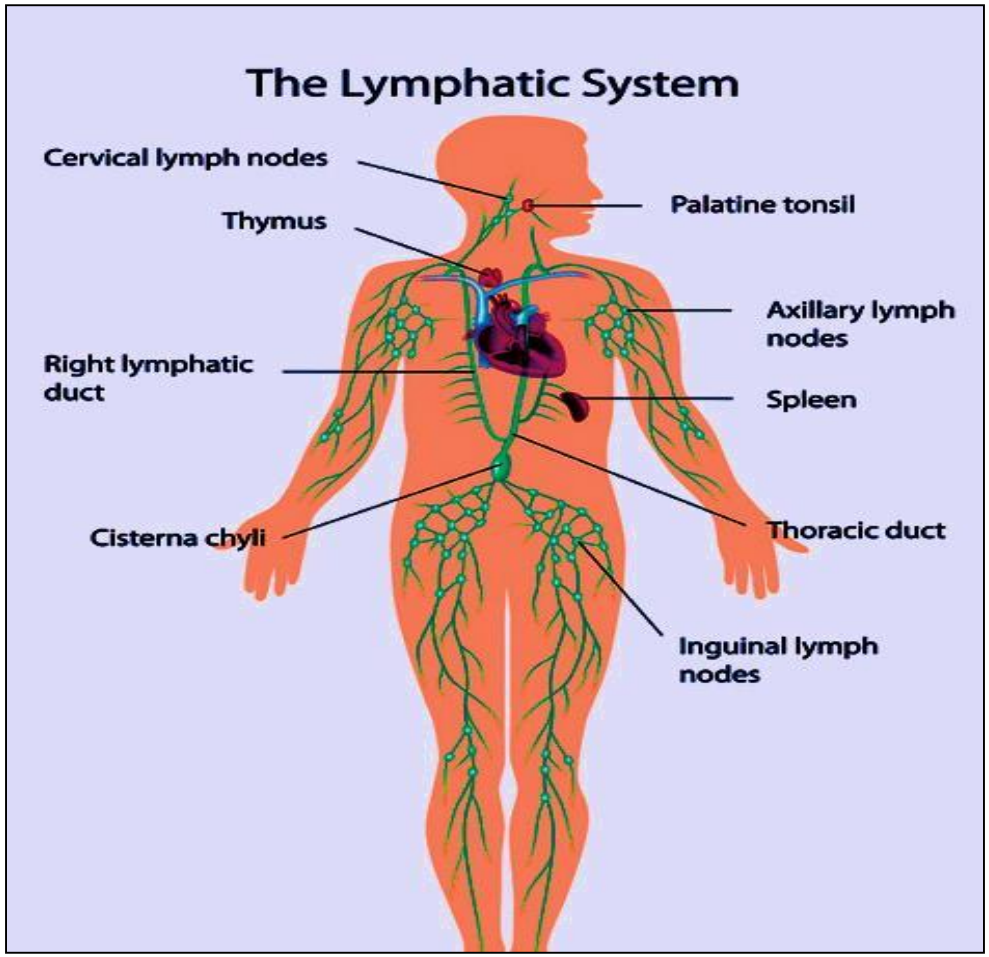
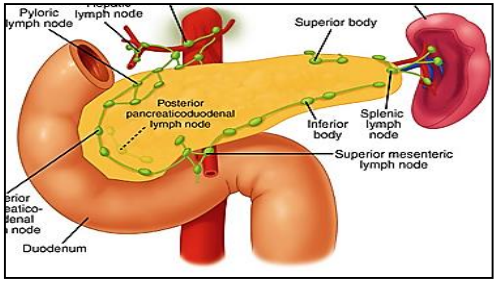
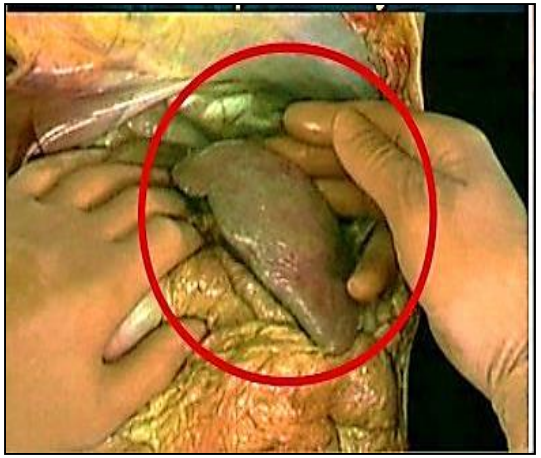
# The lymphatic system
# (Part II)
# Professor Dr. Hala El-mazar





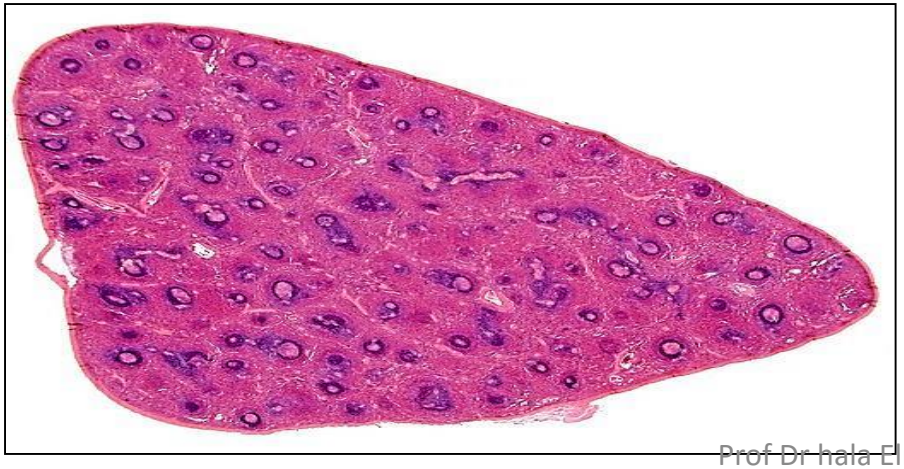

# Spleen



- Largest single hemo-lymphatic organ
- Important blood filter. 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 ).

