatic tissue (lymphocytes and concentric layers of reticular fibers and flattened reticular cells). The follicles are continuous with the PALS and are typically found at bifurcation sites of the central arterioles. They are composed primarily of B-cells. Follicles may contain germinal centers (dividing B cells surrounded by T cells and accessory cells, including macrophages and dendritic cells), which form upon antigenic stimulation, and stain less intensely.



The marginal zone is a unique region of the spleen situated at the interface of the red pulp with the PALS and follicles. Considered by many to be a separate compartment rather than part of the white pulp, it is designed to screen the systemic circulation for antigens and pathogens and plays an important role in antigen processing.

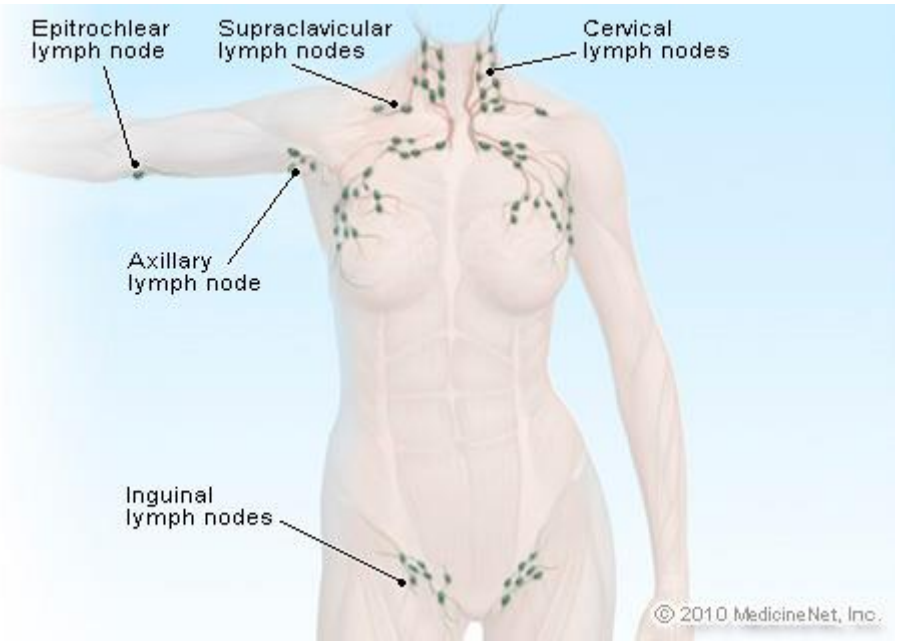


Lymph nodes and nodules

Lymph nodes and **nodules** are masses of lymphatic tissue. Nodes and nodules differ with respect to size and location. Nodes are usually larger, 10 to 20mm in length; nodules range from a fraction of a millimeter to several millimeters in length.

Lymph nodes are found in groups along the pathways of lymph vessels, and lymph flows through these nodes on its way to the subclavian veins. Lymph enters the nodes through several afferent lymph vessels and leaves through one or two efferent vessels. As lymph passes through a lymph node, bacteria and other foreign materials are phagocytized by fixed (stationary) macrophages. Fixed plasma cells (from lymphocytes) produce antibodies to any pathogens in the lymph; these antibodies, as well as lymphocytes and monocytes, will eventually reach the blood.

There are many groups of lymph nodes along all the lymph vessels throughout the body, but three paired groups deserve mention because of their strategic locations. These are the **cervical**, **axillary**, and **inguinal** lymph nodes. Notice that these are at the junctions of the head and extremities with the trunk of the body. Breaks in the skin, with entry of pathogens, are much more likely to occur in the arms or legs or head rather than in the trunk. If these pathogens get to the lymph, they will be destroyed by the lymph nodes before they get to the trunk, before the lymph is returned to the blood in the subclavian veins.



Cervical Lymph Nodes

In the head and neck, lymph nodes are arranged in two horizontal rings and two vertical chains on either side of the neck. The outer, superficial ring consists of the **occipital**, **preauricular** (**parotid**), **submandibular**, **sublingual** and **submental** nodes. The inner, deep ring is formed by clumps of mucosa associated lymphoid tissue (MALT) located primarily in the naso- and oropharynx (**Waldeyer's ring**).

The following describes the main cervical node groups:
The **occipital nodes** are in the superficial group, which includes 3-5 nodes. This group of nodes is localized between the sternocleidomastoid (SCM) and trapezius muscles, at the apex of the posterior triangle. These nodes are superficial to the splenius capitis.
The **deep posterior cervical group** includes 1-3 nodes. This group of nodes is located deep to the splenius capitis and follows the course of the occipital artery. These nodes drain the scalp, the posterior portion of the neck, and the deep muscular layers of the neck.
The **postauricular nodes** vary in number from 2 to 4; they are located in the fibrous portion of the superior attachment of the SCM muscle to the mastoid process. Postauricular nodes drain the posterior parietal scalp and the skin of the mastoid region.

The **preauricular (parotid) nodes** can be divided into intraglandular and extraglandular groups. The extraglandular parotid nodes are located outside but adjacent to the parotid gland, where they drain the frontolateral scalp and face, the anterior aspects of the auricle, the external auditory canal, and the buccal mucosa. Embryologically, the lymphatic system develops before the parotid gland, which surrounds the intraglandular nodes as it develops. This explains why the parotid gland contains lymphoid tissue. The intraglandular nodes drain the same regions as the extraglandular nodes, to which they interconnect and then drain into the upper jugular group of lymph nodes. As many as 20 parotid nodes may be found.
The **submandibular** nodes are divided into 5 groups: preglandular, postglandular, prevascular, postvascular, and intracapsular. The preglandular and prevascular groups are located anterior to the submandibular gland and facial artery, respectively. The postglandular and postvascular groups are posterior to these structures. Differing from the parotid gland in embryological development, there is no true intraglandular node; however, occasionally, a node has been identified inside the capsule of the gland. The submandibular nodes drain the ipsilateral upper and lower lip, cheek, nose, nasal mucosa, medial canthus, anterior gingiva, anterior tonsillar pillar, soft palate, anterior two thirds of the tongue, and submandibular salivary gland. The efferent vessels drain into the internal jugular nodes.

