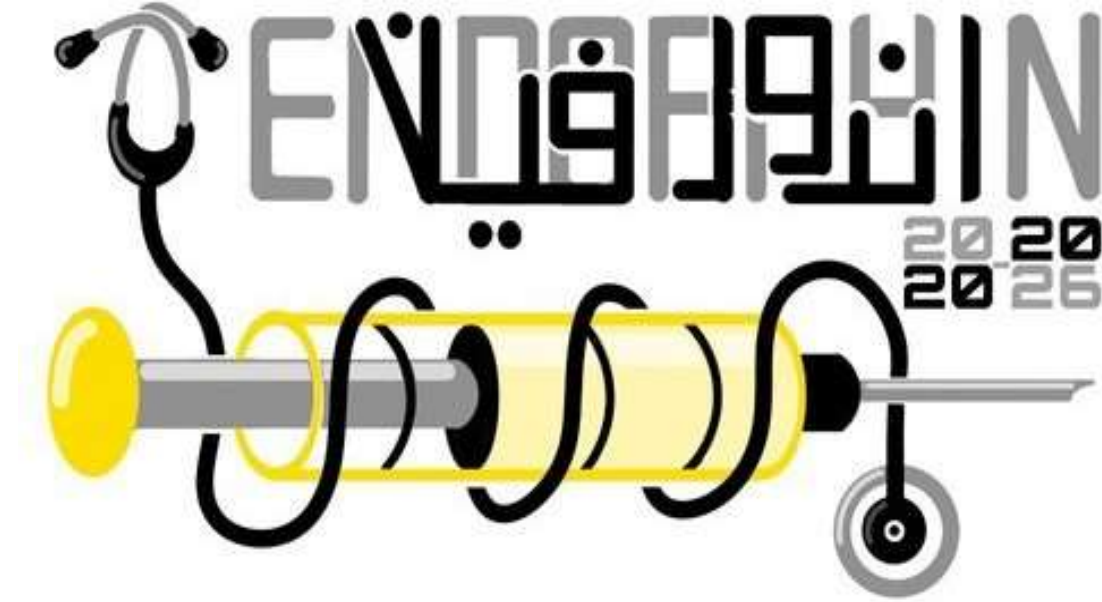


Anatomy



Sheet:#4

Lecture title:lymphatic system

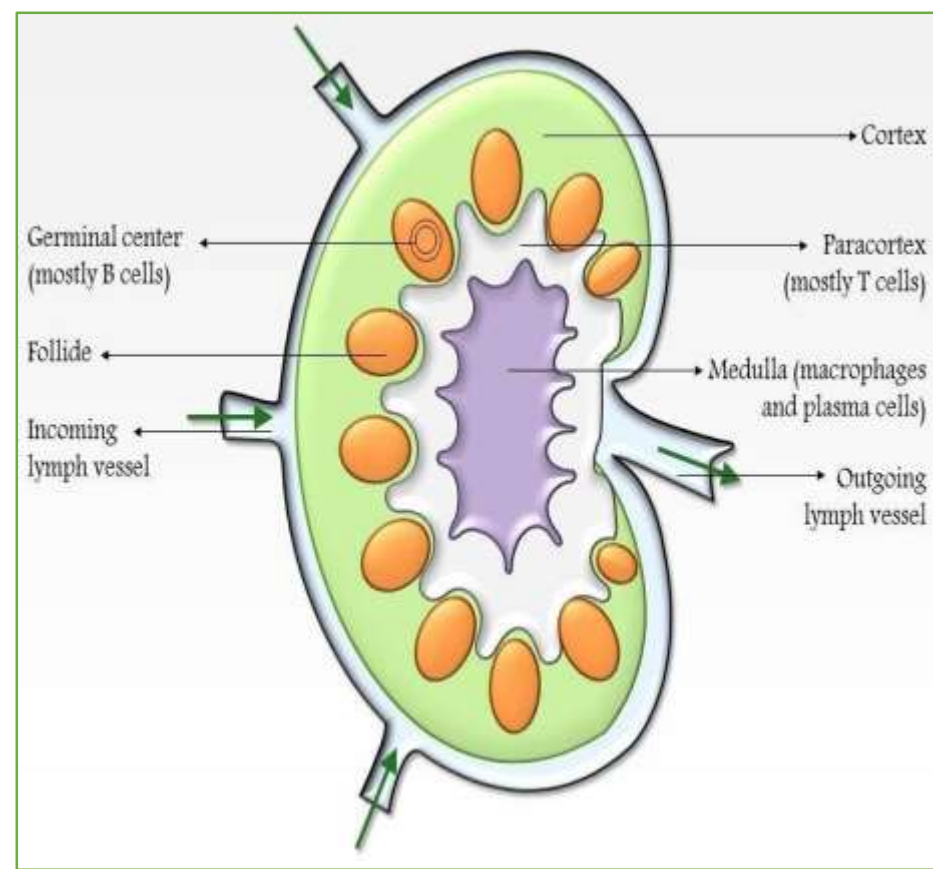
Date:3/3/2022

Done by:Shahed Aljammal

Edited by:Mohammad Abujaber

If you come by any mistake (whether it be spelling , grammatical or scientific) while browsing this sheet,
Kindly report it to [Academic](#)

- The **outer cortex** has **lymphatic follicles** that mostly contain **B-cells**.
- The **inner cortex (paracortex)** contains mostly **T-cells**.
- The **medullary cords** contain mostly **plasma cells**. (and memory cells)
- Other cells in the lymph node:
 - **Macrophages**
 - **Dendritic cells**
 - **Follicular dendritic cells**
 - **Reticular cells**



Both the macrophages, and the dendritic cells trap antigens and present them on their surfaces. As B cells in lymphatic follicle are stimulated, they differentiate into plasma cells. Plasma cells move to medulla (medullary cords)



Small
(6-9 μm)
Inactive lymphocyte

Darkly stained cell



Large
(9-18 μm)
Active lymphocyte

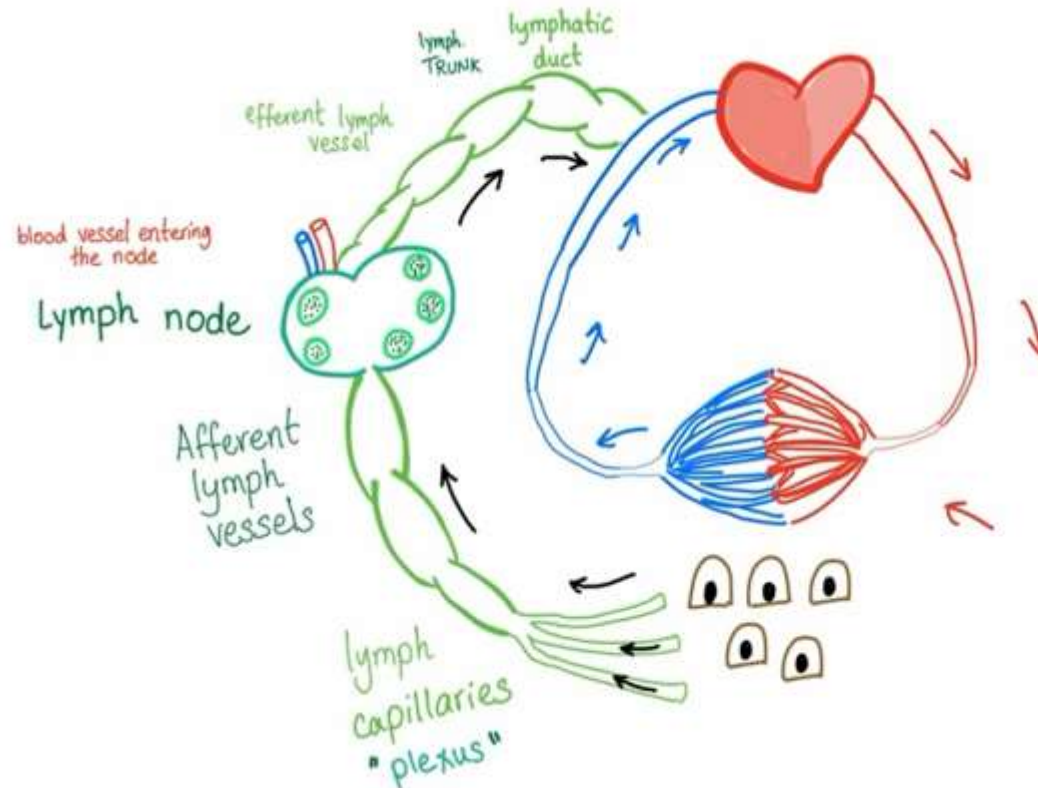
Lightly stained cell

Immunocompetent doesn't necessarily mean an active lymphocyte

Immunocompetent means it is able to differentiate between self and non-self antigen (whether it is active or not; we call it active when it finds the antigen and distinguishes it)

Active lymphocyte is larger and lighter stained.

So according to follicle's activity, there are 2 types: primary and secondary



The outer cortex houses lymphatic follicles (nodules) which are of two types:

1- Primary lymphoid nodules (follicles):

- Lymphoid follicles without a germinal centre
- Spherical aggregates of B lymphocytes (virgin B cells and memory cells)

2- Secondary lymphoid nodules (follicles):

- lymphoid follicles with a germinal centre (pale centre).
- Form only in response to exposure to antigens
- Sites for B memory cell and plasma cell generation
- Outer region: dense accumulation of small lymphocytes that are migrating away from their site of origin within the secondary nodule



When activated by antigens (and T helper cells), B cells migrate to the centre of the follicle, forming a germinal centre.

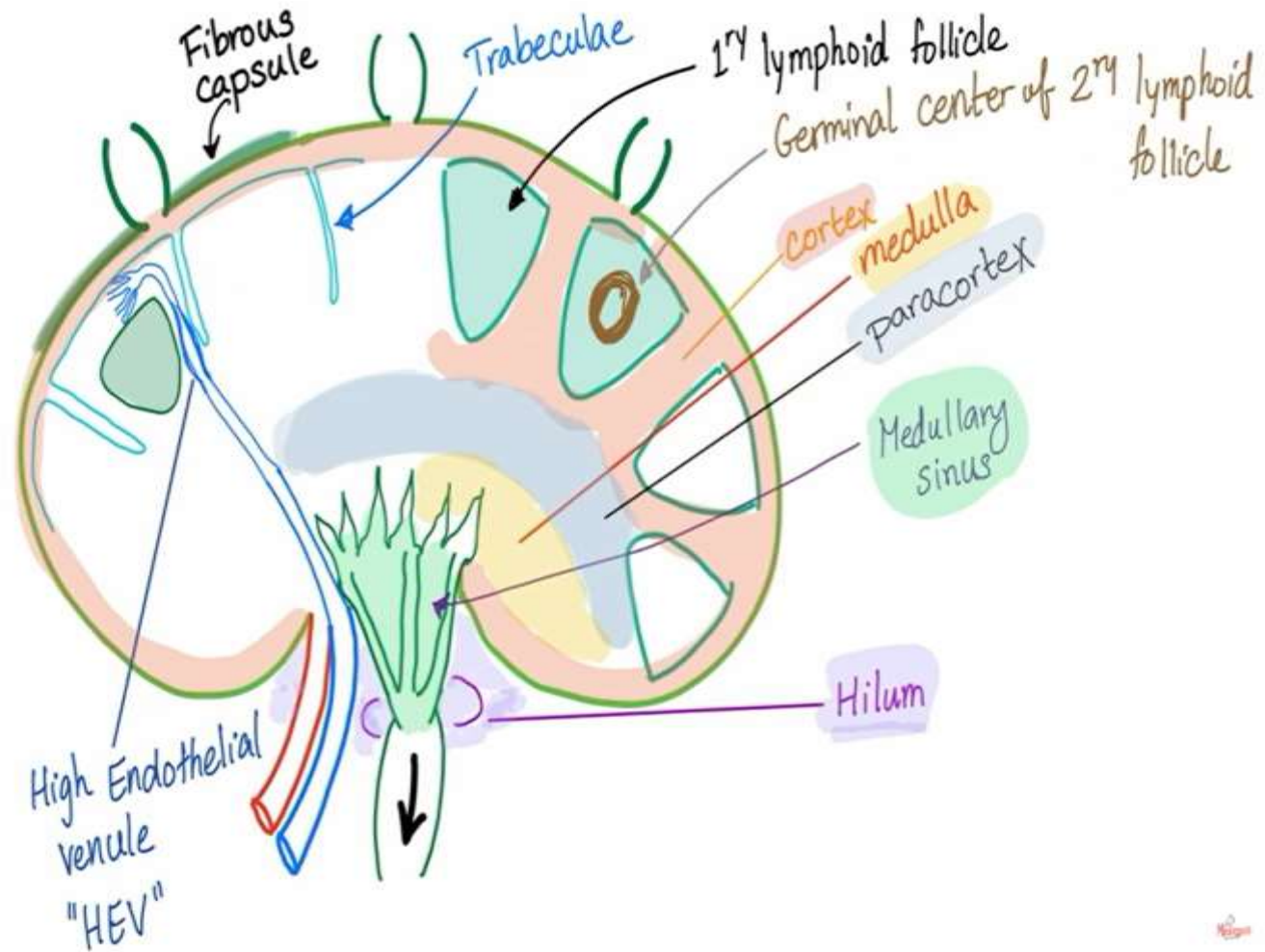
Germinal centres are the central regions of secondary follicles where activated B cells are proliferating (dividing by mitosis) and differentiating into plasma cells and memory B cells.