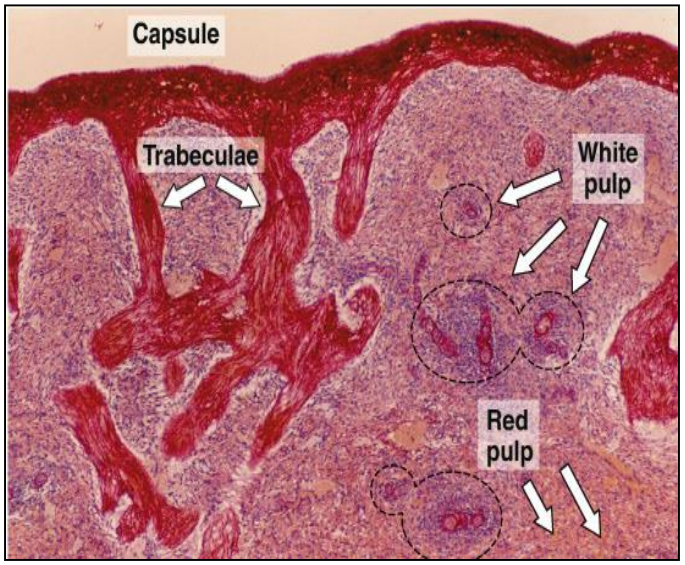
# Spleen

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



# Structure of spleen

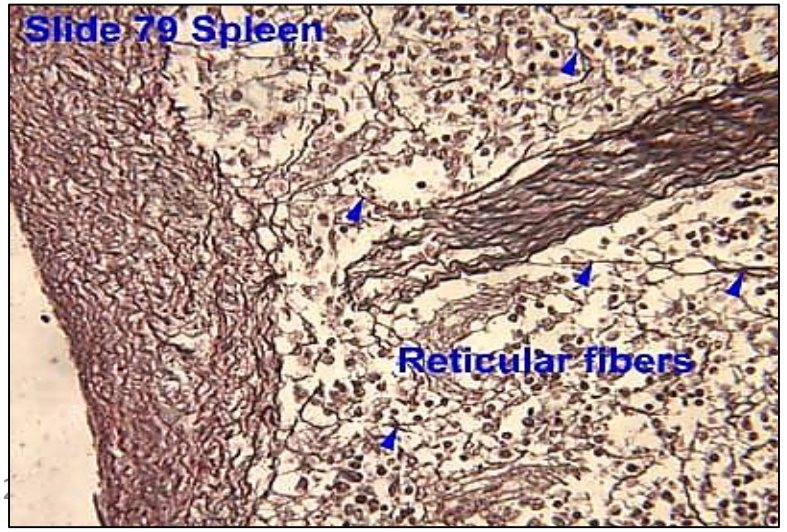
## A-Stroma




**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

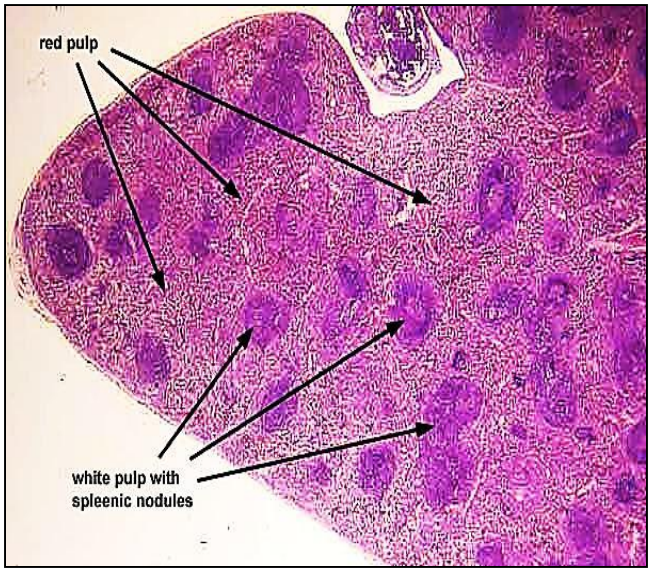
# B-parenchyma

## White pulp

### Lymphoid nodules

#### PALS

Peri-arteriolar lymphatic sheath




## Red pulp

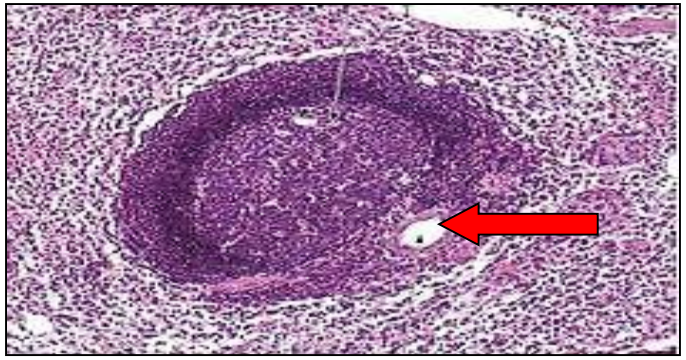
### Blood sinusoids

#### Splenic cords

# I- white pulp

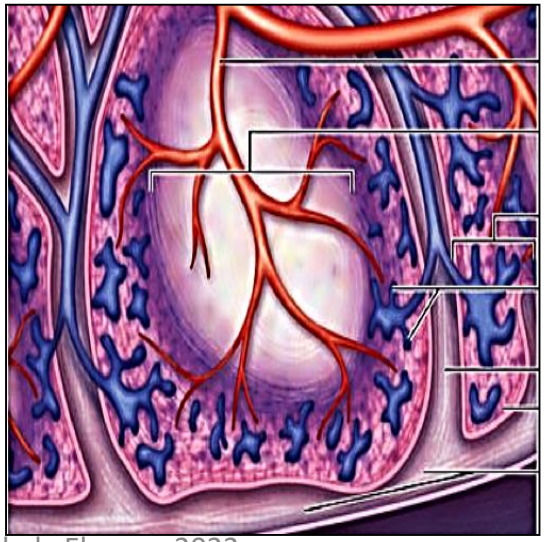
## 1- lymphatic nodules (splenic Malpighian corpuscles):

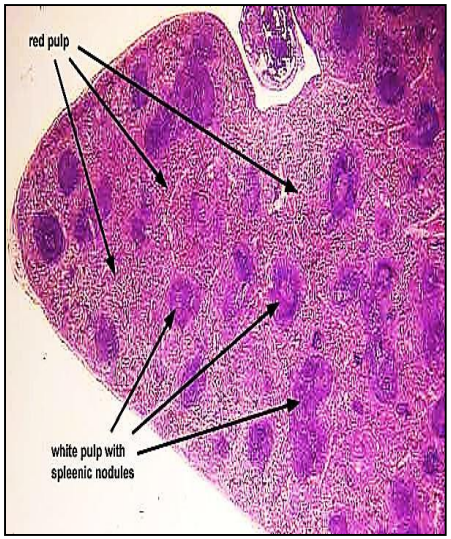
aggregations of lymphocytes forming 1ry or 2ry nodules distributed throughout the parenchyma of the spleen

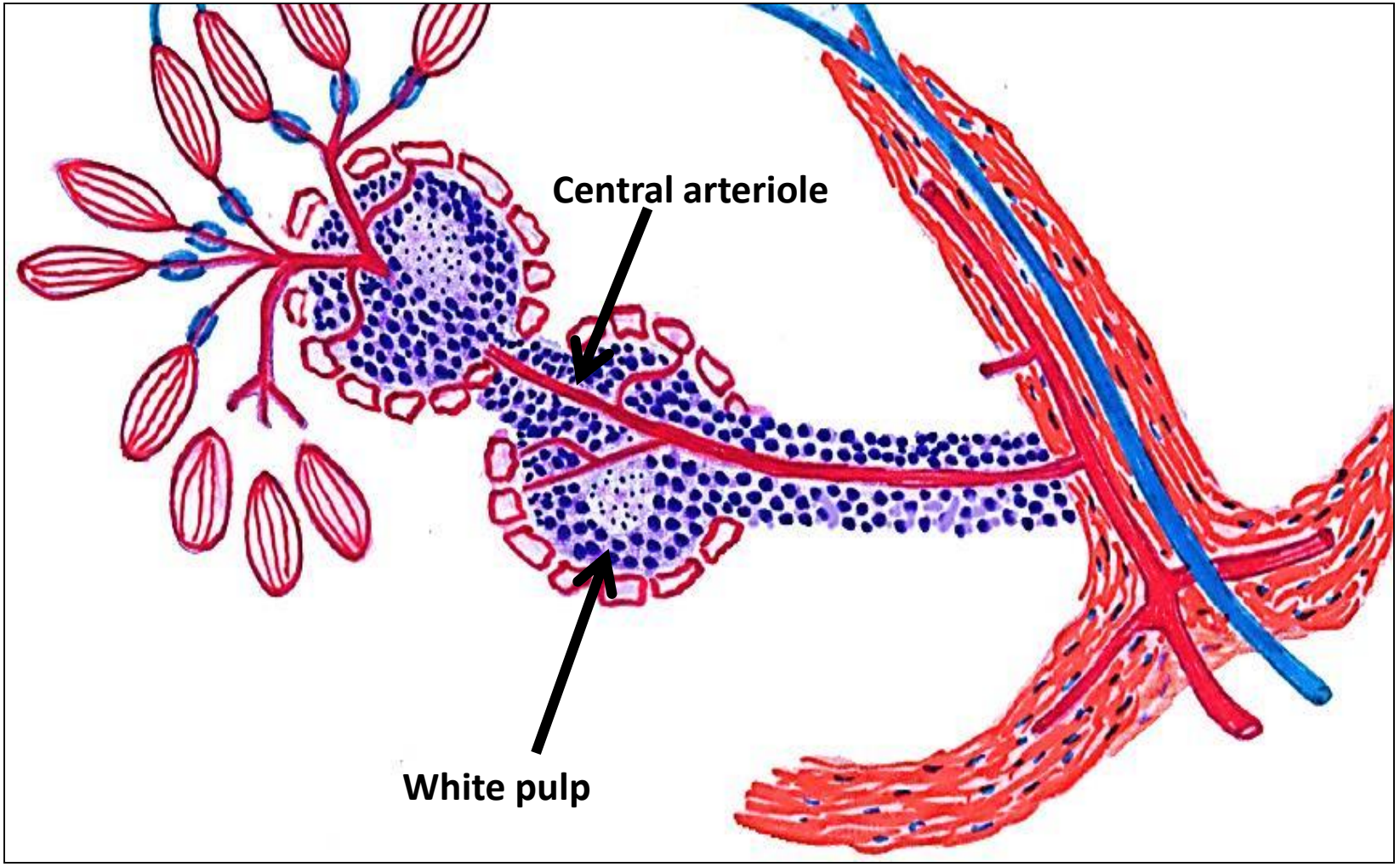


## 2- Central arterioles ( follicular arterioles):

- 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.