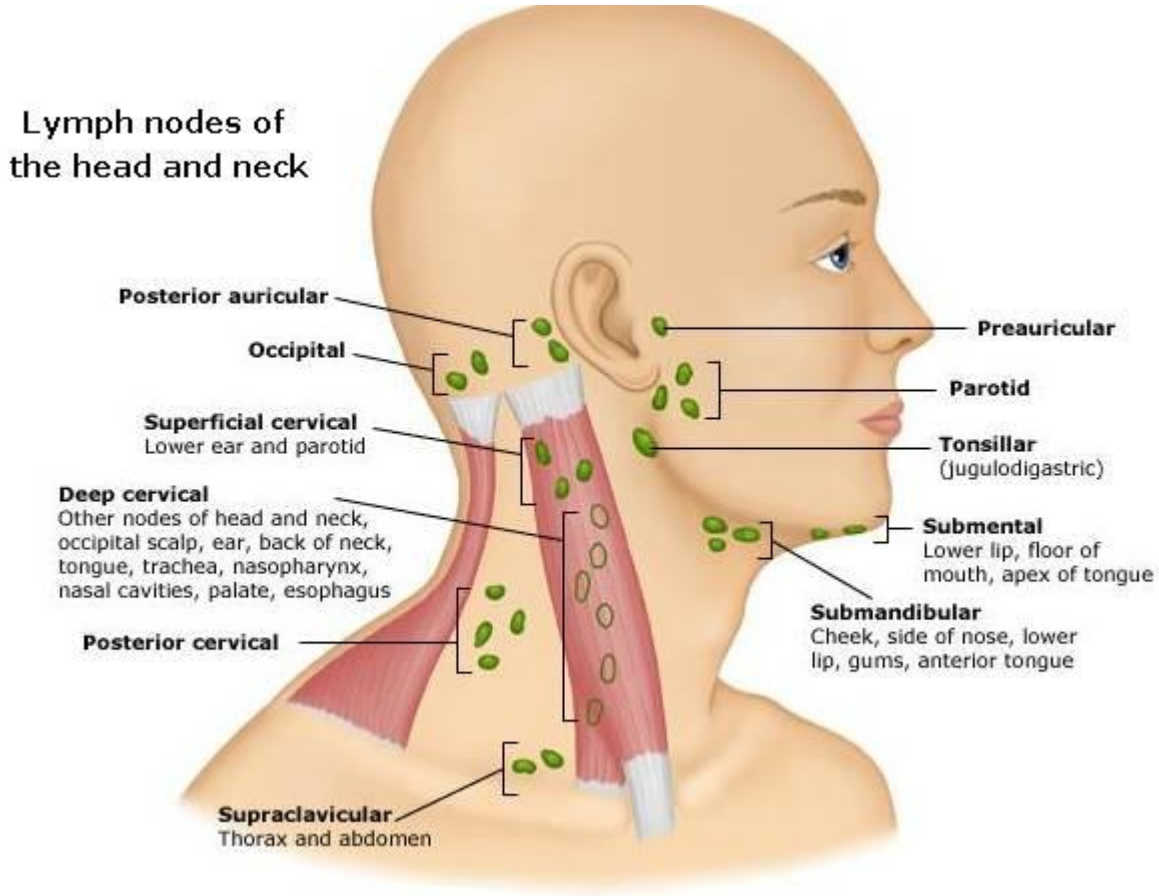
For the **submental** nodes, 2-8 nodes are located in the soft tissues of the submental triangle between the platysma and mylohyoid muscles. These nodes drain the chin, the middle portion of the lower lip, the anterior gingiva, and the anterior third of the tongue. The efferent vessels drain into both the ipsilateral and contralateral submandibular nodes or into the internal jugular group.

The **sublingual** nodes are located along the collecting trunk of the tongue and sublingual gland and drain the anterior floor of the mouth and ventral surface of the tongue. These nodes subsequently drain into the submandibular or jugular group of nodes.

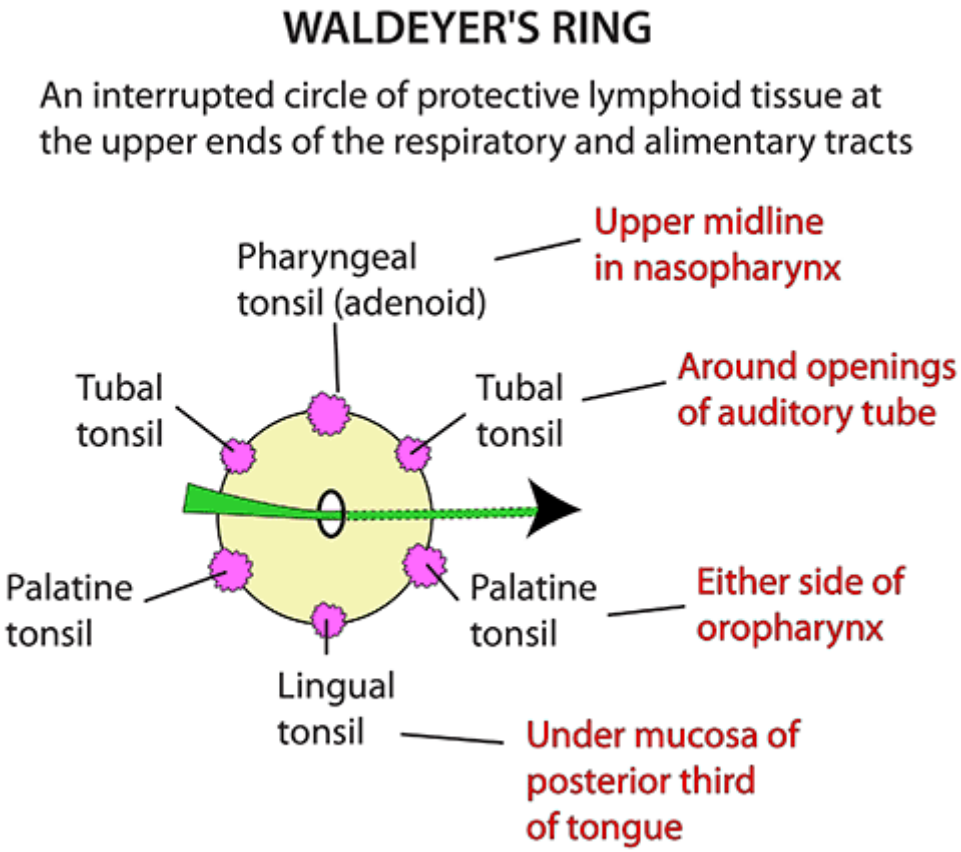
The **retropharyngeal nodes** are divided into a medial and lateral group, located between the pharynx and the prevertebral fascia. The lateral group, located at the level of the atlas near the internal carotid artery, consists of 1-3 nodes, which may extend to the skull base. The medial group extends inferiorly to the postcricoid level. This group drains the posterior region of the nasal cavity, sphenoid and ethmoid sinuses, hard and soft palates, nasopharynx, and posterior

pharynx down to the postcricoid area. Management of these nodes must be considered if any malignancy arises from the mentioned drainage areas.
The **anterior cervical nodes** are divided into the anterior jugular chain and the juxtavisceral chain of nodes. The anterior jugular chain nodes follow the anterior jugular vein, located superficial to the strap muscles. These nodes drain the skin and muscles of the anterior portion of the neck, and the efferent vessels empty into the lower internal jugular nodes.
The **pretracheal group** consists of nodes between the isthmus of the thyroid gland down to the level of the innominate vein. Varying from 2-12 in number, these nodes drain the region of the thyroid gland and the trachea and receive afferent flow from the prelaryngeal group. The pretracheal efferents empty in the internal jugular group and the anterior superior mediastinal nodes.
The **paratracheal** nodes lie near the recurrent laryngeal nerve and drain the thyroid lobes, parathyroid glands, subglottic larynx, trachea, and upper esophagus. The efferent vessels travel to the lower jugular group or directly toward the junction of the internal jugular vein and the subclavian vein. The anterior nodes drain bilaterally because the midline of the neck has no division. Treatment must be planned accordingly when a tumor is located in subjacent draining areas.
The **lateral cervical nodes** are divided into superficial and deep groups. The superficial group follows the external jugular vein and drains into either the internal jugular or transverse cervical nodes of the deep group.
The **deep group** forms a triangle bordered by the internal jugular nodes, the spinal accessory nodes, and the transverse cervical nodes. The transverse cervical nodes, forming the base of the triangle, follow the transverse cervical vessels and may contain as many as 12 nodes. These nodes receive drainage from the spinal accessory group and from collecting trunks of the skin of the neck and upper chest. The spinal accessory chain follows the nerve of the same name and may account for as many as 20 nodes. This chain receives lymph from the occipital, postauricular, and suprascapular nodes and from the posterior aspect of the scalp, nape of the neck, lateral aspect of the neck, and the shoulder.
The **internal jugular chain** consists of a large system covering the anterior and lateral aspects of the internal jugular vein, extending broadly from the digastric muscle superiorly to the subclavian vein inferiorly. As many as 30 of these nodes may exist, and they have been arbitrarily divided into upper, middle, and lower groups. The efferents of these nodes eventually pass into the venous

system via the thoracic duct on the left and multiple lymphatic channels on the right. These nodes drain all the other groups mentioned.



