♣ Objectives

1. State the key differences between cell mediated and humoral immune responses.
2. Know the five classes of antibodies and the main function of each.
3. To know the nature of the MHC and its role in organ transplantation and rejection
4. Compare the functional rules and distinguishing features of two important subclasses of small lymphocyte
5. Compare the basic histological organization and main functions of four different types of lymphoid tissues (MALT, lymph node, thymus and spleen).

♣ Introduction

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). This system has the ability to neutralize or inactivate foreign molecules and to destroy microorganisms or other cells (such as virus infected cells, cells of transplanted organs, and cancer cells).

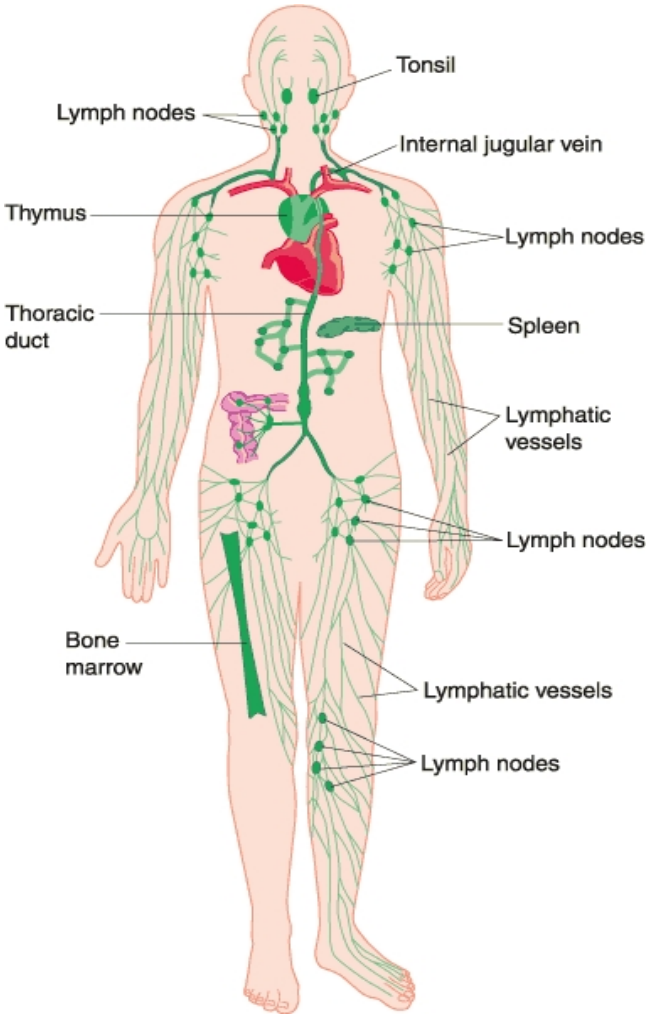
The cells of the immune system are:

(1) Distributed throughout the body in the blood, lymph, and epithelial and C.T؛

(2) Arranged in small spherical nodules called lymphoid nodules found in connective tissues and inside several organs; and

(3) Organized in larger lymphoid organs—the lymph nodes, the spleen, the thymus, and the bone marrow.

The wide distribution of immune system cells and the constant traffic of lymphocytes through the blood, lymph, C.T, and lymphoid organs provide the body with an elaborate and efficient system of surveillance and defense.

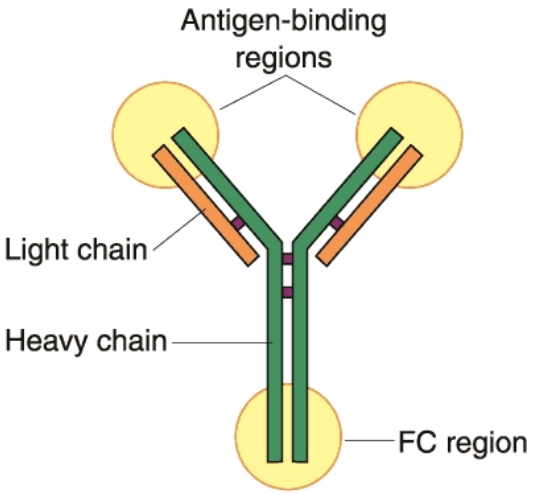


♣ Antigens

A molecule that is recognized by cells of the immune system and may elicit a response from these cells.

The cells of the immune system do not recognize and react to the whole antigen molecule but instead react to small molecular domains of the antigen known as ***antigenic determinants*** or ***epitopes***.

♣ *Antibodies*



An antibody is a glycoprotein that interacts specifically with an antigenic determinant. Antibodies belong to the immunoglobulin (Ig) protein family.

Free molecules of antibodies are secreted by plasma cells that arise by proliferation and terminal differentiation of clones of B lymphocytes whose receptors recognize and bind specific epitopes.

There are several classes of antibody molecules but all have a common design.

Summary of classes of antibodies

	% in serum	Presence (other than blood, C.T, and lymphoid T)	Known functions
IgG	80%	Fetal circulation in pregnant women	Activates phagocytosis, neutralizes antigens, protects newborn
IgA	10–15%	Secretions (saliva, milk, tears, etc.)	Protects the surfaces of mucosae
IgM	10–15%	B lymphocyte surface (as a monomer)	First antibodies to be produced in an initial immune response; activates complement
IgD	0.2%	Surface of B lymphocytes	Functions as a receptor to antigens triggering initial B cell activation
IgE	0.002%	Bound to the surface of mast cells and basophils	Participates in allergy and destruction of parasitic worms

♣ *Cytokines*

The function of the immune system is regulated by a large number of molecules, mainly cytokines, which are peptides or glycoproteins with low molecular masses, they influence both the cellular and humoral immune responses

Cytokines act on many cells that have receptors for them—not only cells of the immune system, but also cells of other systems, such as the nervous system and endocrine system. They are primarily produced by cells of the immune system, mainly lymphocytes, macrophages, and leukocytes, but may also be synthesized by other cell types, such as endothelial cells and fibroblasts.