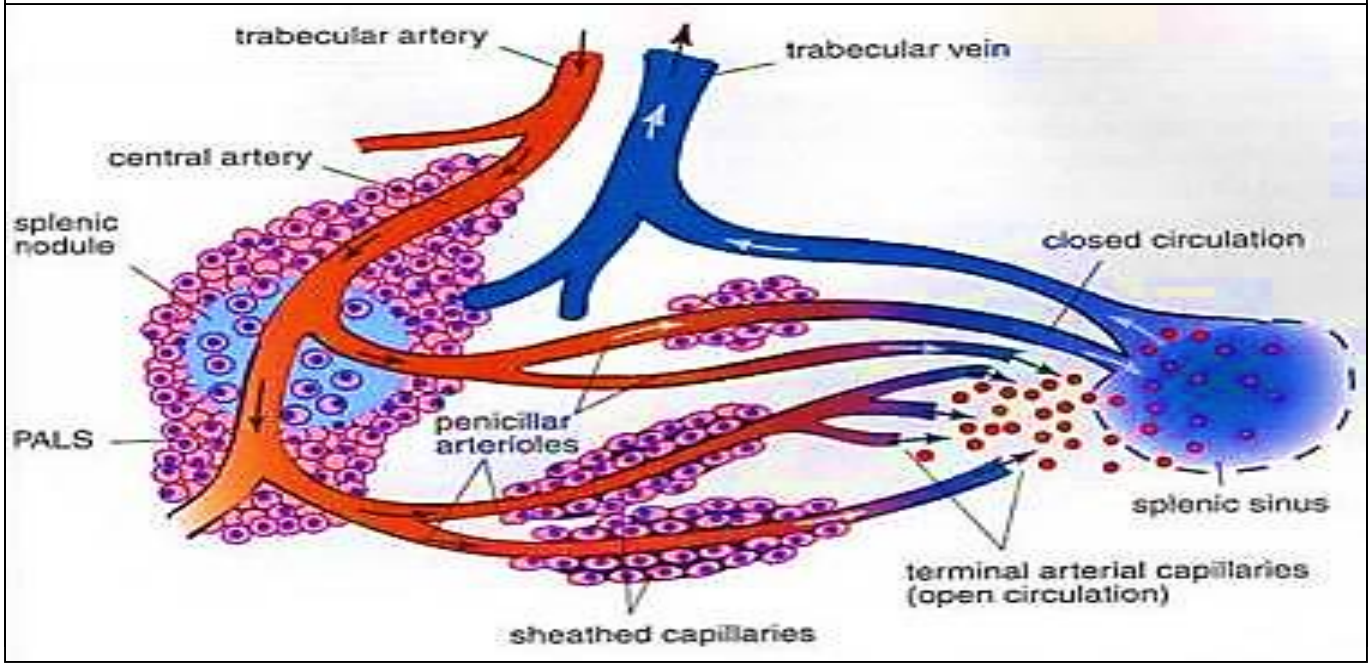







**The sketch shows the lay out of the blood supply of the spleen**

# 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:

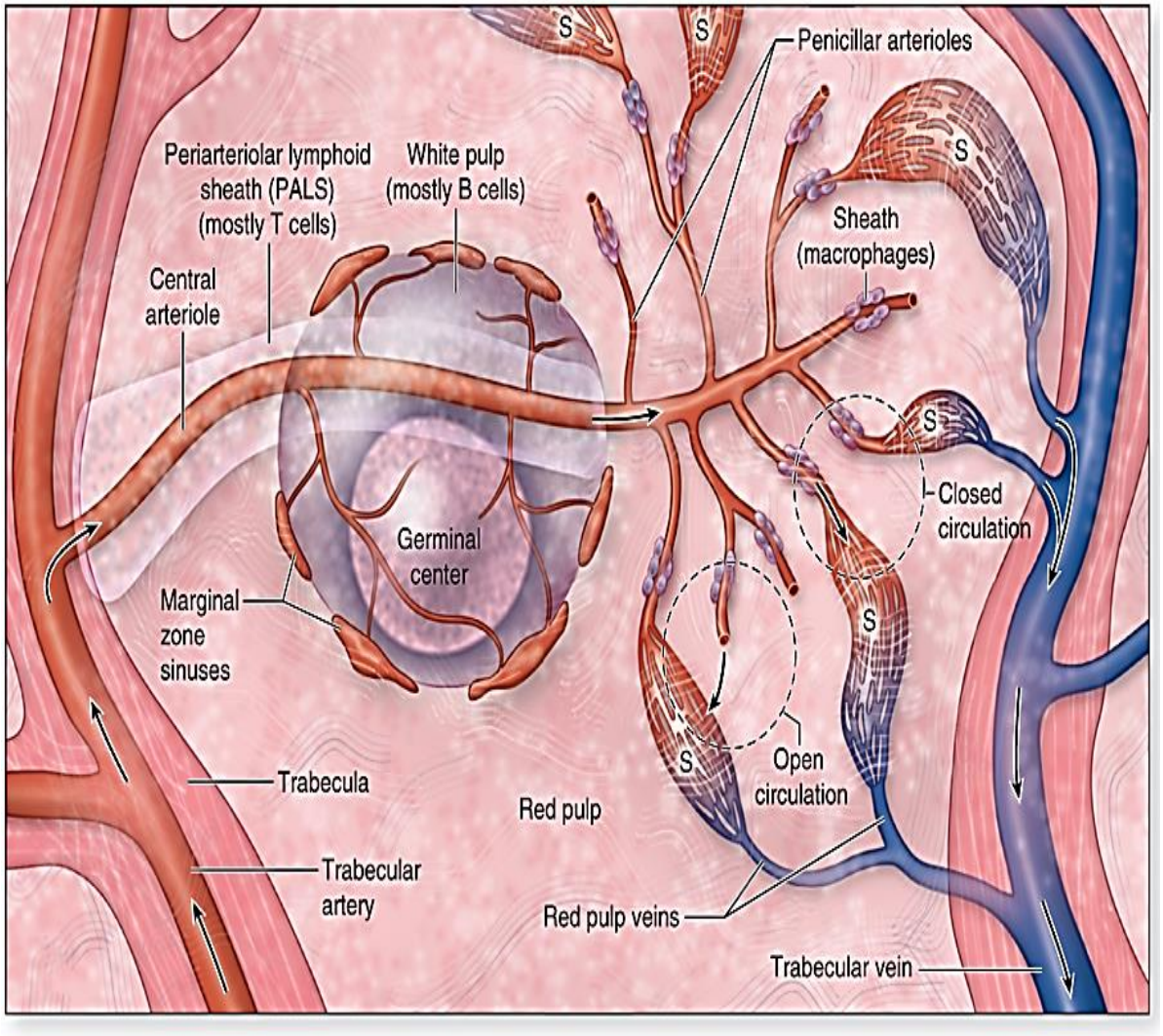
- **Periarteriolar lymphoid sheaths (PALS): mainly T lymphocytes** encircle the central arteriole and called