The palatine tonsils, nasopharyngeal tonsil (adenoid) and lingual tonsil constitute the major part of **Waldeyer's ring**, with the tubal tonsils and lateral pharyngeal bands as less prominent components. The lymphoid tissue of Waldeyer's ring is located at the gateway of the respiratory and alimentary tract and belongs to the mucosa-associated lymphoid tissue (MALT). As tonsils (details discussed below) are the first site of encounter with inhaled and ingested micro-organisms, they are considered the first line of defense against exogenous aggressors. The generation of B cells in the germinal centers of the tonsil is one of the most essential tonsillar functions.



Axillary Lymph Nodes

The lymph nodes of the axillary region are responsible for the lymphatic drainage of a large section of human anatomy. Due to this arrangement and duty, they have a particular clinical relevance. This is particularly evident with breast cancer, where axillary lymph node status, with regards to cancer, defines the treatment algorithm and approach. There are 20-30 lymph nodes divided into five groups; Anterior (pectoral), posterior (subscapular), lateral (humeral), central, and apical.

The **anterior (pectoral) group** is located across the inferior border of the pectoralis minor muscle and the superior border of the pectoralis major muscle. There are usually 4-5 large nodes. The lymph flows from the anterolateral aspect of the abdominal wall superior to the level of the umbilicus and the lateral quadrants of the breast. It conveys the lymph to more central nodes.

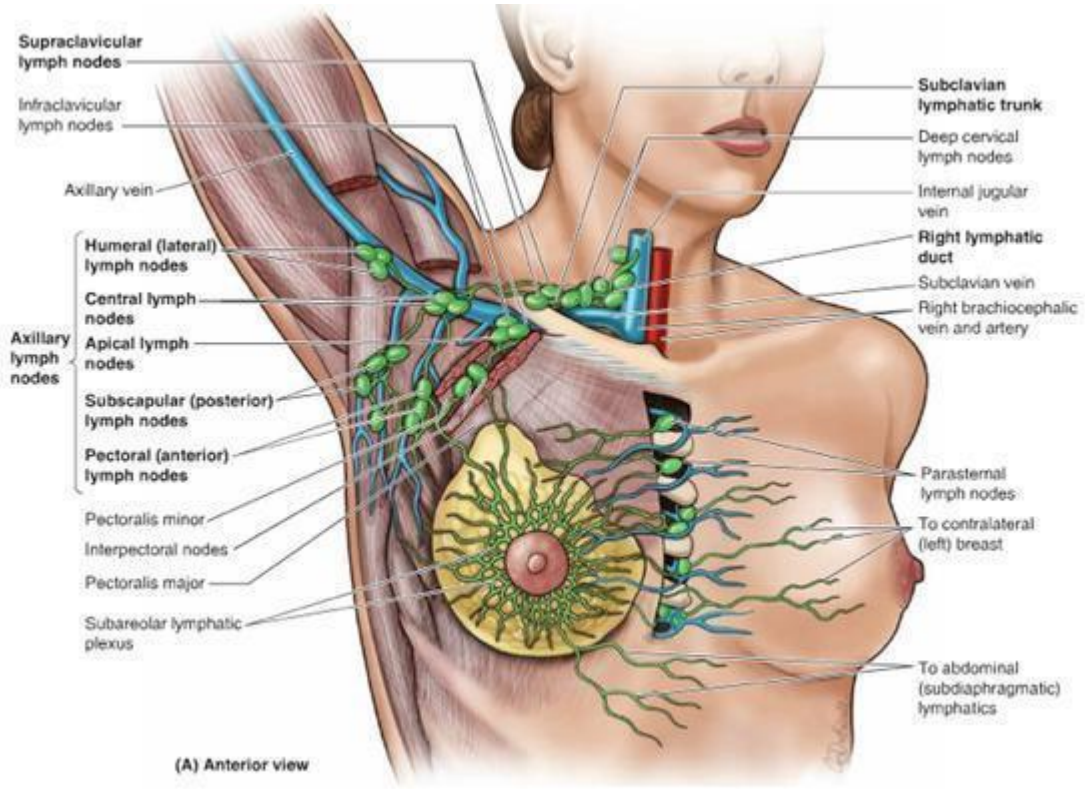
The **posterior (subscapular) group** consists of 6-7 nodes that can be found anterior to the subscapularis muscle and receives superficial lymph vessels

located more commonly within the upper portion of the back and posterior neck. However, these can receive lymph from as far inferior as the superior border of the iliac crests.

The **lateral (humeral) group** is a group of 4-6 nodes that can be found against the axillary vein. The vast majority of the lymph vessels of the upper limb flow into this group. The superficial group of nodes however, drains the lateral aspect of the upper limb and flows into the infraclavicular nodes.

The **central group** consists of 3-4 nodes, and is found at the base and centrally located in the axilla. These nodes are interspread amongst the adipose (fat) of the region. These are the most important group of nodes in terms of drainage because these receive lymph flow from the three groups of nodes mentioned above (anterior, posterior, and lateral).

The **apical group** (4-5 nodes) lies at the apex of the axilla and is located at the lateral border of the first rib. It is also referred to as the subclavicular group. This group receives efferent lymph vessels from the other axillary group of nodes. The apical group of nodes then drains into the subclavian lymph trunk. The drainage is different on the left and right sides. The left side axillary drainage flows into the thoracic duct, whereas on the right side the drainage is into the right lymphatic trunk.



Inguinal Lymph Nodes

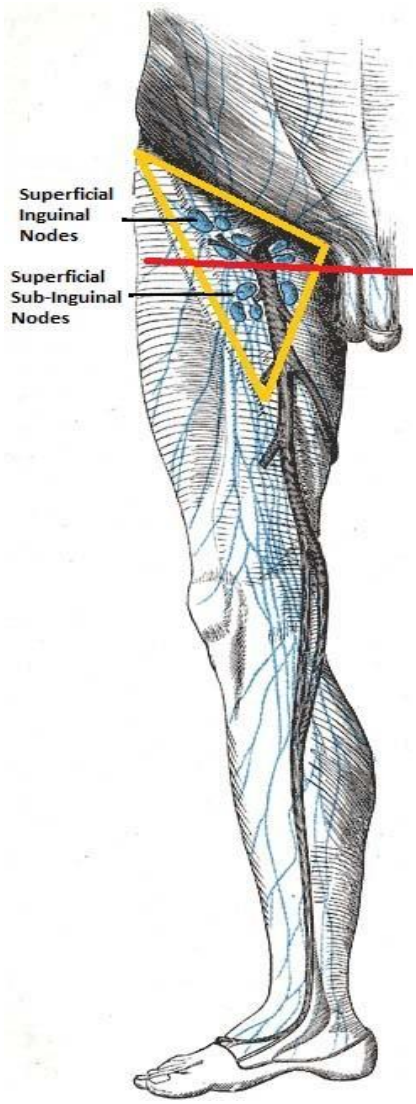
The inguinal nodes are found in the upper aspect of the **femoral triangle** and are around 20 in number.

They are subdivided into 2 groupings determined by their position relative to a horizontal line drawn at the level of termination of the great saphenous vein. Those below this line are the **sub-inguinal nodes** (consisting of a deep and superficial set) and those above are the **superficial inguinal nodes.**

The **superficial inguinal nodes** form a line directly below the **inguinal ligament** and receive lymph from the penis, scrotum, perineum, buttock and abdominal wall.

The s**uperficial sub-inguinal nodes** are located on each side of the proximal section of the great saphenous vein. They receive afferent input primarily from the superficial lymphatic vessels of the lower leg.