When stimulated by antigens, lymph nodes enlarge due to the formation of germinal centres and B cell proliferation

Macrophages and Dendritic cells capture antigen within tissues and transport antigen to secondary lymphoid tissue

Primary; contain only inactive form of lymphocyte-naïve

Secondary; when B-lymphocyte find the antigen, become activated, get larger and lighter, it moves to the center and differentiates to give plasma cells and memory cells

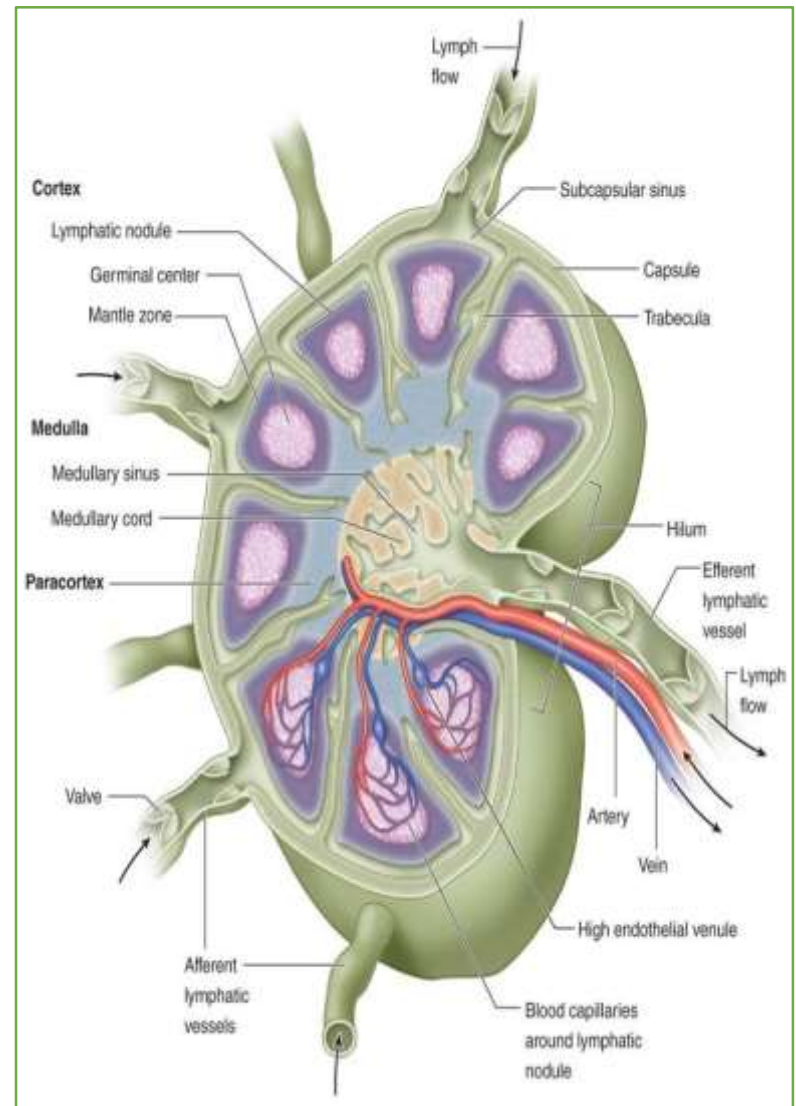


The medulla

is the deep, cavitated part of the lymph node

it is composed of:

large tortuous lymph sinuses surrounded by lymphoid cells that are organized in clusters known as medullary cords
medullary cords: contain B lymphocytes and some plasma cells

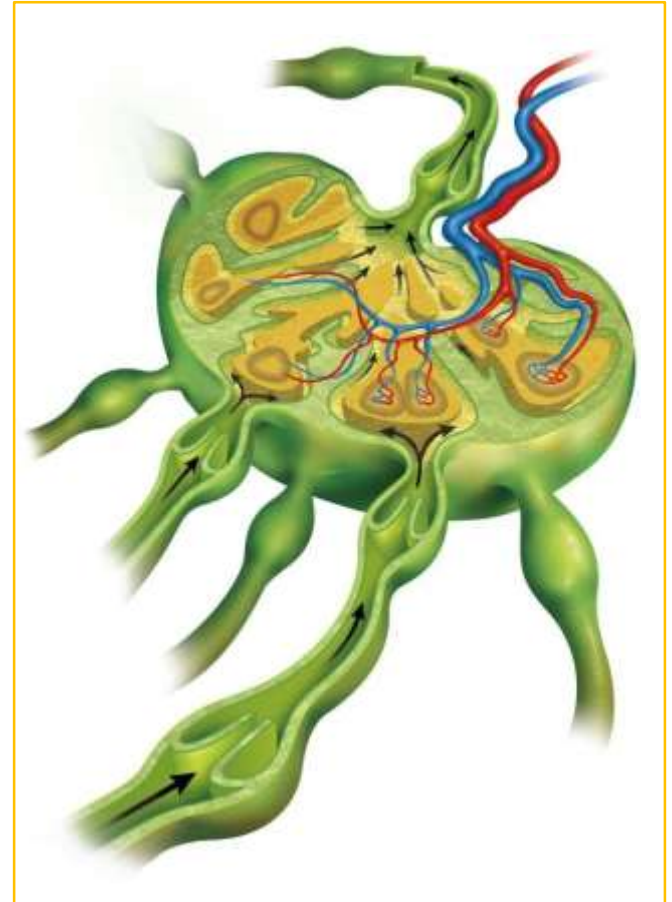


Functions of lymph nodes

- Nodes filter the lymph, removing foreign material and microorganisms.

All lymph is filtered by at least one lymph node before it returns to the blood.

- Antibody-mediated and cell-mediated immune responses occur in the lymph nodes
- Lymph nodes are production sites of antibodies and activated lymphocytes
- Sites for antigen recognition



Lymph nodes contain b cells t cells and antigen presenting cells so its primary function is to initiate immune response,producing anti-bodies and activate lymphocytes

Both types of immune :

- ✓ Cell-mediated→due to T lymphocyte
- ✓ Antibody-mediated→due to B lymphocyte

Afferent vessels

Many afferent lymphatic vessels enter the lymph node at different points over its convex surface

Each containing valves to prevent backflow of lymph.

- **Subcapsular sinuses**

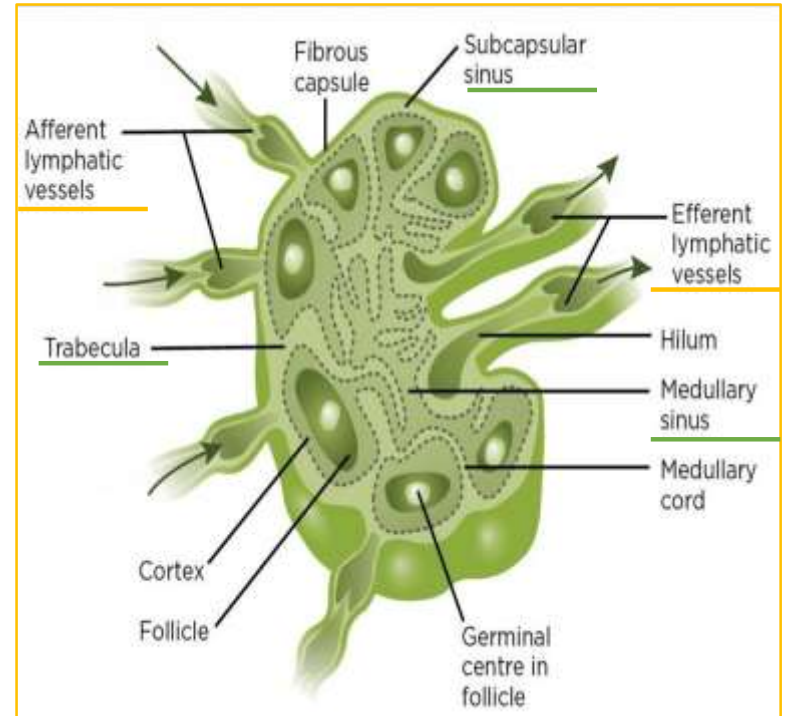
Each afferent vessel empties into the subcapsular sinus.

- **Trabecular sinuses**

The trabecular sinuses are a continuation of the subcapsular sinuses that follow the trabeculae and drain into the medullary sinuses.

- **Medullary sinuses**

Found separating the cords. The medullary sinuses converge at the hilum into the efferent lymphatic vessel.



Lymph slows down when it passes lymph nodes

Efferent vessels

The lymph is removed from the medullary sinus via one or two efferent lymphatic vessels that leave the lymph node at the hilum. Valves in the vessels prevent lymph from flowing in the wrong direction.

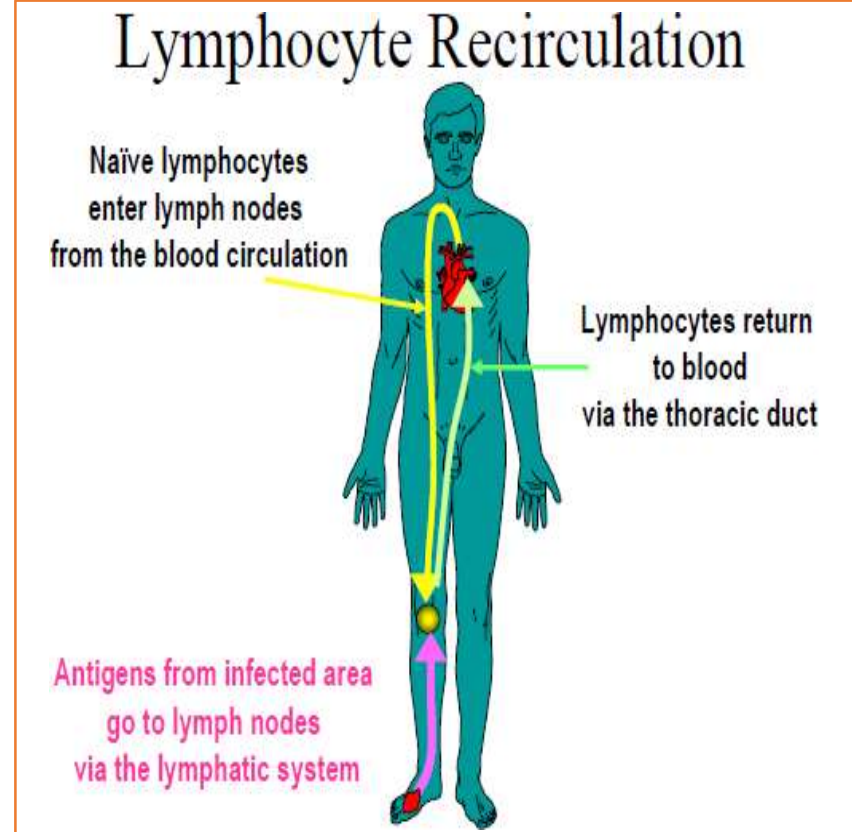
Lymphocyte recirculation

Lymphocyte homing

Serves critical functions in adaptive immune response:

1. It enables the limited number of lymphocytes in an individual that are specific for a particular antigen to search for that antigen throughout the body

2. It ensures that particular lymphocytes are delivered to particular tissue e.g. Recirculation of naive lymphocytes differ from those of effector and memory lymphocytes → specifically naive lymphocytes recirculate through peripheral lymphoid organ and effector lymphocytes migrate to peripheral tissue at sites of infection and inflammation



Afferent vessels is a property exclusive to lymph nodes يعني هي خاصية مميزة لل

Afferent vessels enter below the capsules so we call it SUBCAPSULAR SINUSES

When antigen presenting cells enter lymph nodes → immune response activation → B cells differentiate into plasma cells and memory cells → move from germinal center to medulla and transported through efferent vessels.

Most plasma cells go to bone marrow, so most antibodies are produced within bone marrow

Memory cells will go to other lymph node through its afferent vessel, searching for antigen.

-يعني بتضل تهاجر وتدور عال

antigen

And this explains why we can find memory cells in the primary nodules

Lymphocytes can enter lymphoid

tissues in two ways:

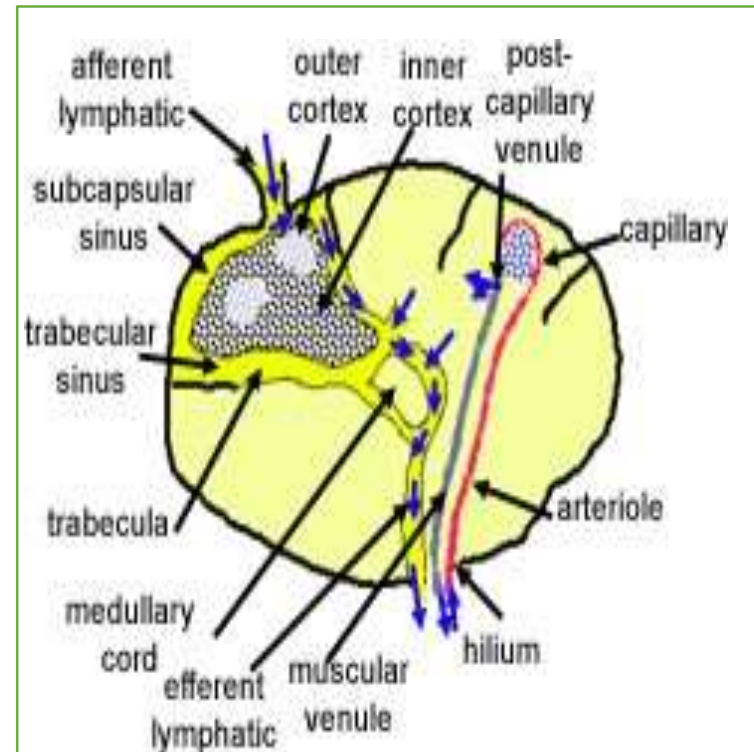
- 1) Direct entry into lymph nodes via afferent lymphatics (10% of lymphocyte enter by this route**)
- 2) Entry from blood capillaries across specialized endothelial cells present in the

How is the process of lymphocyte recirculation regulated?

Why naïve lymphocytes migrate preferentially to lymph node?????

