



# Lymphatic System

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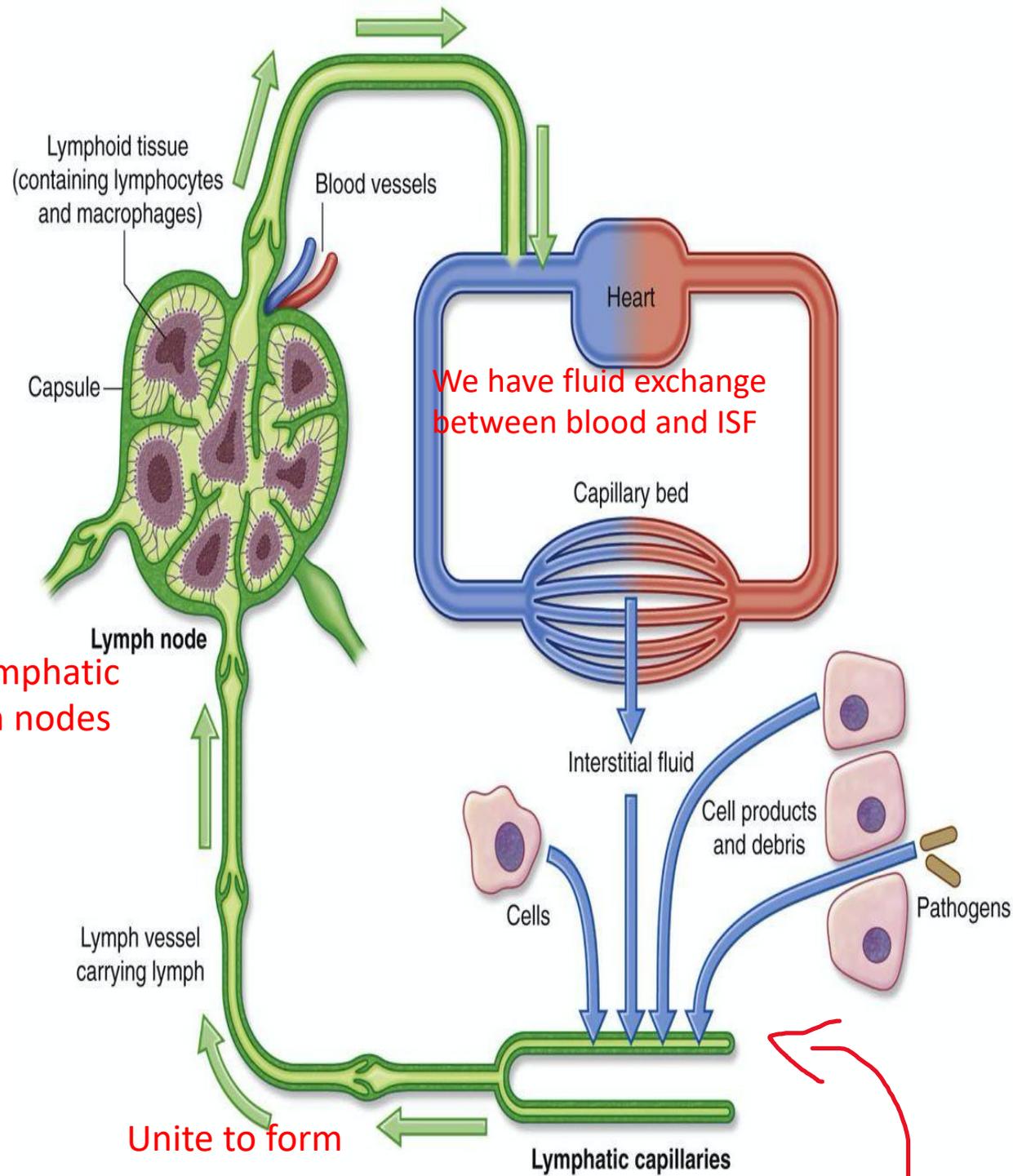
# Lymphatic system

The lymphatic system consists of lymphatic fluid, lymphatic vessels, lymphatic tissue, and lymphatic organs located throughout the tissues of the body.

Along the course of lymphatic vessels we have lymph nodes

It functions to:

- 1- Drain excess interstitial fluid from the tissues and return to blood stream
- 2- Initiate an immune response against disease by producing and transporting lymphocytes
- 3- Transport dietary lipids absorbed by the gastrointestinal tract into the blood.

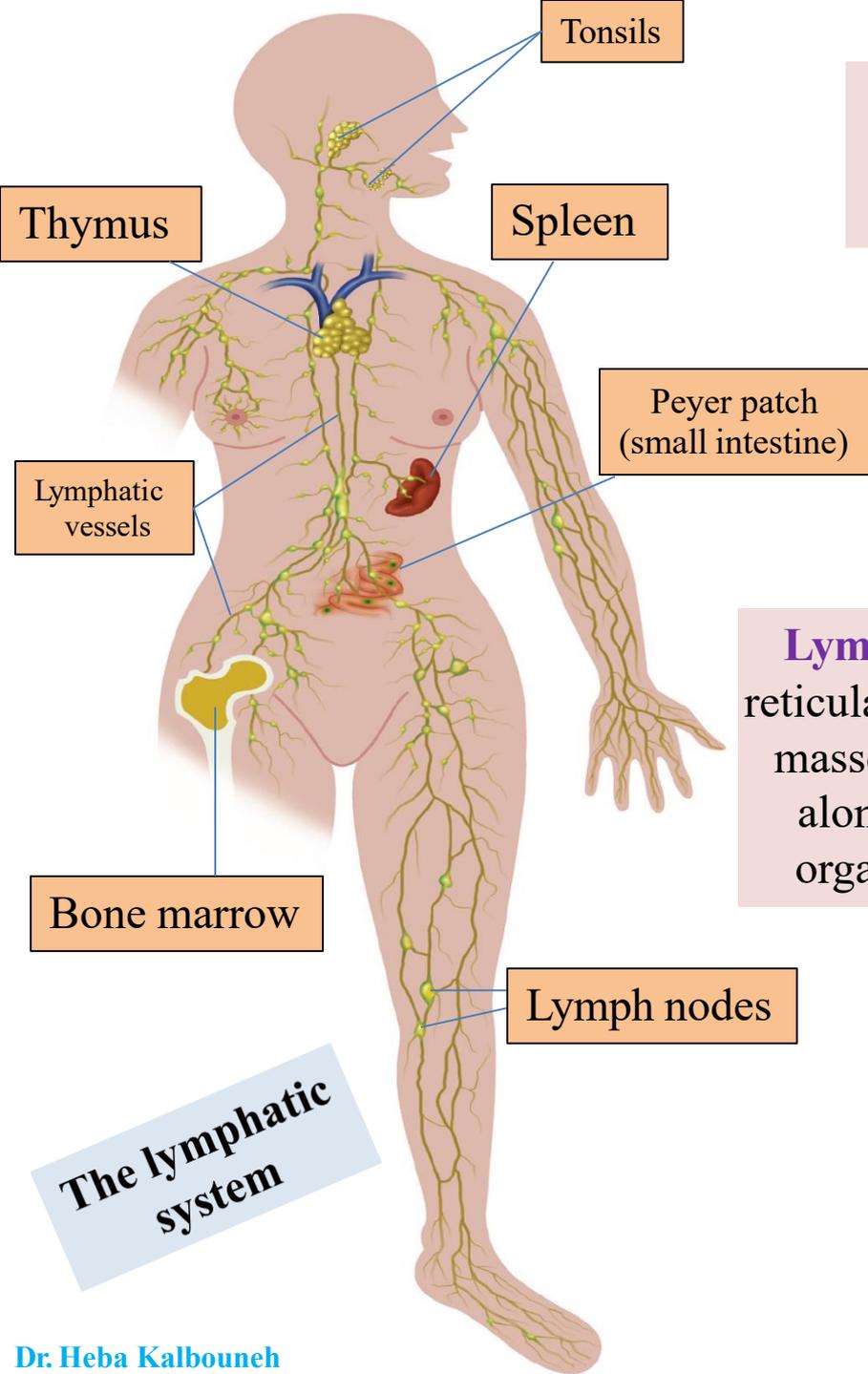


The lymphatic system starts as lymphatic capillaries

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20 liters of blood enters the capillary bed but only 17 liters gets out why?

Because the hydrostatic force of the blood on the capillary forces 3 liters of fluids to leave to the interstitial fluid. And these three liters are drained back to the blood by the lymphatic system



**Lymph** is a colorless fluid that floats in the lymphatic vessels. It is similar in composition to blood plasma

**Lymphatic vessels** are thin vessels that accompany arteries and veins throughout the body and transport lymph.

**Lymphatic tissue** is a specialized form of reticular connective tissue that is composed of masses of lymphocytes. These either occur alone as lymph nodules (follicles) or are organized into various lymphatic organs.

**Lymphatic organs** include the lymph nodes, spleen, thymus, and red bone marrow

# Fluid balance

The tissues of the body are supplied by blood capillaries that bring oxygen-rich blood and remove carbon dioxide-rich blood.