The **deep sub-inguinal nodes** are often found in one to three in number and are most commonly found on the medial aspect of the femoral vein. The afferent supply to these nodes is from the deep lymphatic trunks of the thigh which accompany the femoral vessels.



Lymph nodules are small masses of lymphatic tissue found just beneath the epithelium of all mucous membranes. The body systems lined with mucous membranes are those that have openings to the environment: the respiratory, digestive, urinary, and reproductive tracts. You can probably see that these are also strategic locations for lymph nodules, because any natural body opening is a possible portal of entry for pathogens. For example, if bacteria in inhaled air get through the epithelium of the trachea, lymph nodules with their macrophages are in position to destroy these bacteria before they get to the blood.

Some of the lymph nodules have specific names. Those of the small intestine are called **Peyer's patches**, and those of the pharynx are called **tonsils**. The palatine tonsils are on the lateral walls of the pharynx, the adenoid (pharyngeal tonsil) is on the posterior wall, and the lingual tonsils are those on the base of the tongue. The tonsils, therefore, form a ring of lymphatic tissue around the

pharynx, which is a common pathway for food and air and for the pathogens they contain.

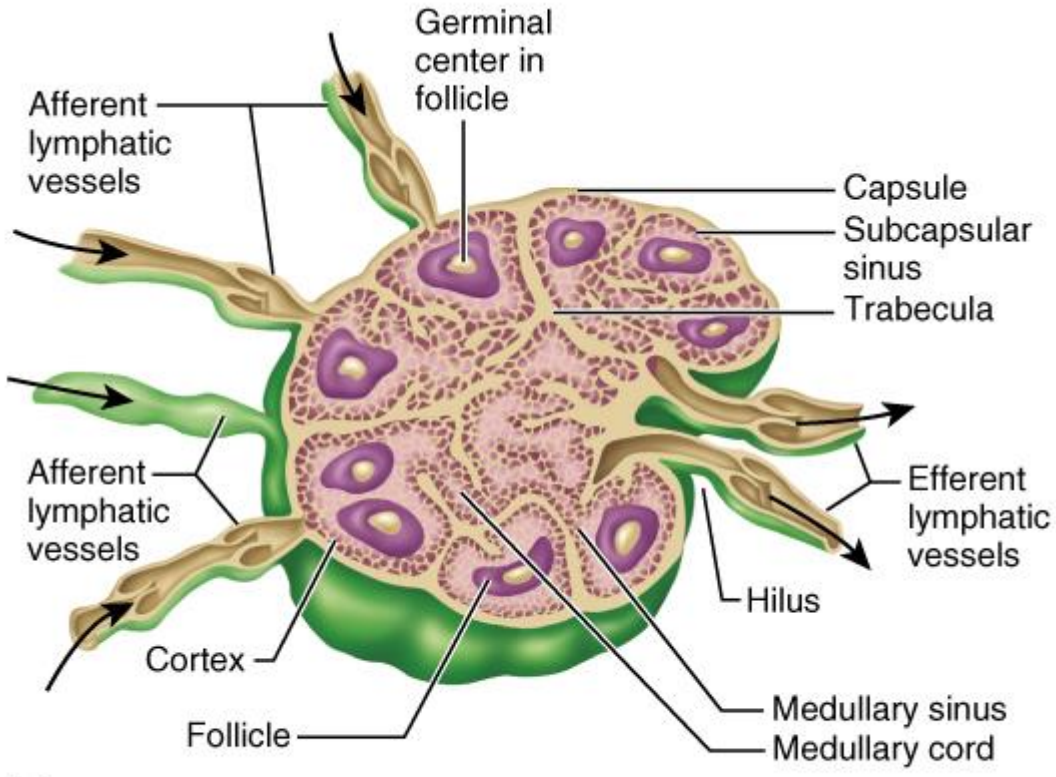
Histology of lymph nodes

The nodes are covered by a **capsule** of dense connective tissue, and have capsular extensions, of connective tissue, called the **trabeculae**, which provide support for blood vessels entering into the nodes.
Lymph, containing micro-organisms, soluble antigens, antigen presenting cells, and a few B-cells, enters the lymph node via **afferent lymphatic** vessels which enter the **subcapsular sinus**.

It then runs through **cortical sinuses** into **medullary sinuses** and leaves through the **efferent lymphatic vessels**, at the **Hilium** as **efferent** lymph.

This contains lots of T-lymphocytes, B-lymphocytes, plasma cells and antibody.

All the **sinuses** are lined by a discontinuous layer of simple squamous endothelium, and they also contain lymphocytes and macrophages. Reticular fibers provide additional support to the matrix/stroma.



(a)

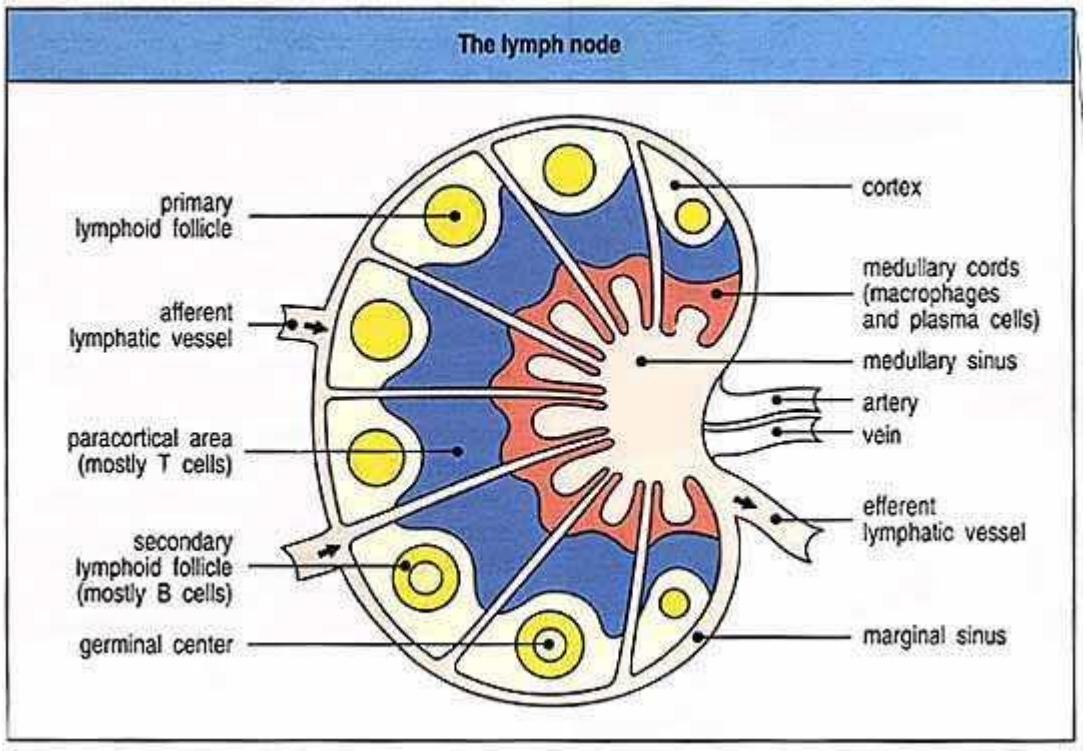
The **cortex** is divided into an outer and an inner cortex (**paracortex**).

The **outer cortex** has lymphatic nodules that mostly contain B-cells. Small lymphocytes sit in the spaces between the reticular fiber meshwork in the cortex. The lighter staining areas are **germinal centers,** where the **B-cells proliferate** into antibody secreting plasma cells. **Macrophages** are also present in these regions, together with **dendritic cells**, and some **T-cells**. Both the macrophages, and the dendritic cells trap antigens and present them on their surfaces to B-cells.

The **inner cortex** contains mostly T-cells.

The **deep cortical**, and **medullary cords** contain B-cells and plasma cells.