The structure of the post-capillary venule, in the 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 paracortex.

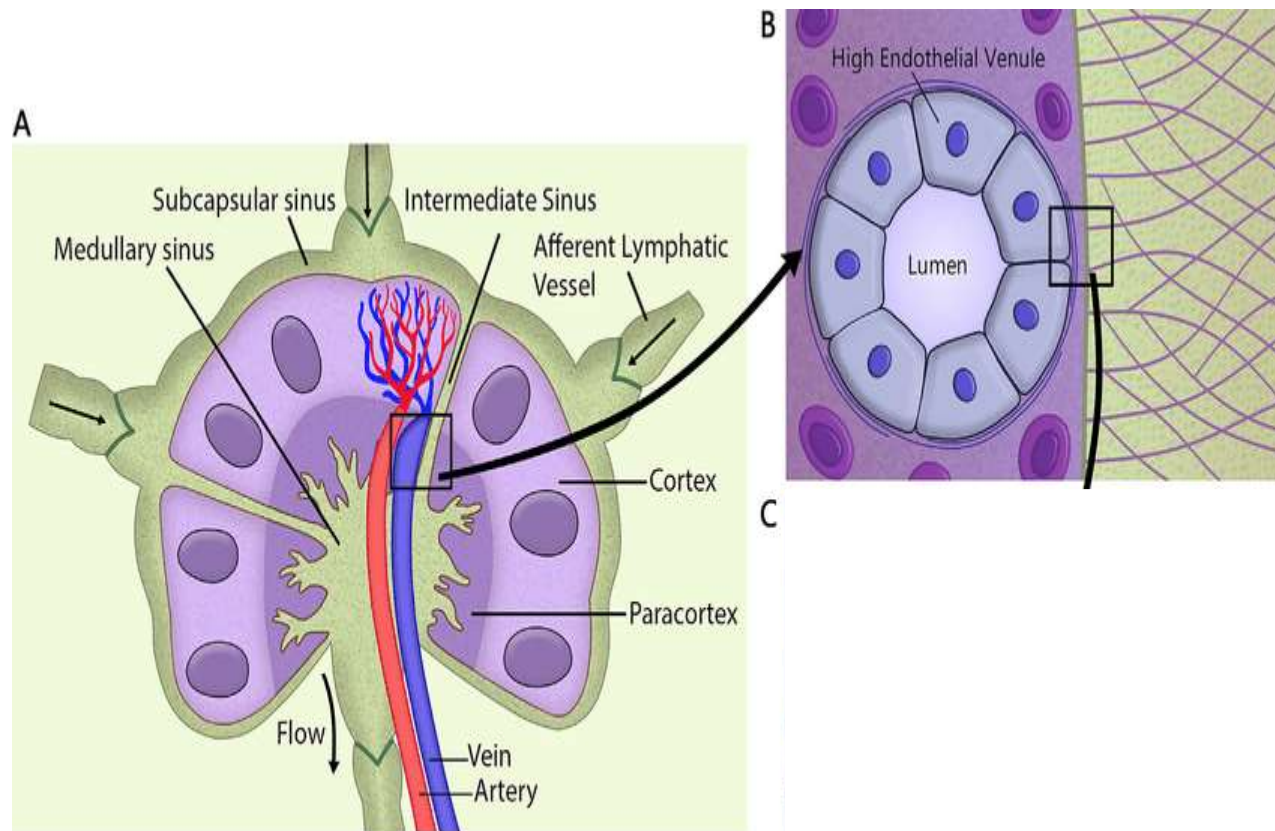
The process of lymphocyte recirculation is regulated by adhesion molecules on lymphocytes called **Homing receptors** and their ligands on vascular endothelial cells called **Adressins**.



This diagram of a lymph node shows the pathways that lymphocytes can take, in and out of the lymph node.

Remember :simple squamous epithelium is the tissue within capillaries and blood vessels
While within High Endothelial Venule(paracortex), the cells are cuboidal in shape.
The ligand presented on HEV attract lymphocytes to enter into lymph nodes (90% of lymphocytes enter through this root)
T-cells remain in paracortex ,B-cells will migrate to the follicles within cortex

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



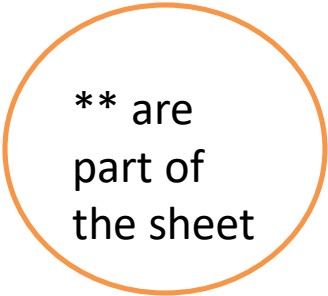
Thank

You

Lymphatic system

II

Dr. Silvia
Boyajian



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part of
the sheet

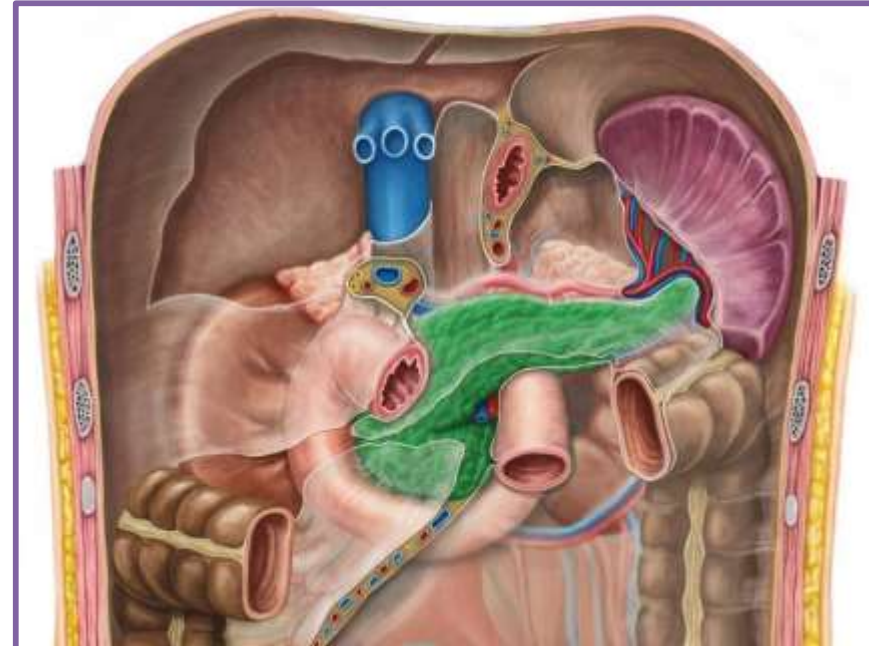
Spleen

- The spleen is an oval-shaped **intraperitoneal organ**
- It is the largest of the lymphoid organs
- Approximately
 - 5 inches in height (12-13 cm)**
 - 3 inches in width (7-8 cm)**
 - 1 inch in thickness (2.5 cm)**
 - Weighs 7 ounces (200gm)**
 - Lies under ribs 9 to 11**

Spleen is the organ of odd numbers

- **Functions**

- I. Filtration of blood (defense against blood-borne antigens)
- II. The main site of old RBCs destruction.
- III. Production site of antibodies and activated lymphocytes (which are delivered directly into the blood)



The spleen resembles a large lymph node
The spleen filters the blood while lymph nodes filter the lymph

Remember:

- lymph node filters the lymph
- Spleen filters the blood

(spleen مقبرة ال)

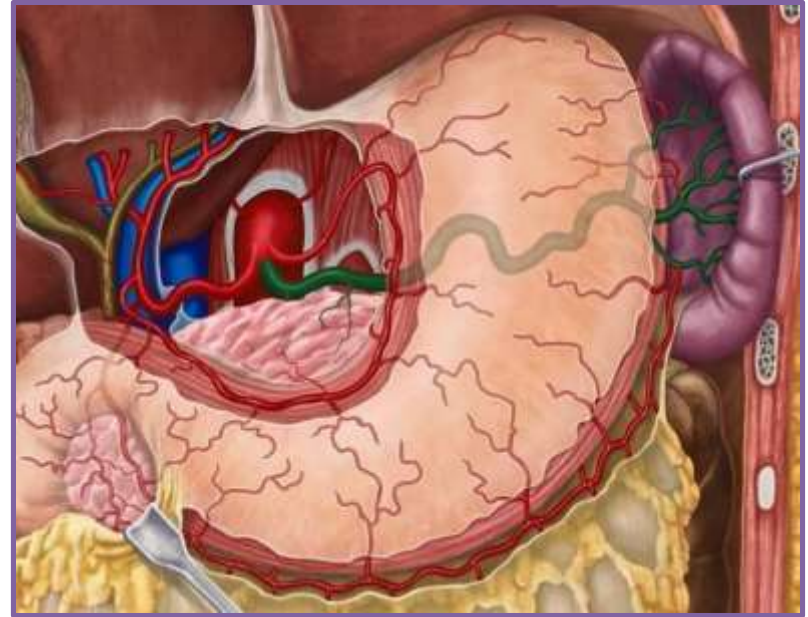
RBC)

Unlike lymph nodes the spleen:

1. has no afferent lymphatics
2. has no lymphatic sinus system
3. Its lymphatic tissue is not arranged into a cortex and medulla

- **The splenic artery is the largest branch of the celiac artery**
- **enter the spleen at the hilum**

sheet**no lymphatic sinuses,instead there are capillary sinuses
-no cortex ,medulla ;instead there are pulps(white and red pulps)



Abdominal Aorta



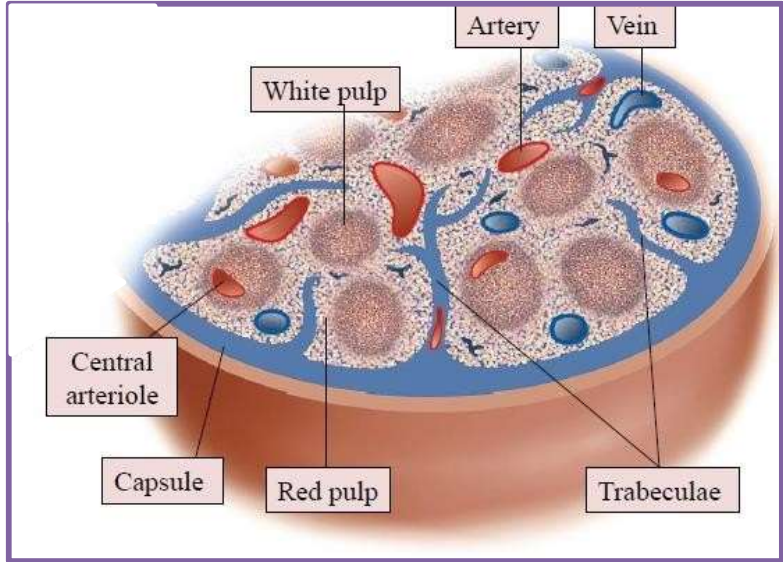
Celiac Trunk



Splenic artery

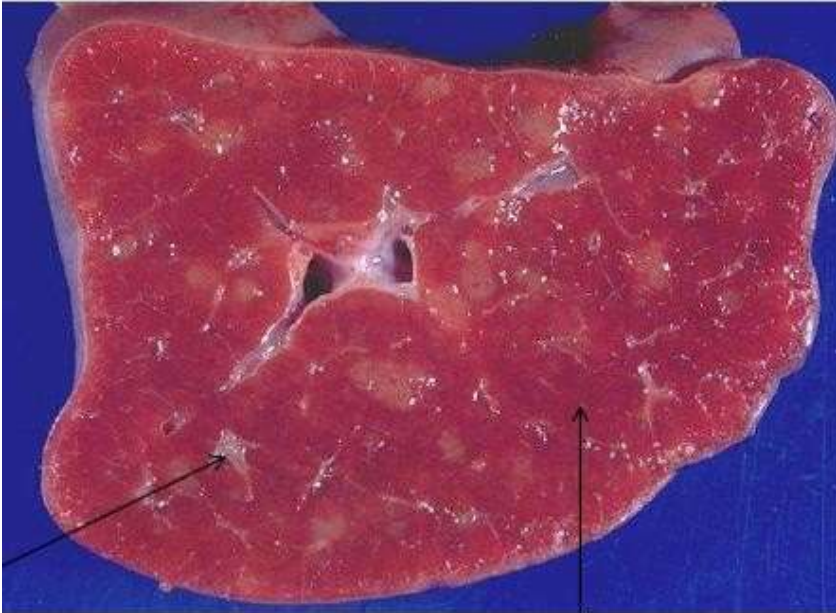
Structure of the

- The spleen is covered by a **capsule of dense connective tissue**, and have **capsular extensions called the trabeculae**
- The spleen is composed of parenchyma and stroma
 1. **Parenchyma:** Splenic pulps
 2. **Stroma:** Reticular tissue (reticular fibres and reticular cells)



The parenchyma of the spleen appears in fresh specimen as:

- White pulp which appears white on gross examination (collection of both B and T lymphocytes)
- Red pulp which appears red on gross examination (blood filled)



Splenic artery

Divides into trabecular arteries as it enters the spleen

Trabecular arteries

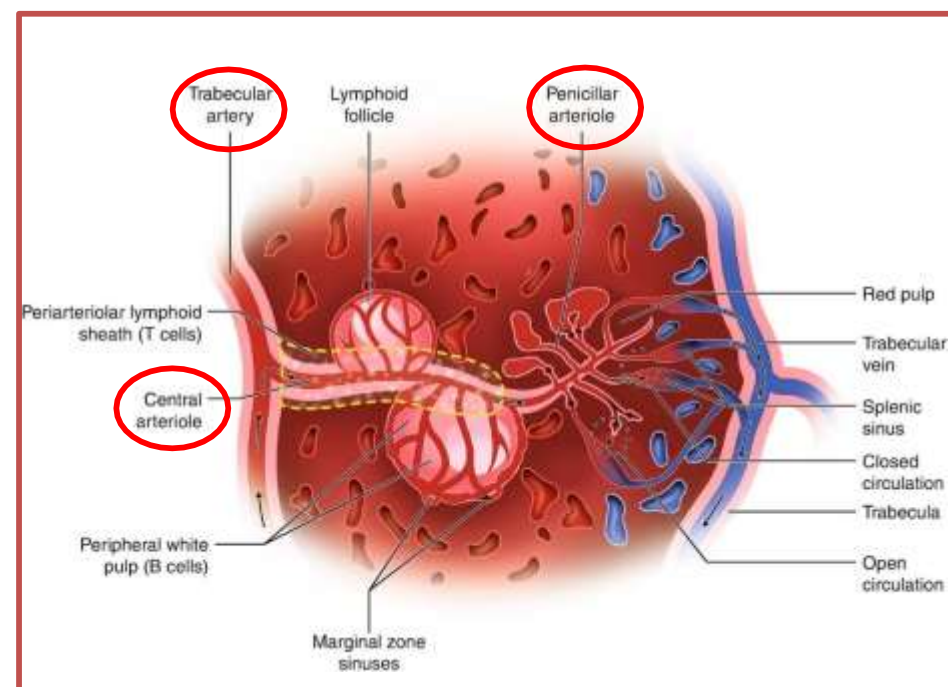
Follow the course of trabeculae

Central arterioles

Are branches of trabecular arteries entering the white pulp. They are surrounded by a sheath of lymphocytes.

