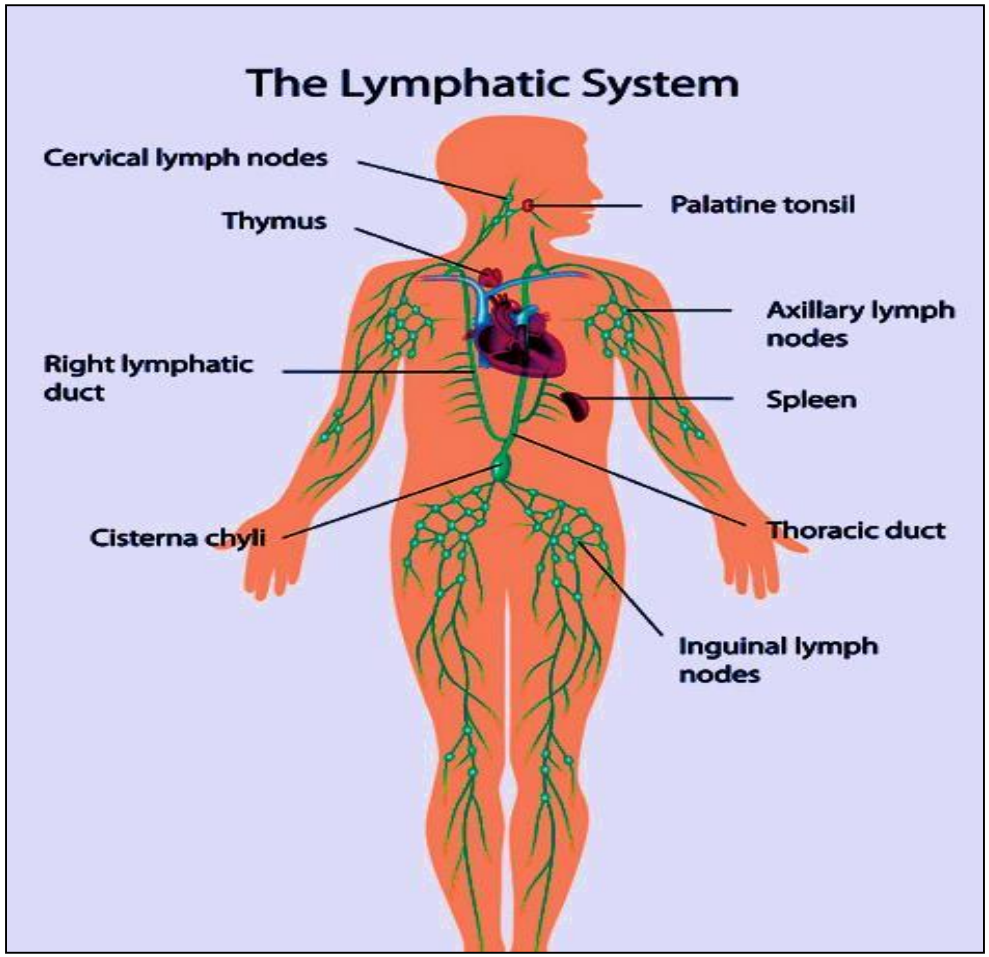
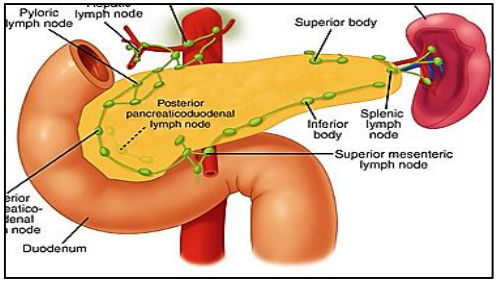
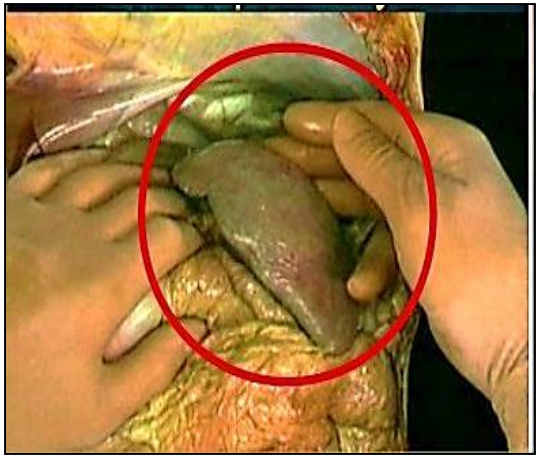
The lymphatic system
(Part II)
Professor Dr. Hala El-mazar





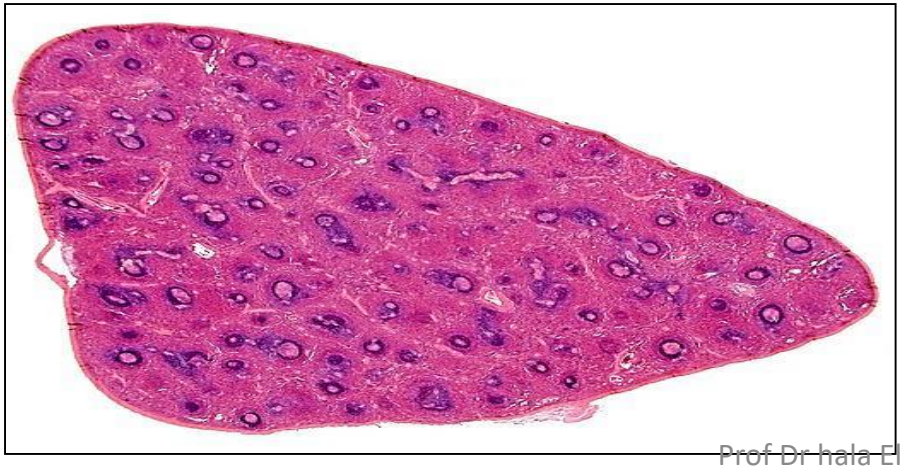
Spleen



- Largest single hemo-lymphatic organ
- Important blood filter. Is the site of destruction of aged RBCs & recycling of iron
- Immunological function through B & T cells (humoral & cell mediate immunity)
- A site of hematopoiesis in the fetus, and stores RBCs & platelets (blood reservoir in animals).

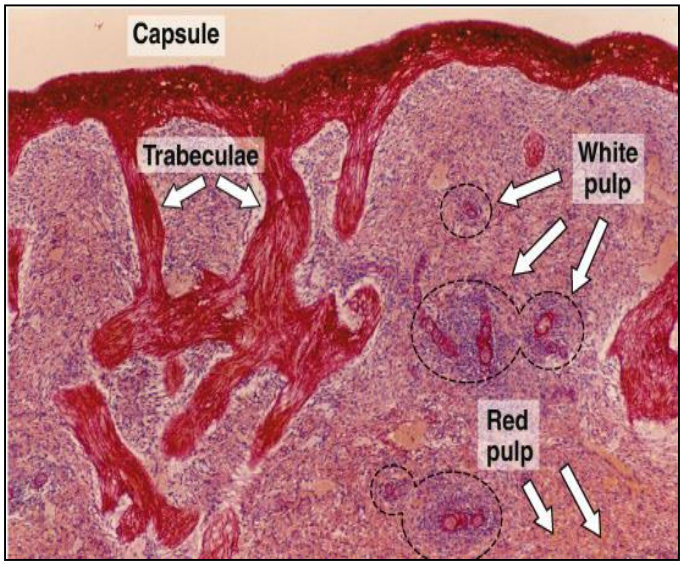
Spleen

- **A- Stroma**
  - Capsule
  - Trabeculae
  - Reticular CT
- **B- Parenchyma**
  - 1- White pulp
    - Lymphatic nodules
  - 2- Red pulp
    - splenic cords
    - Blood sinusoids



Structure of spleen

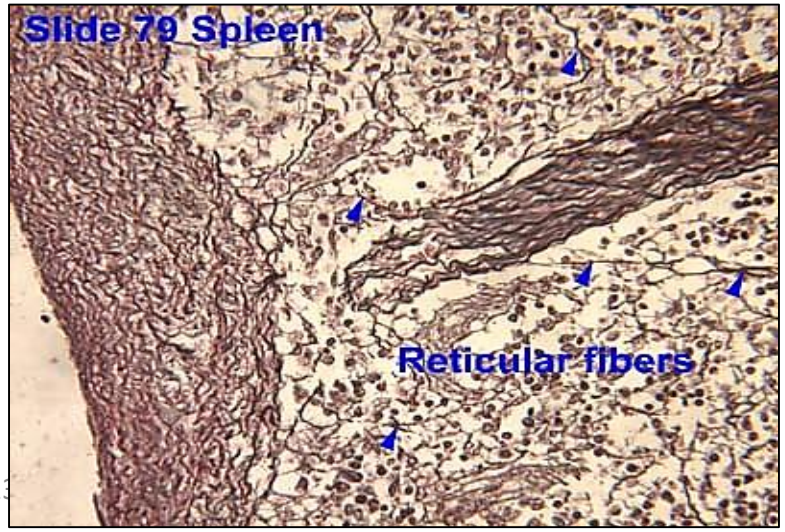
A-Stroma



1-Capsule: thick, rich in collagenous, elastic fibers & **smooth ms cells.**

2-Trabecula: are short ones, extend from capsule.

divide the spleen into incomplete compartment, rich in elastic fibers & smooth ms. cells