  **(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.

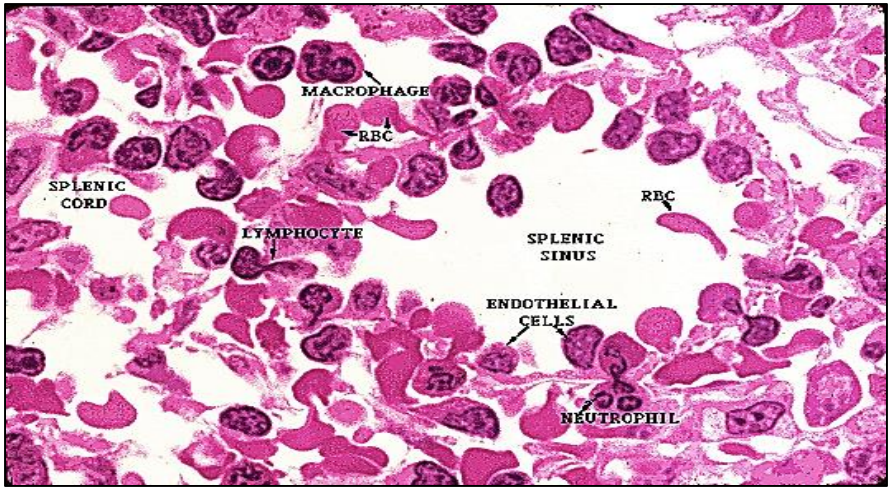


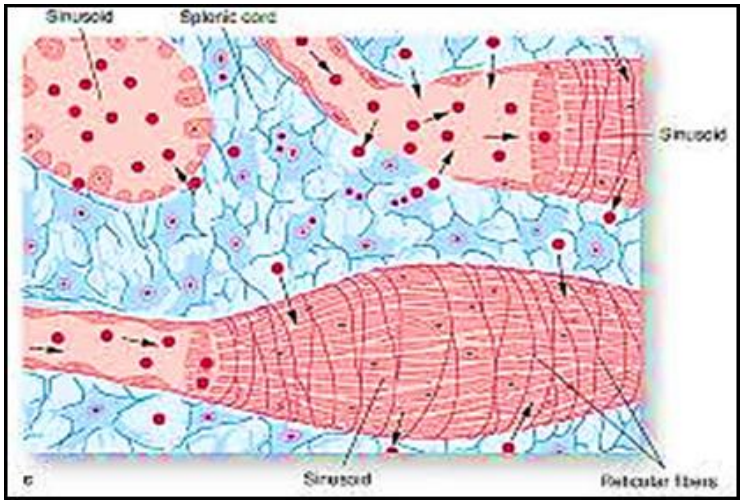

# Organization of Cells in white pulp of spleen

# 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

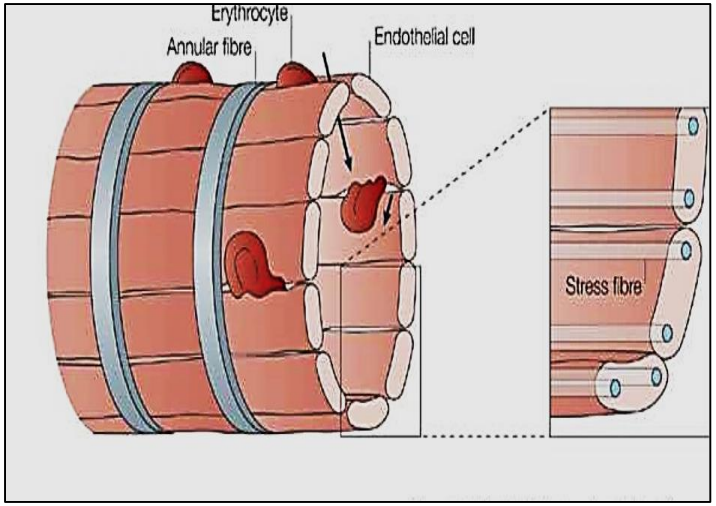


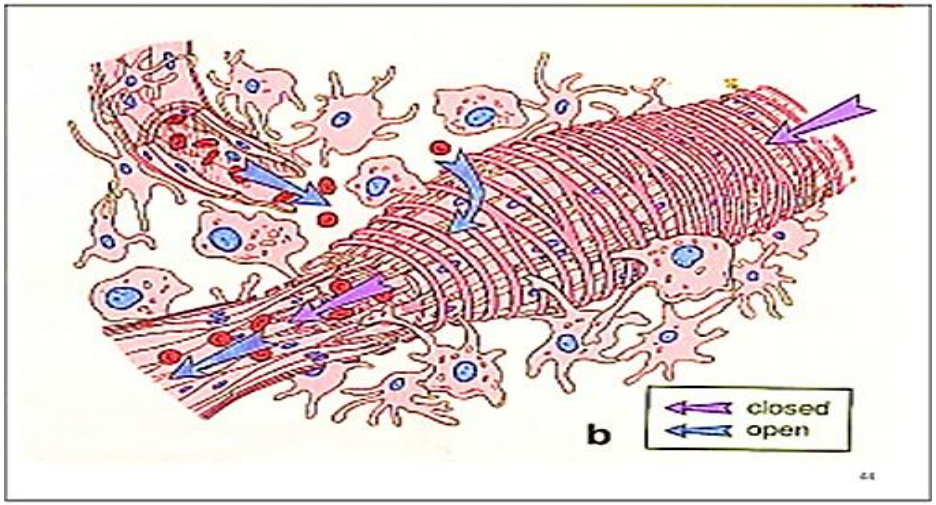




## 2-Blood sinusoids (venous sinuses):

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

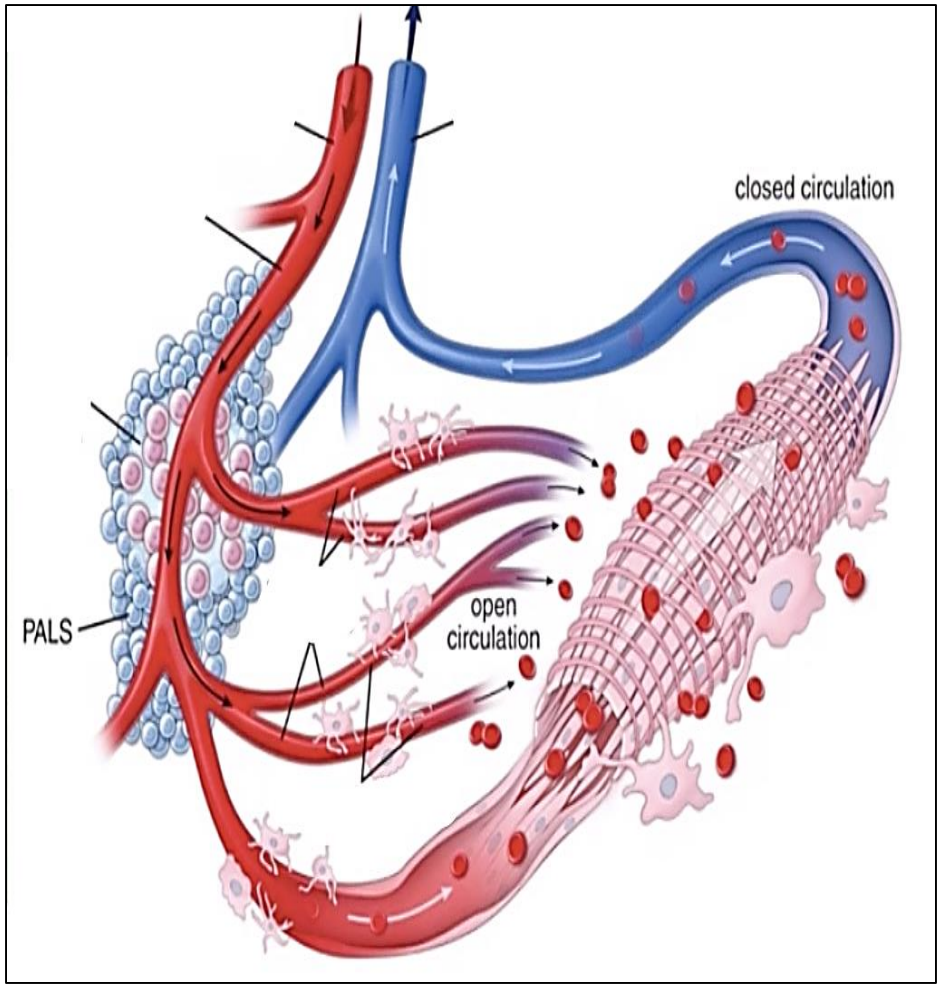
- **Stave cells** , unusual elongated endothelial cells( rod-like) oriented parallel to the sinusoidal blood flow
- These cells have discontinues basement membrane which wrap the cells cross wise

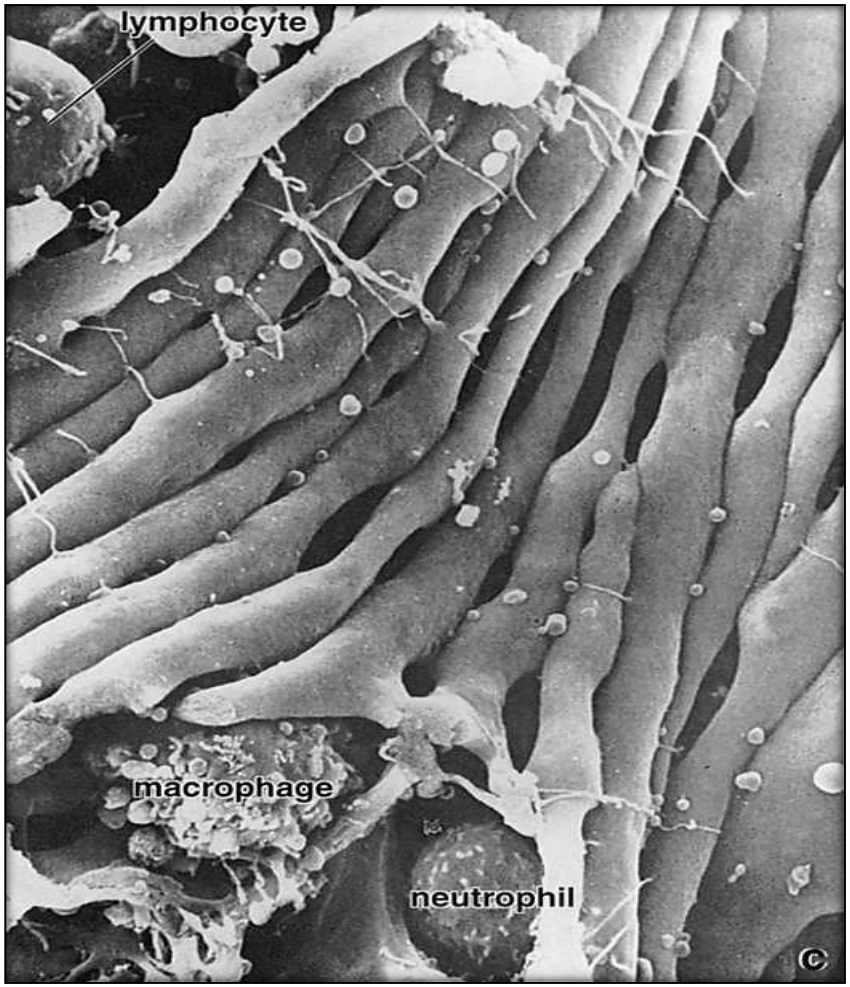



- The gaps between the endothelial cells mechanically filter the blood cells.. Old or abnormal RBCs attempting to squeeze through the endothelial gaps become badly damaged and subsequently removed by macrophages