Penicillar arterioles

Each central arteriole eventually leaves the white pulp and enters the red pulp, losing its sheath of lymphocytes and branching as several short straight penicillar arterioles that continue as terminal capillaries.



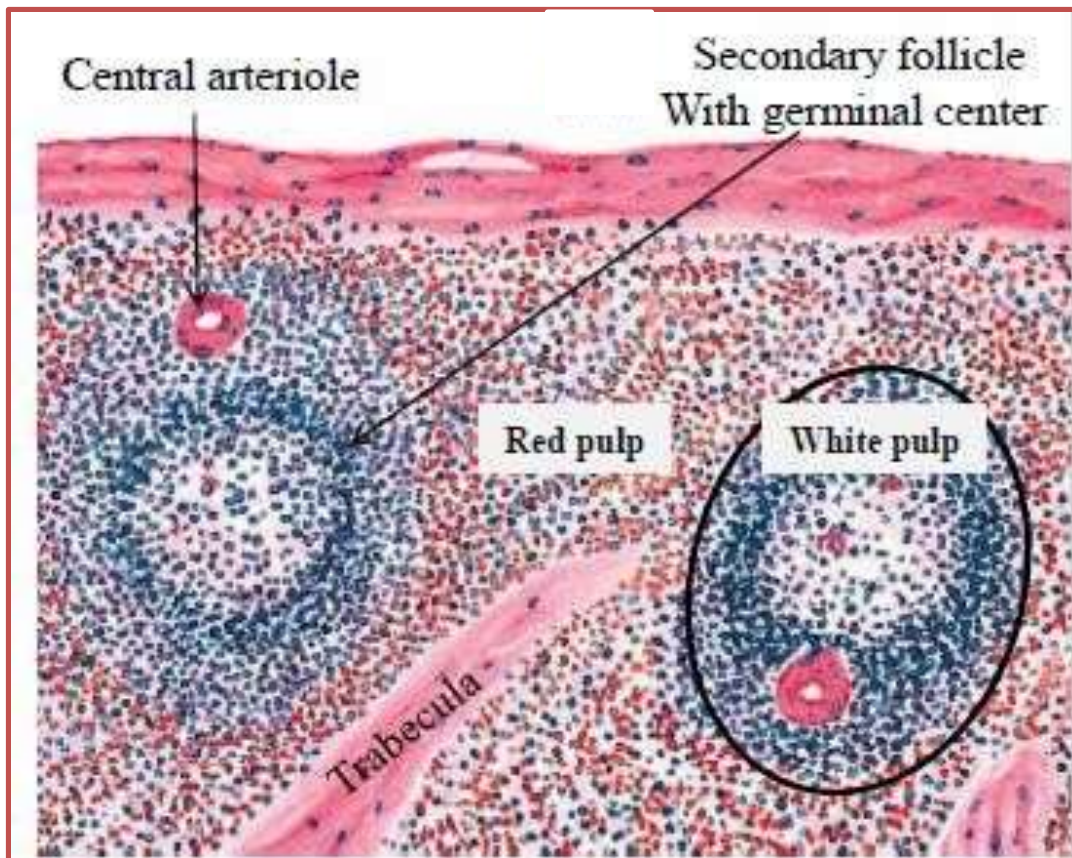
Penicillus

The structure of the spleen is built around its blood supply

Sheet**terminal capillaries are surrounded by macrophages → terminal sheath capillaries

White pulp (lymphoid tissue)

- Constituting 25% of the spleen
- the white pulp is responsible for the immunological (lymphatic) function of the spleen.



- The white pulp contains:

1. **Periarteriolar lymphatic sheaths (PALS):**

tightly packed T cells arranged in cylindrical sheaths around central arterioles

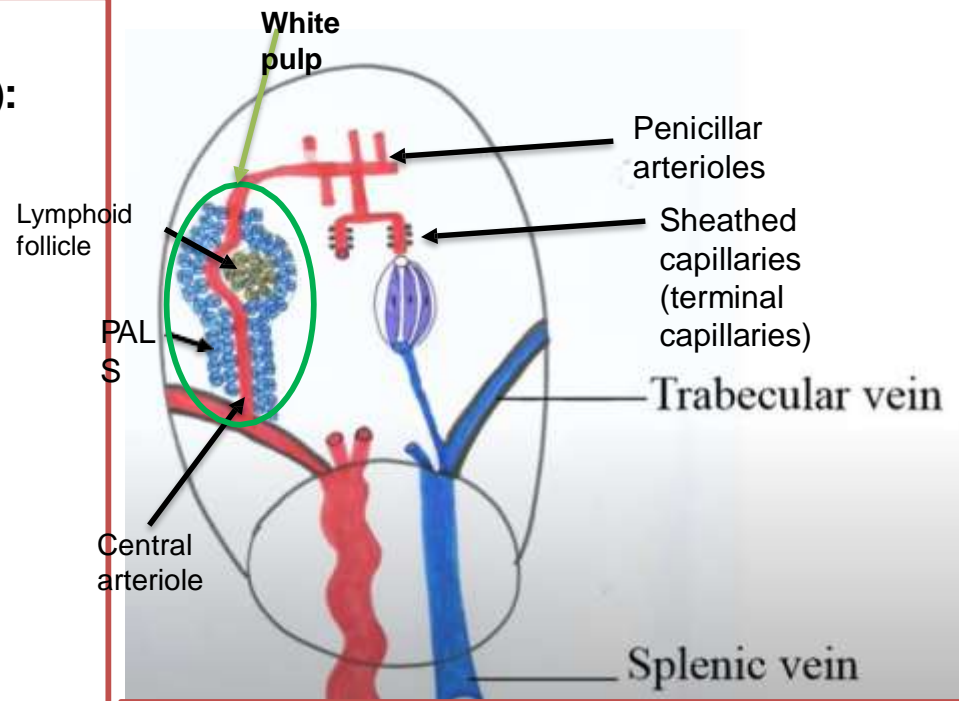
2. **Lymphoid follicles:** spherical aggregations of B cells scattered throughout the PALS Primary (unstimulated) follicles contain resting (inactive) B cells

Secondary (stimulated) follicles contain activated B cells in a central region (germinal center)

↳ **Splenic nodules (Malpighian corpuscles)**

Note: These follicles have the same structural organization as those found in lymph nodes

Function: The lymphocytes and APCs monitor the blood for foreign antigens and respond in a similar way to those in the lymph nodes.



When the lymphatic sheath expands to incorporate the follicles, the central arteriole is displaced to one side and acquires an eccentric position in the follicle but is still called the central arteriole (Follicular arteriole).

****The PALS will surround both Follicles & Central arterioles**

Splenic → trabecular → central → penicillar → terminal capillaries

**RECOMMENDE VIDEO → <https://youtu.be/RezL2xWFCe8>

Blood flow through the splenic red pulp can take either of two routes:

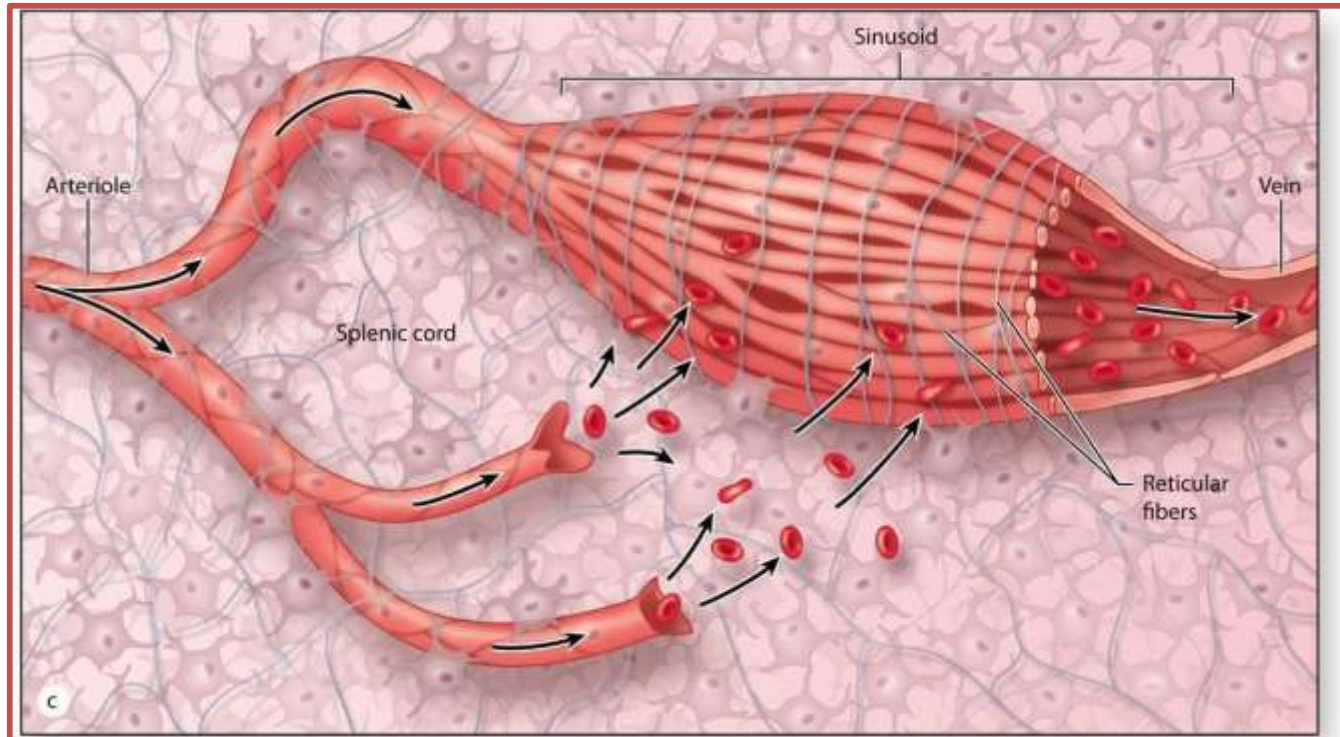
Open circulation: the capillaries open into the spaces of the red pulp (**splenic cords**) and then the blood returns to the venous system through the wall of the splenic sinusoids

90% of blood

Closed circulation: the capillaries open directly into the **splenic sinusoids** (blood is

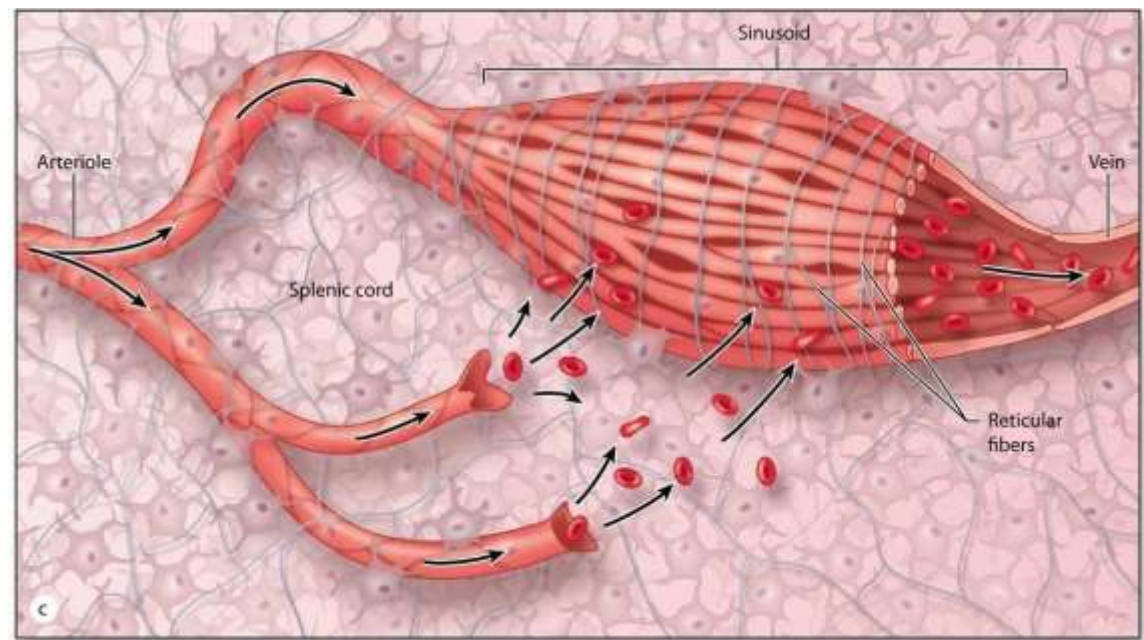
enclosed

by endothelium)