3-Reticular CT:

reticular cells and fibers, form background

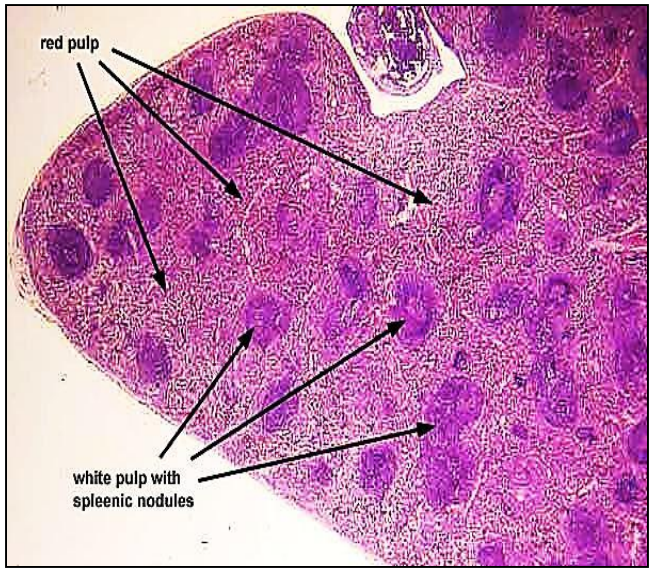
B-parenchyma

White pulp

Lymphoid nodules

PALS

Peri-arteriolar lymphatic sheath



Red pulp

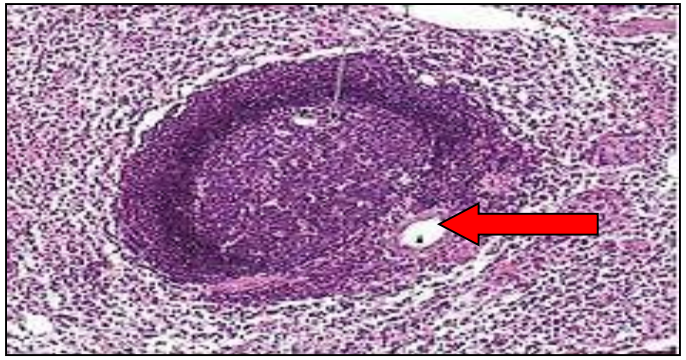
Blood sinusoids

Splenic cords

I- white pulp

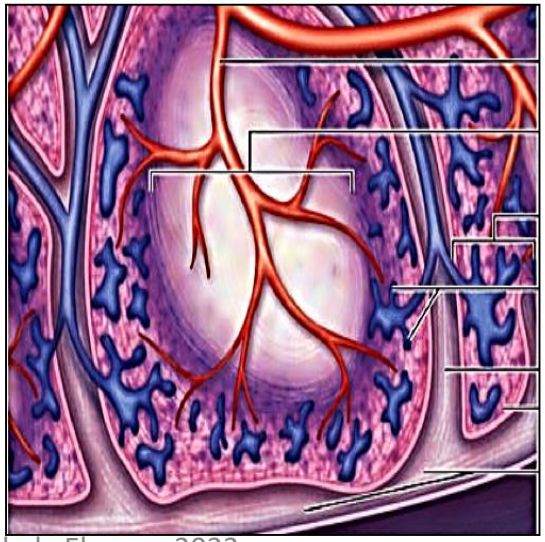
1- lymphatic nodules (splenic Malpighian corpuscles):

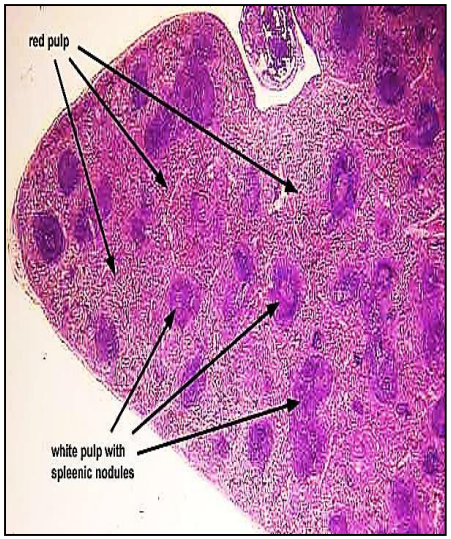
aggregations of lymphocytes forming 1ry or 2ry nodules distributed throughout the parenchyma of the spleen

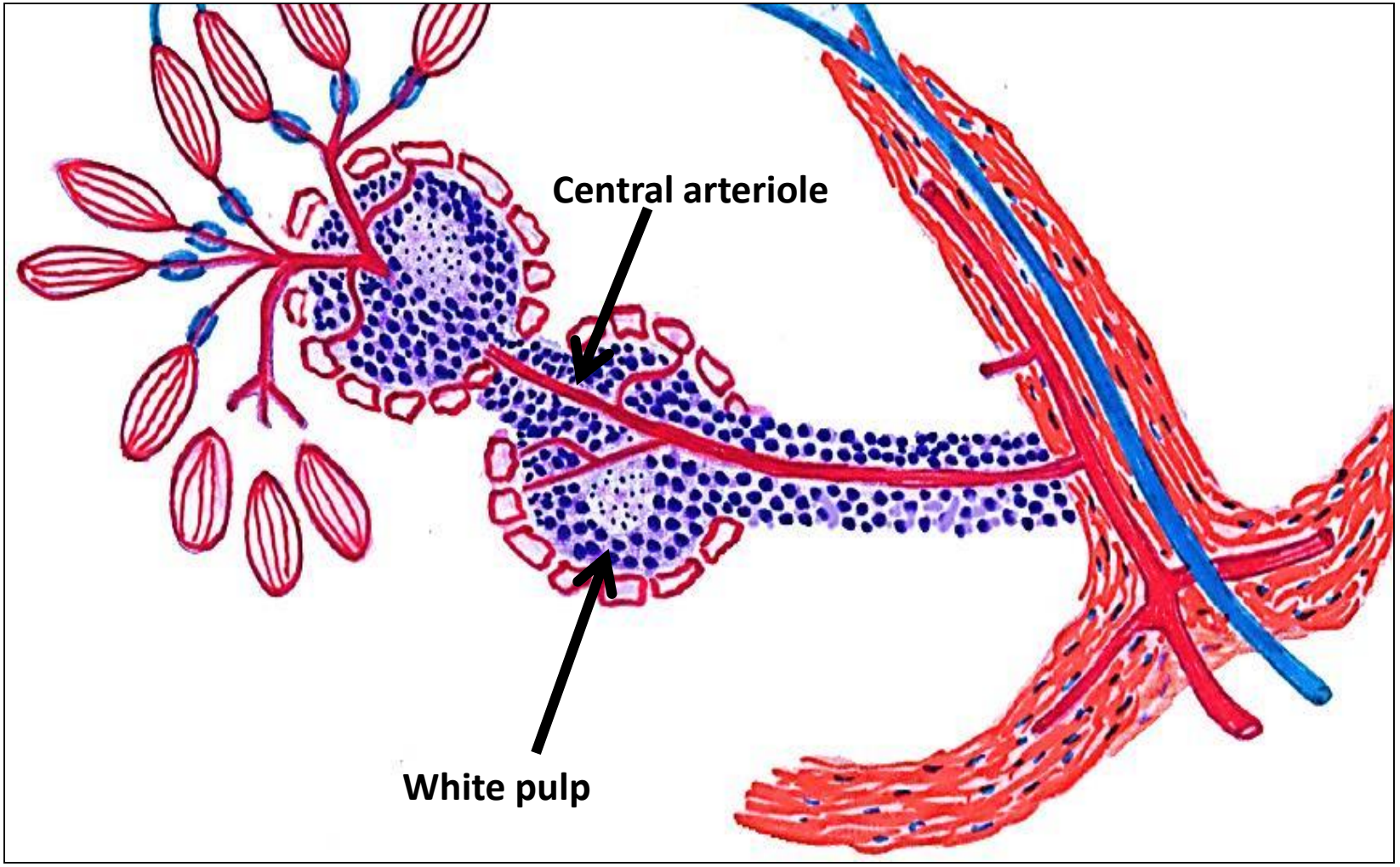


2- Central arterioles (follicular arterioles):

- Run at the **periphery** of the nodules (eccentric). They are branches of splenic artery
- which give numerous branches before leaving the white pulp to enter the red pulp.

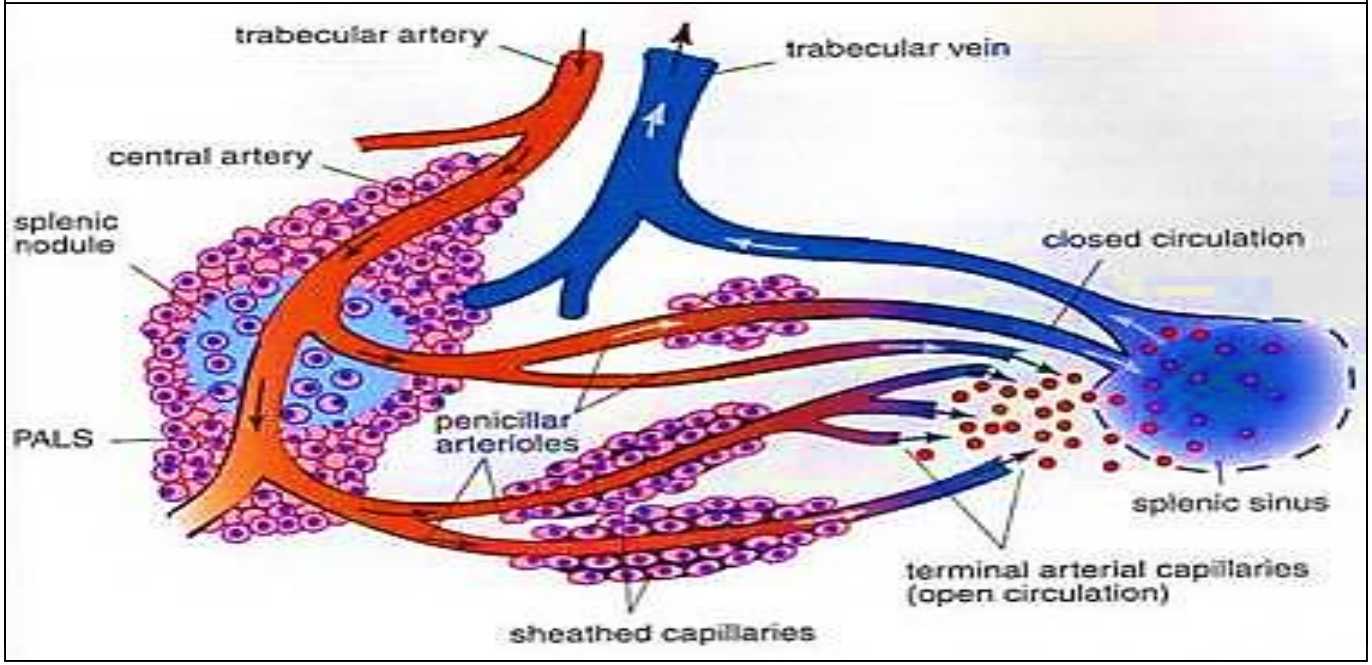






The sketch shows the lay out of the blood supply of the spleen

Open and Closed Circulation in Spleen



Splenic artery → trabecular arteries → central arterioles → penicillinar arterioles enter the red pulp and they terminate as:

- Closed circulation when terminate directly into splenic sinusoids
- Open circulation when terminate in splenic cords

Organization of Cells in white pulp of spleen:

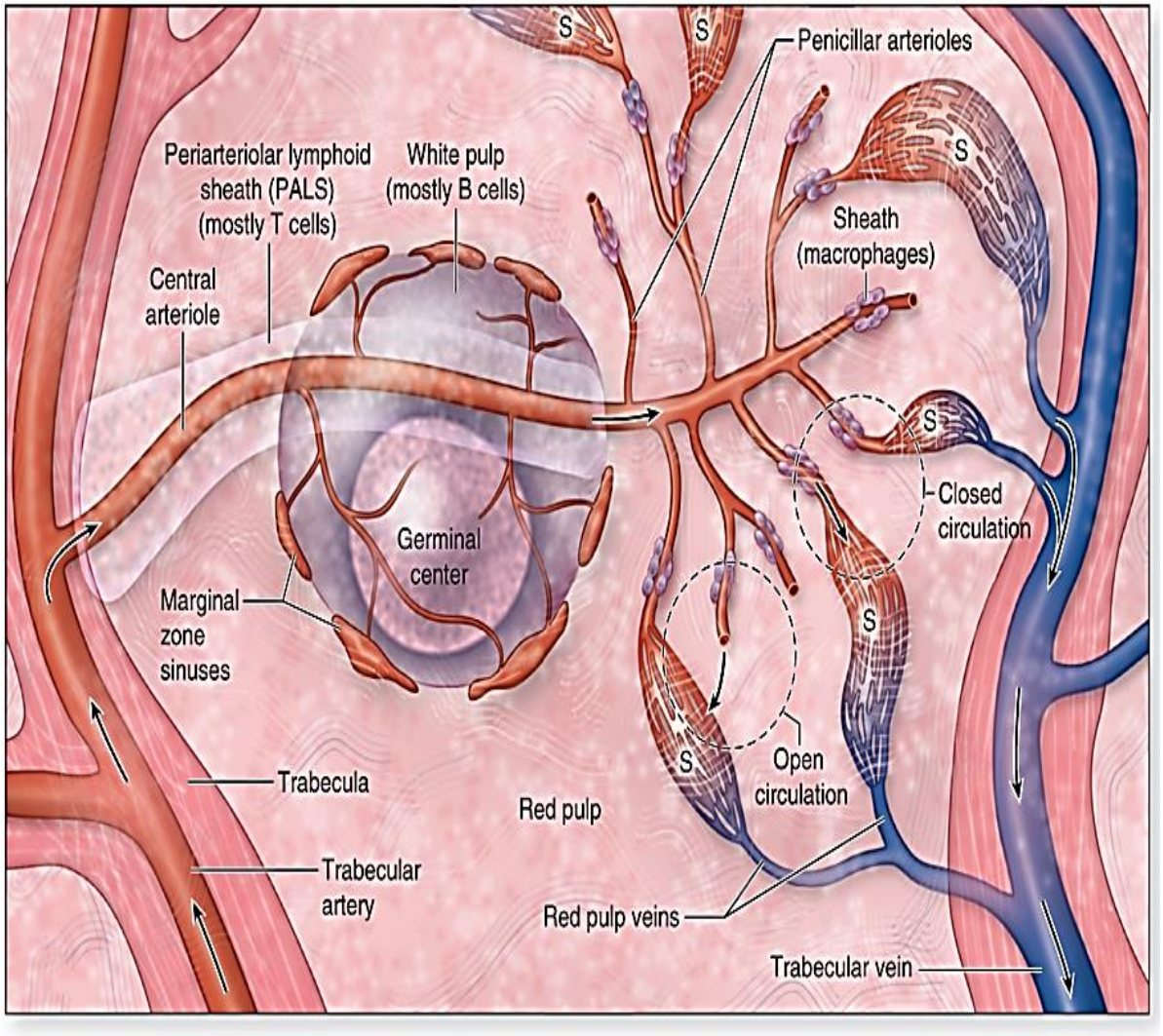
- **Periarteriolar lymphoid sheaths (PALS): mainly T lymphocytes** encircle the central arteriole and called

  (Thymus dependent zone of spleen)

- **Germinal center** : lightly stained, contain activated B cells, plasma cells & macrophages

  (located between PALS and marginal zone)

- **Marginal zone** at the periphery of W. pulp close to red pulp has APCs & macrophages.

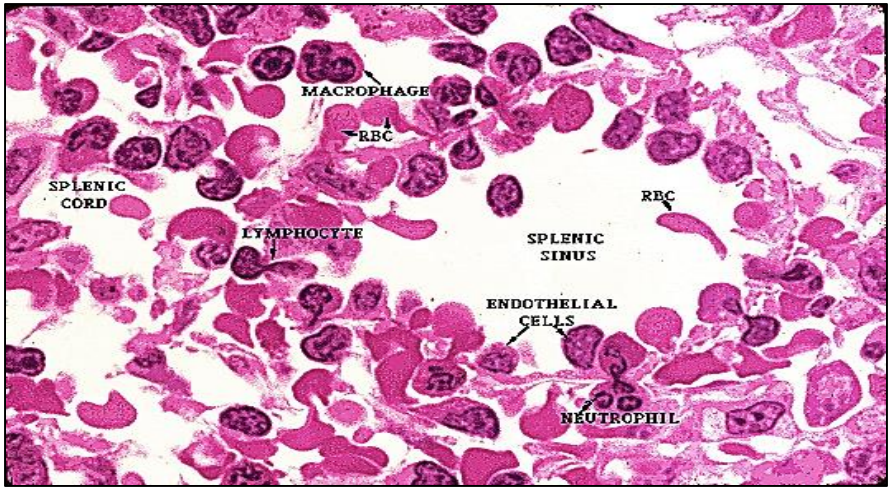


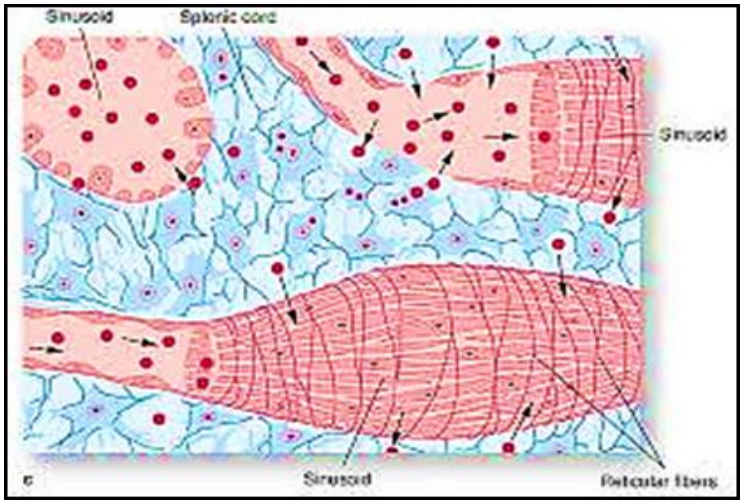
Organization of Cells in white pulp of spleen

II- Red pulp (79%)

1-Splenic cords (Billroth cords):

- Network of reticular fibers between blood sinusoids to support the free cells found e.g. blood cells, T & B lymphocytes , plasma cells , macrophages

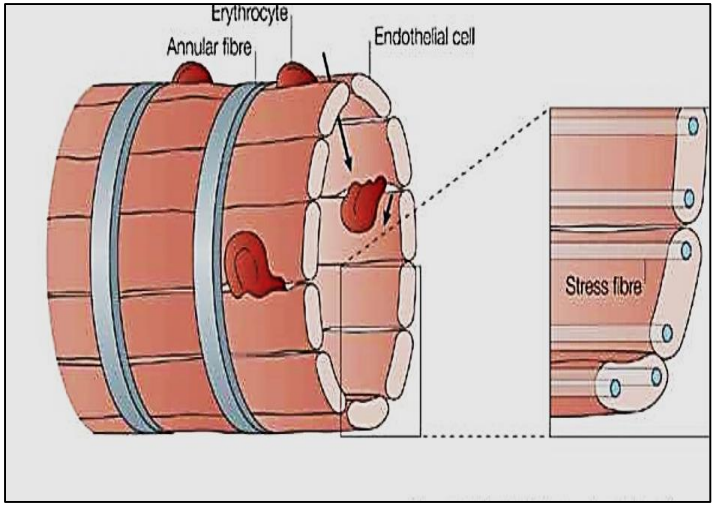


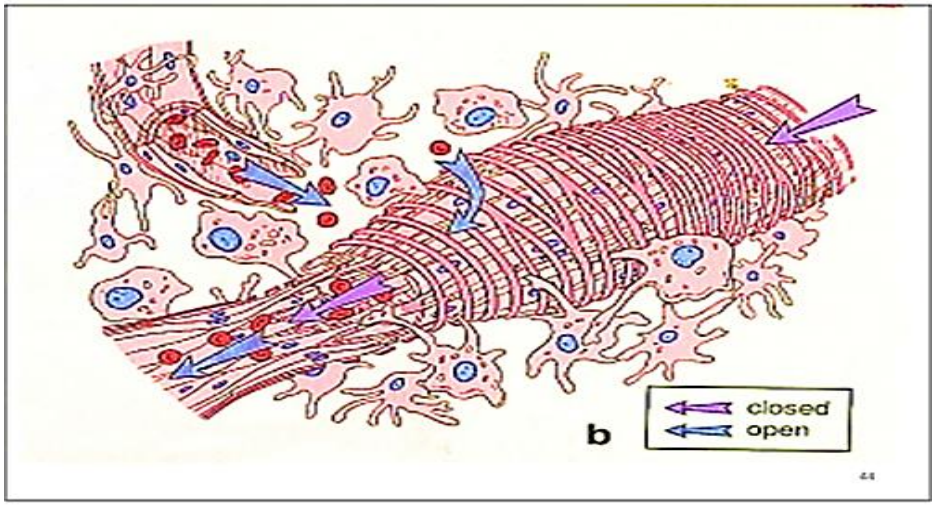


2-Blood sinusoids (venous sinuses):

- wide spaces lined e fenestrated endothelium called **stave cells** which filter the blood & surrounded e *Macrophages called* ***Littoral cells***

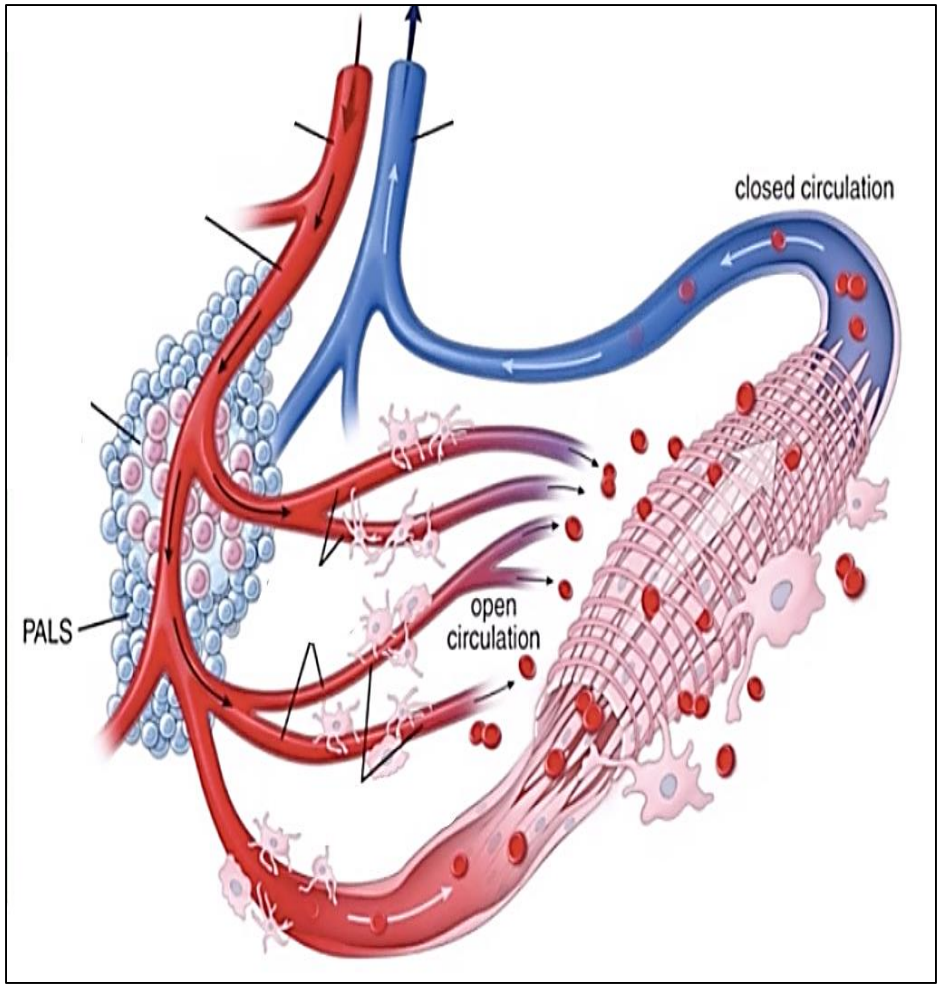
- **Stave cells** , unusual elongated endothelial cells(rod-like) oriented parallel to the sinusoidal blood flow
- These cells have discontinues basement membrane which wrap the cells cross wise