♣ *Cells of the Immune System*

The primary cells that participate in the immune response are: ***Lymphocytes***, ***Plasma Cells***, ***Mast Cells***, ***Neutrophils***, ***Eosinophils***, and cells of the ***Mononuclear Phagocyte System***.

♣ *Lymphocytes*

Lymphocytes can be classified into three major types based on their immunologic functions: ***B lymphocytes*** (B cells), ***T lymphocytes*** (T cells), and ***Null cells***.

Lymphocytes originate in the bone marrow and develop and mature in primary lymphoid organs.

It is impossible to distinguish between the T and B cells without using immunohistochemical stains. However, they have a tendency to reside in certain regions of the lymphoid organs. For example, most B cells reside in lymphatic nodules of the secondary lymphoid organs, whereas T cells reside in the thymus, paracortex of the lymph nodes, and periarterial lymphatic sheath of the spleen (the last two areas are called thymus dependent regions).

Because of their function in lymphocyte production and maturation, the bone marrow and the thymus are called the ***primary*** or ***central lymphoid organs***.

The other lymphoid structures are all ***secondary*** or ***peripheral lymphoid organs*** (spleen, lymph nodes, tonsils، appendix, and Peyer's patches of the ileum).

B and T cells are not anchored in the lymphoid organs; instead, they continuously move from one location to another, a process known as ***lymphocyte recirculation*** so that the cellular composition and microscopic anatomy of lymphoid tissues differ from one day to the next.

♣ *B Lymphocytes*

B lymphocytes originate from precursor cells in the bone marrow and become **naïve (virgin)** B cells in the bone marrow.

These B cells develop their surface antibody (Ig), which enables them to recognize nonself antigens. If B cells recognize self-antigens during the maturation process, these B cells will undergo apoptosis (***negative selection***).

Naïve B cells migrate from the bone marrow to the secondary lymphoid organs through the blood circulation. If naïve B cells do not meet a specific foreign antigen, they will die in a short time. If they encounter such an antigen, recognizing and binding to the antigen will allow them to survive and become ***active B cells***. Activated B cells undergo cell division and differentiate into ***plasma cells*** and ***memory B cells***.

Memory B cells have a long life and can live for decades in circulating blood in an inactive state. They can differentiate into plasma cells, which produce ***antibodies*** to participate in the ***humoral immune response***.

♣ *T Lymphocytes*

T lymphocytes also originate from precursor cells in the bone marrow, but they do not mature in the bone marrow.

Pro–T lymphocytes enter the blood circulation and travel to their primary lymphoid organ (***thymus***) to finish their maturation. They develop into ***thymocytes*** in the cortex of the thymus and undergo a differentiation process to become ***naïve (virgin)*** T cells.

Naïve T cells have surface markers on their cytoplasmic membrane and have a short life as do naïve B cells, they will die if they do not meet an antigen.

Naïve T cells migrate from the thymus to secondary lymphoid organs where they encounter foreign antigens and become ***active T cells***.

Once T cells are activated, they can boost the action of cytotoxic T cells and macrophages and help to expedite proliferation of B lymphocytes, which increase the production of antibodies.

Activated T cells undergo cell division to become ***memory T*** cells or ***effector T*** cells.

MEMORY T CELLS have a much longer life than naïve (virgin) T cells. They can differentiate into effector T cells to participate in a stronger and faster secondary immune response when they encounter the same antigen for the second time.

- **Three important subpopulations of effector T cells are the following:**

1. ***Helper cells***, which produce cytokines that:1) promote differentiation of B cells into plasma cells, 2) activate macrophages to become phagocytic, 3) activate cytotoxic T lymphocytes, and 4) induce many parts of an inflammatory reaction.