Note the wide gaps between endothelial cells which allow for movement of entire cells from cords to sinuses

Red pulp (blood filled)



- Constituting 75% of the spleen

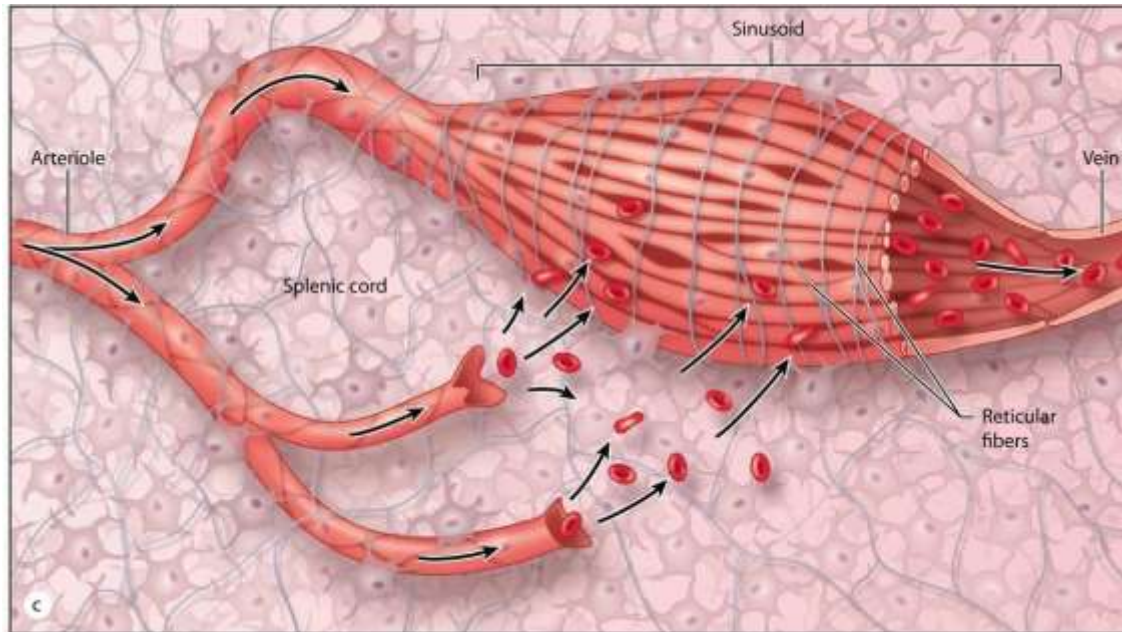
• **The red pulp contains:**

1. **Splenic cords (Billroth's cords):** consist of all cells between the sinusoids in the red pulp (reticular cells, macrophages, plasma cells, lymphocytes, RBCs, platelets, other leukocytes)

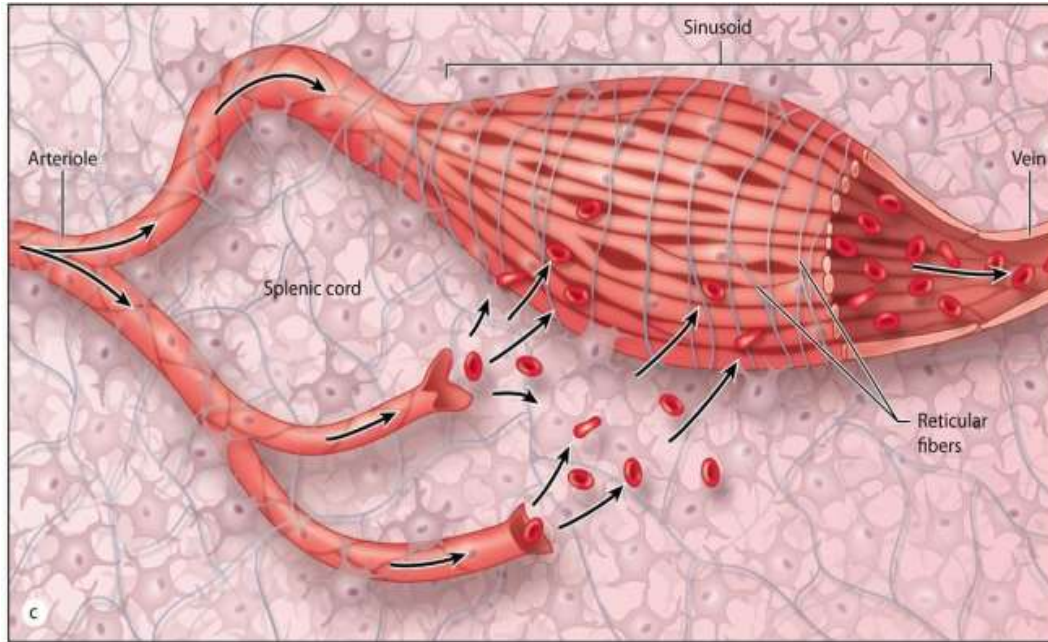
1. **Splenic sinusoids:** are blood-filled spaces located throughout the red pulp. They have large, dilated, irregular lumens and large pores (spaces between the endothelial cells)

1. The endothelial cells (**stave cells**) are **elongated, fusiform cells that lie parallel to the long axis of the vessel**
2. The cells lie side by side around the vessel but not joined by any type of intercellular junctions
3. The endothelial cells are supported by highly discontinuous basal lamina (forms bars and encircles the sinusoid)

Function: Destruction of worn-out RBCs and platelets



****lots of spaces between cells in the vessel because we need to return all the blood into the closed circulation**



- In this route plasma and all the formed elements of blood must re-enter the vasculature by passing through narrow slits between the stave cells into the sinusoids.
- These small openings present no obstacle to platelets, to the motile leukocytes, or to thin flexible erythrocytes.
- However **stiff or swollen RBCs** at their normal life span of 120 days are blocked from passing between the stave cells and undergo selective removal by **macrophages**
- Deformed or less pliable RBCs cannot squeeze effectively from the cord into the sinus and upon their mechanical fragmentation are removed by resident macrophages (lie just next to the sinusoids)

Macrophages monitor erythrocytes as they migrate from splenic cords between the endothelial cells into the splenic sinusoids

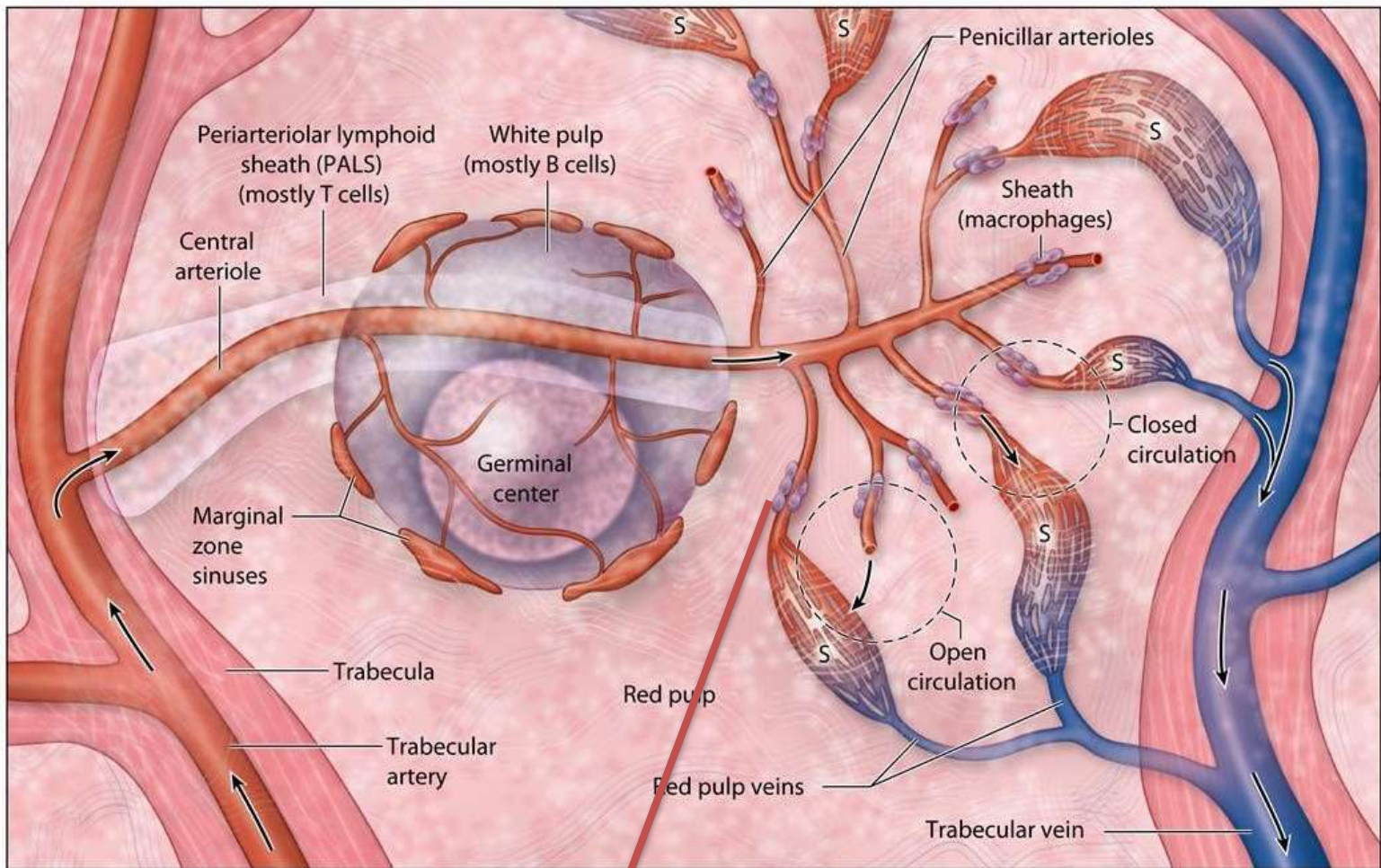
Old erythrocytes **lose their flexibility**

They cannot penetrate the spaces between the endothelial cells and are phagocytosed by macrophages

Old erythrocytes **lose sialic acid** from their cell membranes → **Galactose exposed** **Induce phagocytosis of RBCs**

Clinical note

After surgical removal of the spleen (splenectomy), the number of abnormal erythrocytes in the circulation increases although most such cells are then removed by macrophages in sinusoids of the bone marrow and liver



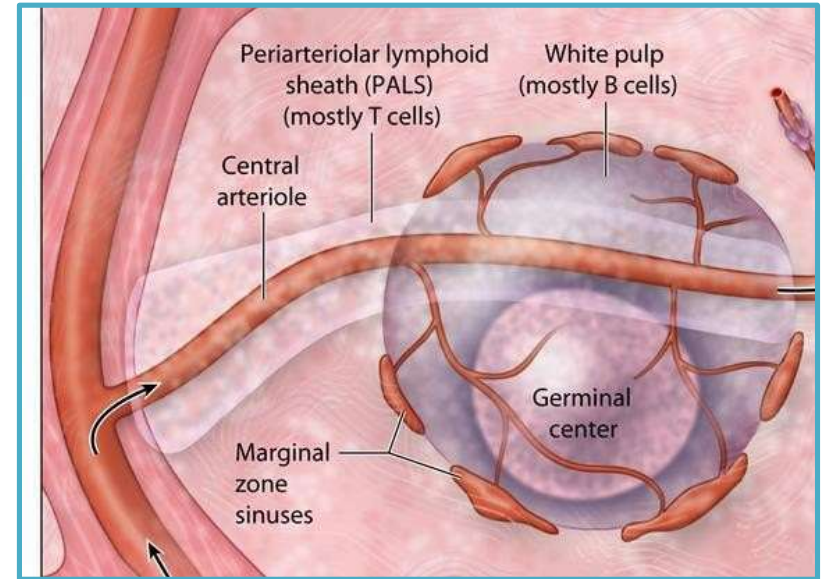
****Macrophages**
The whole structure is called
terminal sheath

Marginal zone

sinuses

Located between the white and the red pulp

- The spaces between these sinuses are wide (2-3 μm)
- It is here the blood-borne antigens and particulate matter have their first free access to the parenchyma of the spleen



The following events occur at the marginal zone:

- 1-APCs sample the material travelling in blood searching for antigens
- 2-Macrophages attack microorganisms present in the blood
- 3-The circulating B and T cells leave the blood stream to enter the preferred location within the white pulp


T cells: PALS

B cells: lymphatic follicles

Lymphocytes come into contact with APCs, if they recognize their antigen, the lymphocytes initiate immune response within the white pulp

Functions of the spleen:

- 1. Blood cell production:** During the fetal life, blood cells are produced in the spleen
- 2. Blood storage:** A small quantity of blood is stored in the sinusoids of the red pulp
- 3. RBC destruction:** Most worn-out or damaged red blood cells are destroyed in the spleen (some in the liver and bone marrow). They are phagocytosed by macrophages
- 4. Defense mechanism:** Macrophages phagocytose microbes that have penetrated the blood. Antigens in the blood activate B and T cells residing in the spleen, triggering an immune response



Production of antibodies and activated lymphocytes (which are delivered directly into the blood)

Summary:

Lymph node	Spleen
Multiple, small	Single, large
Along the course of lymphatic vessels	Intra-abdominal
Filters lymph	Filters blood
Covered by fascia	Covered by peritoneum
Has afferent vessels	No afferent vessels
Cortex and medulla	White pulp and red pulp
Contains Lymphatic sinuses	Contains Blood sinuses

Diffuse lymphatic tissue (lymphatic nodules)

- Is formed by aggregations of lymphatic tissue
- Is found in various mucosal sites of the body

The mucosa or inner lining of the digestive, respiratory, and genitourinary tracts is a common site of invasion by pathogens because their lumens open to the external environment.