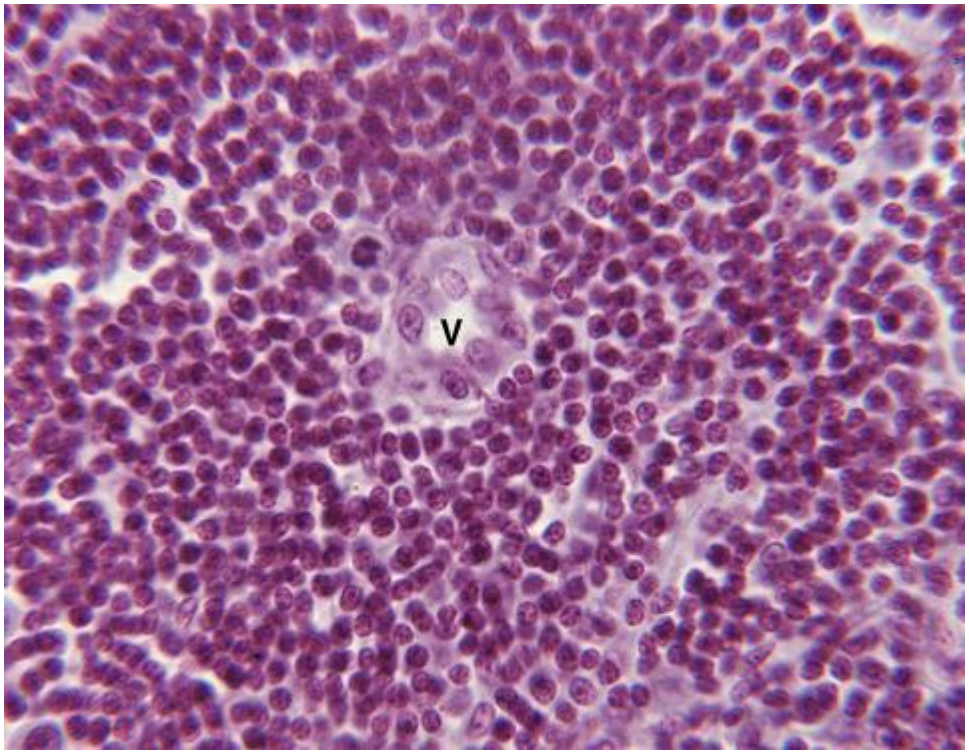
Most of the lymphocytes enter the lymph nodes via blood vessels, and about 10% enter through the lymph.

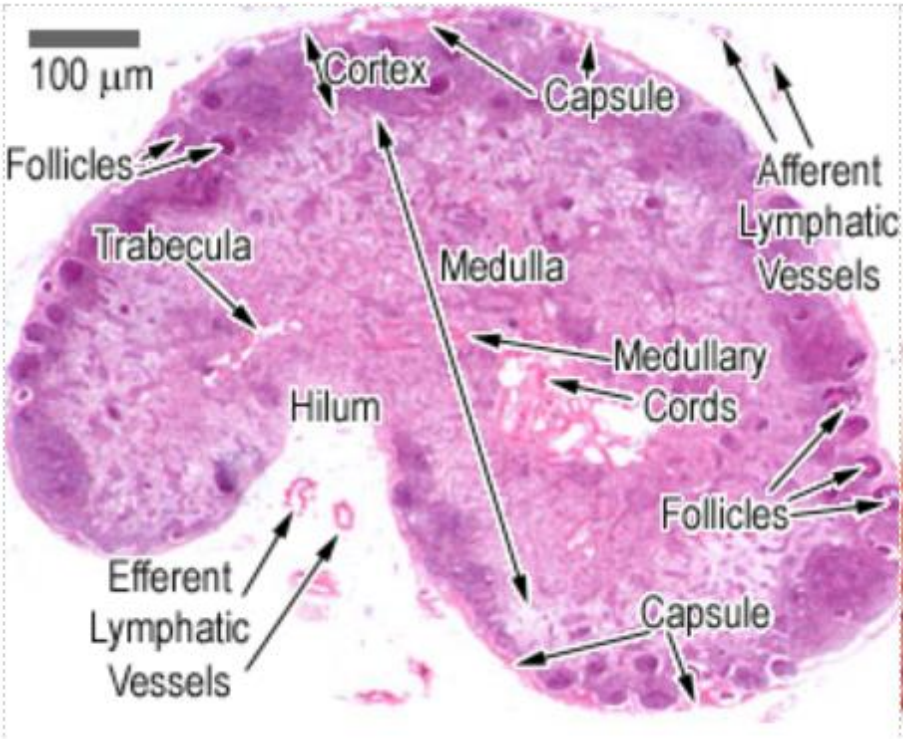


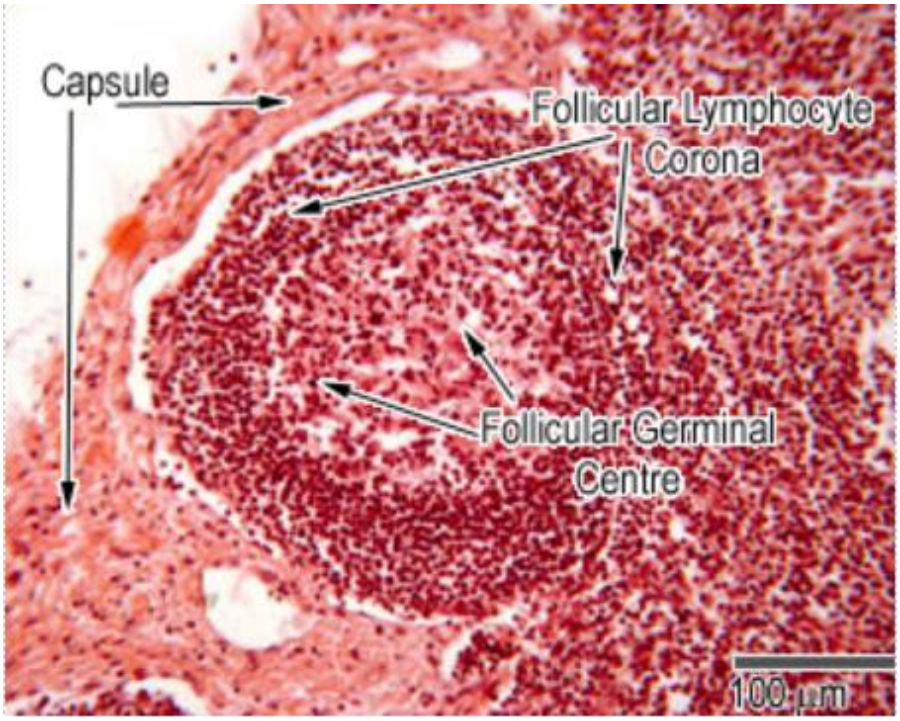
The structure of the post-capillary venule, in the deep cortex (paracortex) is unusual in that it is not lined by simple squamous epithelium, but by a simple cuboidal epithelium. These are called high endothelial venules (HEVs). Lymphocytes recognize and adhere to these endothelial cells, and squeeze