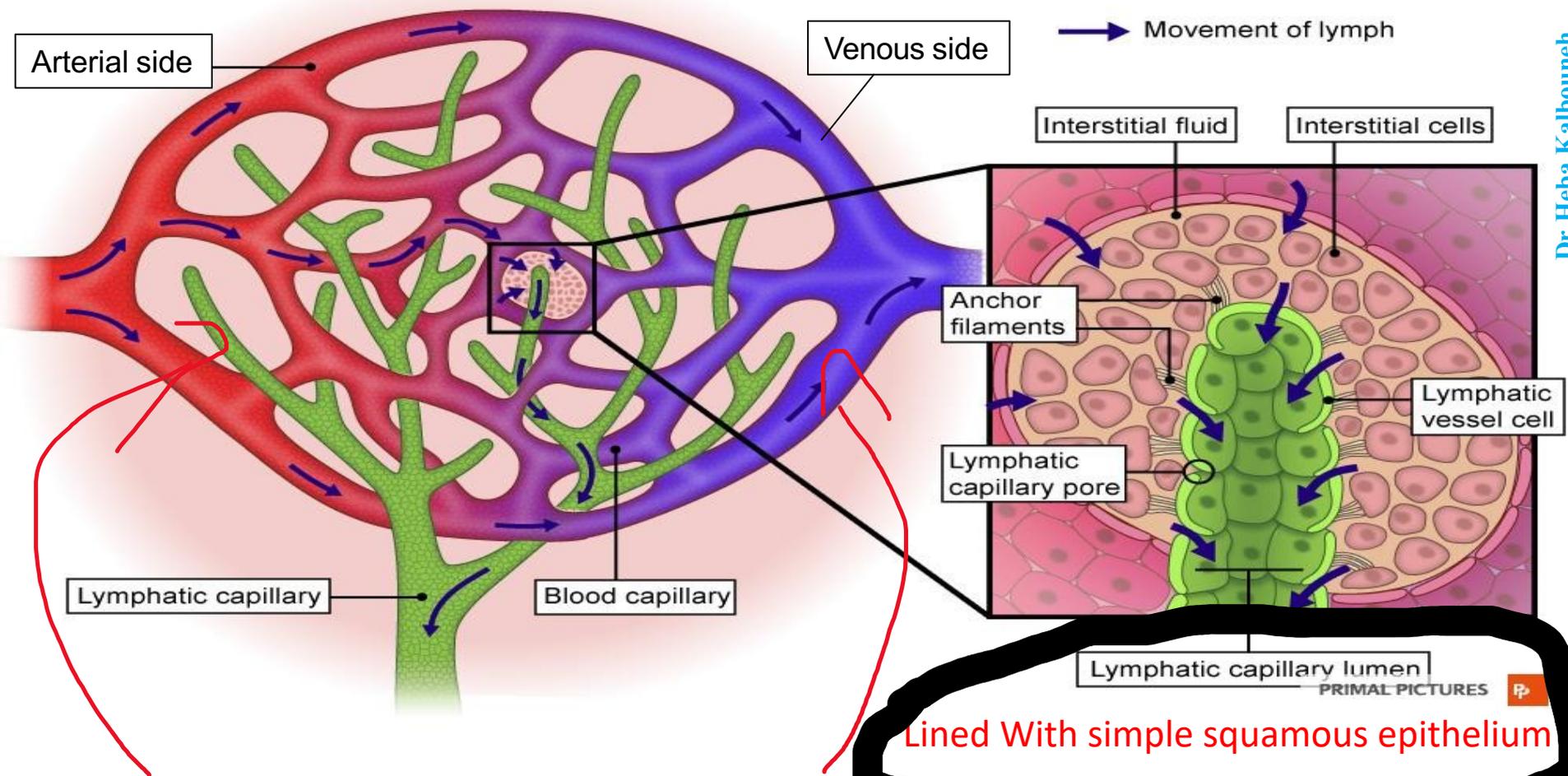


Fluid similar to blood plasma, called **interstitial fluid**, leaches from these vessels into the surrounding tissue.

Around 20 liters of fluid leaves the arterial capillaries every day, but only 17 liters of fluid returns to the venous capillaries.



Lymphatic vessels function to drain this excess fluid from the tissues as lymph and return this fluid to the blood.



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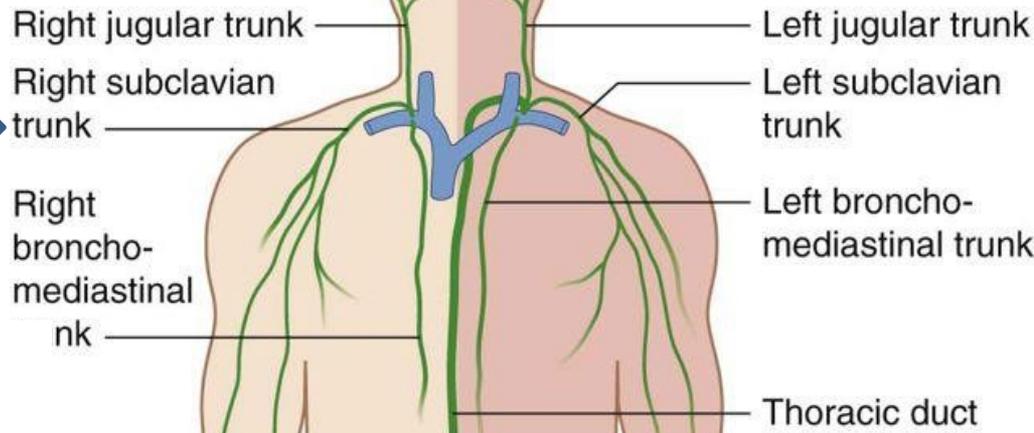
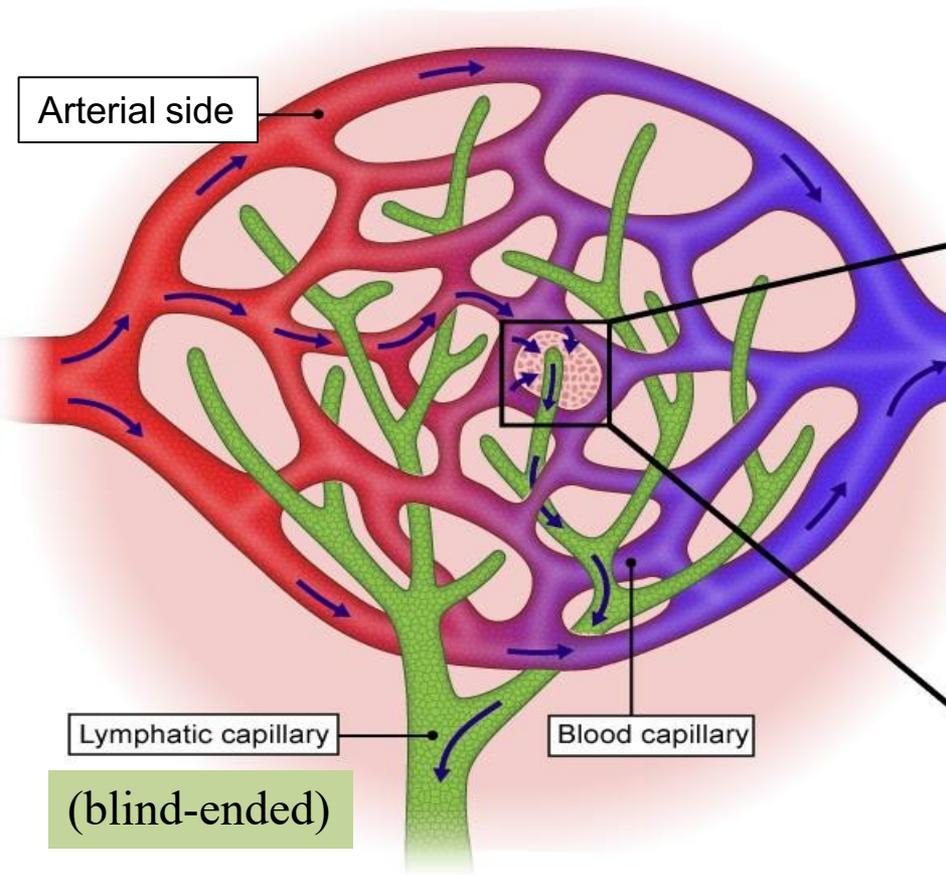
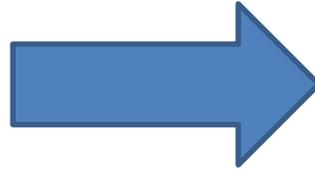
The arterial side is Rich in O<sub>2</sub> and nutrients

The venous side is Rich in CO<sub>2</sub> and waste products

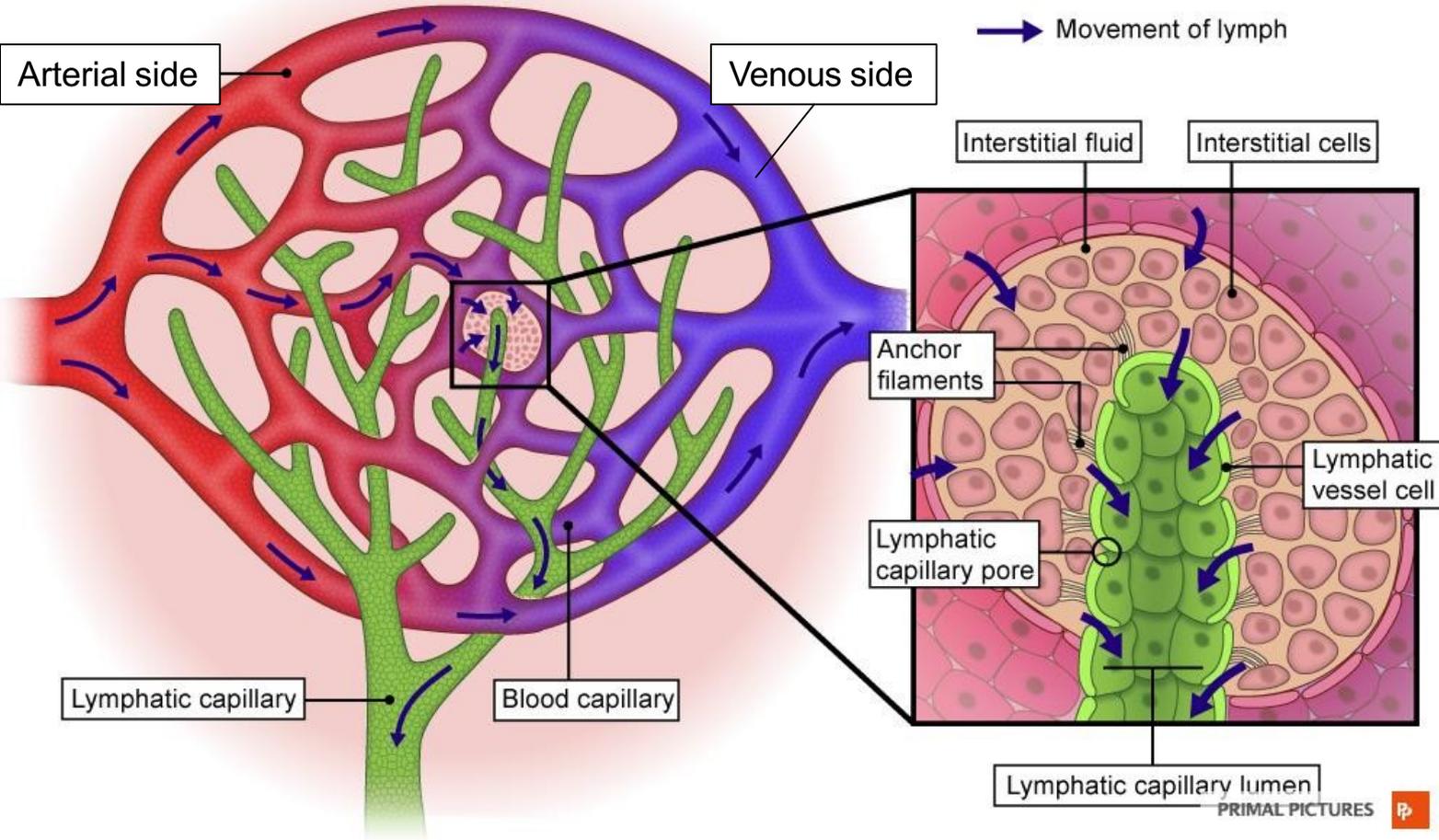
Lined With simple squamous epithelium

the lymphatic vessels start as blindended lymphatic capillary

**Lymphatic vessels** begin as “porous” blind-ended lymphatic capillaries in tissues of the body and converge to form a number of larger vessels, which ultimately connect with large veins in the root of the neck.