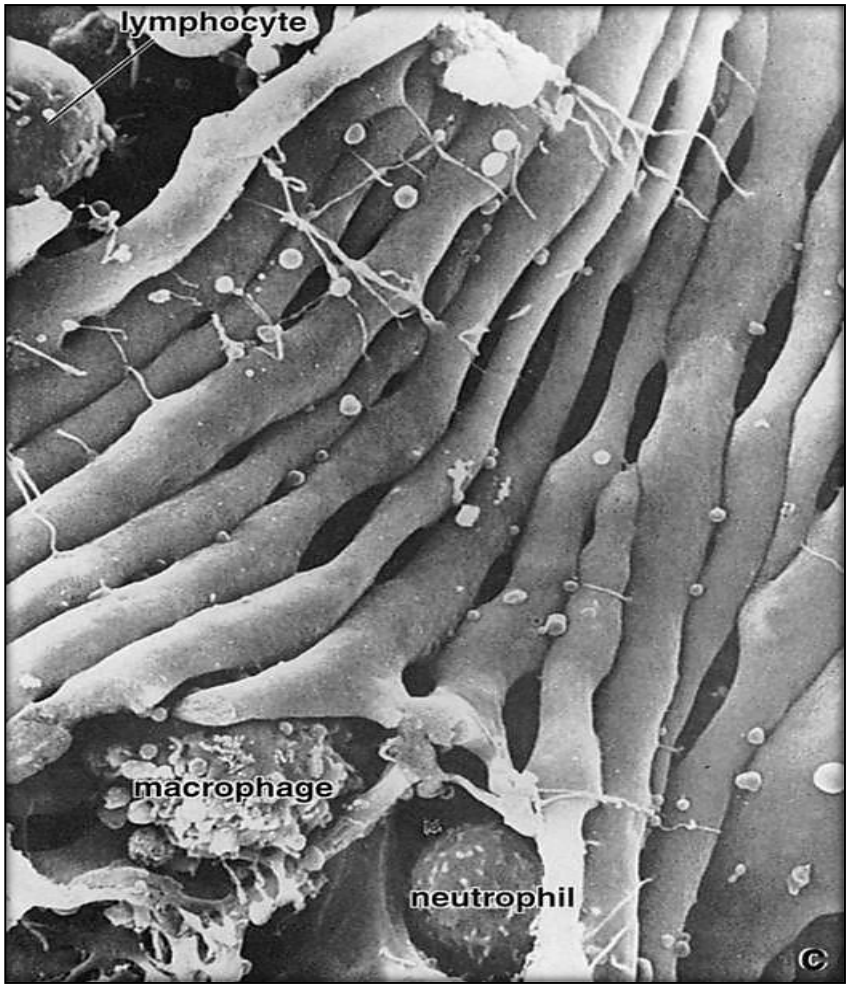




- The gaps between the endothelial cells mechanically filter the blood cells.. Old or abnormal RBCs attempting to squeeze through the endothelial gaps become badly damaged and subsequently removed by macrophages

After about 120 days the erythrocytes undergo membrane changes & swell , signals for their engulfment by macrophages in the cords of the reticular between the venous sinuses





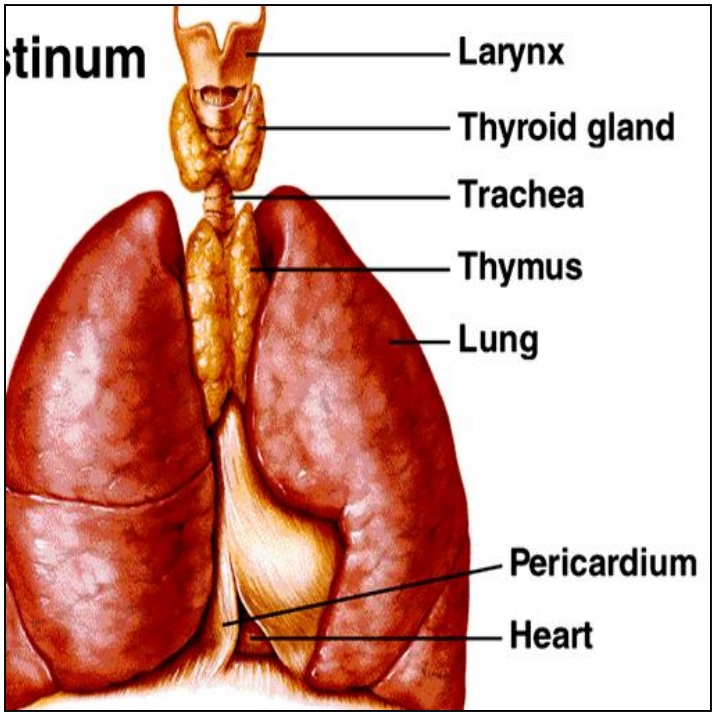
The lining of splenic sinusoids and the EM of Stave cells

Thymus

- is a **1ry** lymphatic organ e an endocrine function

- Location: behind the sternum in the mediastinum

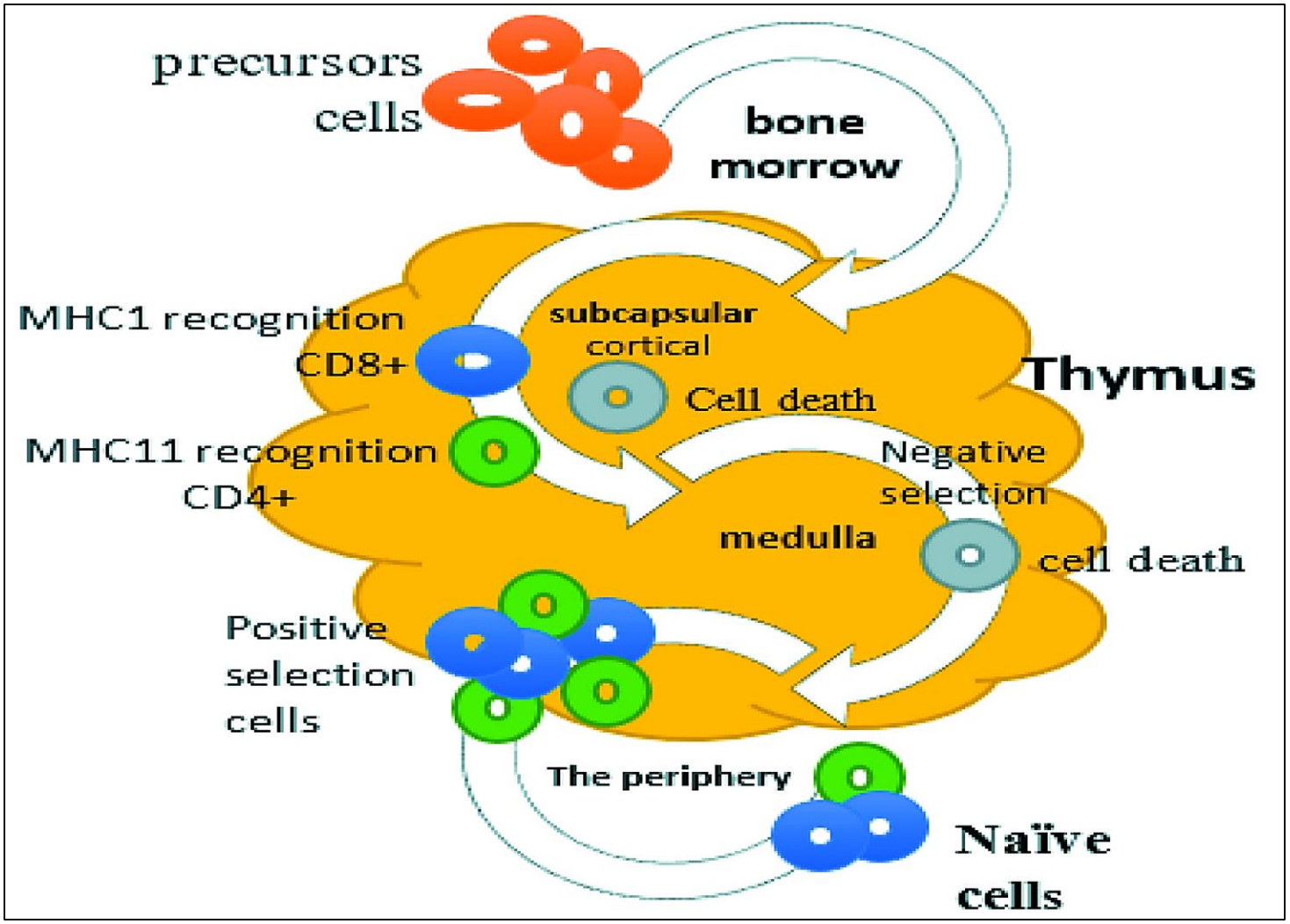
- Single bi-lobed structure, highly lobulated organ



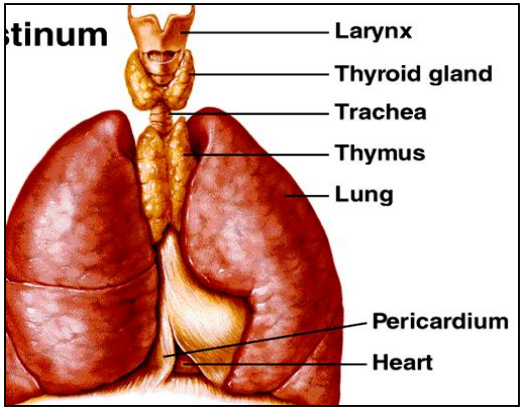
- Development:
  - Infant – ↑ in size
  - Puberty – maximum size
  - Adult – ↓ in size
- **Function**