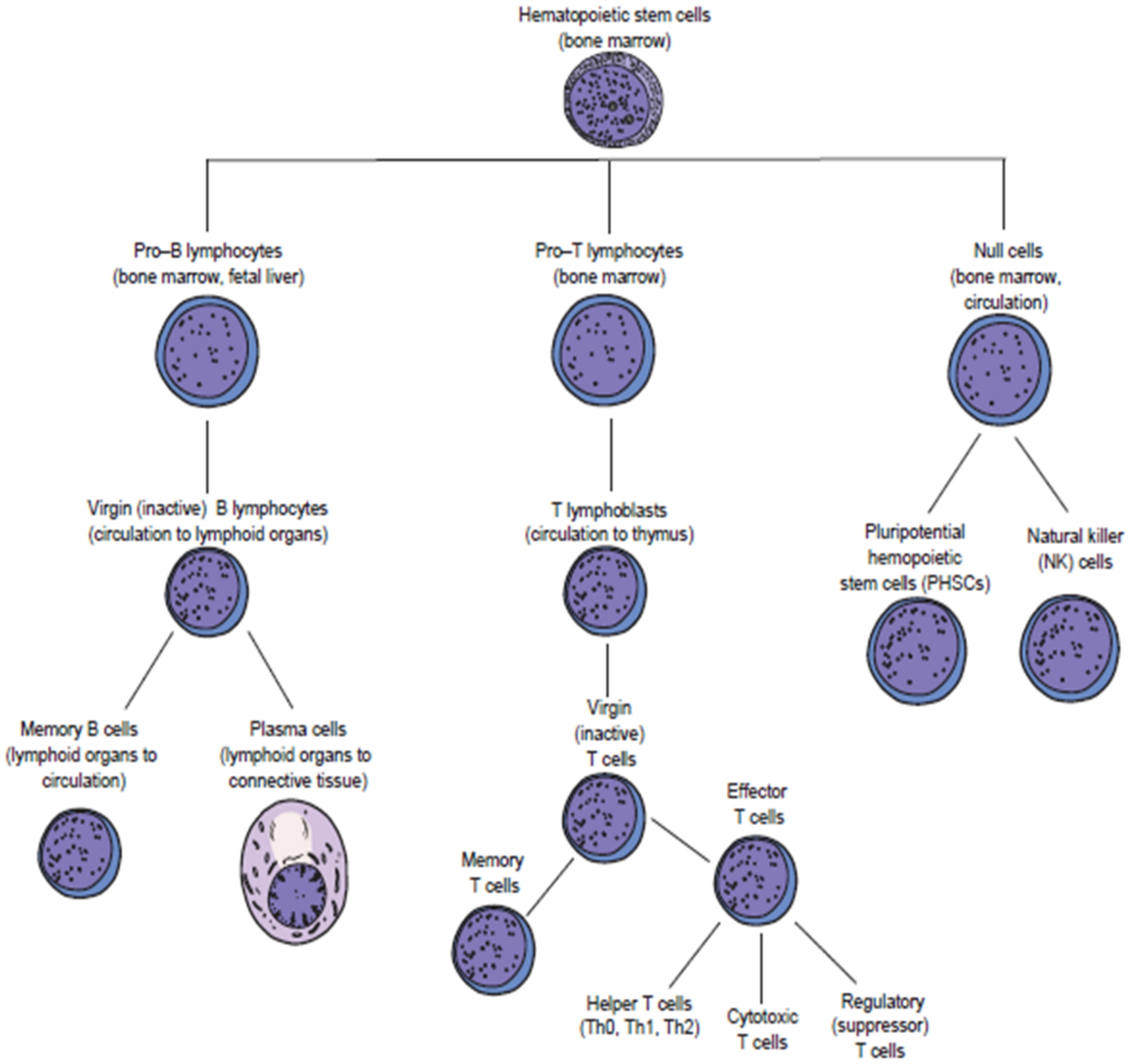
   Helper cells have a marker called CD4 on their surfaces and are, hence, called ***CD4+ T cells***.
2. ***Cytotoxic T*** cells are ***CD8+*** and act directly against foreign cells or virus-infected cells by two main mechanisms. *In one*, they attach to the cells to be killed and release proteins called perforins that create holes in the cell membrane of the target cell, with consequent cell lysis. *In the other*, they attach to a cell and kill it by triggering mechanisms that induce programmed cell death (apoptosis).
3. ***Regulatory (suppressor) T*** cells are ***CD4+CD25+*** and play crucial roles in allowing immune tolerance, maintaining unresponsiveness to self-antigens and suppressing excessive immune responses. These cells produce peripheral tolerance, which backs up the central tolerance emerging in the thymus.

♣ *Null Cells*

Null cells resemble lymphocytes but do not have surface markers، which B and T cells have. They include ***pluripotential hemopoietic stem cells (PHSCs***) and ***natural killer (NK) cells***.

PHSCs function as stem cells and can give rise to various types of blood cells.

NK cells do not require exposure to antigens to become activated. They function similarly to cytotoxic T cells but do not have the surface markers CD8 or CD4. They kill invading target cells, such as virus-infected cells and tumor cells.



♣ *Antigen-Presenting Cells (APCs)*

These cells present antigens to lymphocytes. Most of them are MHC-II class.
These cells present antigen to T cells.
They include **macrophages**, **dendritic cells**, **Langerhans cells**, and **B cells**.

♣ *Major Histocompatibility Complex (MHC) & Antigen Presentation*

MHC is a complex of chromosomal loci encoding several proteins known as ***class I*** and ***class II*** MHC molecules. Because a great many alleles exist within each of the loci, there is great variation of these molecules among the general population. One individual, however, expresses only one set of class I proteins and one set of class II proteins؛these proteins are **unique** to that person.
All nucleated cells have class I proteins, but class II proteins exist on antigen-presenting cells only.

♣ *Organ Transplantation*

Tissue grafts and organ transplants are classified as ***autografts*** when the transplanted tissues or organs are taken from the individual receiving them, ***isografts*** when taken from an identical twin, ***homografts or allografts*** when taken from an individual (related or unrelated) of the same species, and ***heterografts or xenografts*** when taken from an animal of a different species.
The body readily accepts autografts and isografts. There is no rejection in such cases, because the transplanted cells are genetically identical to those of the host and present the same MHC on their surfaces. The organism recognizes the grafted cells as self (same MHC) and does not react with an immune response.
Homografts and heterografts, on the other hand, contain cells whose membranes have class I and class II MHC molecules that are foreign to the host; they are therefore recognized and treated as such.

♣ *Types of immune responses*

The two basic types of immune response are the **innate** and **adaptive** response

Innate Response	**Adaptive Response**
Simple	Complex
Fast	Slow
Non Specific	Specific
Olderfrom an evolutionary point of view	Newer
does not produce memory cells	produce memory cells
Occur through the action of Macrophages, neutrophils, mast cells and NKC	Humoral or Cellular responses

The adaptive mechanisms that lead to the elimination of antigens are classified as:

A. ***Humoral immunity*** is accomplished by antibodies produced by plasma cells derived from clones of activated B lymphocytes.

B. ***Cellular immunity*** is mediated by T lymphocytes that:

1. Secrete cytokines that act on B lymphocytes, on other T cells, and on inflammatory cells such as macrophages and neutrophils, and
2. Attack foreign cells or cells that exhibit foreign epitopes on their surfaces, such as cells infected by viruses or parasites, and some tumor cells.