It can therefore be referred to as:

Mucosa-Associated Lymphatic Tissue (MALT)

- These aggregations are **not encapsulated**
- MALT can be found in the following locations:

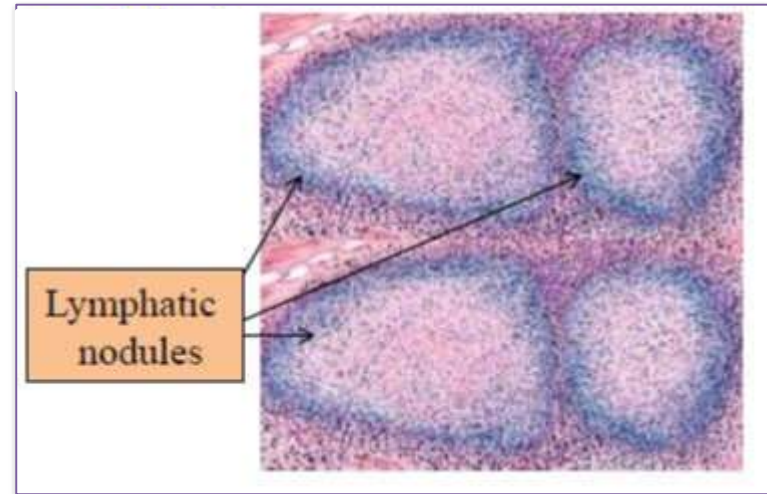
Palatine tonsils

Lingual tonsils

Pharyngeal tonsils

Gut-associated lymphoid tissue (GALT)

Bronchus-associated lymphatic tissue (BALT)



MALT is populated by:

T cells

B cells

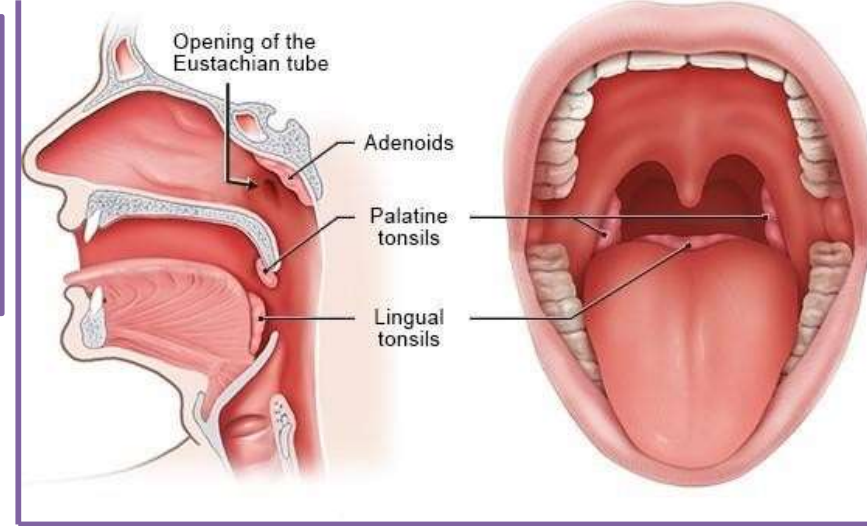
Plasma cells

APCs

Each of which is well situated to encounter antigens passing through the mucosal epithelium

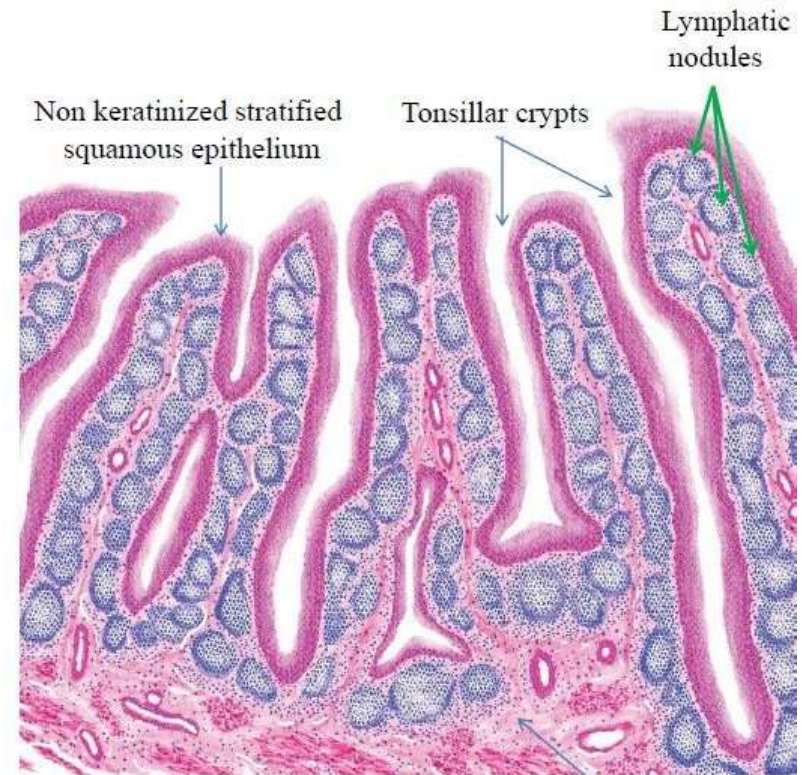
sheet**MALT is found mostly in
GI ,Urinary,respiratory system

- **Tonsils are large, irregular masses of lymphoid tissue embedded in the mucous membranes of the throat**
- **Function of tonsils:** Protect the body from inhaled and ingested pathogens.

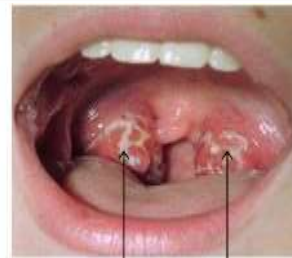


Palatine tonsils

- Are located at the lateral wall of oropharynx**2 in number
- Are covered by stratified squamous epithelium.
- The surface area of each is enlarged with 10-20 tonsillar crypts (deep invaginations)
- Many lymphoid nodules around the crypts
- Has an underlying capsule (partial capsule)



**when inflammation occurs ,pus will be collected within crypts→
As strawberry



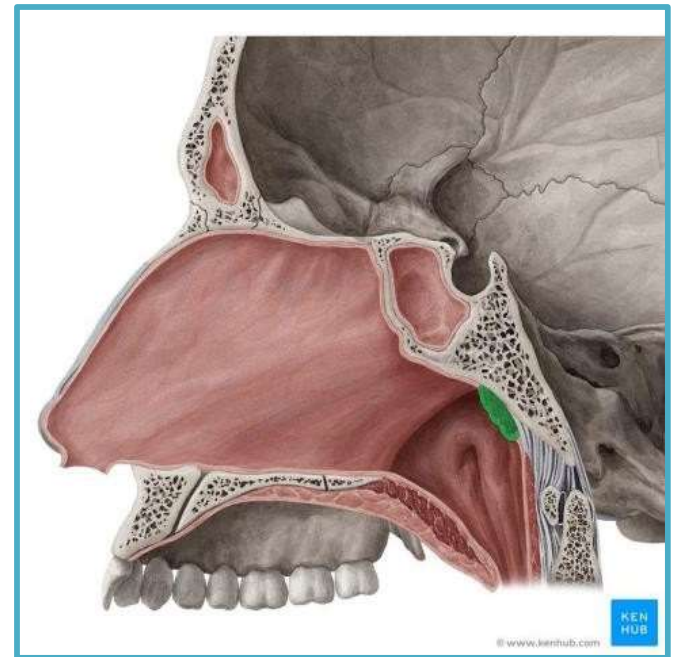
Pus in tonsillar crypts

Palatine tonsils

Capsule

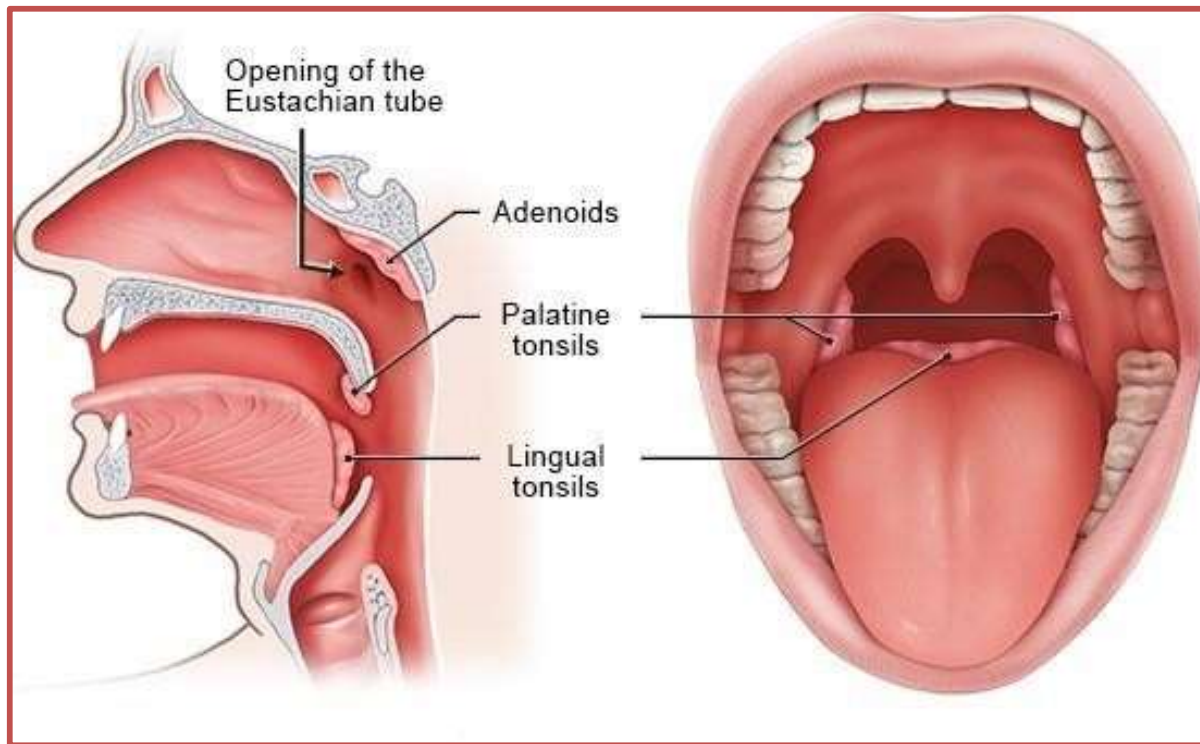
Pharyngeal tonsils

- Are located in the posterior wall of the nasopharynx.
- It is most prominent in children, but begins to atrophy from the age of seven.
- Epithelium: respiratory epithelium (ciliated pseudostratified columnar epithelium)
- Contain diffuse lymphoid tissue and lymphatic nodules
- No crypts
- Thin capsule
- Hypertrophied regions of pharyngeal tonsils resulting from chronic inflammation are called **adenoids**.



Lingual tonsils

- Are located on the posterior 1/3 of the tongue.
- Smaller and more numerous than palatine and pharyngeal tonsils
- Covered by stratified squamous epithelium

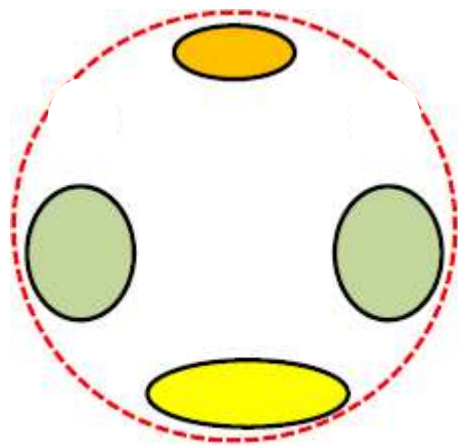


Waldeyer's tonsillar ring (Waldeyer's lymphatic ring) is a ringed arrangement of lymphoid tissue

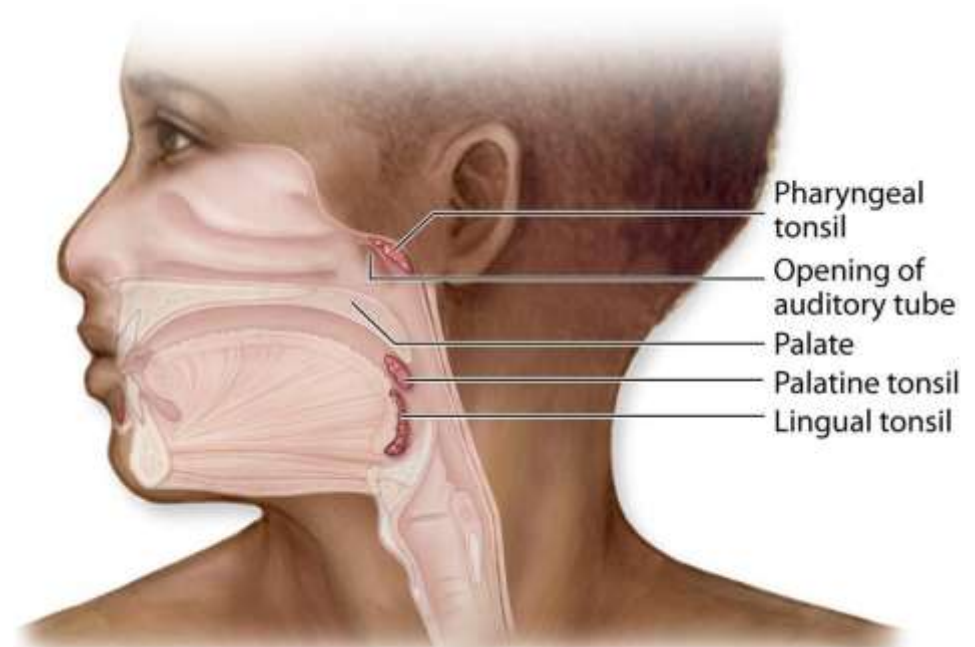
In the nasopharynx, oropharynx, and base of the tongue.