Lymph returns back to the big veins (**venous angle**: the junction between subclavian and internal jugular veins) through the Thoracic duct and Right lymphatic duct.



Lymphatic capillaries are made of overlapping endothelial cells with large gaps. The overlapping flaps function as a one-way valve.

When fluid accumulates in the tissue, interstitial pressure increases pushing the flaps inward, opening the gaps between cells, allowing fluid to flow in.

As pressure inside the capillary increases, the endothelial cells are pressed outward, closing the gaps, thus preventing backflow.

Unlike blood capillaries, the gaps in lymphatic capillaries are so large that they allow bacteria and immune cells (ex. Macrophages/ dendritic cells) to enter. This makes the lymphatic system a useful way for large particles to reach the bloodstream.

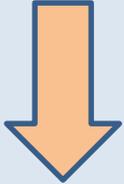
*Remember: lymphatic system is used, for example, for dietary fat absorption in the intestine.*

The cells in the lymphatic capillary are overlapped in a way that they act as a one-way valve

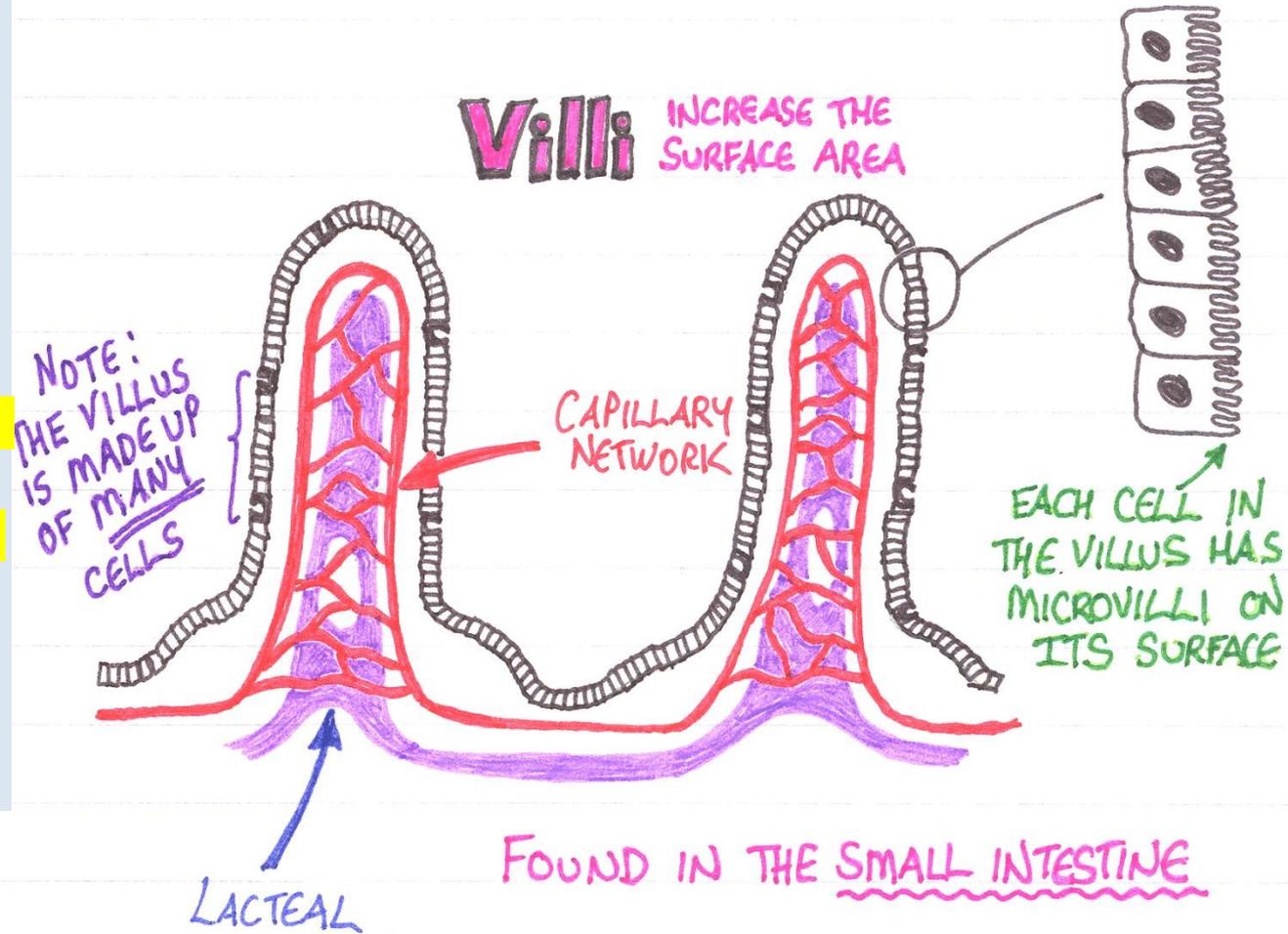


# Transport

Some lipids are too large to pass through the capillary walls of the small intestine and therefore cannot be absorbed.



The lymphatic capillaries within the small intestine, known as **lacteals**, can absorb these large lipid molecules and transport them into the venous circulation via the thoracic duct. Lymph containing these lipids becomes a creamy white color and is referred to as **chyle**.



# Lymphatic Organs and Tissues

Lymphocytes can be found throughout the body, however, they aggregate in places where they are most likely to come into contact with pathogens.

Lymphocytes are produced within the red bone marrow and are transported via the blood vessels to lymphatic tissues and organs.

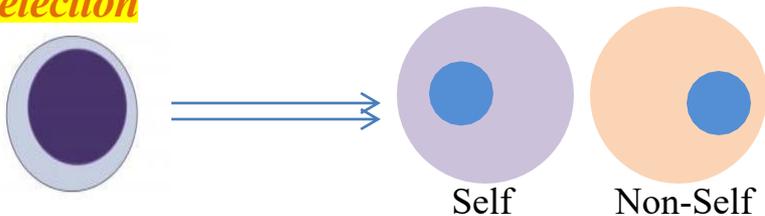
Lymphatic organs are divided into:

## Primary lymphatic organs

**Bone marrow.**

**Thymus gland.**

*Are sites of Lymphocyte production, maturation, selection*



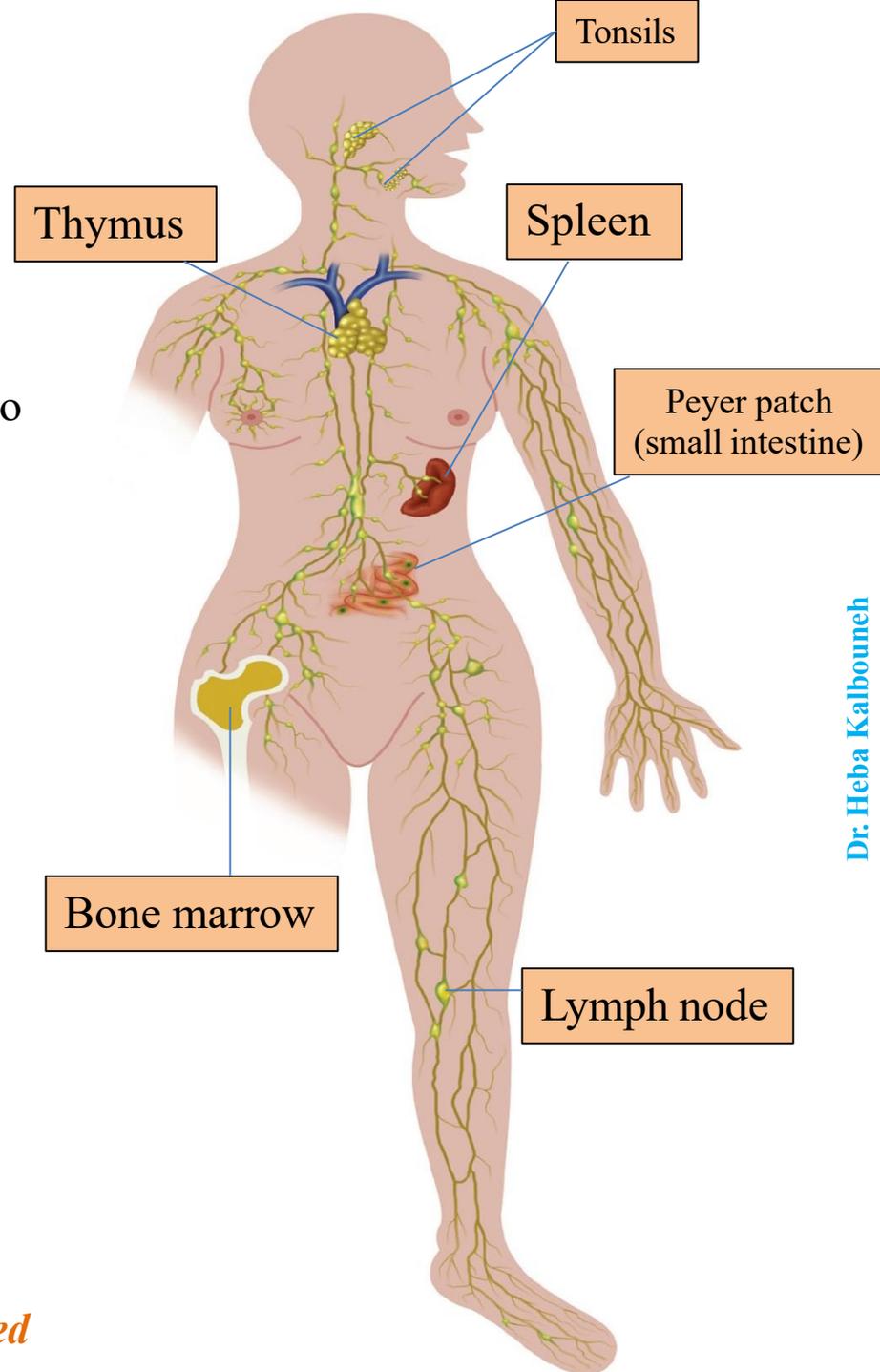
## Secondary lymphatic organs

**Diffuse lymphatic tissue (lymphatic nodules).**

**Spleen.**

**Lymph nodes.**

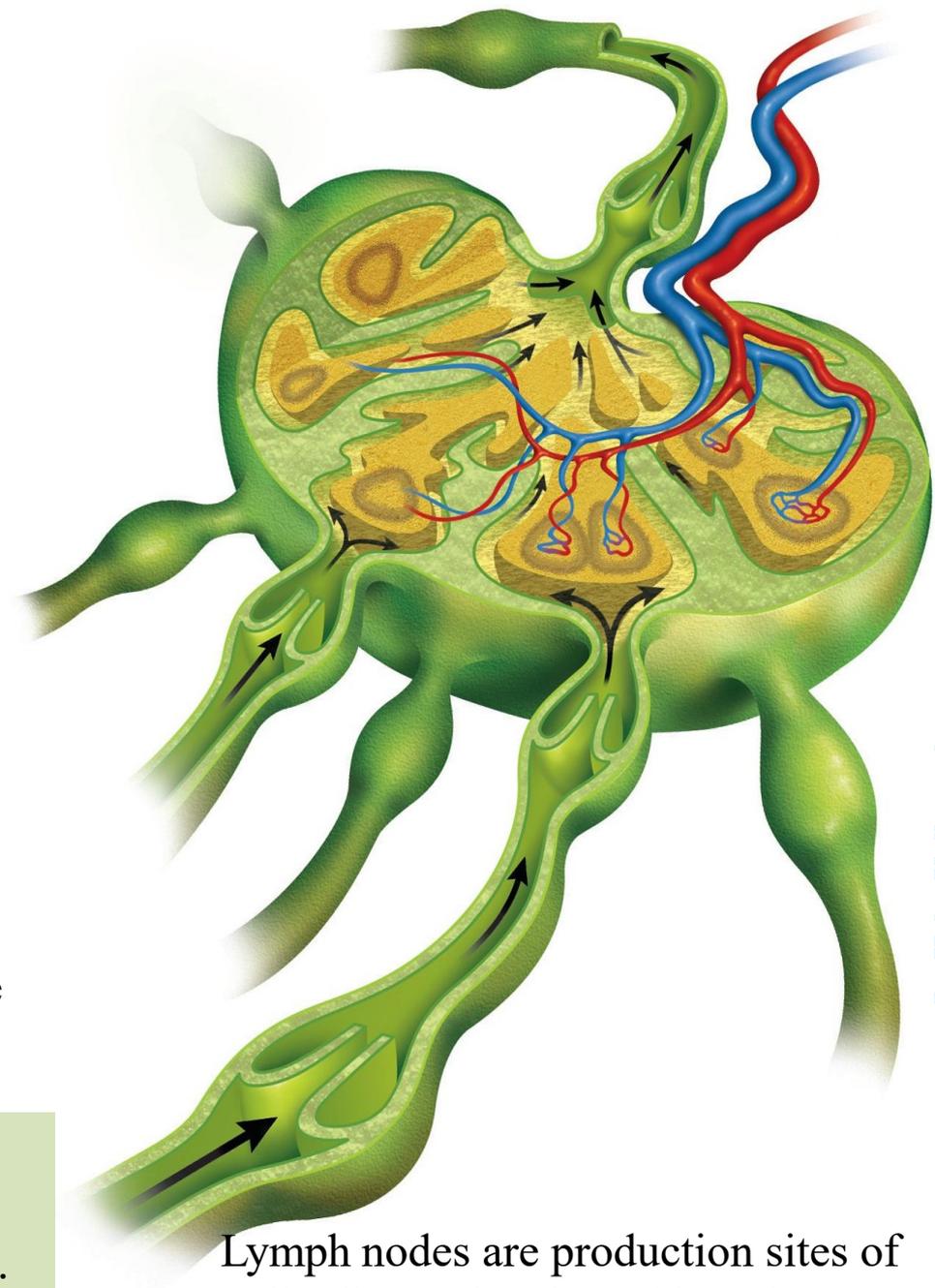
*Are sites to encounter pathogens and become activated*



# Lymph nodes

- ✓ Are kidney-shaped small encapsulated bodies located along the course of lymphatic vessels (Approximately 600 lymph nodes )
- ✓ Reticular tissue forms the stroma of the lymph node
- ✓ Lymph nodes are up to 3 cm in length
- ✓ Immunocompetent B cells and T cells are suspended throughout the lymph node
- ✓ 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 congregate around blood vessels in clusters and are usually named according to the vessel or location that they are associated with.

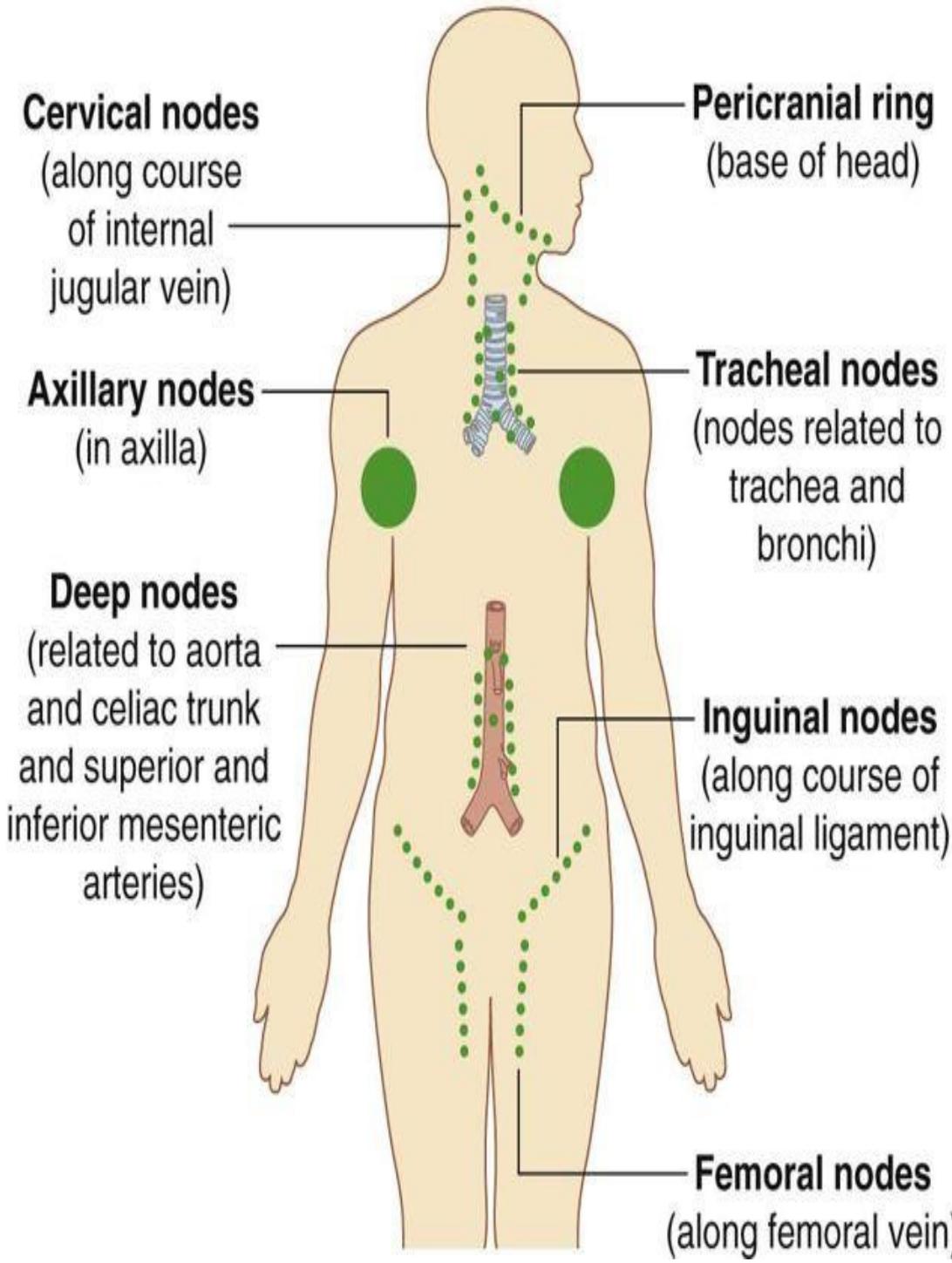
Lymph node enlargement can happen in cases of lymphoma (painless lymphadenopathy) or infection (painful).



Lymph nodes are production sites of antibodies and activated lymphocytes

The main groups of lymph nodes include:

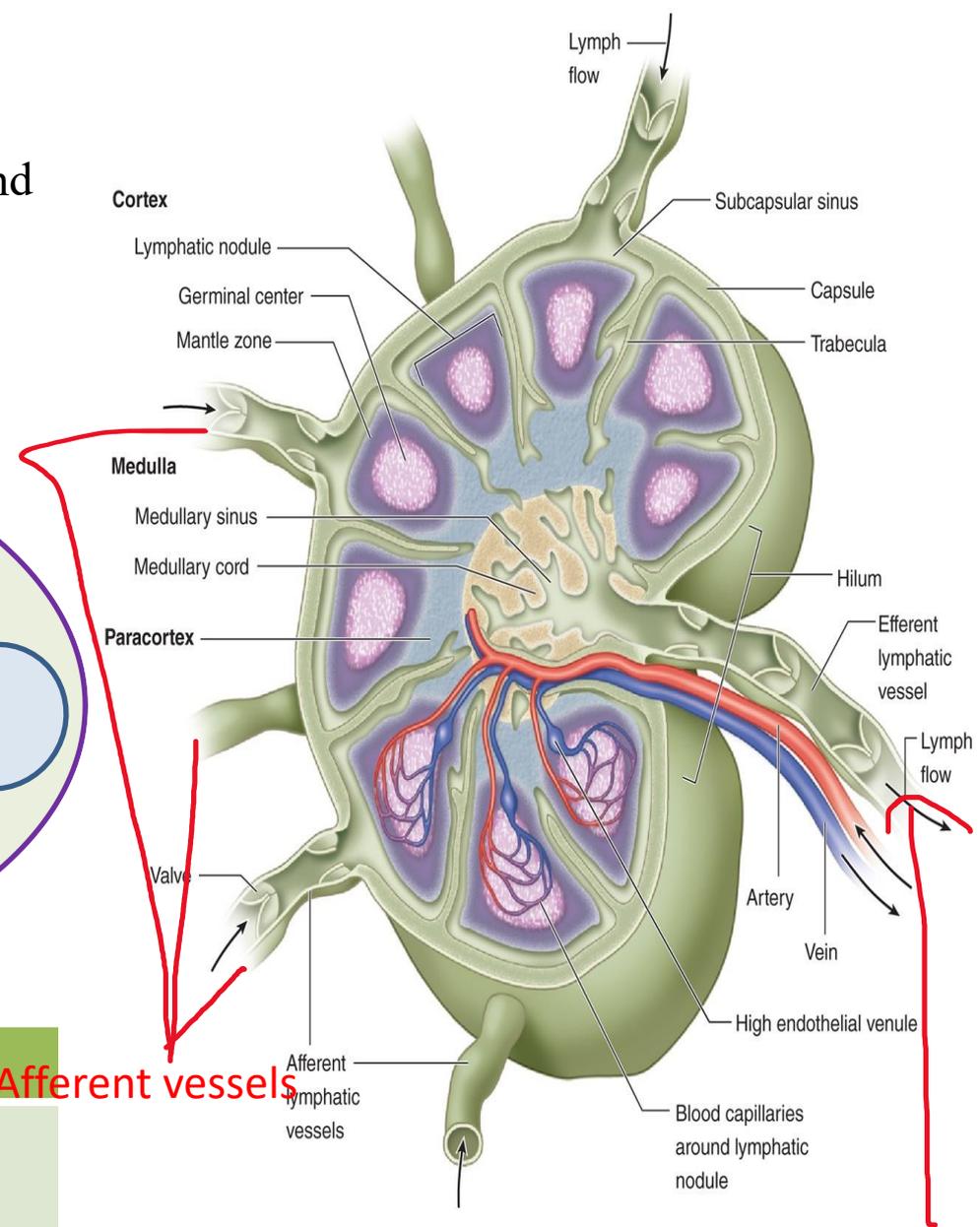
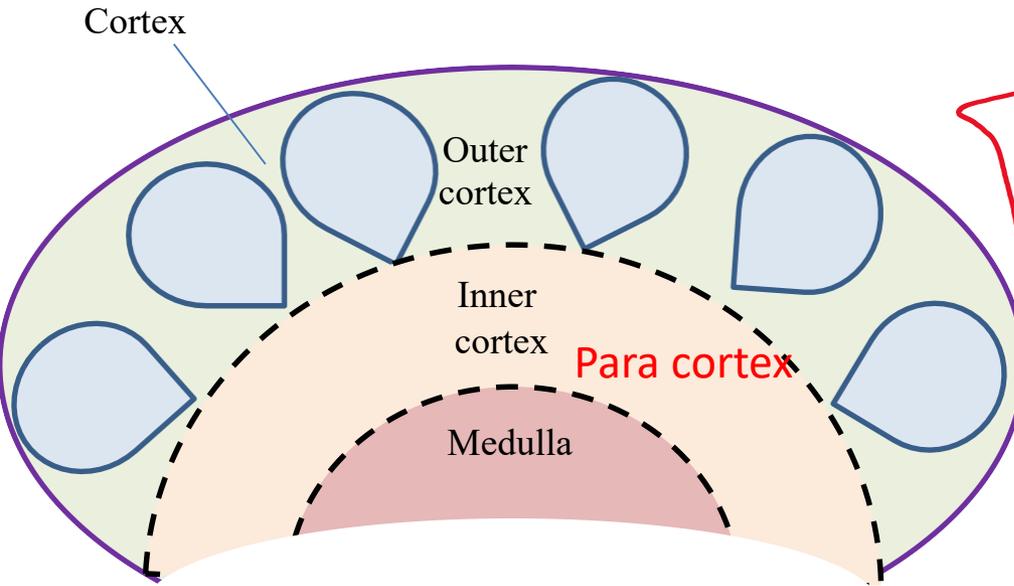
Name	Location	Associated vessel
Axillary nodes	Armpit	Axillary vein
Cubital nodes	Elbow	Basilic vein
Popliteal nodes	Posterior knee	Popliteal vein
Inguinal nodes (superficial and deep)	Groin	Great saphenous vein Femoral vein
Cervical lymph nodes (superficial and deep)	Neck	Internal jugular vein External jugular vein



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**Important table**

The lymph node consists of an outer cortex and an inner medulla



Cortex	Medulla
Contains lymphatic follicles	No follicles
Receives lymph from afferent vessels	Forms sinuses that lead to efferent vessels at the hilum

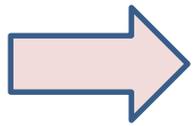
Afferent vessels

Efferent vessels

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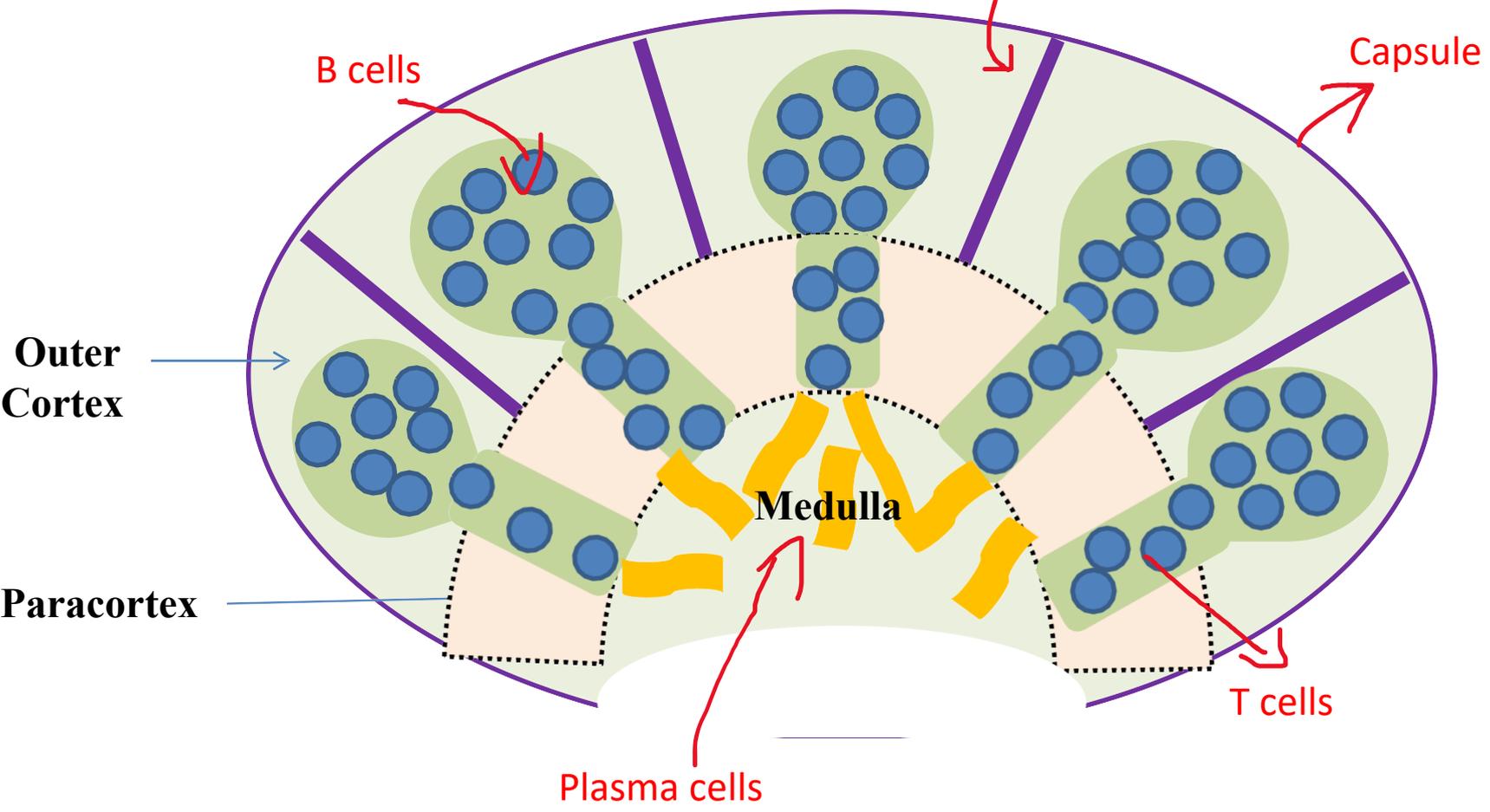
Afferent vessels: carries lymph to the lymph node (usually multiple)  
 Efferent vessels: carries lymph from the lymph node (usually single)  
 An Efferent vessel for a lymph node could be an Afferent for another lymph node

The nodes are covered by a **capsule** of dense connective tissue, and have capsular extensions called the **trabeculae**, which provide support for blood vessels entering into the nodes.



*When lymph nodes become enlarged, the capsule is stretched and becomes painful*

The cortex is the outer, highly cellular part of the lymph node; it can be divided into an outer cortex and inner paracortex.



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**.

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)

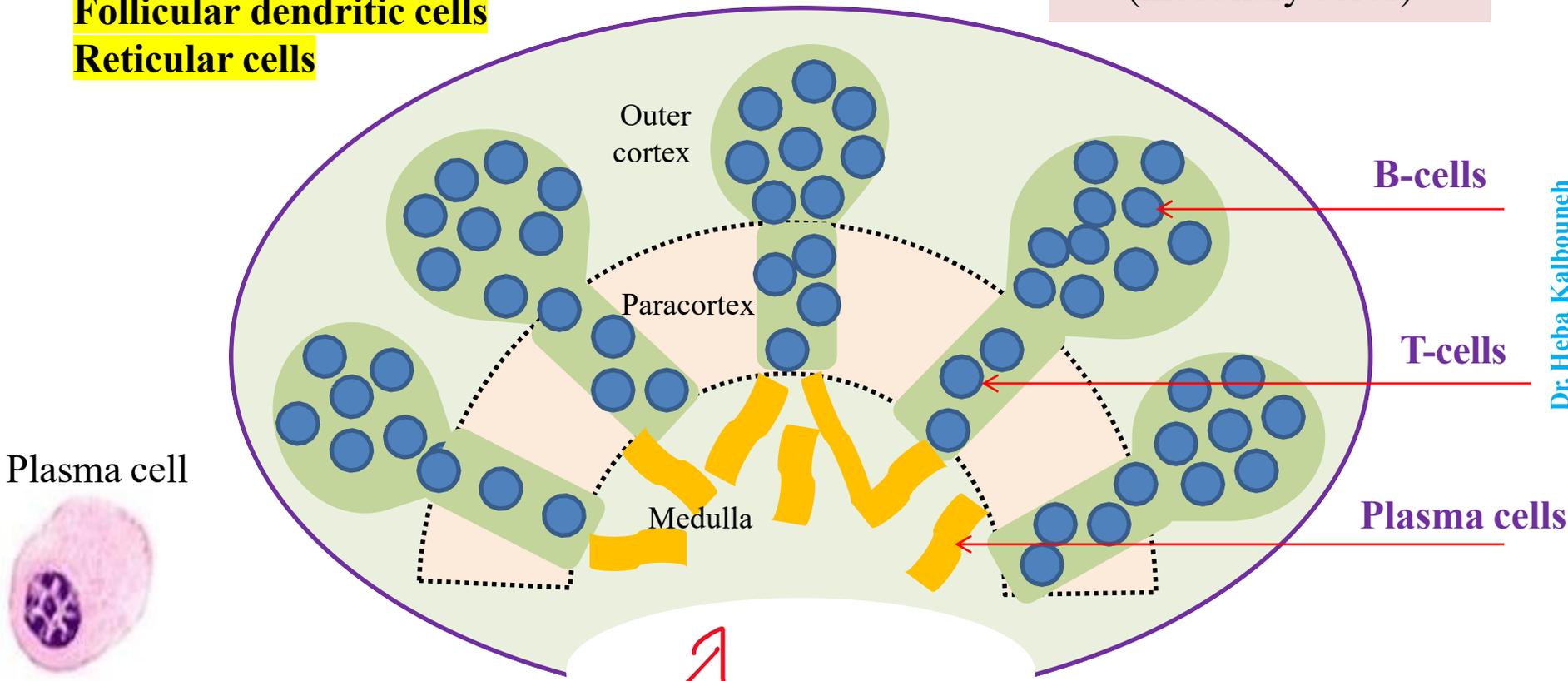
Other cells in the lymph node:

**Macrophages**

**Dendritic cells**

**Follicular dendritic cells**

**Reticular cells**

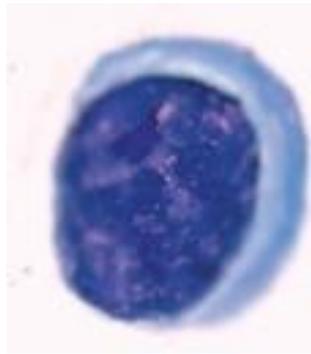


Plasma cell



Cartwheel  
Clock face appearance

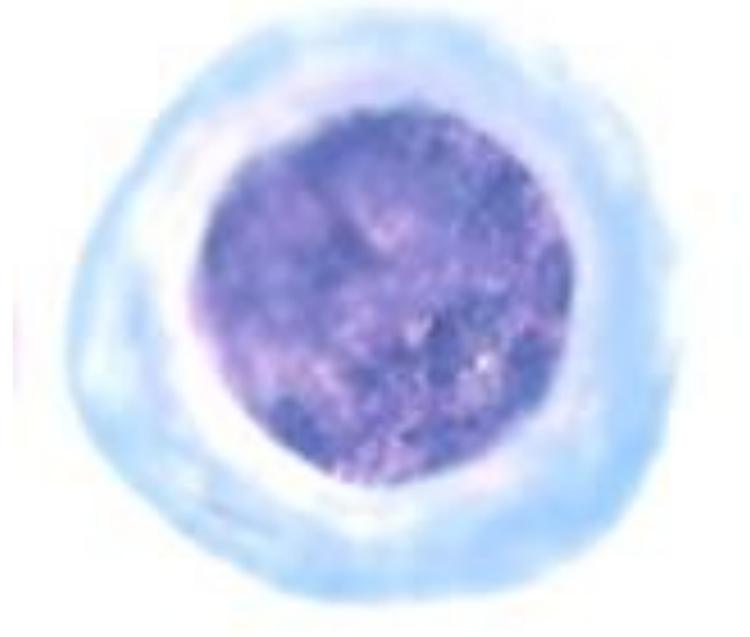
Plasma cells are located peripherally



Small  
(6-9  $\mu\text{m}$ )  
Inactive lymphocyte

Darkly stained cell

Appears basophilic  
Heterochromatic nucleus

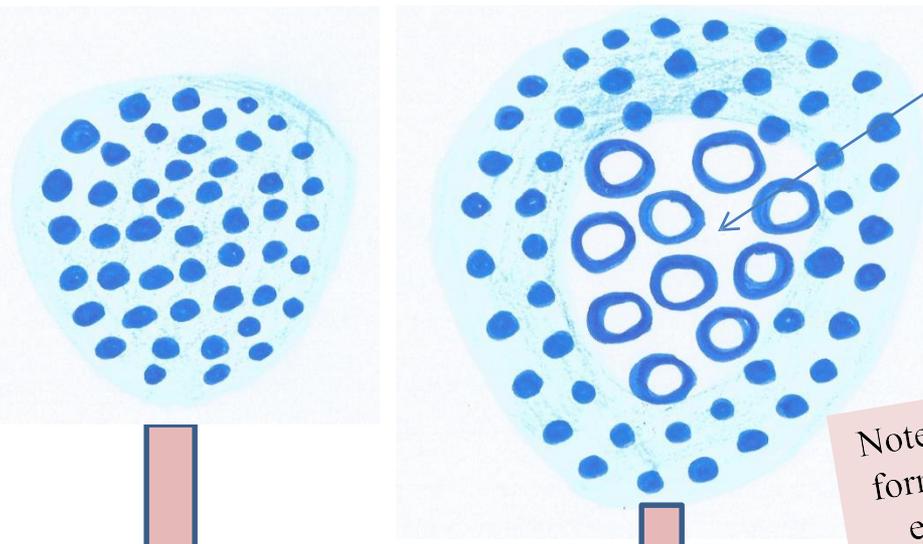


Large  
(9-18  $\mu\text{m}$ )  
Active lymphocyte

Lightly stained cell

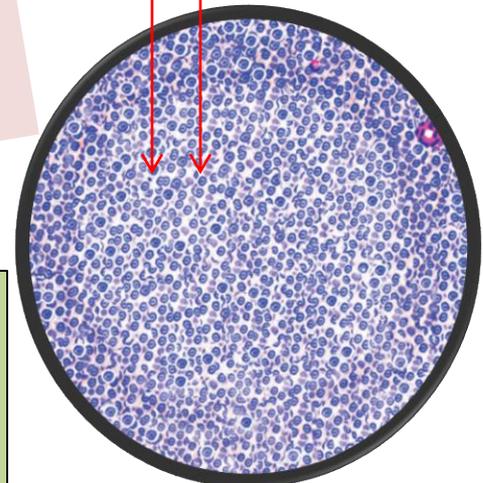
Appears lightly basophilic  
Euchromatic nucleus

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



The lighter staining areas are germinal centers, where the B-cells proliferate and activate into antibody secreting plasma cells and B memory cells