♣ *Diseases of the Immune System*

The diseases of immune system can be broadly grouped into three types:

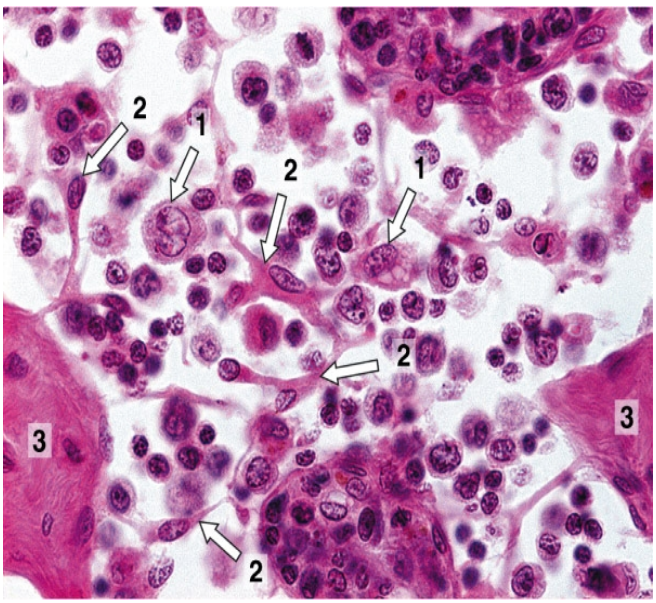
1. Some individuals develop abnormal and intense reactions in an attempt to neutralize the effects of some antigens. This exaggerated intolerance produces the numerous processes called ***allergic reactions***.
2. The immune response can be impaired, a condition generally called ***immunodeficiency***; this may have several causes, such as genetic or infectious (e.g., by measles and human immunodeficiency virus).
3. ***Autoimmune diseases*** are caused by T or B cell responses directed to self-molecules. Tissues are affected or even destroyed by cytotoxic T lymphocytes or by autoantibodies.

♣ *Lymphoid Tissue (L.T)*

L.T is a type of C.T characterized by a rich supply of lymphocytes.

It exists free within the regular C.T or is surrounded by capsules (lymphoid organs). Because lymphocytes have very little cytoplasm, L.T stains **dark blue** in H&E sections.

L.T are basically made up of free cells; as a result, they typically have a rich network of reticular fibrils. In most lymphoid organs, the fibrils are produced by a fibroblastic cell called a ***reticular cell***, whose many processes rest on the reticular fibrils. The thymus is an exception in so far as its cells are supported by a reticulum of epithelial cells of endodermic origin.



Medullary sinus of a lymph node containing reticular cells with long processes and elongated nuclei, macrophages, and many lymphocytes.

(1) Macrophage

(2) Reticular cell

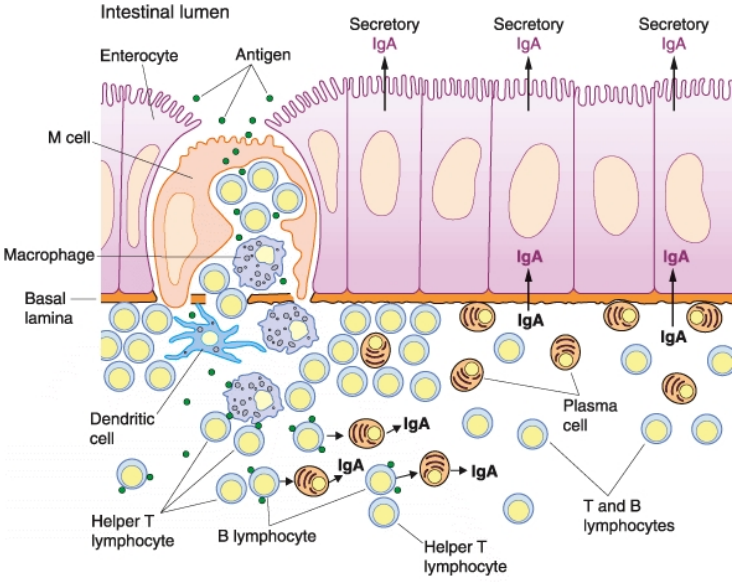
(3) Trabeculae

In the nodular lymphoid tissue, groups of lymphocytes are arranged as spheres, called ***lymphoid nodules*** or ***lymphoid follicles*** that primarily contain B lymphocytes.
When lymphoid nodules become activated as a result of the arrival of antigen-carrying APCs and recognition of the antigens by B lymphocytes, these lymphocytes proliferate in the central portion of the nodule, which then stains lighter and is called a ***germinative center***. After completion of the immune response, the germinative center may disappear. The germinative centers contain a special cell, the follicular dendritic cell (distinct from the epithelial dendritic APCs), that has many processes that bind antigen on their surfaces, to be presented to B lymphocytes .
Lymphoid nodules are found free in C.T anywhere in the body or within lymphoid organs (lymph nodes, spleen, tonsils, ***but not*** in the thymus). They are, however, ***never*** covered by a capsule.
Free lymphoid nodules are commonly present in the lamina propria of several mucosal linings, where, together with free lymphocytes, they constitute the mucosa-associated lymphoid tissue (***MALT***).

♣ *Mucosa-Associated Lymphatic Tissues (MALT)*

Diffuse lymphatic tissues or nodules are often located in the C.T, which support the wet epithelial membranes of the body mucosae. The lymphatic tissues found in the mucosa of the GIT, respiratory, and genitourinary tracts are called **MALT**.
They can be subdivided into gut-associated lymphatic tissue (GALT) and bronchus-associated lymphatic tissue (BALT), according to their locations.
GALT is found in the digestive tract, such as Peyer's patches in the ileum and lymphatic nodules in the appendix and large intestine.
BALT is found in the respiratory tracts, mostly in bronchi and bronchioles.

- In the Peyer's patches, some of the regular surface epithelial cells may be replaced by ***special M cells***. The M cells do not have microvilli as do the regular cells that line the intestine. By pinocytosis they actively capture and transport antigens from the intestinal lumen to the connective tissues where APCs and B lymphocytes are usually present. The plasma cells derived from these lymphocytes secrete mostly IgA, which is transported through the epithelium toward the intestinal cavity.



TONSILS

Tonsils belong to the MALT.