**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**

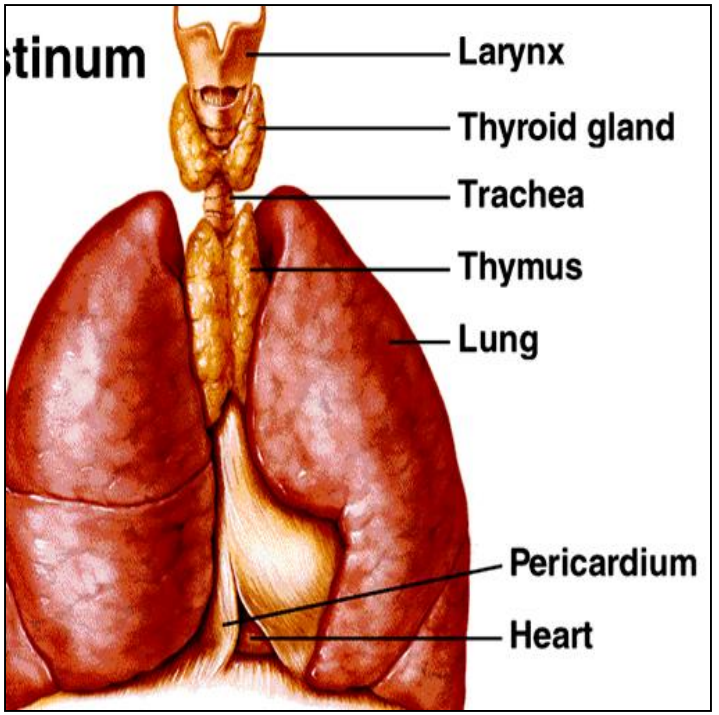



**The lining of splenic sinusoids and the EM of Stave cells**

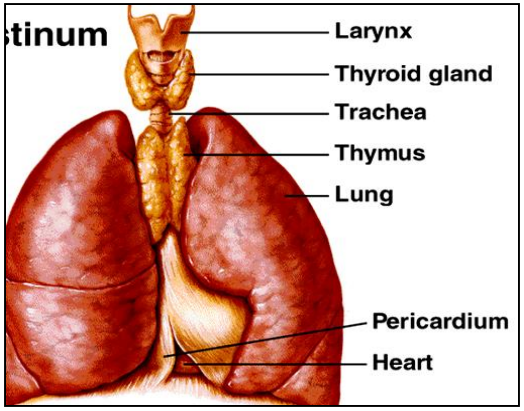
# Thymus

- is a **1ry** lymphatic organ e an endocrine function
- Location: behind the sternum in the mediastinum
- Single bi-lobed structure, highly lobulated organ

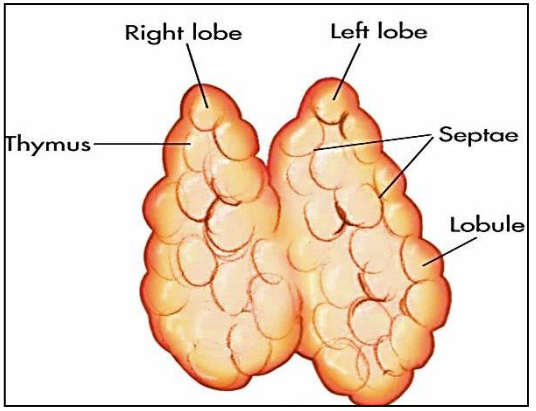



- Development:
  - Infant – ↑ in size
  - Puberty – maximum size
  - Adult – ↓ in size
- **Function**

  Differentiation and maturation of T cells




# Thymus



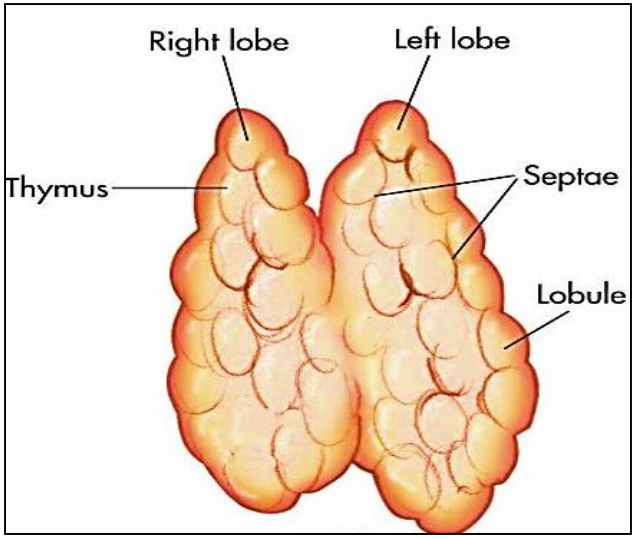

**A-Stroma**
1-Capsule
2-Trabeculae

**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

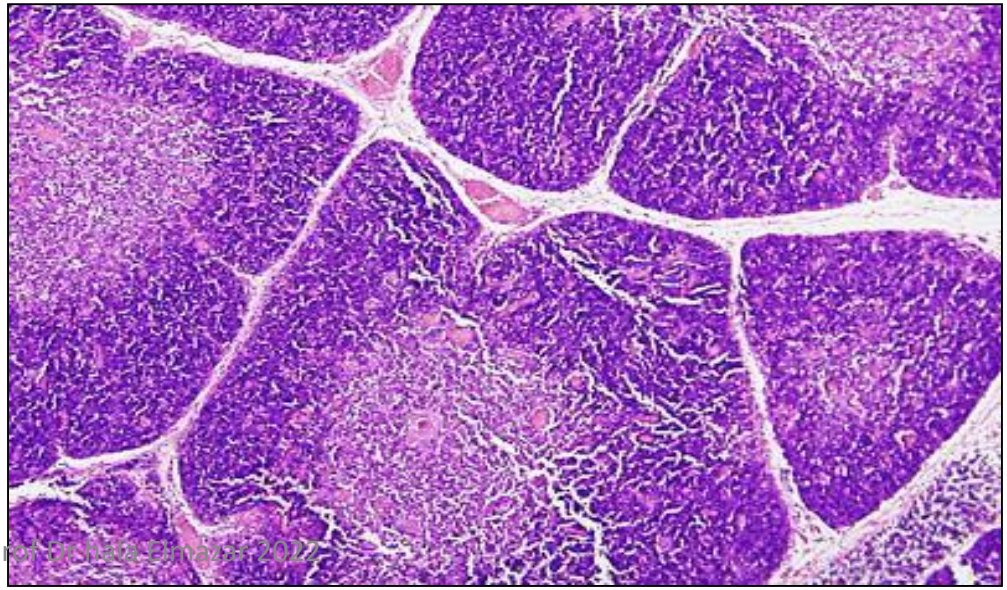
**3- Thymus** **has no reticular fibers** . Reticulum is formed by the processes of epithelial reticular cells

# B-parenchyma

- Cortex
  - Outer & dark
  - Inner & pale
- Medulla

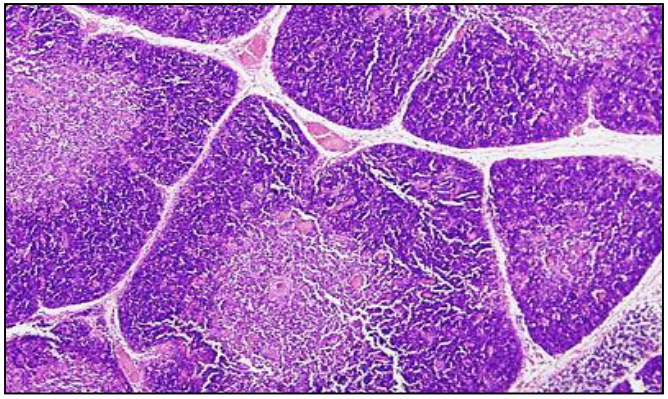
**Both contain:**

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



Prof Dalia Elmazar 2022

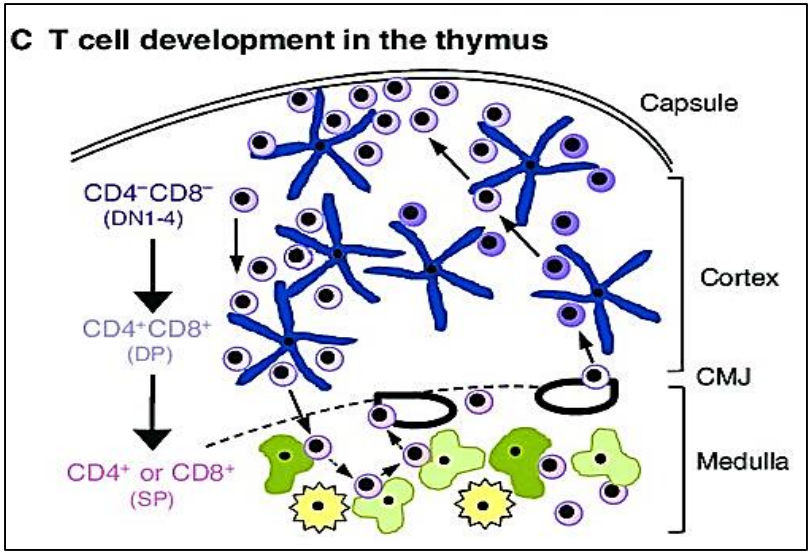
## 1- Cortex:



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

- Cortex contains **thymocytes.**

The hematopoietic precursors which migrated from bone marrow → thymus. Thymocytes 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.**

# T- lymphocytes:

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

➢ **Naïve**

➢ **Memory**

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

## The progression 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

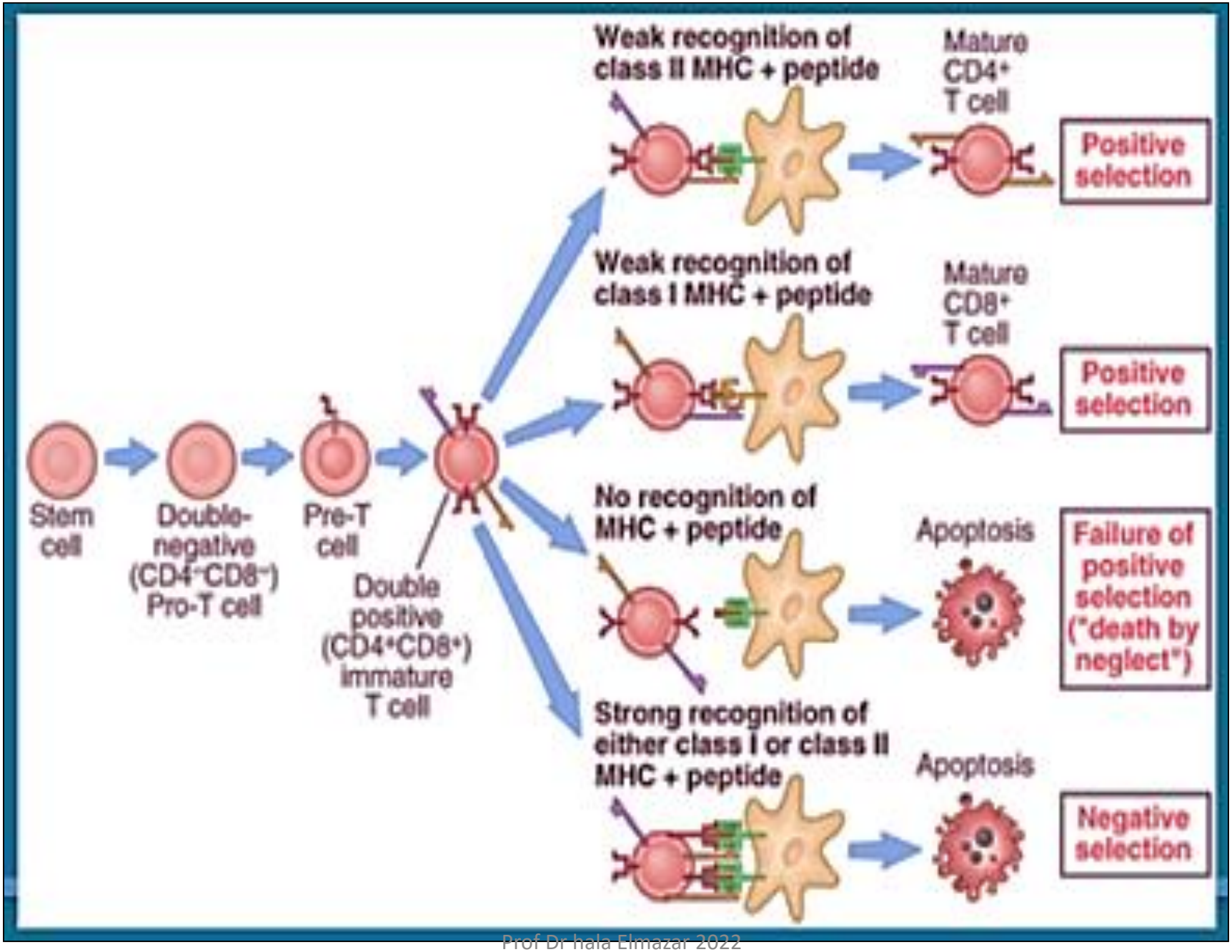
- Double +ve T cells contact ER cells carry MHC-II stop expressing $CD8^+$ marker & become single +ve T cells that express only $CD4^+$ marker

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

- Only **1- 3% of Double +ve T cells will** survive the **selection process and will** allow to enter the medulla

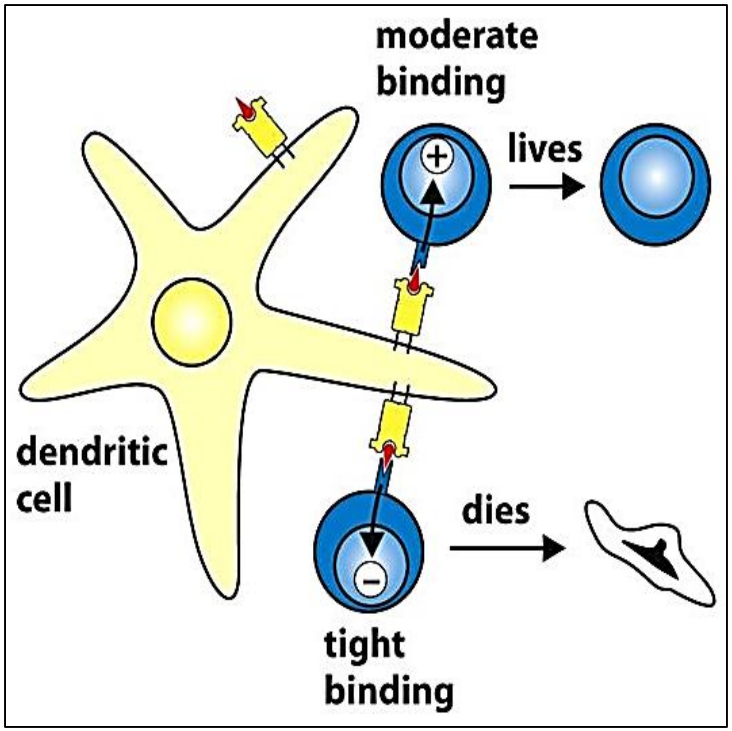
- The previous process is called **positive selection** and take place in the **thymus cortex**

- The final step in maturation of T cells occurs in the medulla


Weak recognition of class II MHC + peptide
Mature CD4+ T cell
Positive selection
Weak recognition of class I MHC + peptide
Mature CD8+ T cell
Positive selection
No recognition of MHC + peptide
Apoptosis
Failure of positive selection ("death by neglect")
Strong recognition of either class I or class II MHC + peptide
Apoptosis
Negative selection
Stem cell
Double-negative (CD4⁻CD8⁻) Pro-T cell
Pre-T cell
Double positive (CD4⁺CD8⁺) immature T cell

- The medullary ER cells will do another test & present self-epitopes of MHC-I & MHC-II to the single +ve T cells & those who bind **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

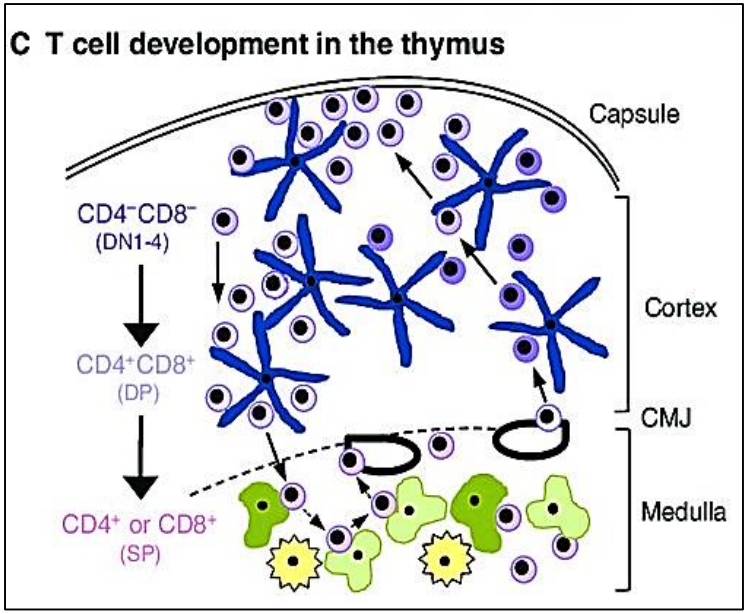
➢ Expression of surface markers

- 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
- 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