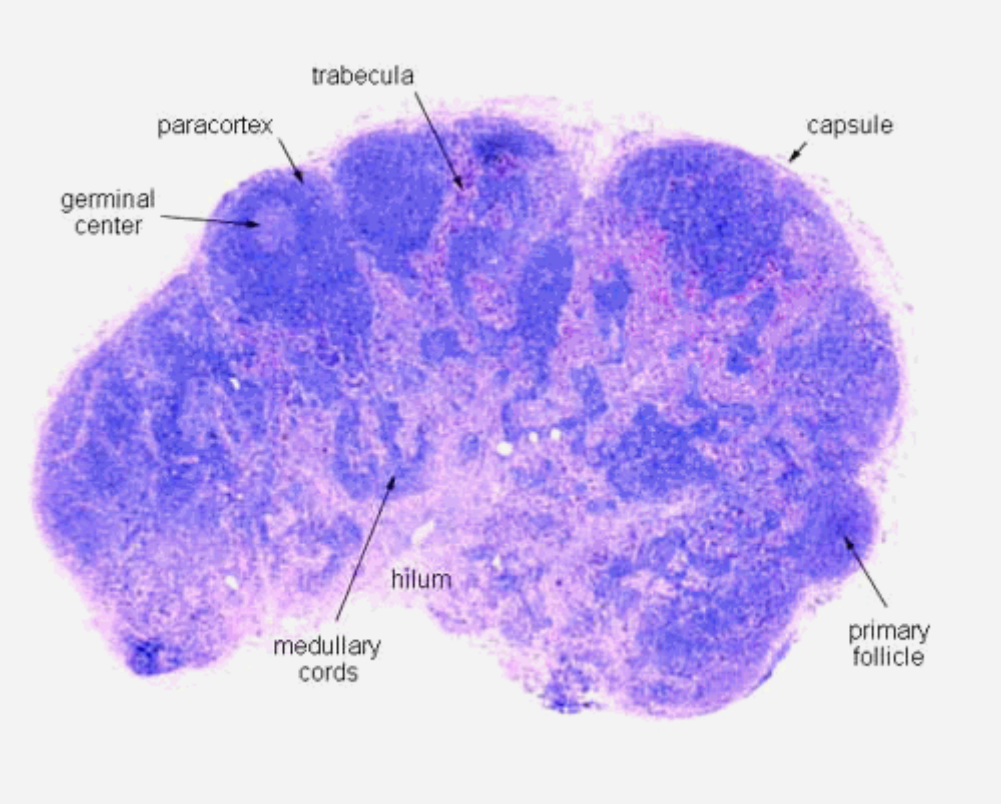
through them into the deep cortical regions of the nodes. This region of the lymph has lots of T-cells, as well as the antigen presenting dendritic cells.

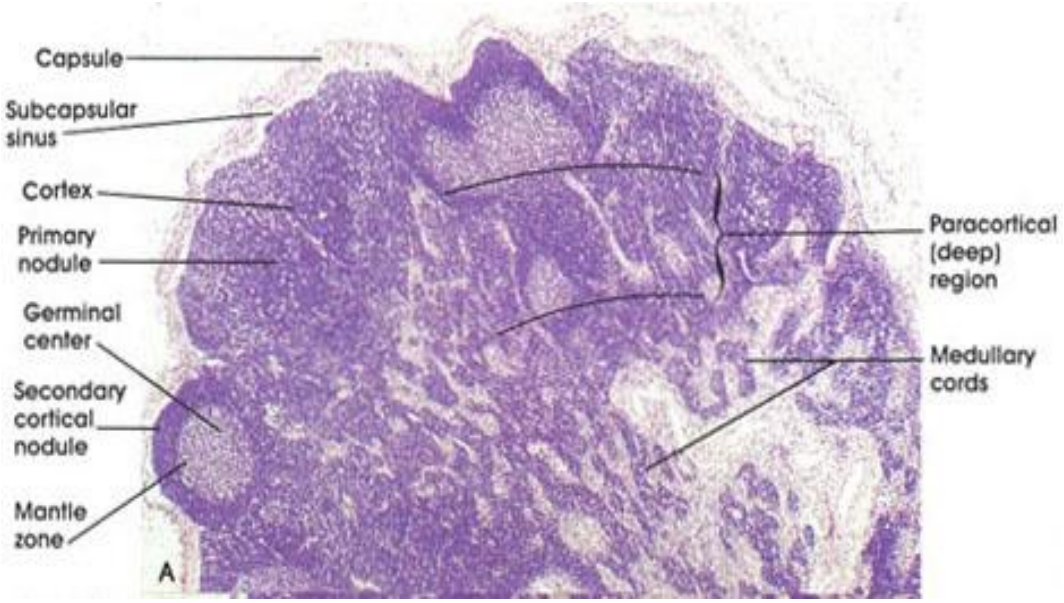
T-cells entering here become activated in the cortex, between lymphoid follicles.

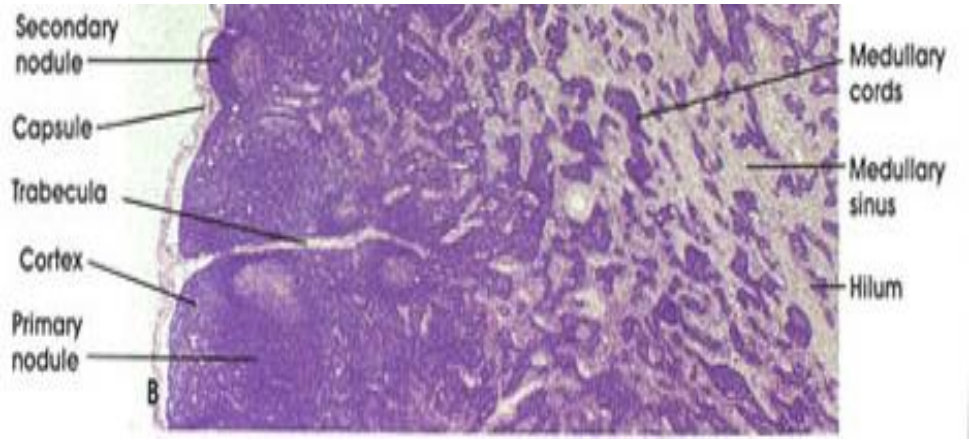



100 µm
Cortex
Capsule
Follicles
Afferent
Lymphatic
Vessels
Trabecula
Medulla
Medullary
Cords
Hilum
Follicles
Efferent
Lymphatic
Vessels
Capsule


Capsule
Follicular Lymphocyte
Corona
Follicular Germinal
Centre
100 µm


trabecula
paracortex
capsule
germinal center
hilum
medullary cords
primary follicle


Capsule
Subcapsular sinus
Cortex
Primary nodule
Germinal center
Secondary cortical nodule
Mantle zone
Paracortical (deep) region
Medullary cords
A