The tonsils constitute a lymphoid tissue that lies beneath, and in contact with, the epithelium of the initial portion of the digestive tract. Depending on their location, tonsils in the mouth and pharynx are called ***palatine***, ***pharyngeal***, or ***lingual.***

Tonsils	Location	Capsule	Lining	Crypt	Lymphoid tissues
Palatine	lateral walls of the oropharynx	A band of dense C.T. separating the lymphoid tissue from subjacent structures. It acts as a barrier against spreading tonsillar infections.	Stratified squamous epithelium (non-keratinized)	10–20 epithelial invaginations that penetrate the tonsil deeply, whose lumens contain desquamated epithelial cells, live and dead lymphocytes, and bacteria.	contains numerous lymphatic nodules, most having a germinal center
Pharyngeal	Superior—posterior portion of the pharynx	Thinner than the capsule of the palatine tonsils	Ciliated pseudostratified columnar epithelium	No, only epithelial invagination	Mostly diffuse lymphoid tissues and some lymphatic nodules
Lingual	At the base of the tongue	No	Stratified squamous epithelium (non-keratinized)	Single crypt	Rows of lymphatic nodules supported by connective tissuesepta

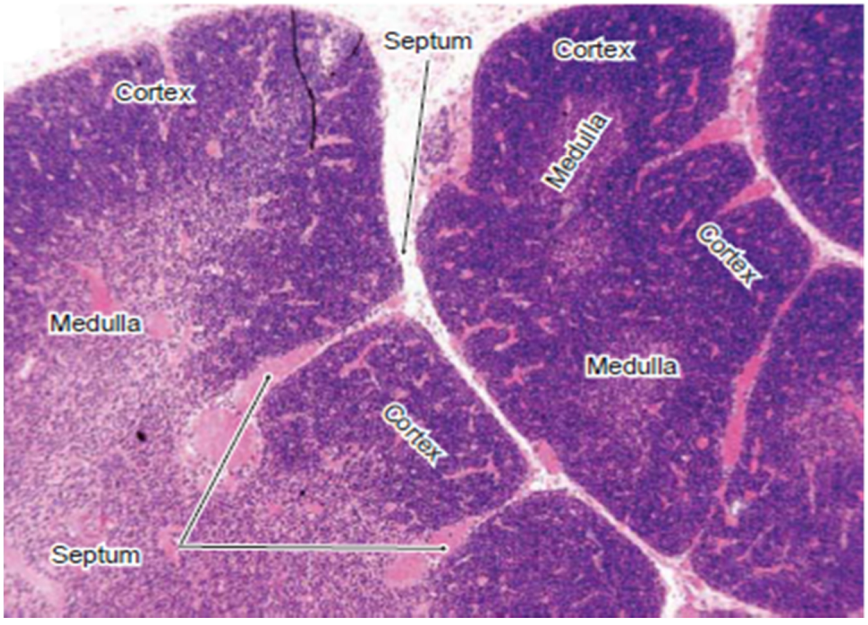
- **Adenoids** are hypertrophied pharyngeal tonsils resulting from chronic inflammation.

THYMUS

The thymus is the primary lymphoid organ for maturation of T cells.
It is located in the superior mediastinum.
The thymus continues to grow until puberty and then gradually atrophies. In elderly, a large portion of the thymus tissue is replaced by adipose tissue.
The thymus is covered by a thin layer of connective tissue (capsule) and has two lobes. Each lobe is composed of many lobules, and the lobules can be divided into a cortex and medulla.
Unlike other lymphatic organs, the thymus:

1. Does not have lymphatic nodules.
2. It has dual embryonic origin: Its lymphocytes arise in the bone marrow from cells of mesenchymal origin that invade an epithelial primordium that has developed from the endoderm of the 3rd&4th pharyngeal pouches), whereas the other lymphoid organs originate exclusively from mesenchyme (mesoderm).

The thymus has a C.T capsule that penetrates the parenchyma and divides it into incomplete lobules, so that there is continuity between the cortex and medulla of adjoining lobules. Each lobule has a peripheral dark zone (the **cortex**) and a central light zone (the **medulla).**
The cortex contains thymocytes (developing T cells), macrophages, dendritic cells, and epithelial reticular cells. A subpopulation of epithelial reticular cells present in the cortex consists of **thymic nurse cells** (**TNCs**), which contain many (20–100) maturing lymphocytes in their cytoplasm. T-cell maturation occurs in the cortex.
The medulla contains virgin T cells, which have developed and migrated from thymocytes in the cortex. Also contains a large number of epithelial reticular cells, Hassall corpuscles (thymic corpuscles), which are formed by concentrically arranged epithelial reticular cells, are found in the medulla, they are characteristic of this region, although their function is unknown.



♣ *Vascularization of the Thymus*

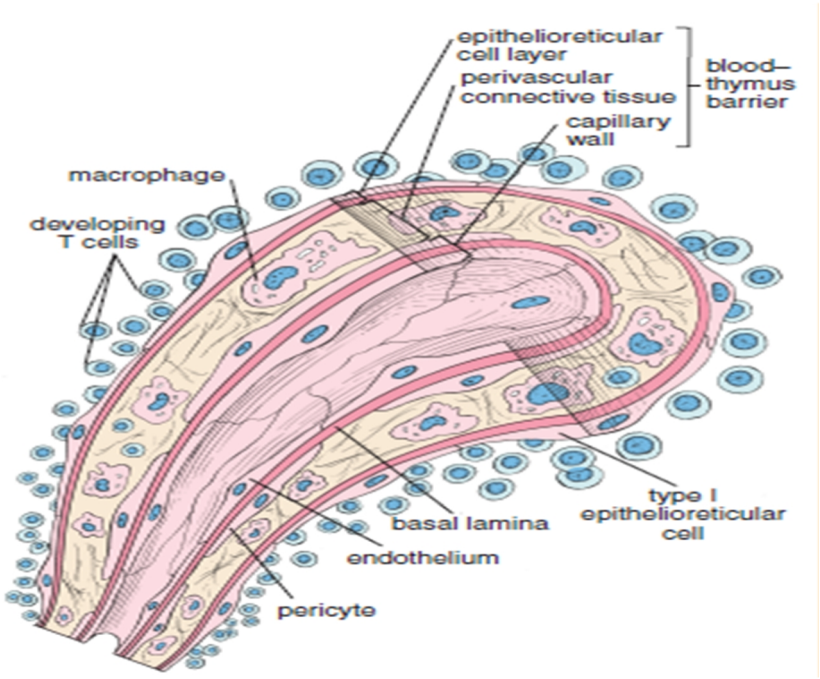
The only blood vessels supplying the thymic cortex are looped capillaries that extend out into the cortex from arterioles at the corticomedullary border.
No afferent lymphatics supply the thymus, as they do in the case of lymph nodes. The thymus is provided only with efferent lymphatics that transport lymph and lymphocytes away from the organ.