ملاحظة غير مهمة ال

W هون بتقرأ v



Anterior view



**found as a ring in the entry of respiratory and digestive system
So ,any pathogen we inhale or digest pass through tonsils first!

Gut-associated lymphoid tissue

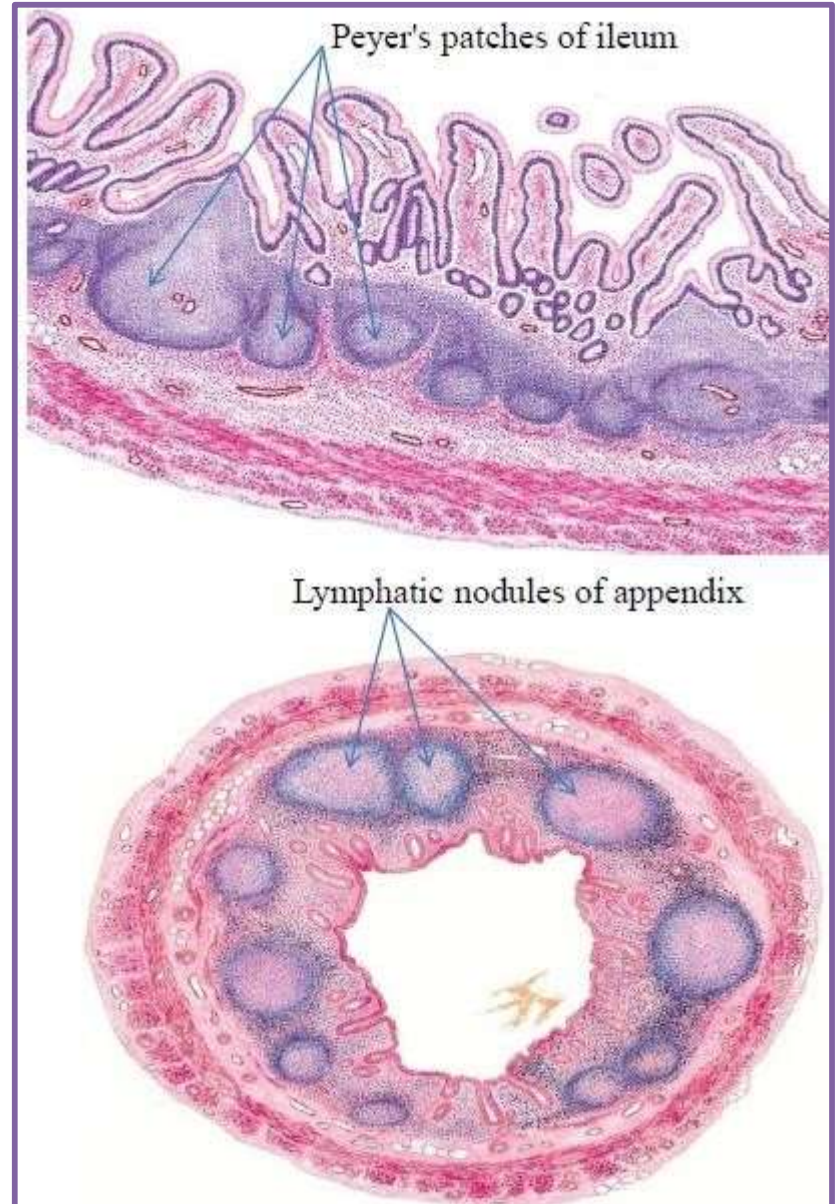
(GALT) Is located in the mucosa of the intestine. **Examples:**

- 1 Peyer's patches of ileum
- 2 Lymphatic nodules of appendix

Function:

Protects the body from ingested pathogens.

*Remember:
Diffuse MALT extends from the pharynx along the entire gastrointestinal tract but becomes very well-developed again in the mucosa and submucosa of the **ileum**. Here large aggregates of lymphoid nodules comprise the Peyer patches, each containing dozens of nodules with no underlying connective tissue capsule.
Another significant collection of MALT occurs in the mucosa of the **appendix***

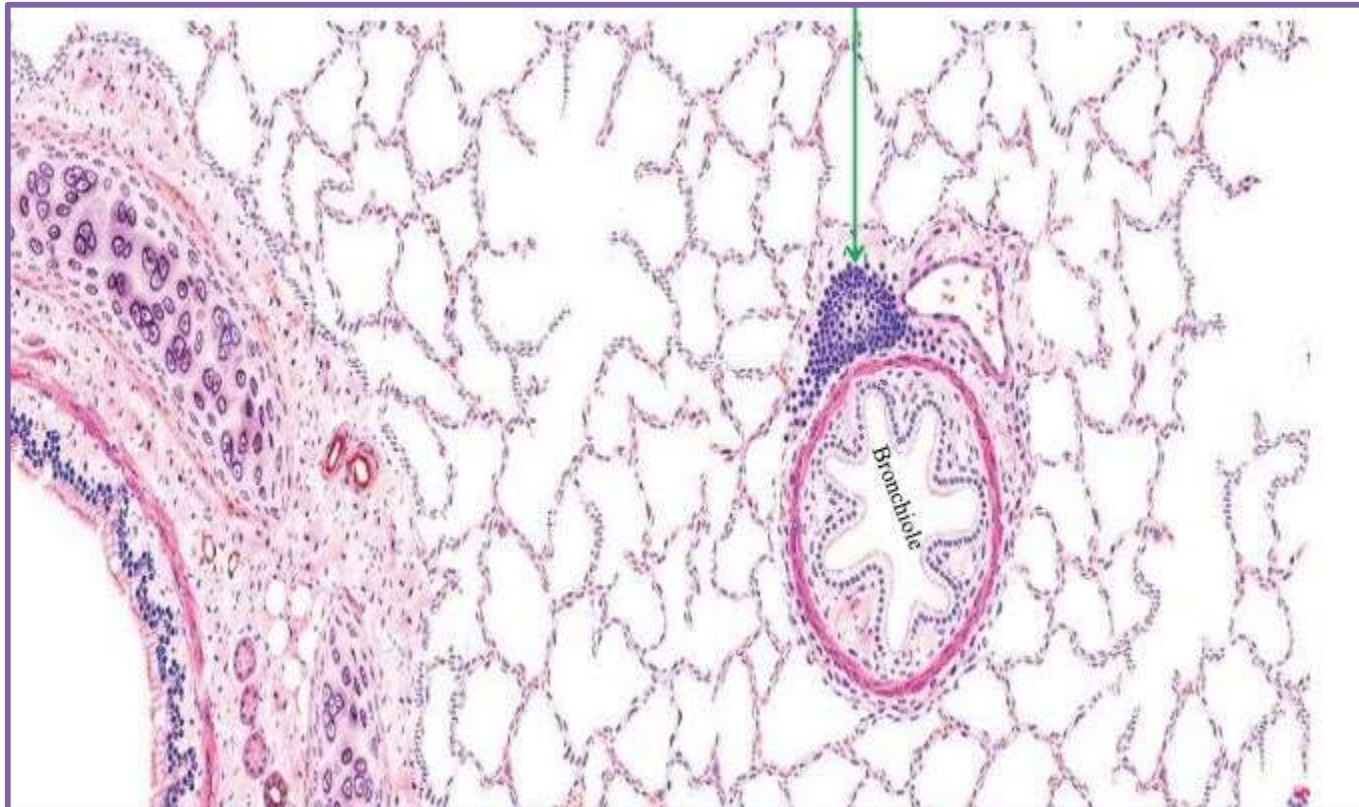


Bronchus-associated lymphatic tissue (BALT)

Is located in the mucosa of the bronchioles.

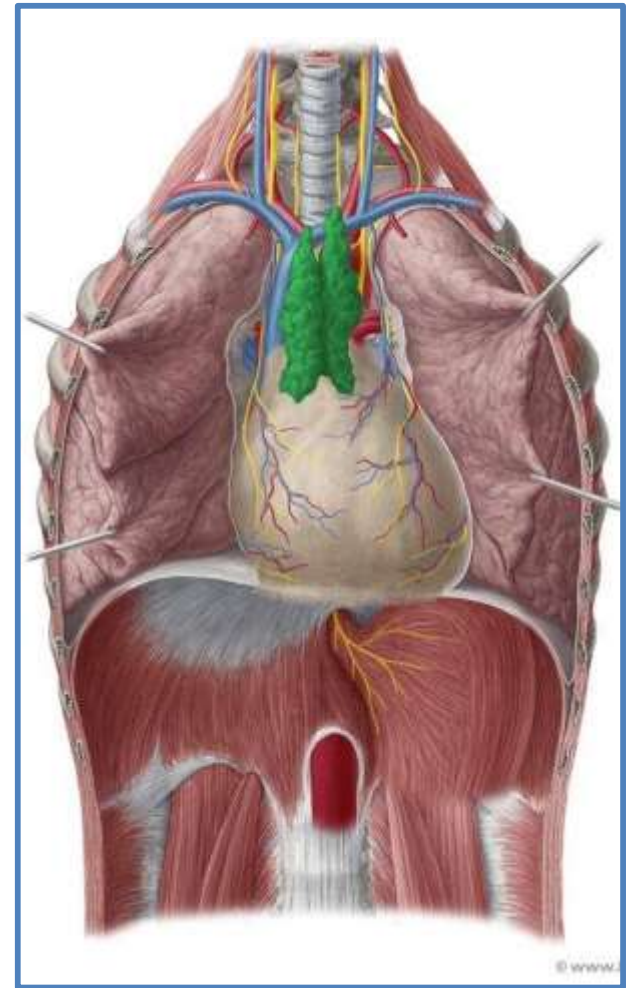
Function:

Protects the body from inhaled pathogens.



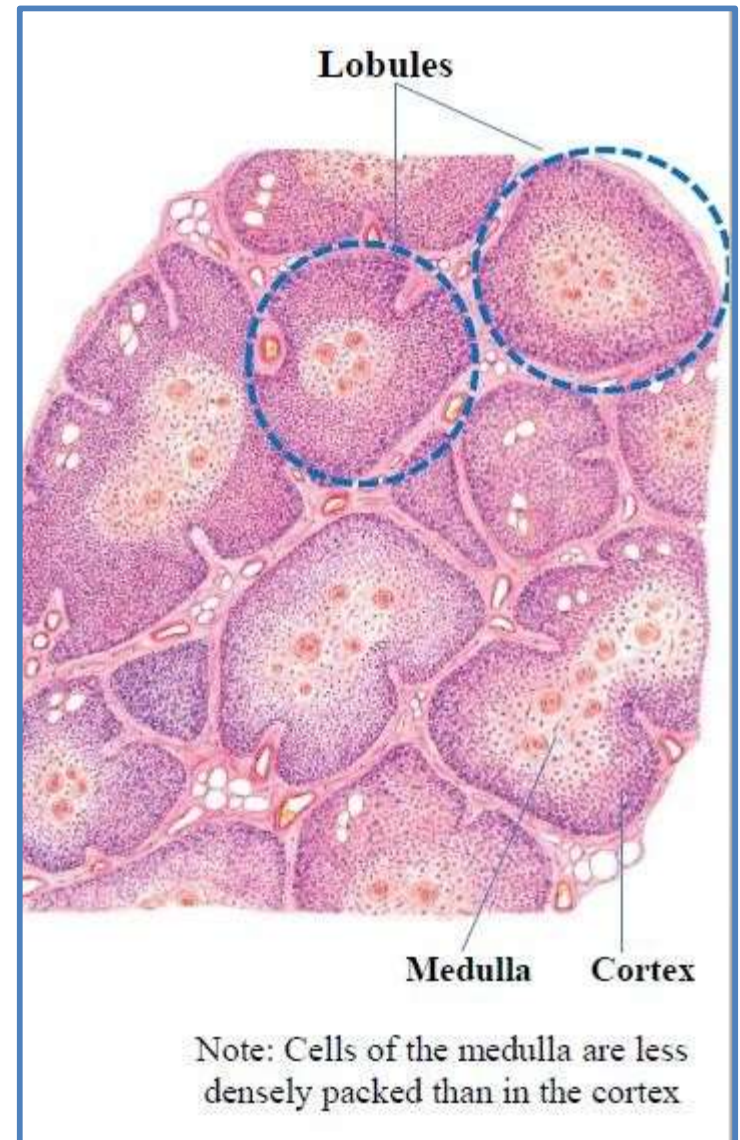
Thymus

- The thymus is a bi-lobed gland located in the anterior mediastinum, posterior to the sternum and anterior to the trachea
- Within the thymus, immature T-cells develop, differentiate, and multiply, as well as gaining their antigen specificity and immune tolerance to the body's own tissues.
- It is large in the newborn and young child
- From puberty onwards, it gradually becomes replaced by fat.