Note: Secondary follicles form **only** in response to exposure to antigens



**Primary follicles:** lymphoid follicles without a germinal center. (virgin B cells)

**Secondary follicles:** lymphoid follicles with a germinal center. Sites for B memory cell and plasma cell generation

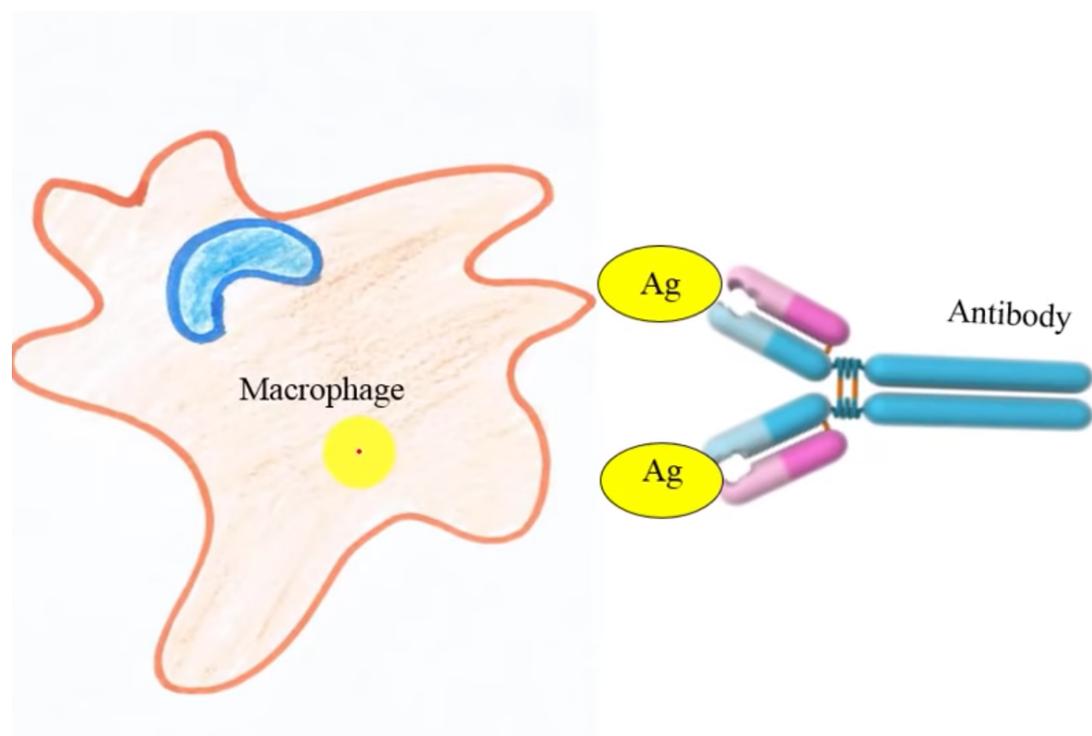


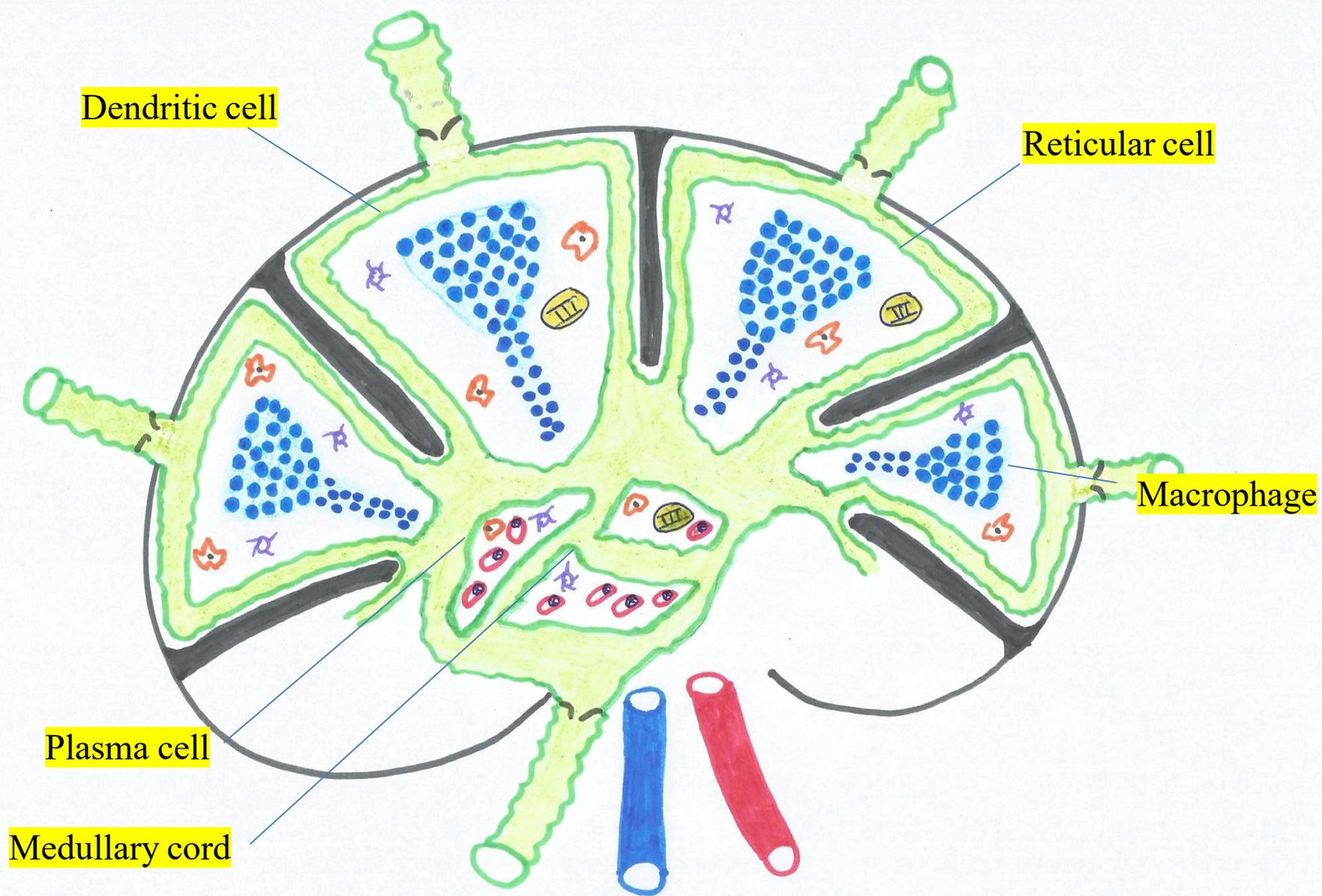
When activated by antigens (and T helper cells), B cells migrate to the center of the follicle, forming a germinal center. Germinal centers are the central regions of secondary follicles where activated B cells are proliferating (dividing by mitosis) and differentiating into plasma cells and memory B cells. When stimulated by antigens, lymph nodes enlarge due to the formation of germinal centers and B cell proliferation

Lymphatic follicle → Aggregation of B lymphocyte  
virgin cells → not yet exposed to antigen  
secondary follicle (activated , stimulated follicle )

The enlarged secondary follicle are the cause of lymph node enlargement in bacterial infections

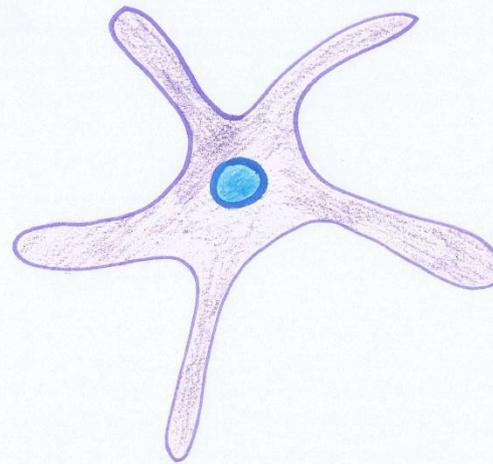
- After activation of B cells, germinal centers will be formed in the center of the follicle forming secondary follicles and these activated B cells are going to differentiate into plasma cells and memory cells.
- The plasma cells move from the germinal center in order to populate inside the medullary cords and then they secrete antibodies directly into the lymph, and this lymph leaves the lymph node through efferent vessels and eventually will reach the blood and circulate everywhere inside the body.
- At the infection site these antibodies form complexes with the antigens and these complexes are completely eliminated by the resident macrophages or the recruited macrophages (monocytes)







Macrophage

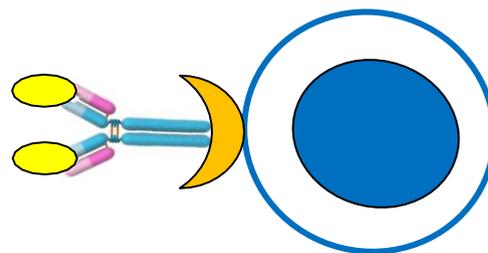


Dendritic cell

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

	Macrophage	Dendritic cell	Follicular dendritic cell
<b>Phagocytosis</b>	Most phagocytic	Moderately phagocytic	X
<b>Antigen presenting (via MHC-II)</b>	Moderate Ag-presenter	Very powerful Ag-presenter	X
<b>Location in lymph node</b>	Cortex and medulla	Cortex and medulla	Outer cortex

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Are antigen **HOLDING** cells  
Holds the Ag for long time

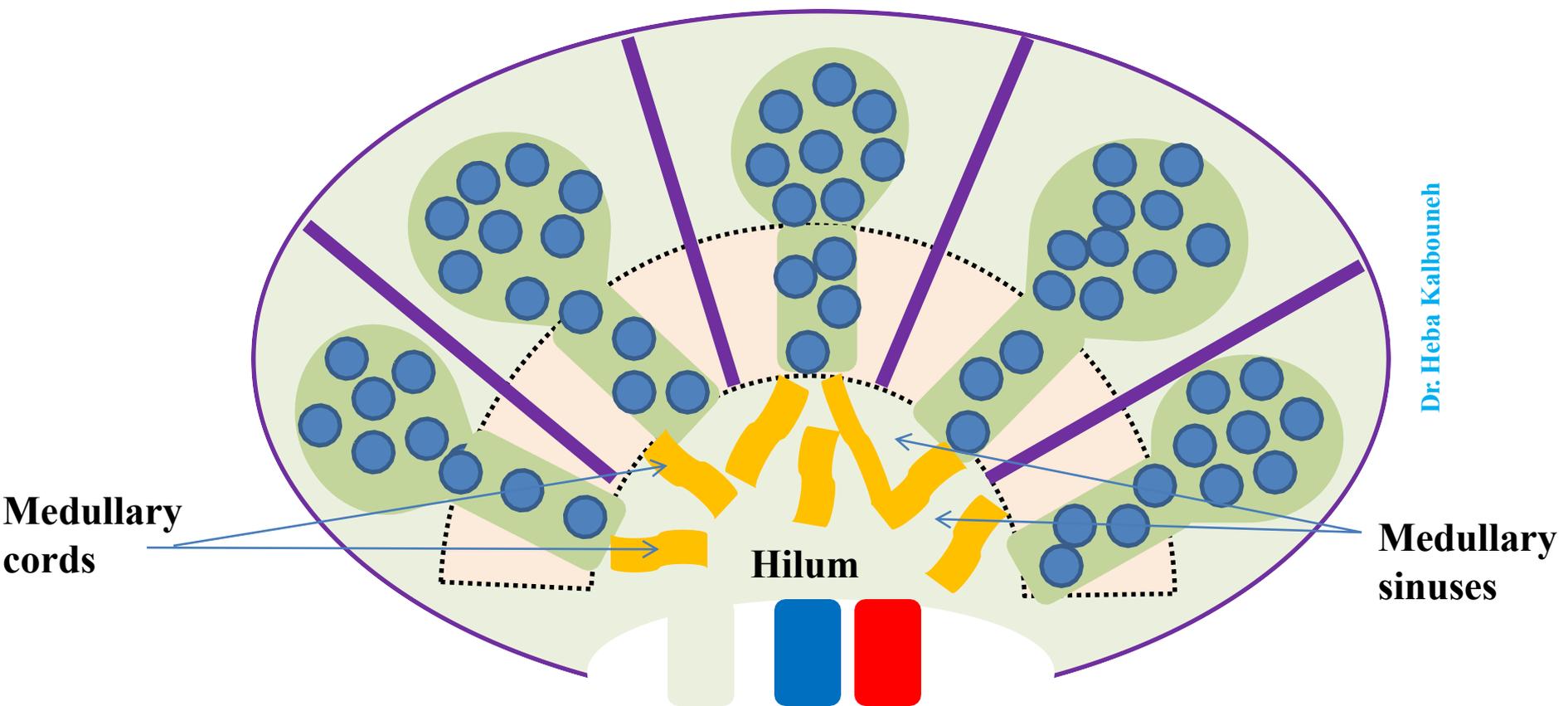
These cells are not phagocytic cells, instead these cells have special receptors for Ag-Ab complexes, so that after the infection is eliminated they hold these complexes to keep our immune system active and in a semi-stimulated state.

The **medulla** is the deep, cavitated part of the lymph node; it is composed of **medullary cords**

The cords are separated by spaces known as **medullary sinuses**

The medullary sinuses converge at the **hilum**.

The hilum is a slight indentation on one side of the node. Here, an artery, vein, and an efferent lymphatic vessel enter and leave the node.



The paracortex can also be called, thymus dependent zone so if there is a defect in the thymus this zone will be underdeveloped --> can't defend intracellular pathogens

## Afferent vessels 1

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 2

Each afferent vessel empties into the subcapsular sinus.