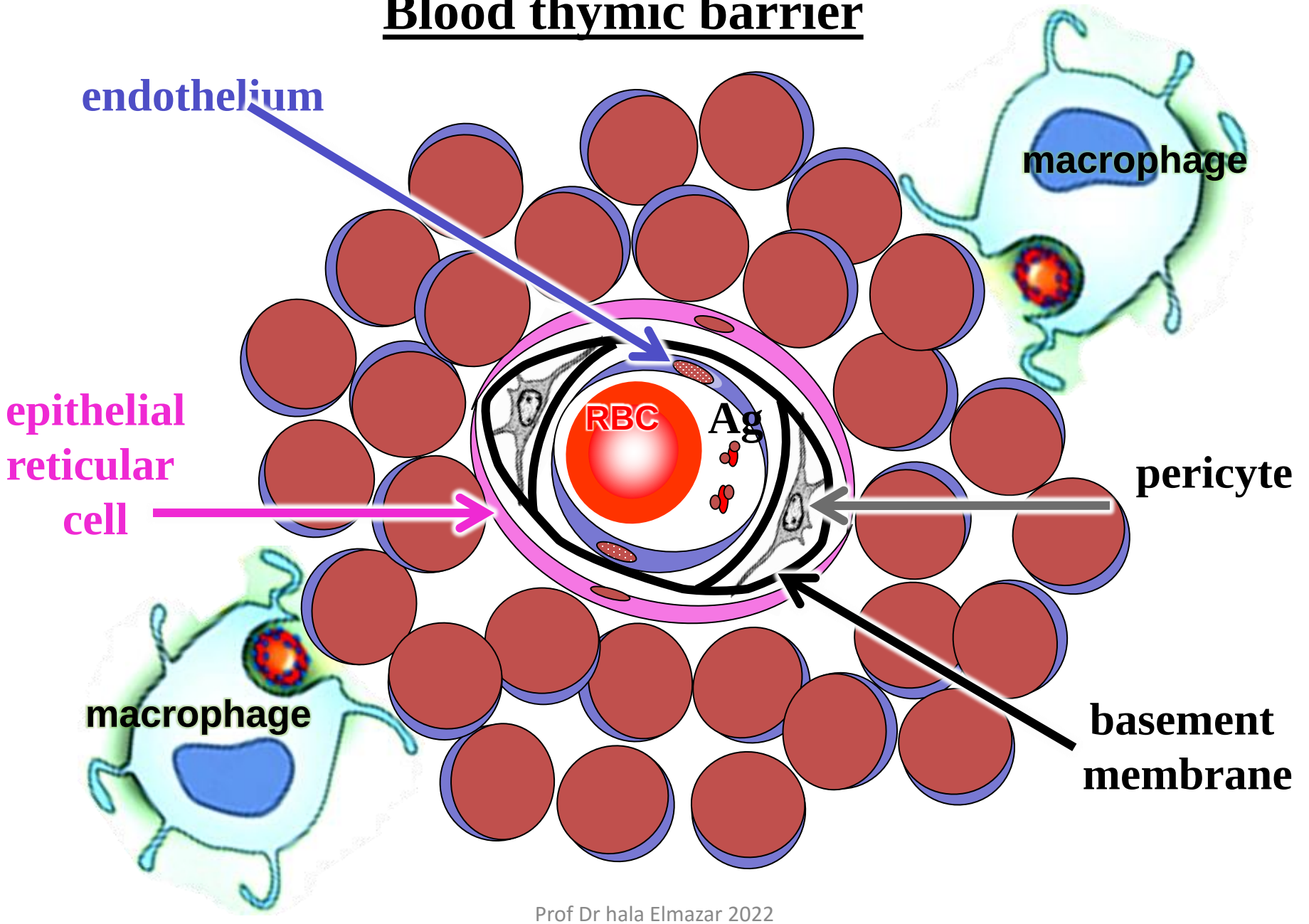
3-thick, continuous basal lamina around endothelium

4- perivacular 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

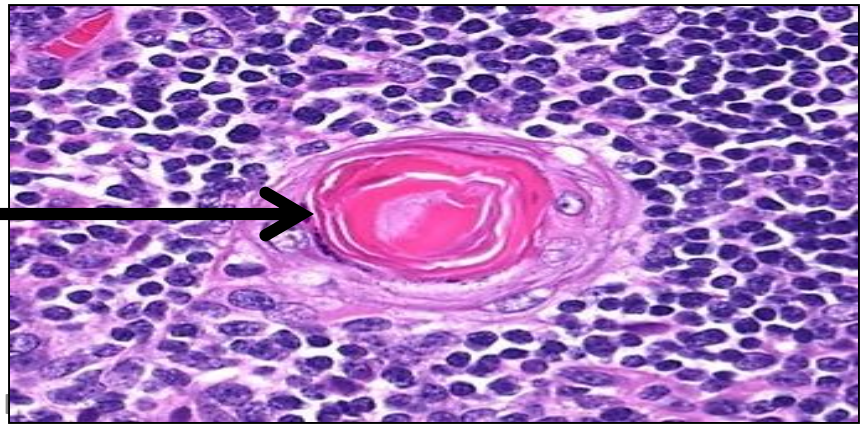


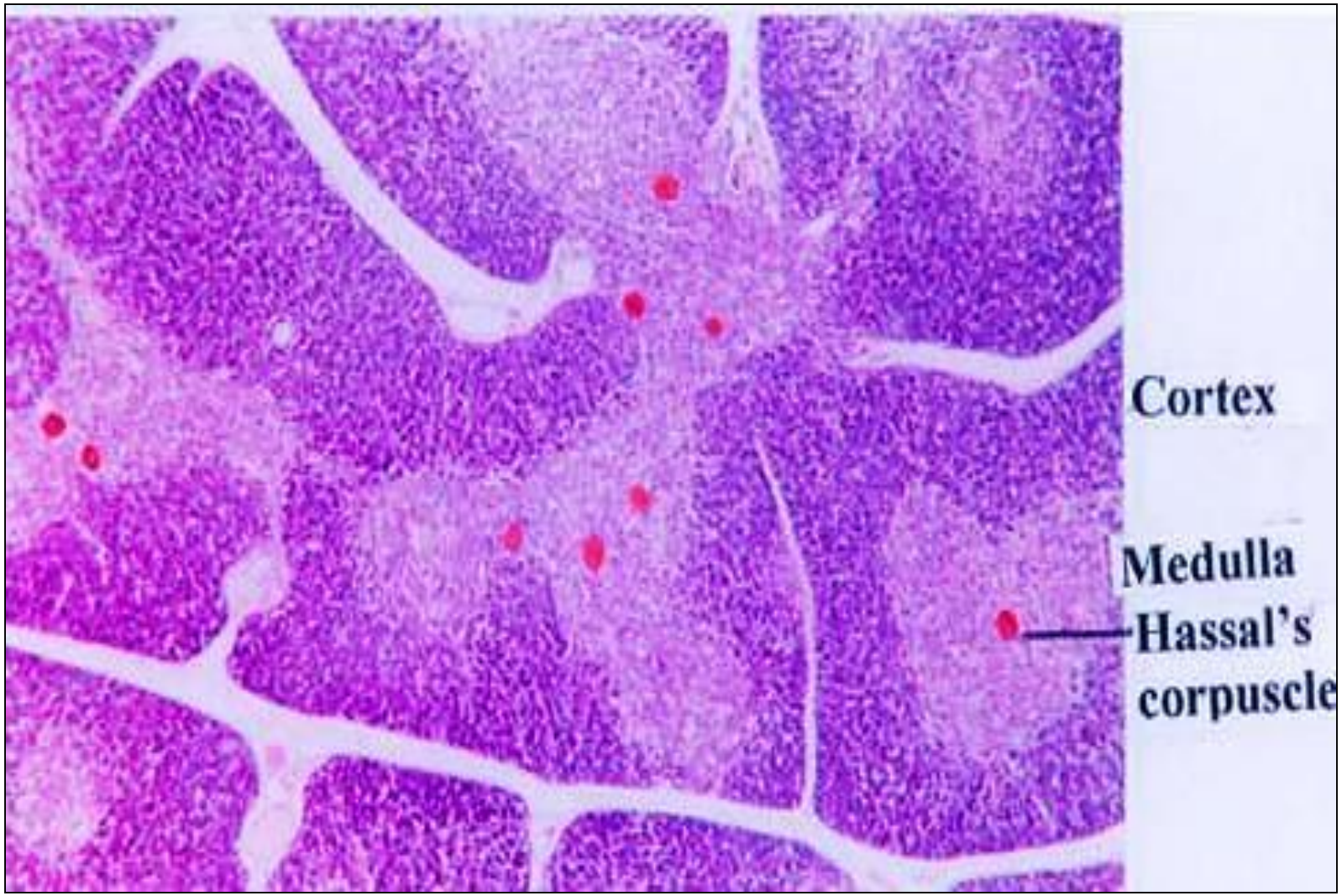
## 2-Medulla:

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

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

Contains **Hassall's corpuscles** (diagnostic feature), which vary in size from 25 to 200 µm in diameter & are acidophilic in reaction.