Differentiation and maturation of T cells

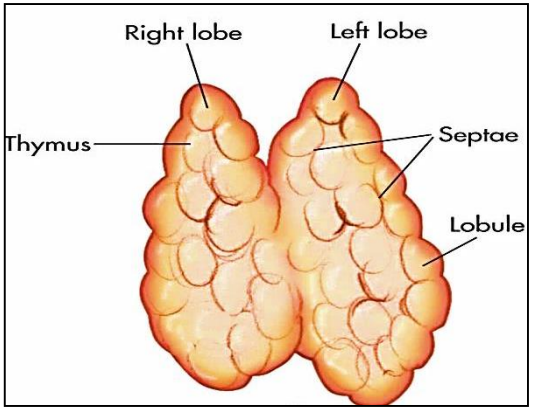
Antigen-independent maturation



Children born without a thymus because of an inability to form a proper third pharyngeal pouch during embryogenesis (DiGeorge Syndrome)



Thymus



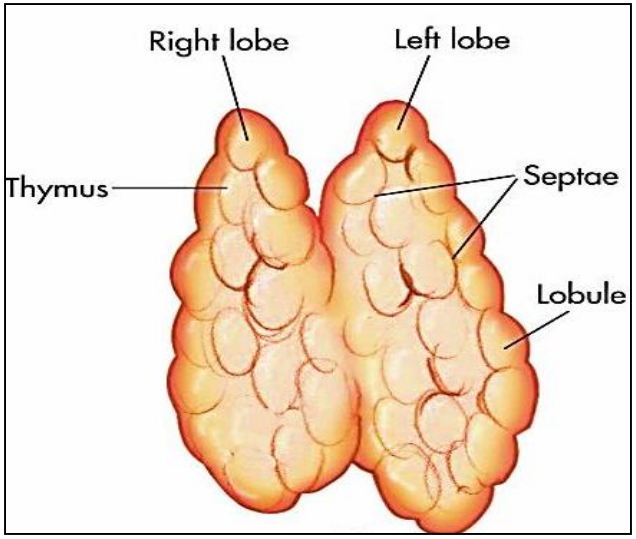
A-Stroma
1-Capsule
2-Trabeculae

B-Parenchyma
1- Lymphocytes
2- Epithelial R cells

1. Cortex

2. Medulla

A- Stroma:

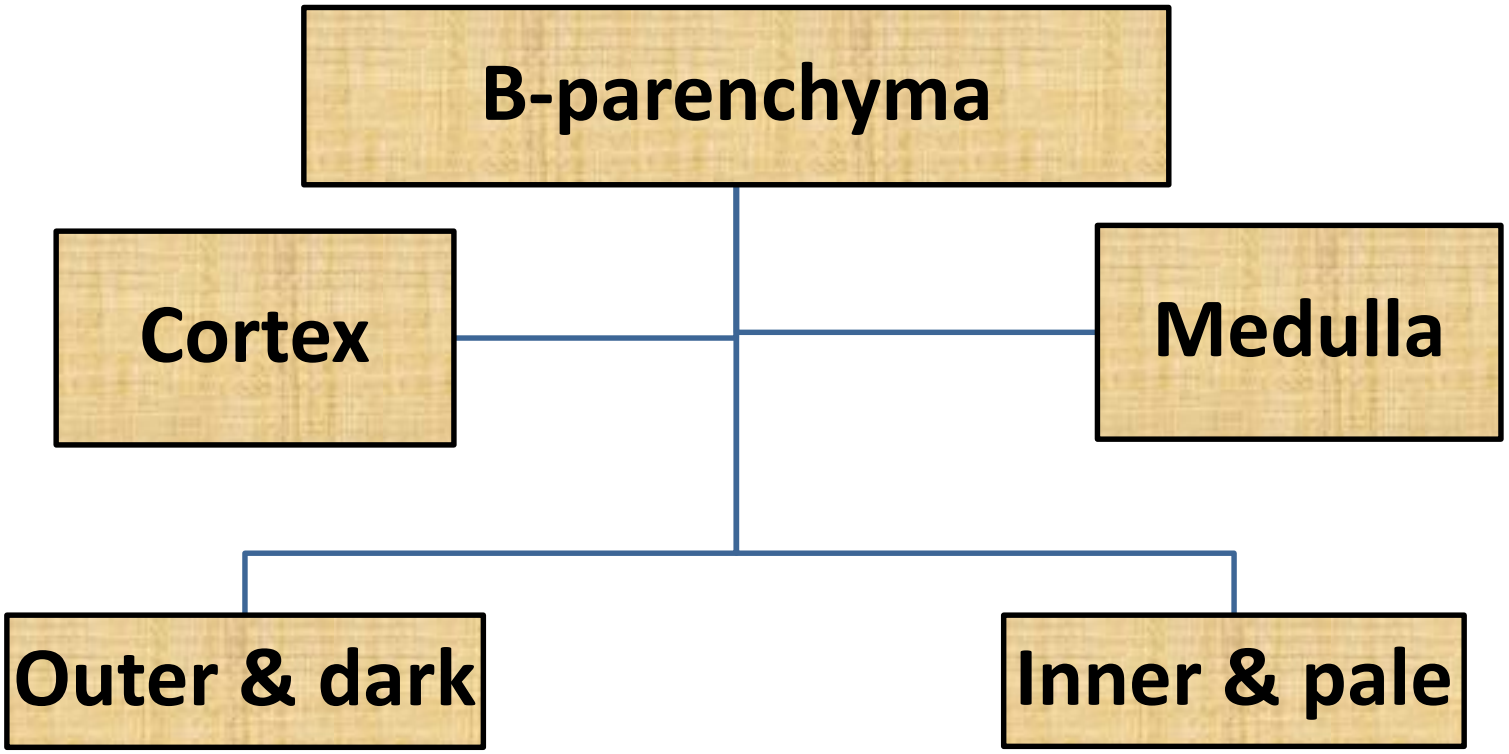


1- Capsule: loose CT

2- Trabeculae (septa):

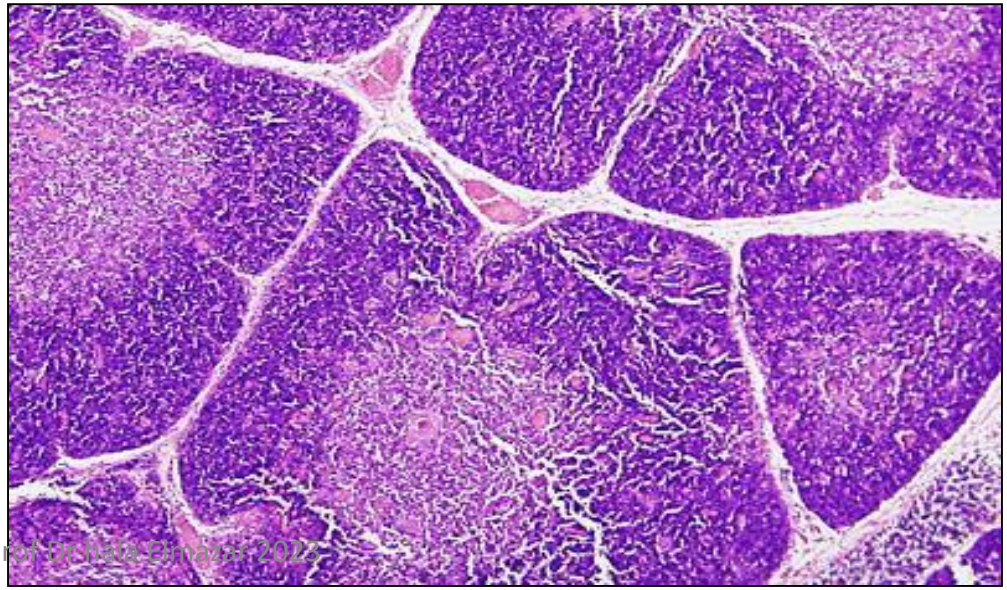
Arise from capsule, penetrate its substance forming lobes, carry blood vessels. Each lobe is divided into incomplete lobules

3- Thymus **has no reticular fibers** . Reticulum is formed by the processes of epithelial reticular cells

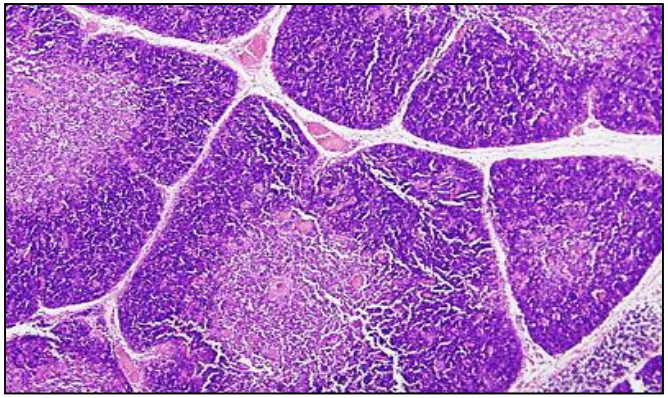


Both contain:

1- T. Lymphocytes.
2- Epithelial reticular cells.
3- Few macrophages.
4- Blood capillaries



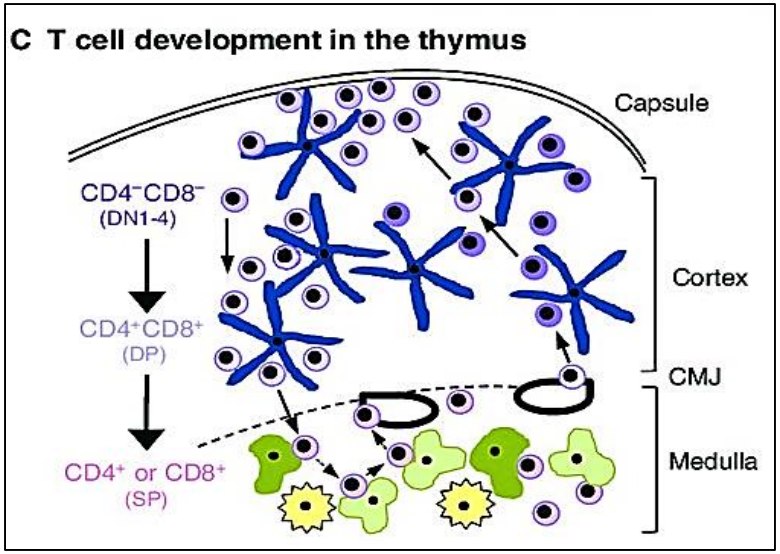
1- Cortex:



- Peripheral dark-stained zone, **where T cell maturation occur**

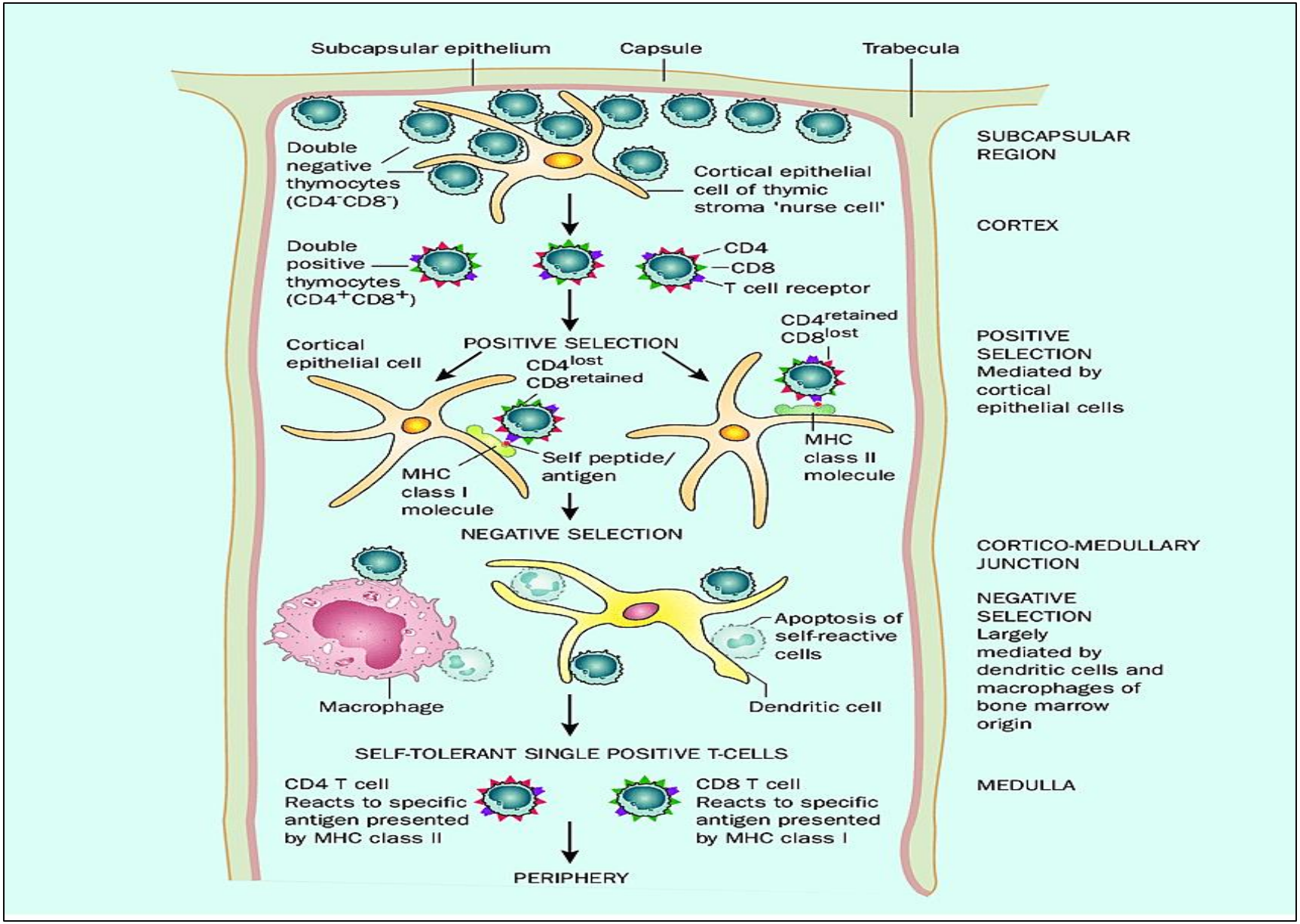
- Cortex contains **thymocytes.**

The hematopoietic precursors which migrated from bone marrow → thymus. Thymocytes is supported by a network of finely branched epithelial reticular cells



- Thymocytes **are completely** surrounded epithelial reticular cells

- The cortex is the site of **earliest events in thymocyte development,** where T cell receptor mature & positive selection take place
- **Mature T lymphocytes** leave the **cortex → the medulla.**



All the steps are controlled by the Thymic hormones

T- lymphocytes:

- Responsible for cell mediated immunity & also assist B lymphocytes in initiating the humoral response (T- helper)
- T- cells are several subtypes:

➢ **Naïve (how they leave the thymus)**

➢ **Effector** (T- helper, T- cytotoxic , T- suppressor (T reg cells) & T- killer cells)

➢ **Memory**

The steps of T- cell development:

- The Stem cells from bone marrow travel to the thymus to reside in the **outer part of cortex,** once there they are called **thymocytes**

- These thymocytes have neither CD4 nor CD8 surface markers (double –ve T cells)

- Within outer cortex the thymocytes will proliferate & undergo genetic arrangement & express 2 cell markers:

✓ **TCR (T cell receptor)**

✓ **Cluster differentiation**: $CD4^+$ & $CD8^+$ (double positive T cells)

- Double positive T cells that don't recognize **self –MHC epitope** offered to them by cortical ER cells are forced into apoptosis

- (MHC: is a large section on vertebrates DNA contains all genes that code for cell surface proteins)

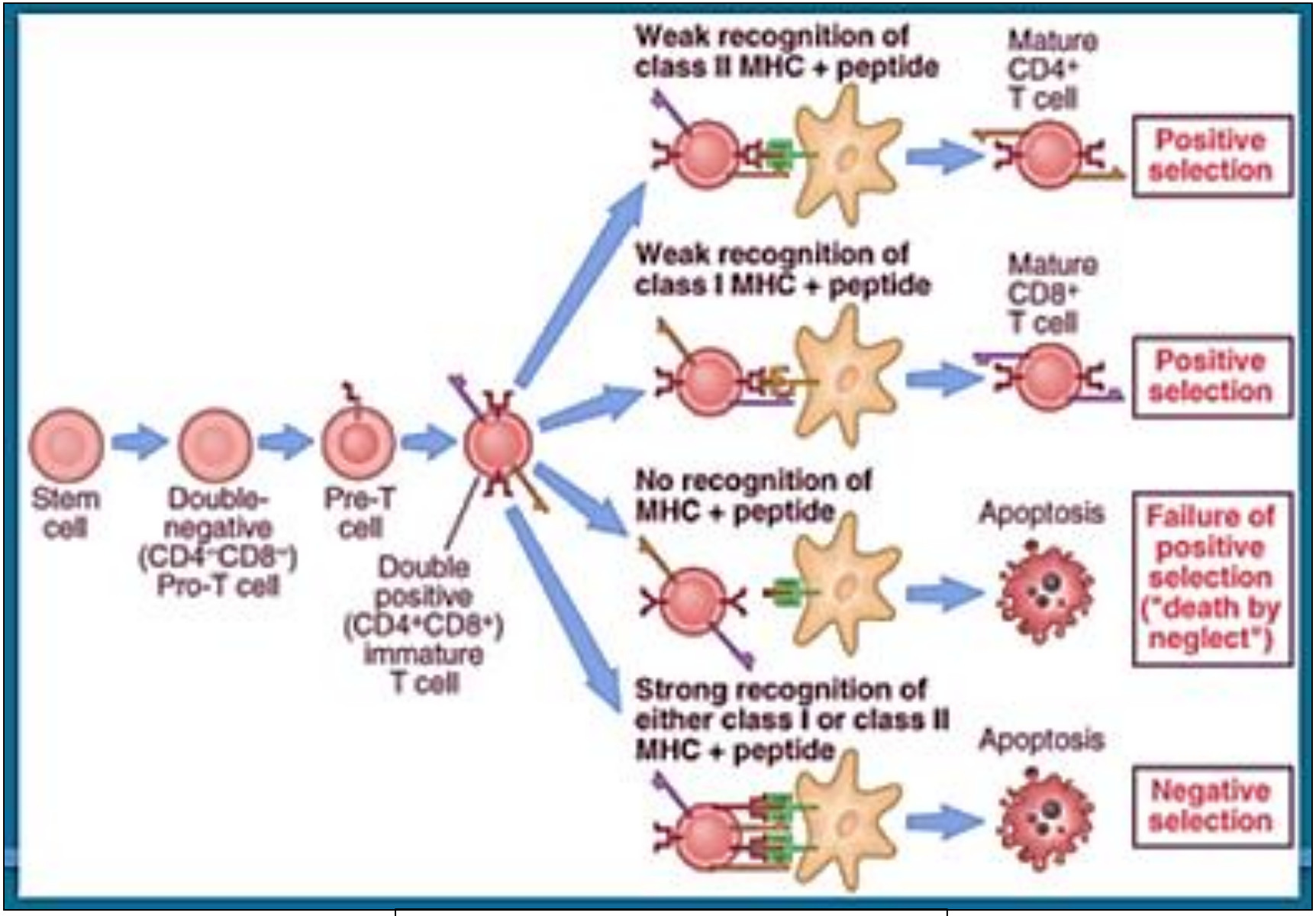
- Still in cortex: double +ve cells that in contact e ER cells that carry MHC I will stop expressing $CD4^+$ marker & become single +ve T cells that express only $CD8^+$ maker

- Double +ve T cells in contact with ER cells carry MHC-II will stop expressing $CD8^+$ marker & become single +ve T cells that express only $CD4^+$ marker

- The previous process is called **positive selection** and takes place in the **thymus cortex**

- By doing that the T cells acquired the **Thymic education** which was done under the influence of thymic hormones secreted by epithelia R cells

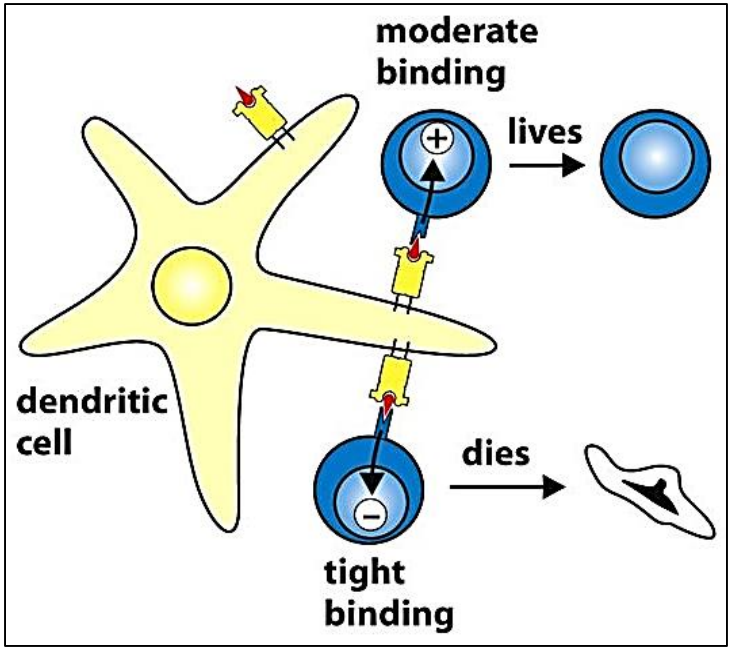
- Only **1- 3% of Double +ve T cells will** survive the **selection process and will** be allowed to enter the medulla where The final step in maturation of T cells occurs