♣ *The blood–thymus barrier*

Consists of three major elements:

1. Capillary endothelium and its basal lamina
2. Perivascular connective tissue space occupied by macrophages
3. Epithelial reticular cells with their basal lamina.

The perivascular connective tissue is enclosed between the basal lamina of the epithelial reticular cells and the endothelial cell basal lamina.These layers provide the necessary protection to the developing immature T cells and separate them from mature immunocompetent lymphocytes circulating in the bloodstream.

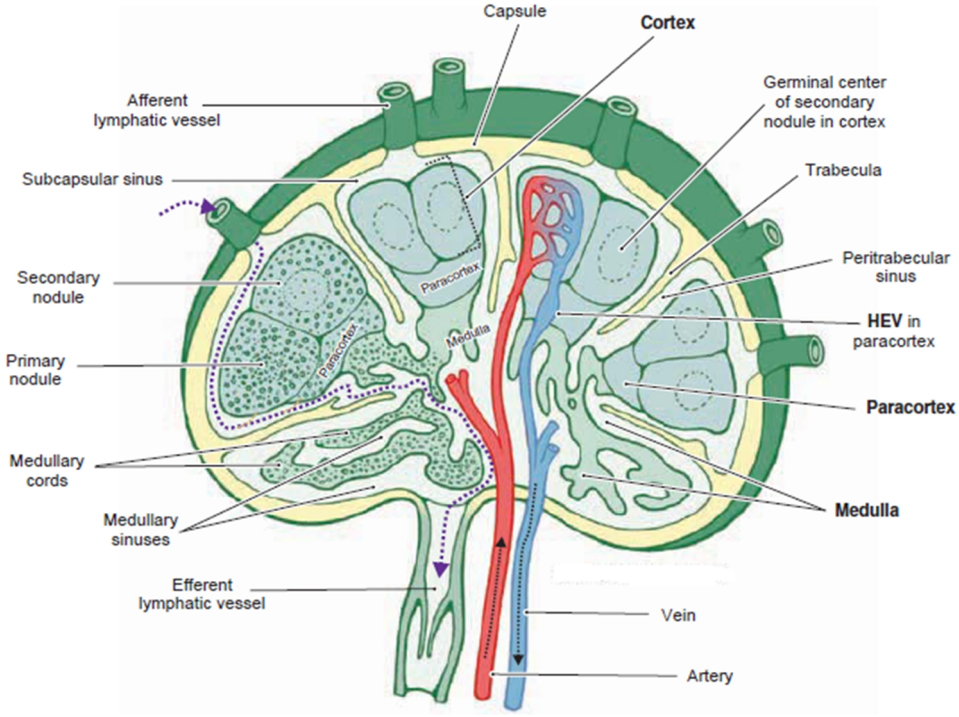


♣ *Secretion by the Thymus*

The thymus produces several proteins that act as growth factors to stimulate proliferation and differentiation of T lymphocytes. They seem to be paracrine secretions, acting in the thymus. At least four hormones have been identified: ***thymosin-∝, thymopoietin, thymulin, and thymus humoral factor.***

LYMPH NODES

Lymph nodes are bean-shaped organs that are covered by a C.T (capsule).
They are distributed throughout the body. The regions that are associated with rich clusters of L.N include the neck, axilla, thorax, abdomen, groin, and femoral regions.
They play important roles in circulating and filtering lymph, defending against microbial invasion, and providing a place for lymphocytes to meet antigens.
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
L.N can be divided into three regions: **cortex، paracortex, and medulla**.

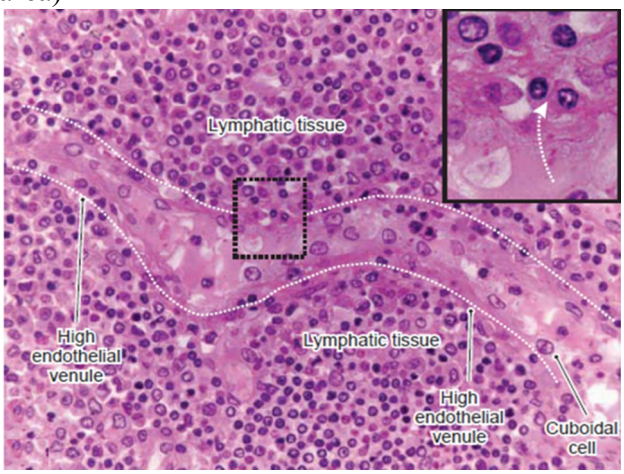


The **cortex**, situated under the capsule, consists of the following components:

- Many reticular cells, macrophages, APCs, and lymphocytes
- Lymphoid nodules, with or without germinal centers, formed mainly of B lymphocytes, embedded within the diffuse population of other cells
- 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.
- 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

The **paracortex** is located between the cortex and the medulla.

- ☒ Most T cells are hosted here (thymus-dependent area)
- ☒ High endothelial venules (HEVs) are found in this region. HEVs are postcapillary venules، which have a cuboidal cell lining instead of the common, flat endothelial cell lining, they are specialized venules, which allow lymphocytes to pass through their walls to enter the lymphatic tissue. HEVs can also be found in other lymphatic organs (but not spleen).