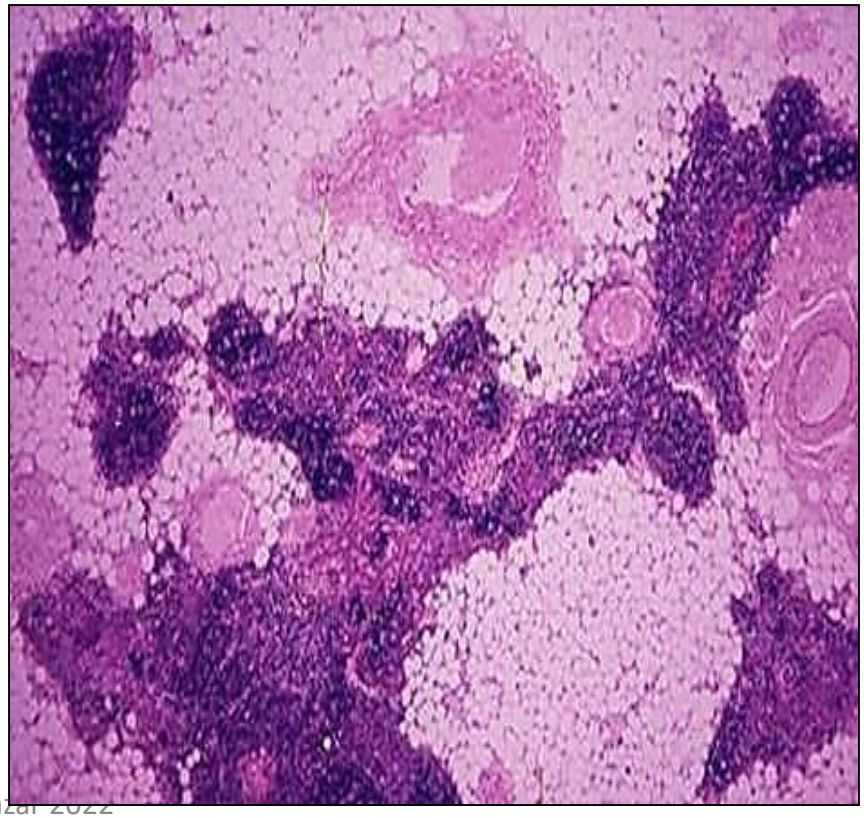

**Thymus gland showing Hassall's corpuscles in medulla**

Hassall’s corpuscle consist  mass of degenerated reticular cells surrounded e concentric layers of epithelial reticular cells

## 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

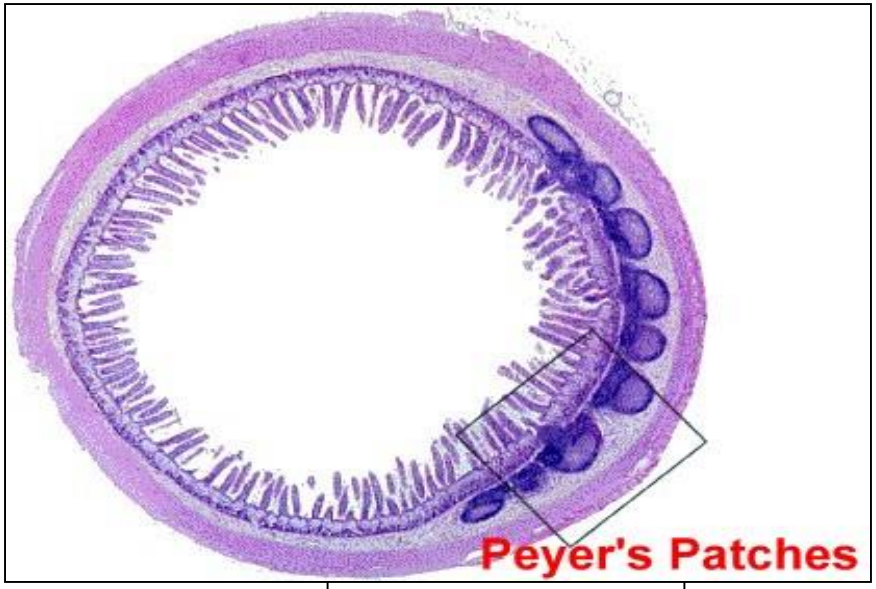
✓ Bronchus : BALT

✓ Gut: GALT

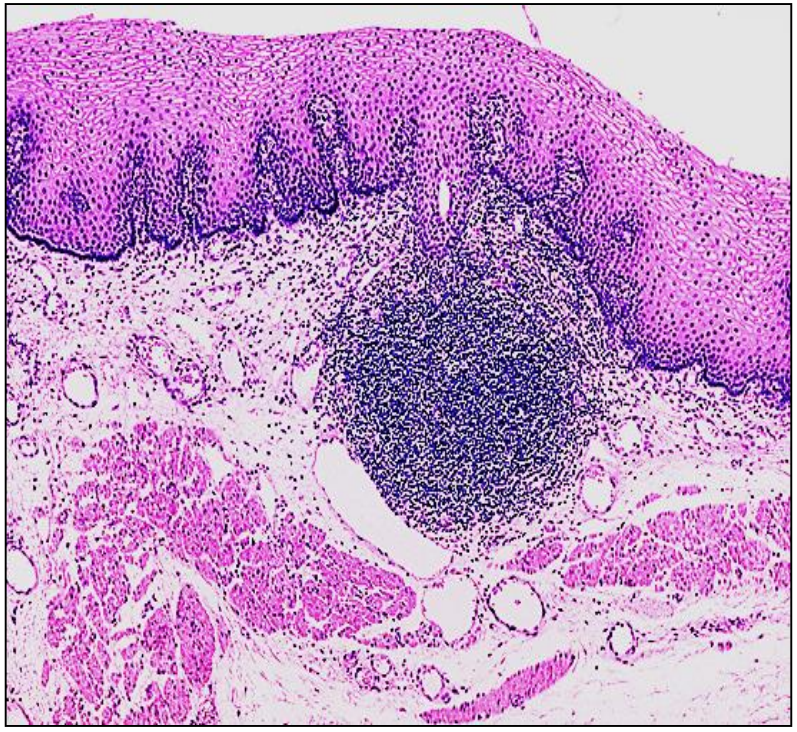
## MALT Examples are:

1 .Payer's patches of ileum .

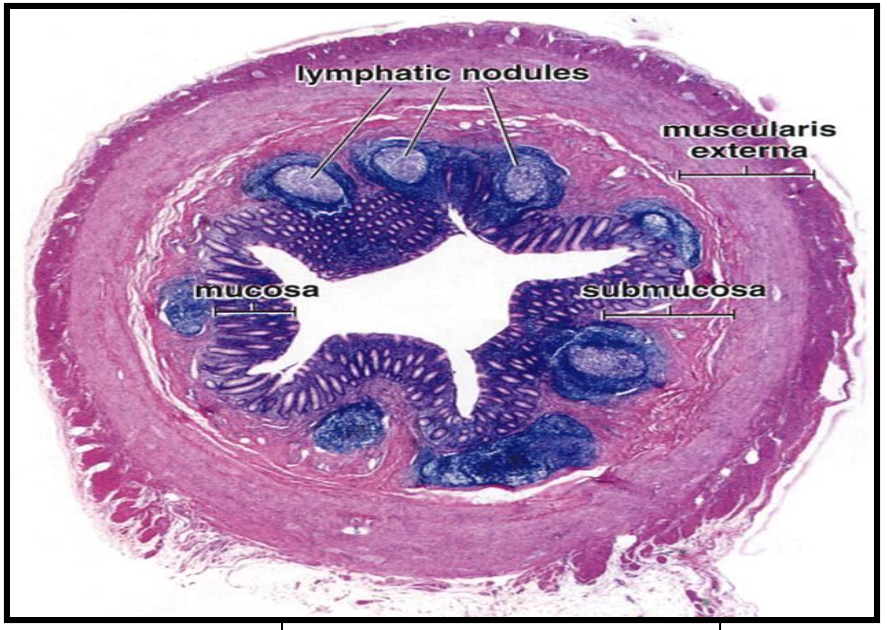
2. MALT of appendix.




**MALT in ileum**



**MALT in wall of esophagus**




**MALT in appendix**

# Thank you