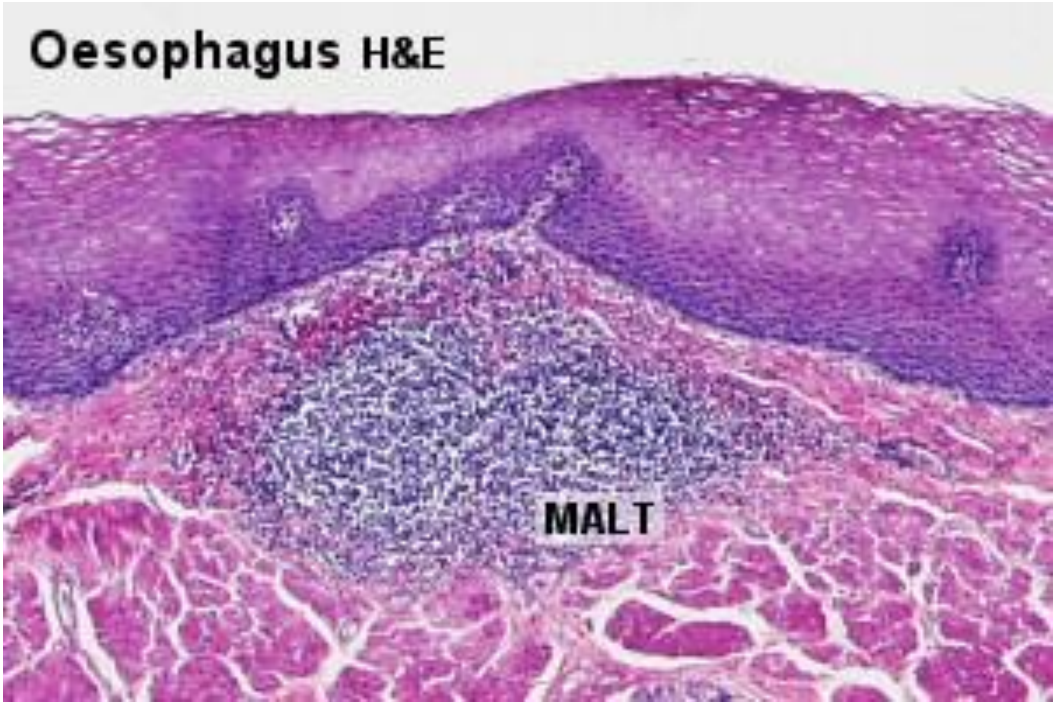


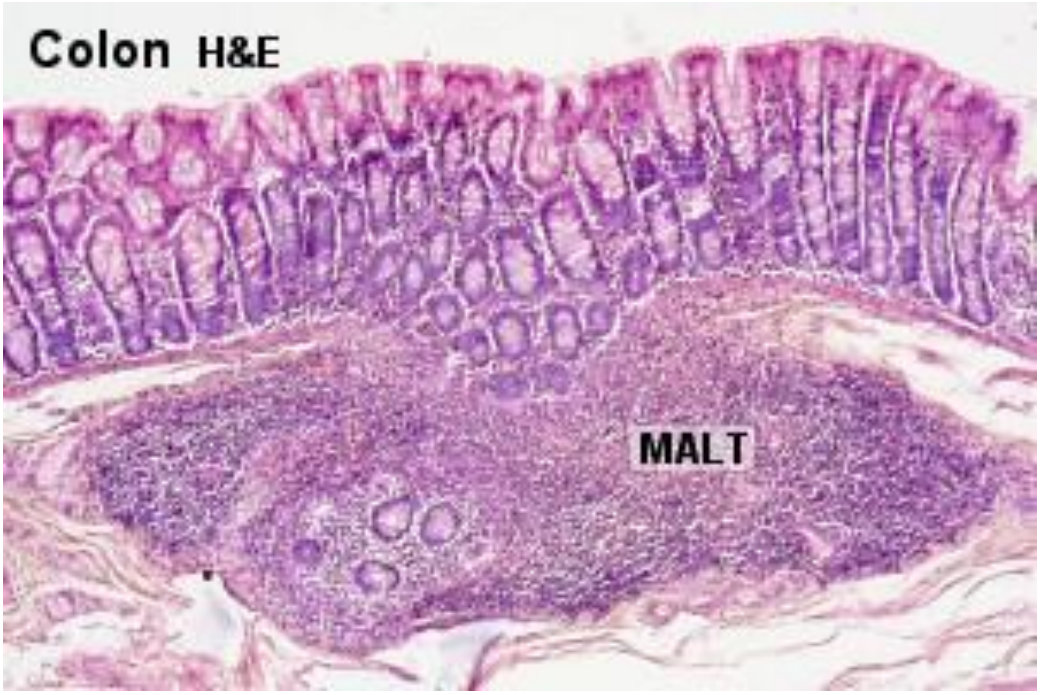
Mucosa-Associated Lymphoid Tissue

The mucosal lining of the alimentary canal and airways is in many ways specialized to facilitate the exchange of substances between the external environment and the body. Unfortunately, these specialization do not just apply e.g. to components of the digested food but also pathogens. This is combined with excellent living conditions for bacteria in parts of the alimentary canal - in particular the ileum and the colon. Lymphoid tissue located beneath the mucosal epithelia, *mucosa-associated lymphoid tissue* (MALT), protects the body against pathogens that may enter the body via the mucosa. The importance of this task is reflected in the mass of the MALT, which corresponds to the combined mass of the other lymphoid organs and tissues.

The task that the immune cells of the MALT have to accomplish is different from that of other parts of the immune system. We do need a defense against pathogens, but it would not be a good idea to mount an immune response against components of the food. Immune cell activation therefore differs between the MALT and other lymphoid tissues.
This difference is mediated by different receptors expressed by immune cells of the MALT and by different substances which they release upon contact with an antigen. Because of their specific functions, immune cells of the MALT do not mingle with other immune cells. Epithelial cells of the vessels supplying the MALT express specific receptors which are recognized by MALT immune cells and allow their homing to the MALT during recirculation. Lastly, MALT plasma cells produce a secretable form of antibodies, immunoglobulin type A dimers, which can be taken up by epithelial cells and then released onto the epithelial surface.
Specialization of MALT immune cells occur at the molecular level. In routine

histological preparations, immune cells of the MALT look pretty much like immune cells of other lymphoid tissues.