The **medulla** has two major components:

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

♣ ***Lymph Circulation***

Afferent lymphatic vessels cross the capsule and pour lymph into the subcapsular sinus. From there, lymph passes through the cortical sinuses and then into the medullary sinuses. During this passage, the lymph infiltrates the cortex and the medullary cords and is filtered and modified by immune cells. The lymph is collected by efferent lymphatics at the hilum and valves in both lymphatics assure the unidirectional flow of lymph.

Afferent Lymphatic Vessel

↓

Subcapsular Sinus

↓

Intermediate Sinus

↓

Medullary Sinus

↓

Efferent Lymphatic Vessel

♣ *Role of Lymph Nodes in the Immune Response*

L.N are distributed throughout the body and lymph formed in tissues must pass through at least one node before entering the bloodstream.

The lymph that arrives at a L.N contains antigens have the opportunity to be presented to B lymphocytes, to T helper cells, and to T cytotoxic lymphocytes for these cells to initiate an immune response.

The lymph node is an important site of lymphocyte proliferation (especially of B cells in the germinal centers) as well as of transformation of B lymphocytes into plasma cells. Because of this, the lymph that leaves a lymph node may be enriched in antibodies. When the lymph is returned to the blood circulation, these antibodies will be delivered to the entire body.

When antibody-producing plasma cells are formed, they migrate to the medulla Stimulation of the lymphocytes by antigens can accelerate the migration process to about 10 times normal, resulting in characteristic swelling of the lymph nodes.

♣ *Recirculation of Lymphocytes*

Because all lymph formed in the body normally drains back into the blood, lymphocytes that leave the lymph nodes by efferent lymphatics eventually reach the bloodstream. These lymphocytes may then leave the blood vessels by entering the tissues and return with other lymph to another lymph node.

However, most (90%) lymphocytes return to a lymph node by crossing the walls of the HEVs (a process called **homing**).

♣ *Lymphadenopathy*

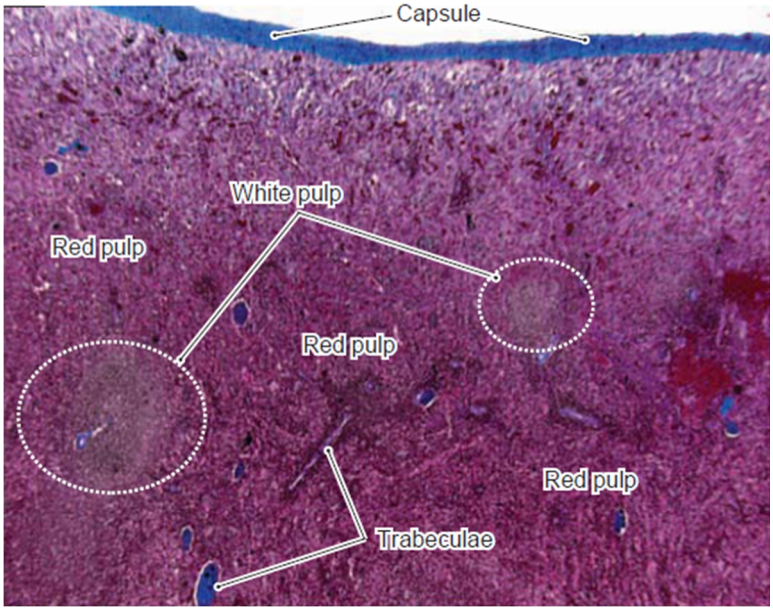
Is a term meaning "disease of the lymph nodes.

It is, however, almost synonymously used with "swollen/enlarged lymph nodes ."

It could be due to infection, auto-immune disease, or malignancy.

SPLEEN

Is the largest lymphatic organ; the only one that located in the path of the blood.
Is surrounded by a dense C.T capsule from which emerge trabeculae, which partially subdivide the parenchyma (splenic pulp) in to incomplete compartments.
The spleen is composed of a network of reticular tissue that contains:reticular cells, lymphocytes and other blood cells, macrophages, and APCs .
Splenic pulp divides in to: **White pulp & Red pulp**, these names derive from the fact that :on the surface of a cut through an unfixed spleen, white spots (lymphoid nodules) are observed within a dark red tissue that is rich in blood.



♣ *White Pulp*

The white pulp is an immune component in the spleen, composed of nodules, central arteries, and a periarterial lymphatic sheath (PALS). Lymphatic nodules are often secondary nodules, which have germinal centers and are often called splenic nodules.
Central arteries pass through the white pulp and give rise to sinuses in the marginal zone (peripheral region of the nodule). The central artery also gives rise to the penicillar arterioles in the red pulp.
The PALS is a sheath of concentrated T cells surrounding a central artery.

♣ *Marginal Zone*

Surrounding the lymphoid nodules is a marginal zone consisting of many blood sinuses and loose lymphoid tissue. A few lymphocytes but many active macrophages can be found there. The marginal zone contains an abundance of blood antigens and thus plays a major role in the immunological activities of the spleen.

♣ Blood flow in the spleen

Splenic A. at the hilum → Trabecular A. → Envloped by a sheath of T lymphocytes (PALS) which part of White pulp

↓

Central A or White pulp A → PALS receive large collections of lymphocytes (mostly B cells) → Lymphoid nodule