Positive selection process

- The medullary dendritic cells will do another test & present self-epitopes of MHC-I or MHC-II to the $CD^{+}8$ & $CD^{+}4$ cells & those whose binds **strongly are forced to apoptosis**
- **It has to be weak reaction** to the MHC - epitopes complex to prevent autoimmune response. This called **negative selection** and takes place in the **Thymic medulla**

- T cells re-enter blood stream & travel to 2ry lymphatic organs (LN & spleen) where they settle in **thymus dependent zones**



- Epithelial Reticular cells secrete thymic hormones that stimulate:

➢ T cell differentiation

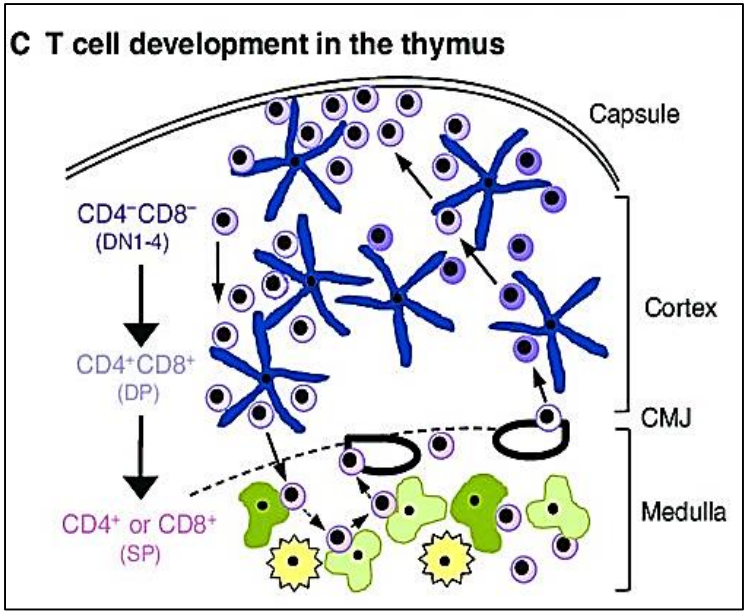
➢ Expression of surface markers

- CD4+ cells called helper T cells: indirectly can kill cells indicated as foreign.
- CD8+ cells called cytotoxic T cells are able directly to kill virus infected & tumor cells

- MHC I molecule is expressed on all nucleated cells *Except RBCs*
- MHC II molecule is expressed on antigen presenting cells: macrophages , dendritic cells…etc

Epithelial reticular cells (ERCs) :

- Branched, acidophilic cells e oval nuclei, their long processes contain tonofilaments (Keratin filaments)
- Also called thymic **nurse cells**
- They are connected together by desmosomes
- Do not produce reticular fibers.



- Found in both cortex & medulla (Cortical ERCs & medullary ERCs)
- Contain secretory granules which contain the thymic hormones

Functions of ERCs:

1- nursing cells for T cells during their differentiation

2- Secrete the thymic hormones

- Thymulin
- Thymopoietin
- Thymosins
- Thymic humoral factor

3- Share in the blood-thymus barrier

4- Antigen presenting cells for developing T lymphocytes

5- in medulla form Hassall's corpuscles

Blood- thymus barrier

Barrier exists in the **cortex only** to separate the developing T-lymphocytes from antigens in blood

The barrier is formed by:

1- Continuous capillary endothelium

2- Pericytes

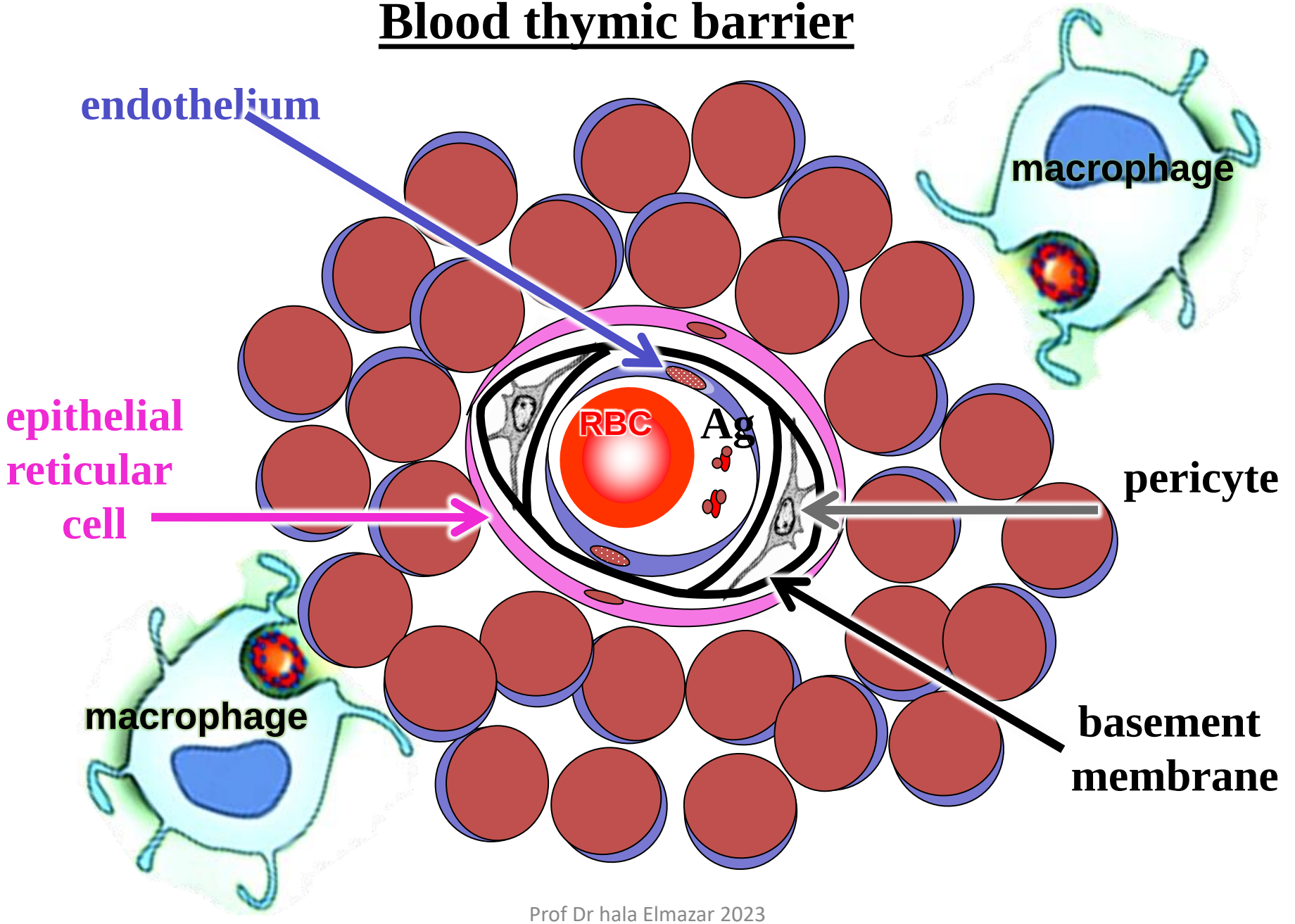
3- Continuous basal lamina around endothelium

4- Perivascular space contains macrophages to deal e any antigen escape

5- Complete layer of epithelial reticular cells around capillaries

The barrier allow immature T lymphocytes to multiply & differentiate free from foreign Ags before they migrate to medulla & leave thymus to blood

Blood thymic barrier



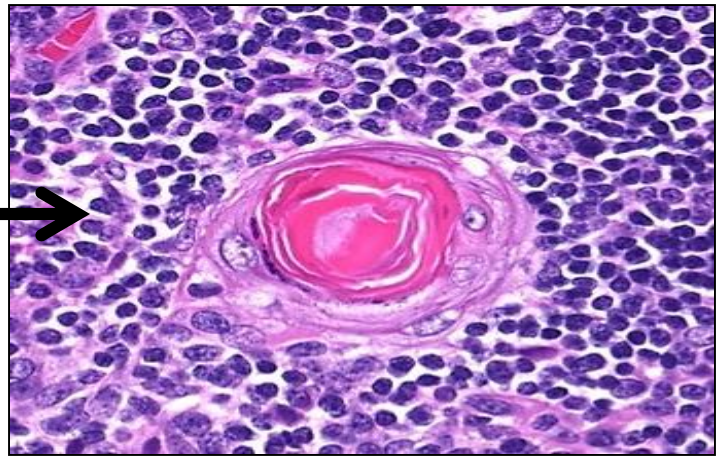
2-Medulla:

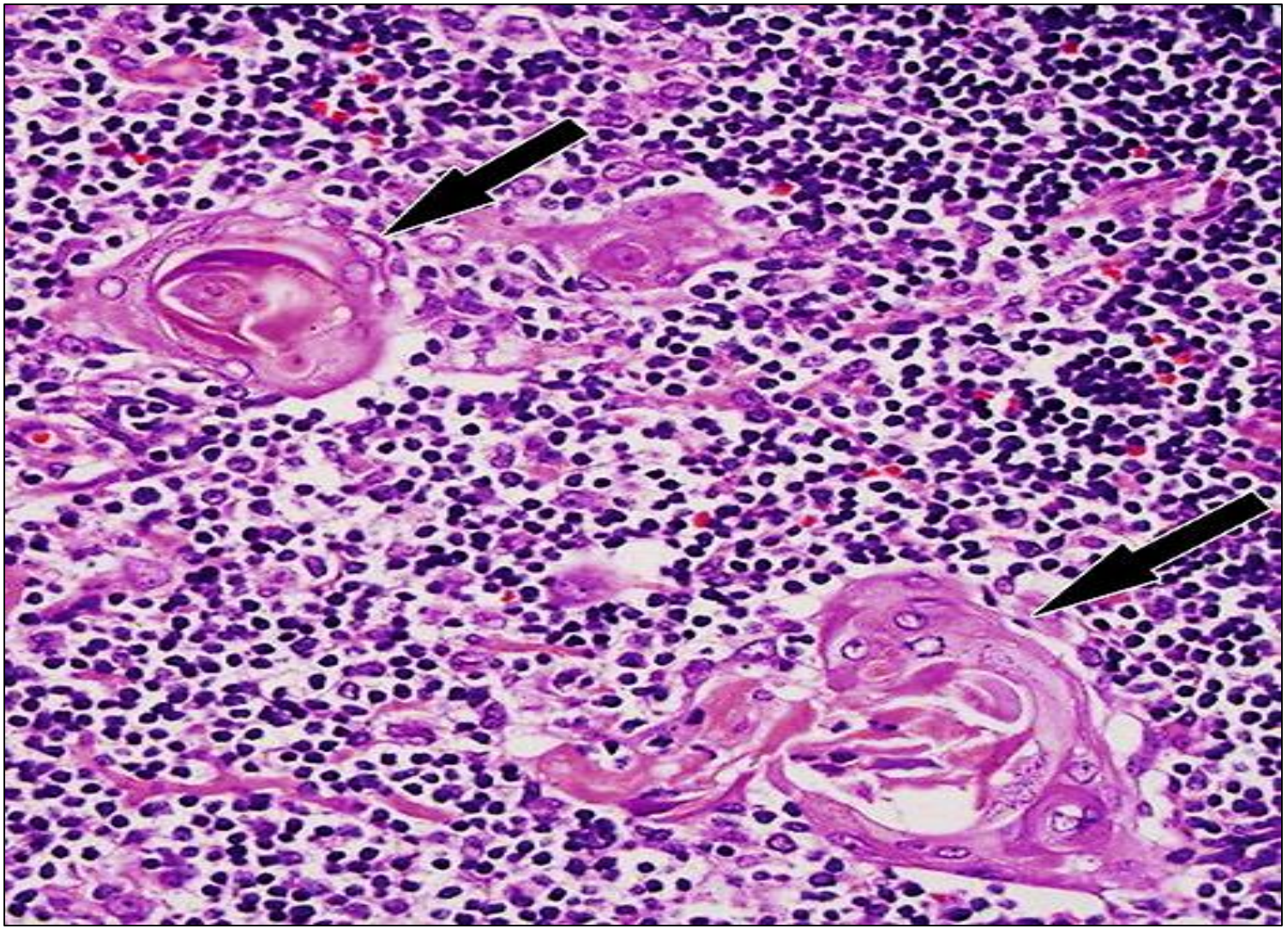
Contains fully differentiated T lymphocytes, which leave medulla through post capillary venules.

T cells will travel to 2ry lymphatic organs (LN & spleen) where they settle in thymus dependent zones

Contains **Hassall's corpuscles** are acidophilic strucureless mass surrounded by concentric layers of epithelial reticular cells responsible for the release of cytokines that regulate dendritic activity.

Hassall's corpuscle





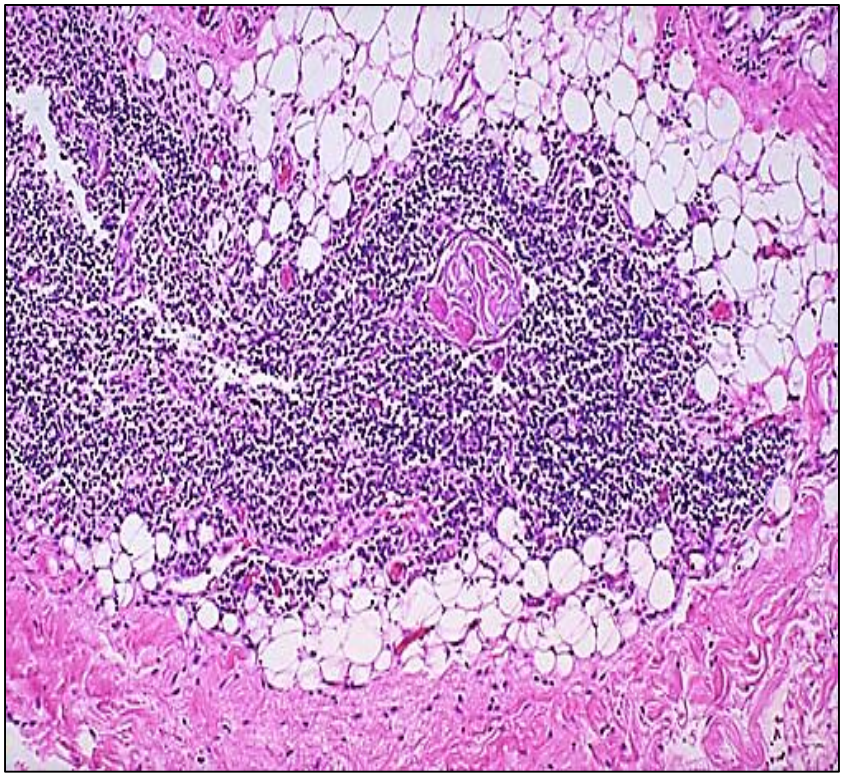
Thymus gland showing Hassall's corpuscles

Hassall’s corpuscles provide developing thymocytes with paracrine and juxtacrine signals to ensure their proper functional maturation

Thymus gland of adult

Formed by:

* Fibrous & adipose tissue.
* Few lymphocytes, ↓ ER cells.
* ↑ Hassall's corpuscles



MALT- mucosa associated lymphoid tissue

- Collective name for the cells of the immune system in the mucosa of respiratory , alimentary , urogenital tracts

- Function : is to augment the mechanical & chemical barriers of surface mucosal epithelium

- Distribution :

✓ Tonsil

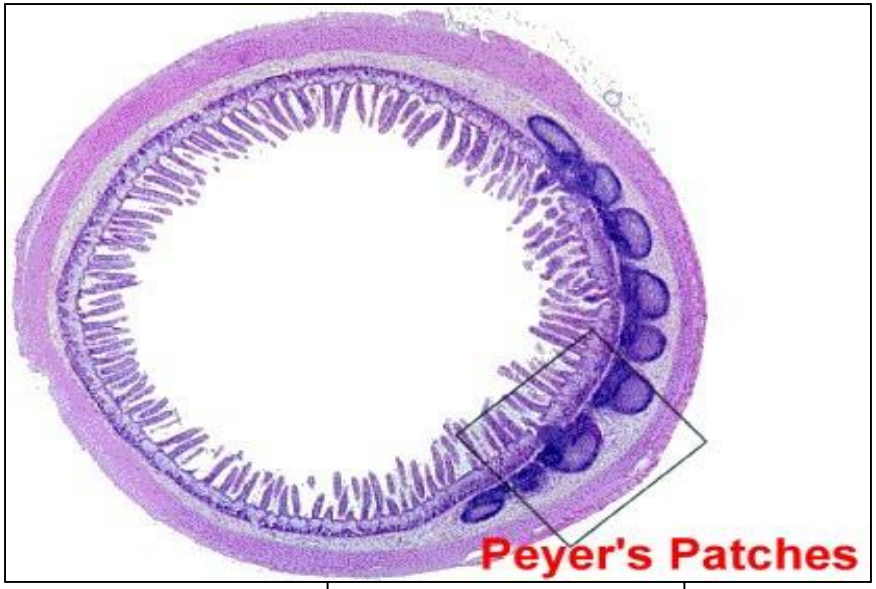
✓ Bronchus : BALT

✓ Gut: GALT

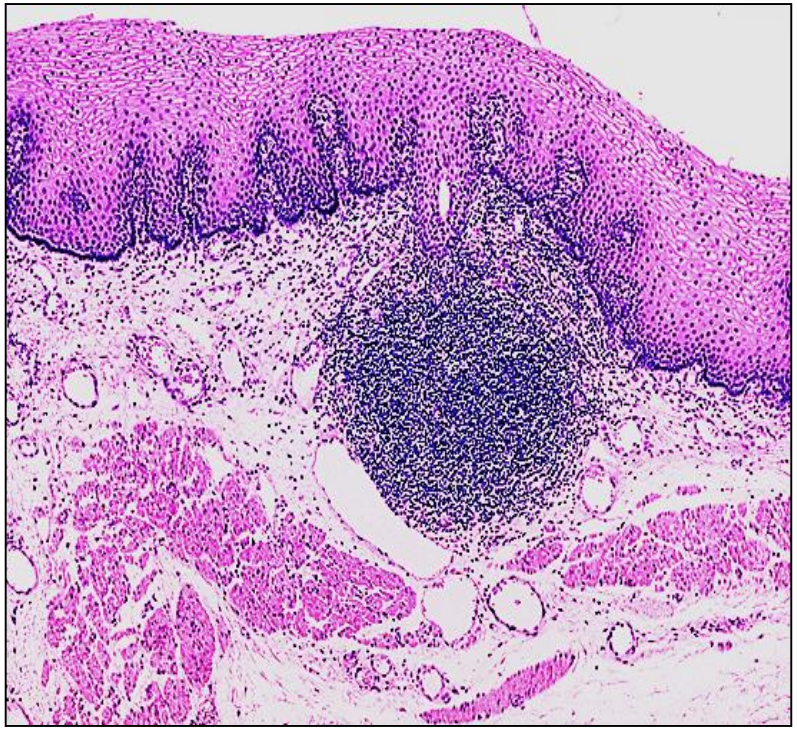
MALT Examples are:

1 .Payer's patches of ileum .

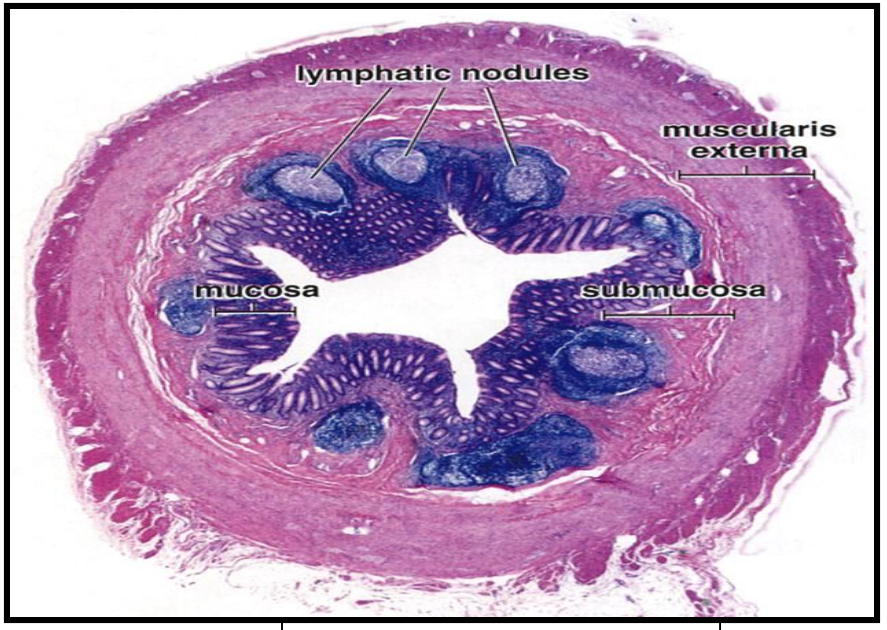
2. MALT of appendix.



MALT in ileum



MALT in wall of esophagus



MALT in appendix

Thank you