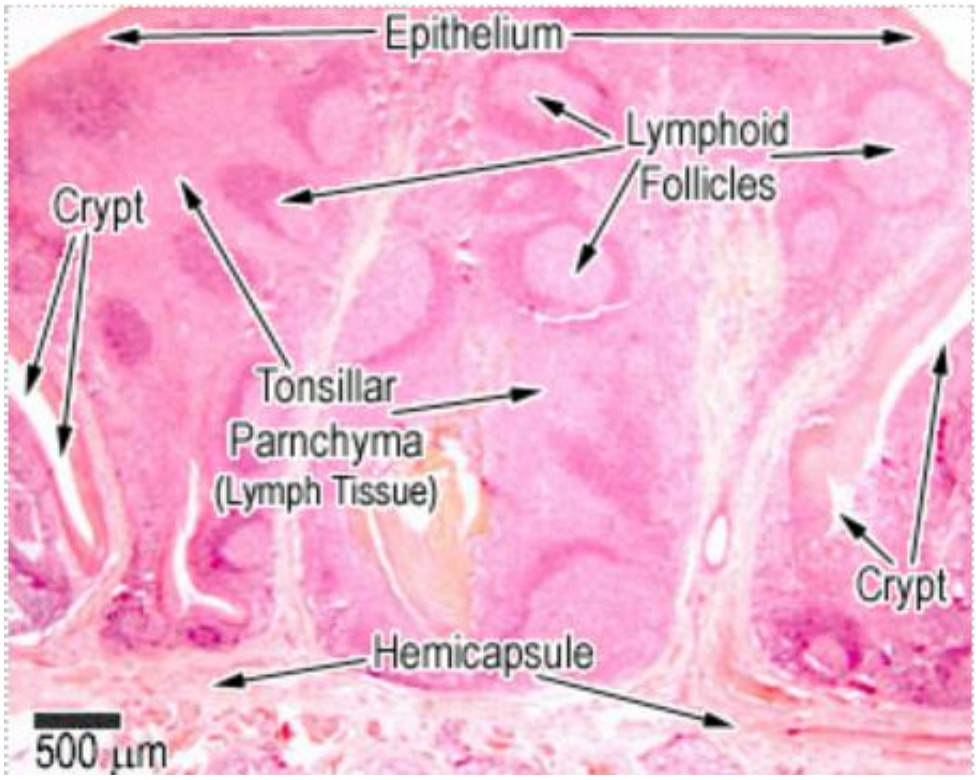


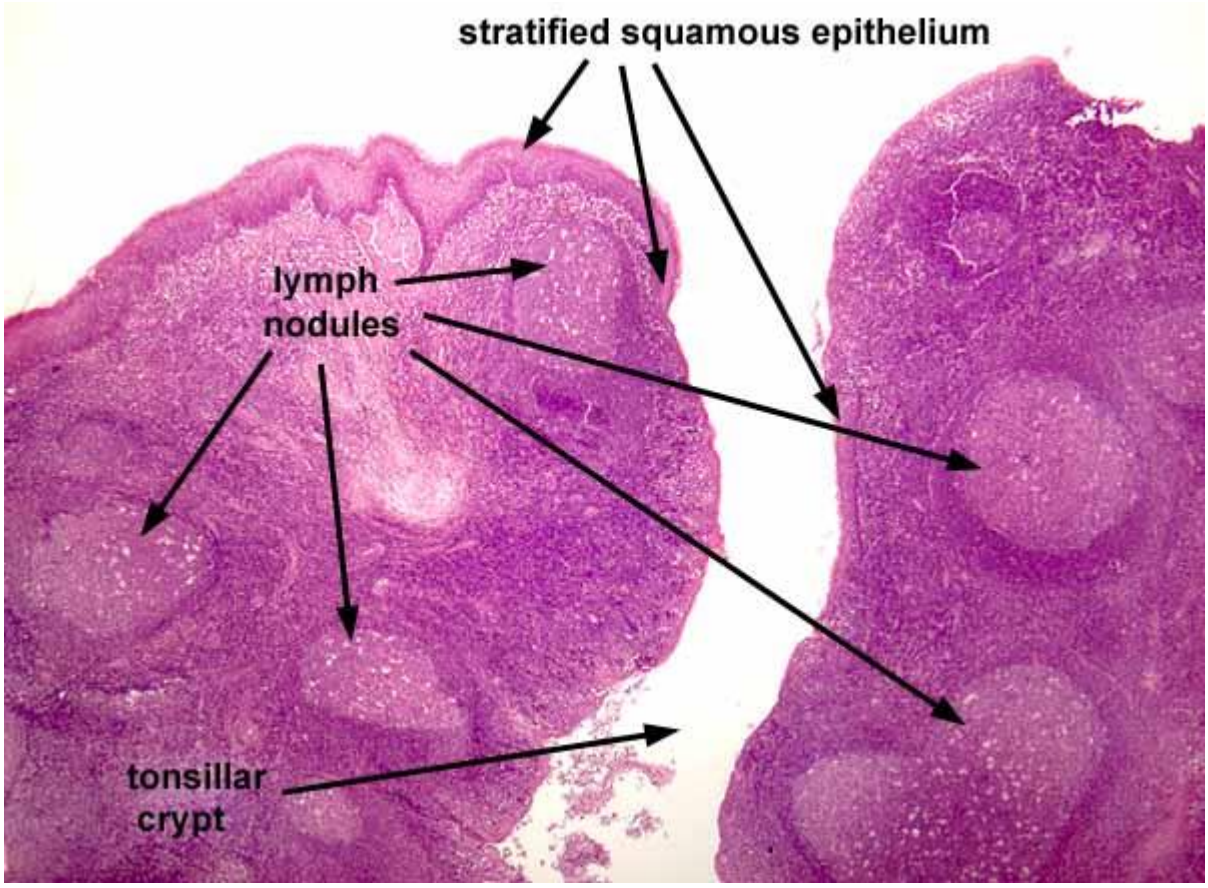
Often MALT consists of small accumulations of lymphoid cells or one to a few lymph follicles beneath the epithelium and possibly extending into the submucosa. The tonsils and Peyer's patches are large accumulations of lymphoid tissue with associated specializations of the epithelium.

Histology of Tonsils

Tonsils are large non-encapsulated (or partially encapsulated) masses of lymphoid tissue, that lie in the walls of the pharynx and nasopharynx and at the base of the tongue.
The **luminal surface** of the tonsils are covered with a stratified squamous epithelium (in common with the oral epithelia).

The tonsils have many invaginations which form **blind crypts.**
Below the epithelium, there are many lymphoid follicles beneath which have germinal centers like the lymph nodes.
The epithelial cells are able to phagocytose bacteria, and transfer them to macrophages, which then present the foreign antigens to B-cells, which are activated (with the help of T cells). The activated cells mostly secrete IgA type antibodies, which are secreted locally.

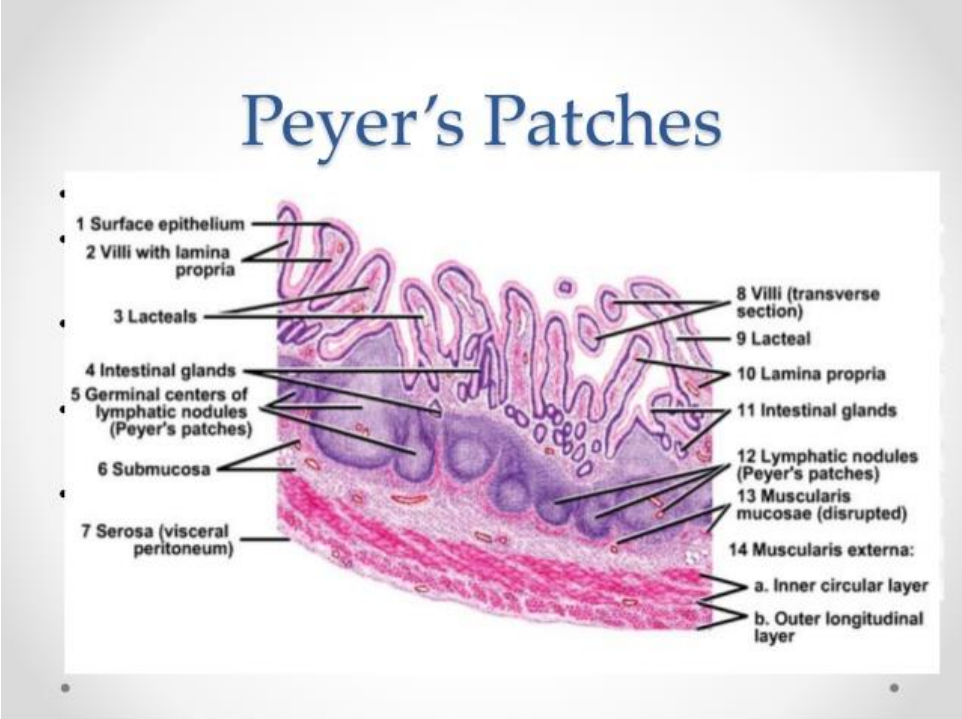




Histology of Peyer's patches

Small accumulations of lymphocytes or solitary lymph follicles are found scattered in beneath the epithelium throughout the gastrointestinal tract. However, the most prominent accumulations occur in the ileum and appendix in the form of Peyer's patches. In the ileum, they form dome-shaped protrusions into the lumen. Beneath the epithelial lining of the domes, Peyer's patches extend from the lamina propria to the submucosa. Within Peyer's patches, lymph follicles with germinal centers are typically located deep in the submucosa.

The epithelium in contact with the lymphoid tissue is specialised to facilitate the contact of antigens with cells of the immune system. The epithelium appears columnar and contains cells with deeply invaginated basal surfaces - *microfold cells or M-cells*. Immune system cells can enter these invaginations (intraepithelial pockets) where they are exposed to materials which have been endocytosed by the epithelial cells and then released into the invaginations. Goblet cells are rare or absent in the epithelium which covers the domes.


Peyer's Patches
1 Surface epithelium
2 Villi with lamina propria
3 Lacteals
4 Intestinal glands
5 Germinal centers of lymphatic nodules (Peyer's patches)
6 Submucosa
7 Serosa (visceral peritoneum)
8 Villi (transverse section)
9 Lacteal
10 Lamina propria
11 Intestinal glands
12 Lymphatic nodules (Peyer's patches)
13 Muscularis mucosae (disrupted)
14 Muscularis externa:
a. Inner circular layer
b. Outer longitudinal layer


Peyer's Patch H&E
domes
villi
lymph follicle
germinal center
muscularis externa