- The thymus has a connective tissue capsule that extends septa, dividing the organ into many incomplete **lobules**.
- Each lobule has an outer **darkly basophilic cortex surrounding a more lightly stained medulla**.
- The staining differences reflect the much greater density of lymphocytes in the cortex than the medulla

**90% of T-lymphocyte get destructed within the cortex
(selecting the immunocompetent cells and destroying the rest)
→ cortex appear darker than medulla



The cortex contains:

- .Immature T cells (T lymphoblasts, thymocytes) (in various stages of differentiation and maturation)
- .Macrophages
- Unique thymic epithelial cells (TECs)

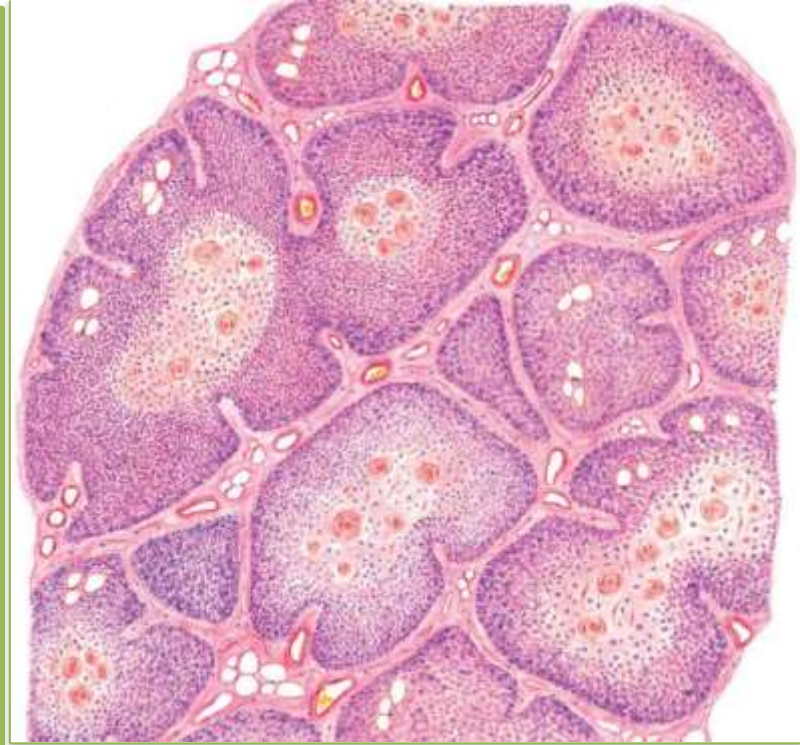
The medulla contains:

- 1.Fewer and more mature lymphocytes.
- 2.Macrophages
- 3.Dendritic cells (APCs)
- 4.Unique thymic epithelial cells (TECs)
- 5.Large aggregates of TECs called **Hassall corpuscles**

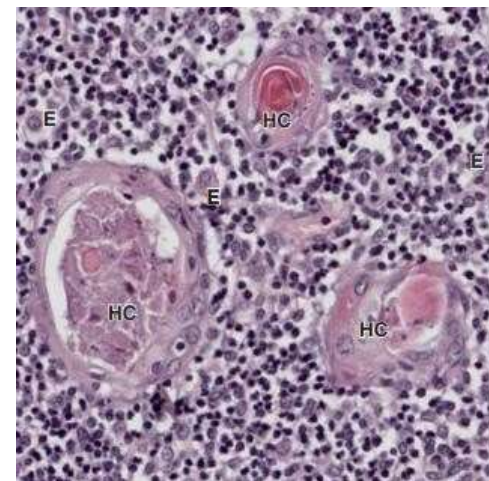
As T cells mature, they migrate to the medulla

Hassall corpuscles are unique to the thymic medulla

- 20-100 μm in diameter
- Are concentric aggregates of squamous cells with central keratinization(acidophilic)
- Consists of flattened epithelial reticular cells wrapped about one another in concentric lamellation
- Tend to grow larger with age
- Function \rightarrow unknown



*Ex;lymphocytes that identify self antigen as a pathogen ;will be destroyed to prevent autoimmune disease



Blood-thymic barrier

The developing T cells of the cortex are protected from contracting blood-borne macromolecules. However self-molecules are permitted to cross blood thymic barrier (probably controlled by epithelial reticular cells) → possibly to eliminate those T cells that are programmed against self-antigens

*4 layers //for isolation

Endothelium, BM, CT, Reticular cells

Thymic Epithelial Cells (TECs) (Epithelial reticular cells)

1 Form a stroma to which macrophages and developing lymphocytes attach instead of reticular fibres

2 Line the capsule and septa and surround all blood vessels in the **cortex**



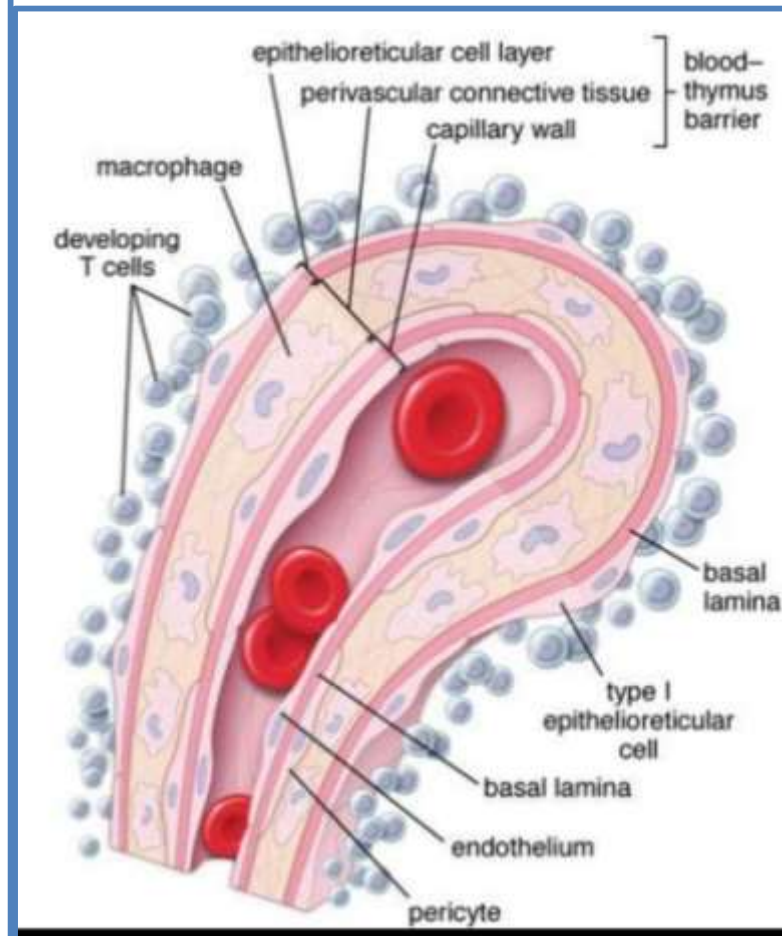
Form a **blood-thymus barrier preventing antigens in the blood from making contact with the developing T cells (in cortex)**

3 Envelop groups of T cells that are multiplying and maturing (**in cortex**)

4 Act as APCs, expressing MHC class II and MHC class I molecules (**in cortex**)

5 Express many specialized proteins specific to cells of other organs, tissue specific antigens (**in medulla**)

6 Secrete hormones that promote the differentiation of T cells (endocrine thymus) → **Thymosin, Thymopoietin**



**Has role in

- ✓ Programming
- ✓ Stroma
- ✓ Secrete hormones

Note

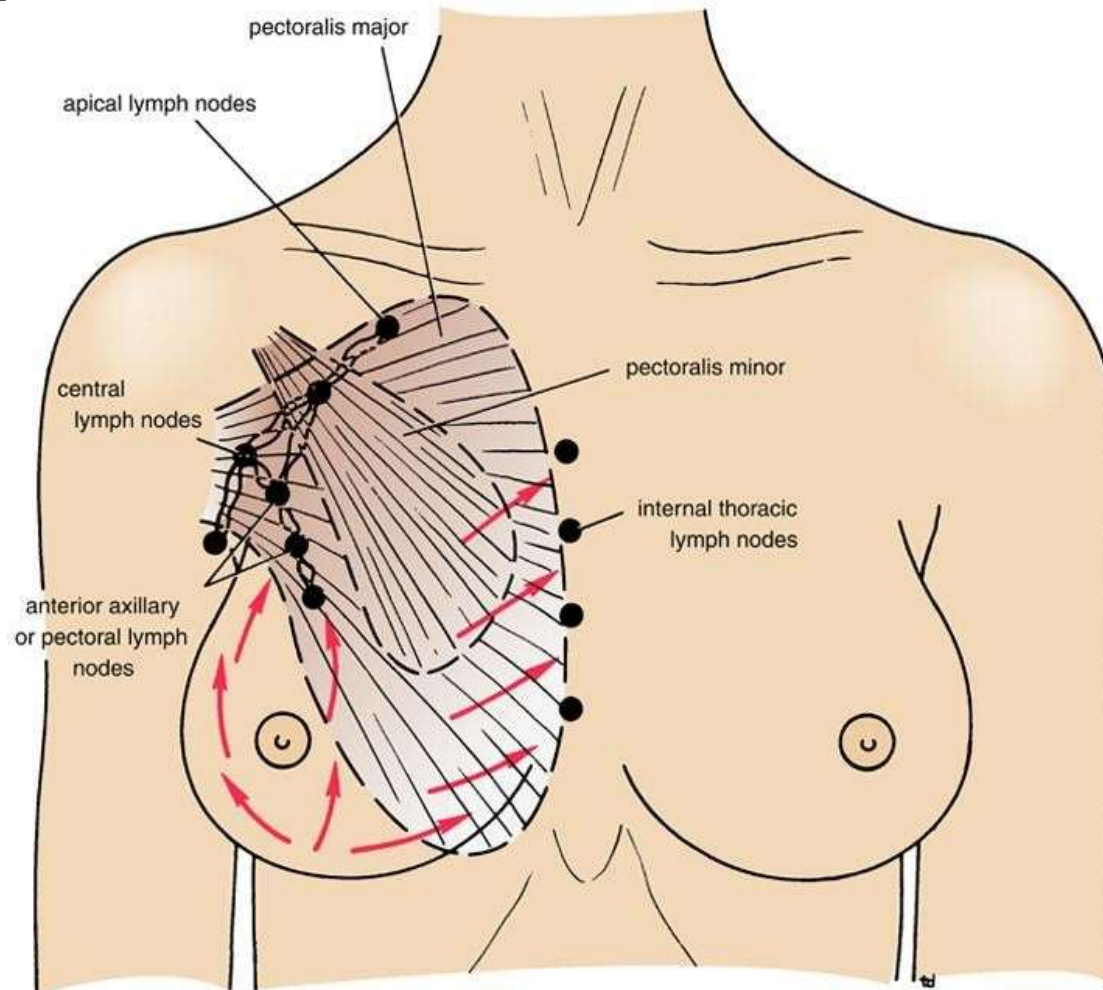
Thymic epithelial cells are also
called

Nursing cells



They form sheets for cells deep to the capsule, around septa and blood vessels, to isolate developing T lymphocytes in the cortex from contact with antigens (present in the blood), while they are programmed

Lymph Drainage of Breast



2 pathways

Medially ,Lateral

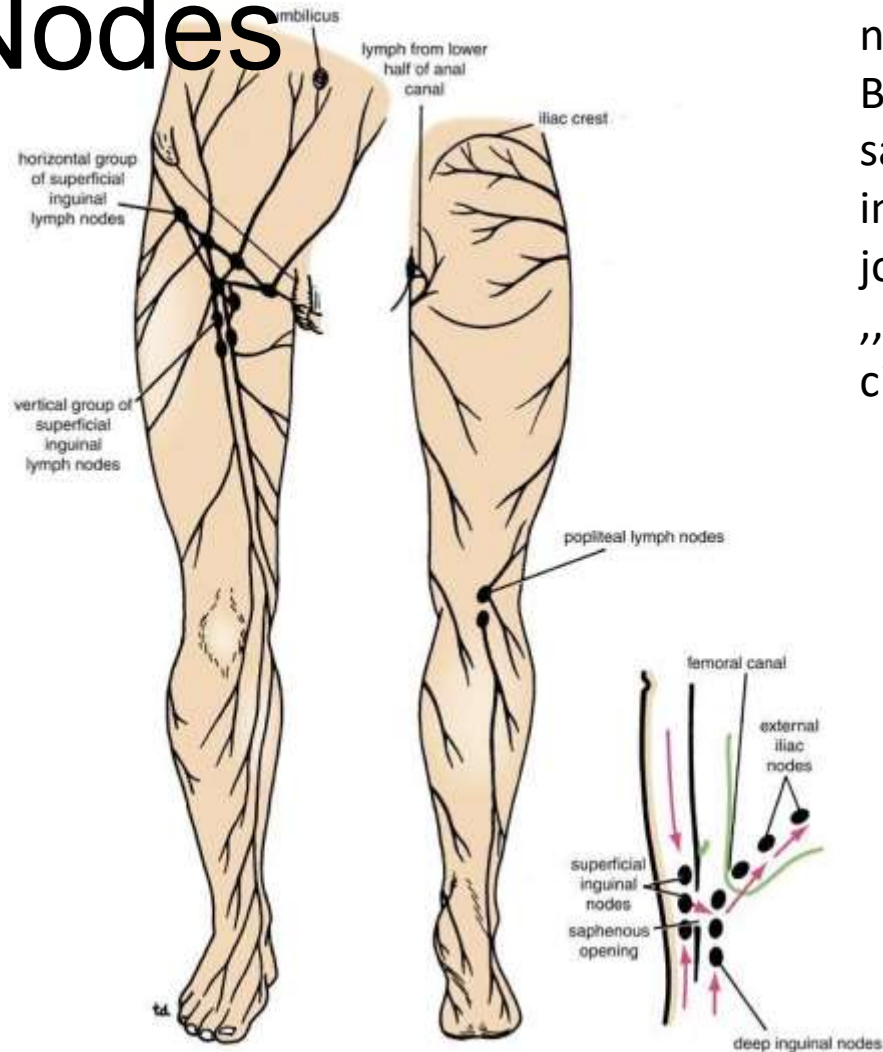
- ✓ Medially→drainage in the internal thoracic lymph node(also called intermamillary lymph node),25% of lymph
- ✓ Lateral→75%

There is connection between right and left side ,so if cancer develop in the right breast it can metastasize to left breast through lymph nodes- لا سمح الله

Enlarged ,tender,soft lymph node→immune response

Hard,no pain زي حبة الحمص →usually cause by metastasis.

Inguinal Lymph Nodes



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**superficial lymph node
Beside Great saphenous vein then inguinal lymph node join with the deep ,,complete the circulation



Thank
You