↓

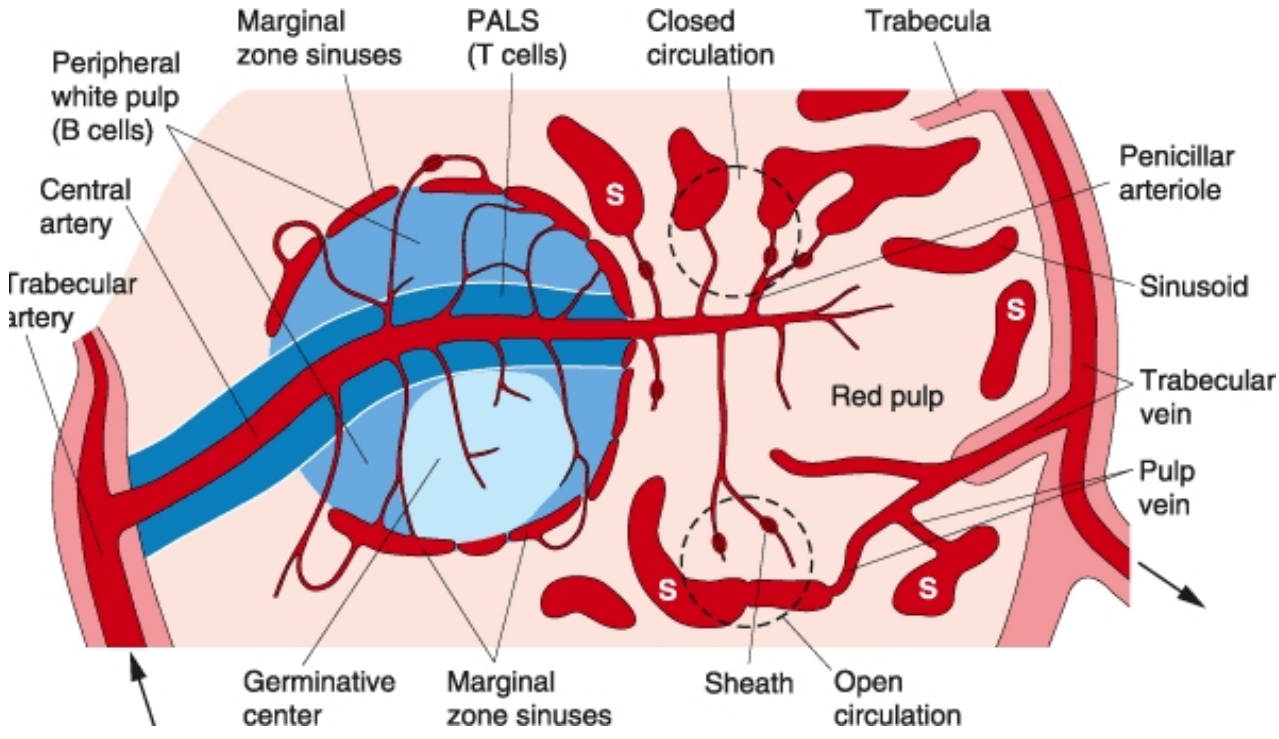
The artery now turned into an Arteriole, occupies an Eccentric position but is still called the Central artery → Radial branches that supply the surrounding lymphoid tissue

↓

After leaving the white pulp, subdivides to form straight Penicillar arterioles → Splenic sinusoids → Trabecular V.

↓

Splenic V. at the hilum

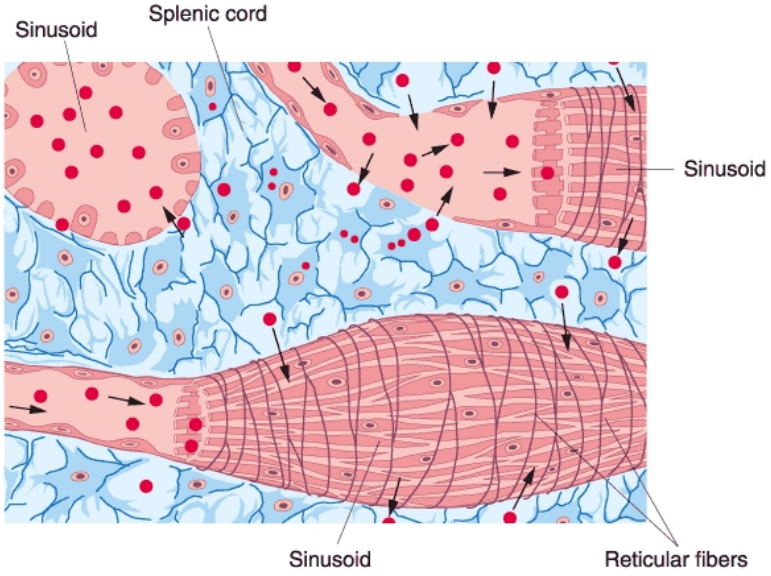


✓ *Closed and Open Blood Circulation in the Spleen*

The manner in which blood flows from the arterial capillaries of the red pulp to the interior of the sinusoids has not yet been completely explained.
Some investigators suggest that the capillaries open directly into the sinusoids, forming a closed circulation in which the blood always remains inside the vessels. Others maintain that the prolongations of the penicillar arteries open into the splenic cords, and the blood passes through the space between the cells to reach the sinusoids (open circulation).

♣ *Red Pulp*

The red pulp is composed of splenic (Bilroth's) cord sand splenic sinusoids.
The cords contain a network of reticular cells supported by reticular fibers. They contain T and B lymphocytes, macrophages, plasma cells, and many blood cells.
The splenic cords are separated by irregularly shaped wide sinusoids. Elongated endothelial cells line the sinusoids of the spleen with the long axes parallel to the long axes of the sinusoids. These cells are enveloped in reticular fibers set primarily in a transverse direction, much like the hoops on a barrel.



Surrounding the sinusoid is an incomplete basal lamina. Because the spaces between the endothelial cells of the sinusoids are 2–3 μm in diameter or smaller, only flexible cells are able to pass easily from the red pulp cords to the lumen of the sinusoids. Unfortunately, because the lumen of sinusoids in the red pulp may be very narrow and the splenic cords are infiltrated with red blood cells, microscopic observation of a spleen section is not always easy; observation of PALS may also be difficult.

♣ *Functions of the Spleen*

The two main functions are architecturally distinct, lymphoid function occurring in the white pulp and phagocytic activity in the red pulp

A. Filtration function

Removal of old or abnormal RBCs, Removal of abnormal WBCs, Removal of normal and abnormal platelets and cellular debris

B. Immunological function

1. Opsonisation: while opsonised bacteria can be removed from the circulation by entire lymphoid system, the spleen is well suited for removing poorly opsonised or encapsulated pathogens.
2. Antibody synthesis occurs chiefly in the white pulp.
3. Protection from infection

THE END