## Trabecular sinuses 3

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

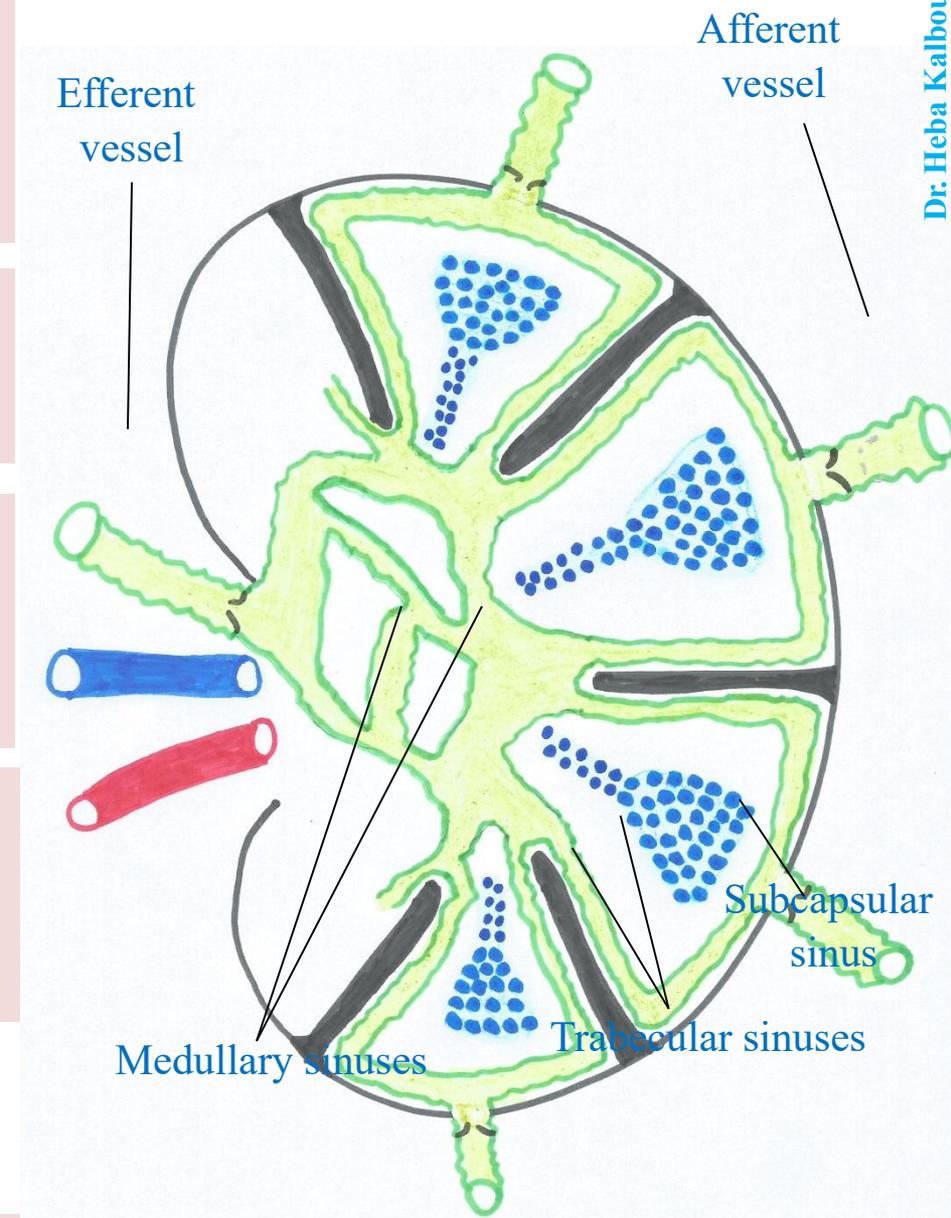
## Medullary sinuses 4

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

## Efferent vessels 5

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.

## How lymph moves in a lymph node

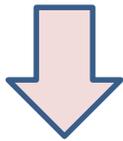


**Sinuses are irregular spaces through which the lymph percolates**

## Lymph flow

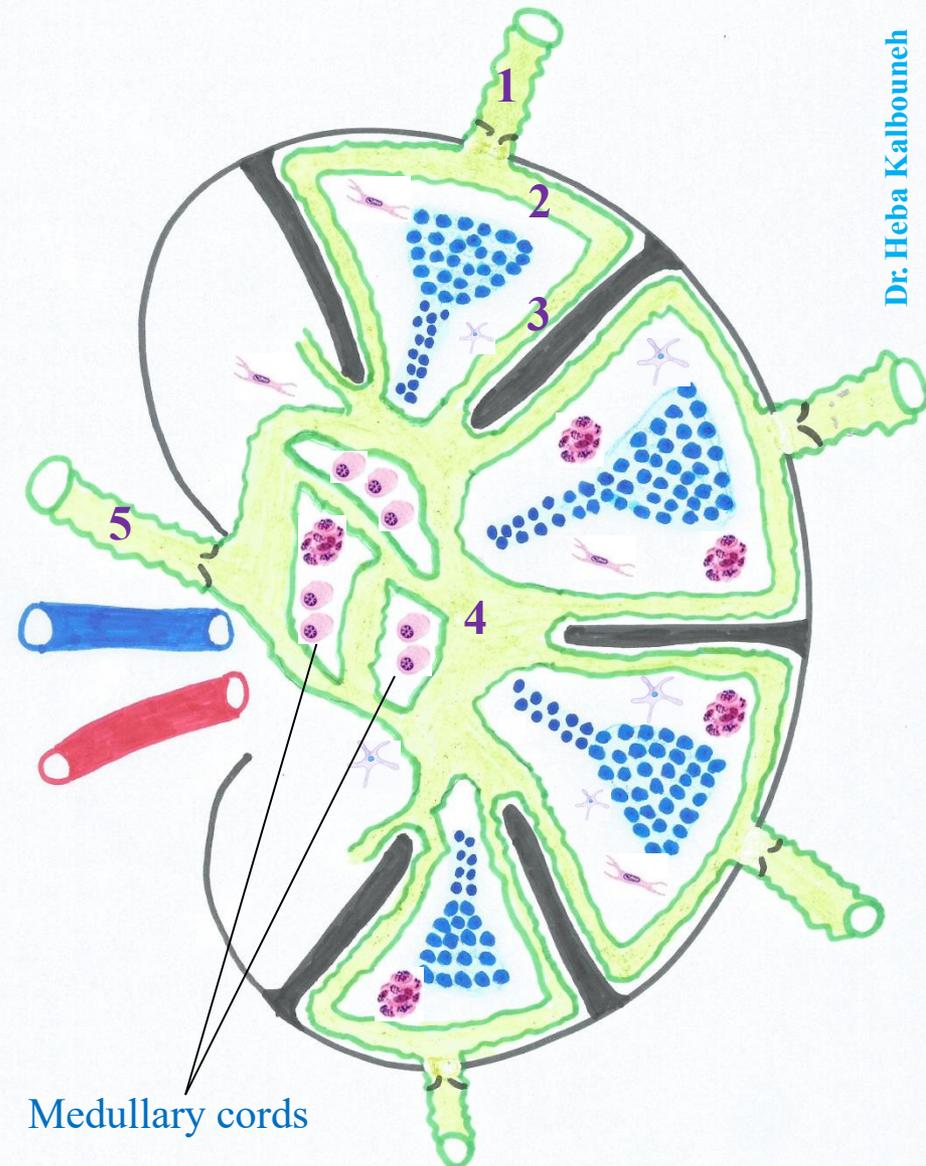
Lymph nodes are linked together by lymphatic vessels. Lymph flows through a lymph node via a series of sinuses and lymphatic tissue

**Lymph**, containing micro-organisms, soluble antigens and antigen presenting cells, enters the lymph node via **afferent lymphatic vessels (1)** which enter the **subcapsular sinus (2)**. It then runs through **trabecular (cortical) sinuses (3)** then into **medullary sinuses (4)** and leaves through the **efferent lymphatic vessels (5)**, at the **Hilum** as **efferent lymph**.

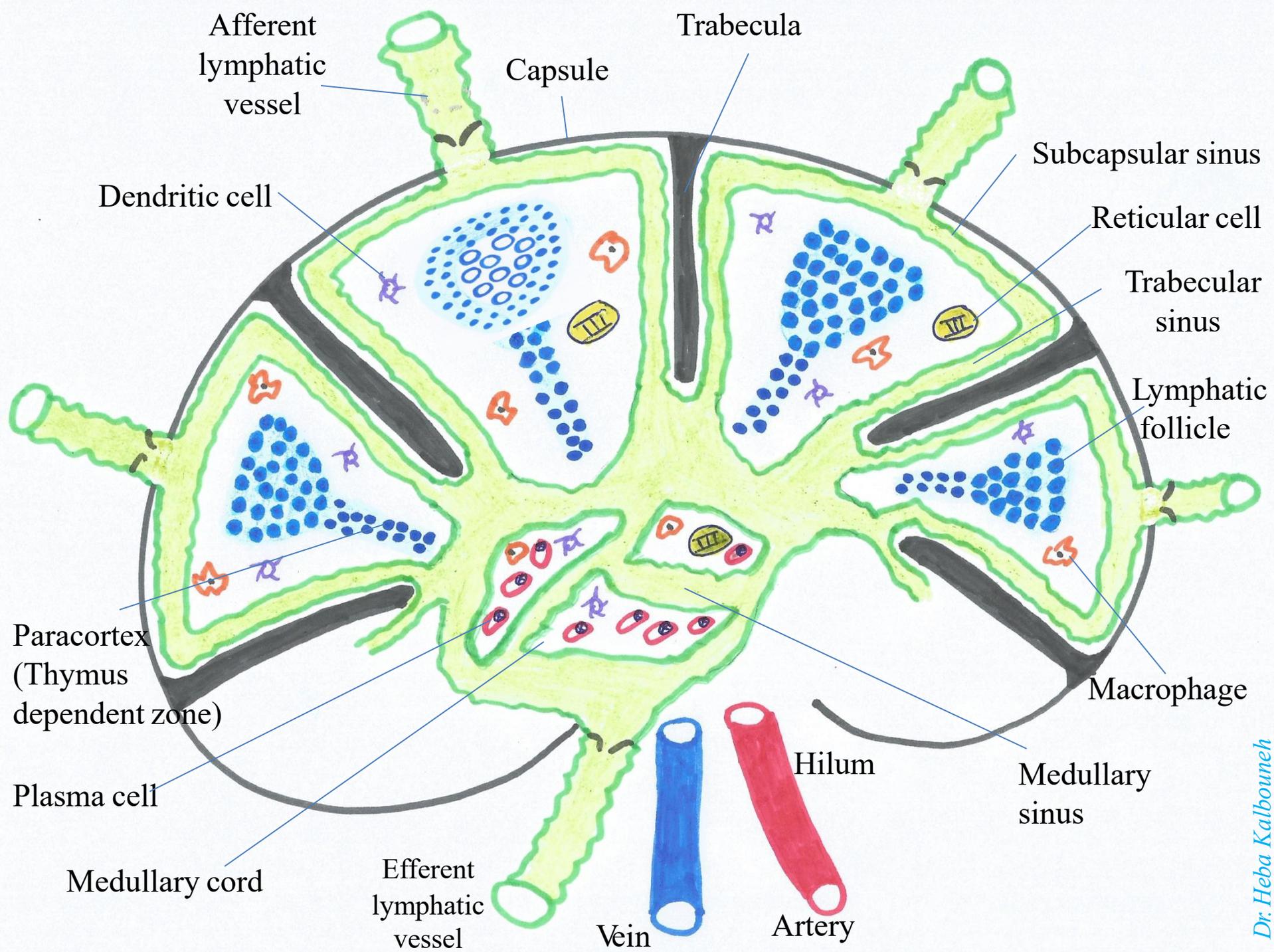


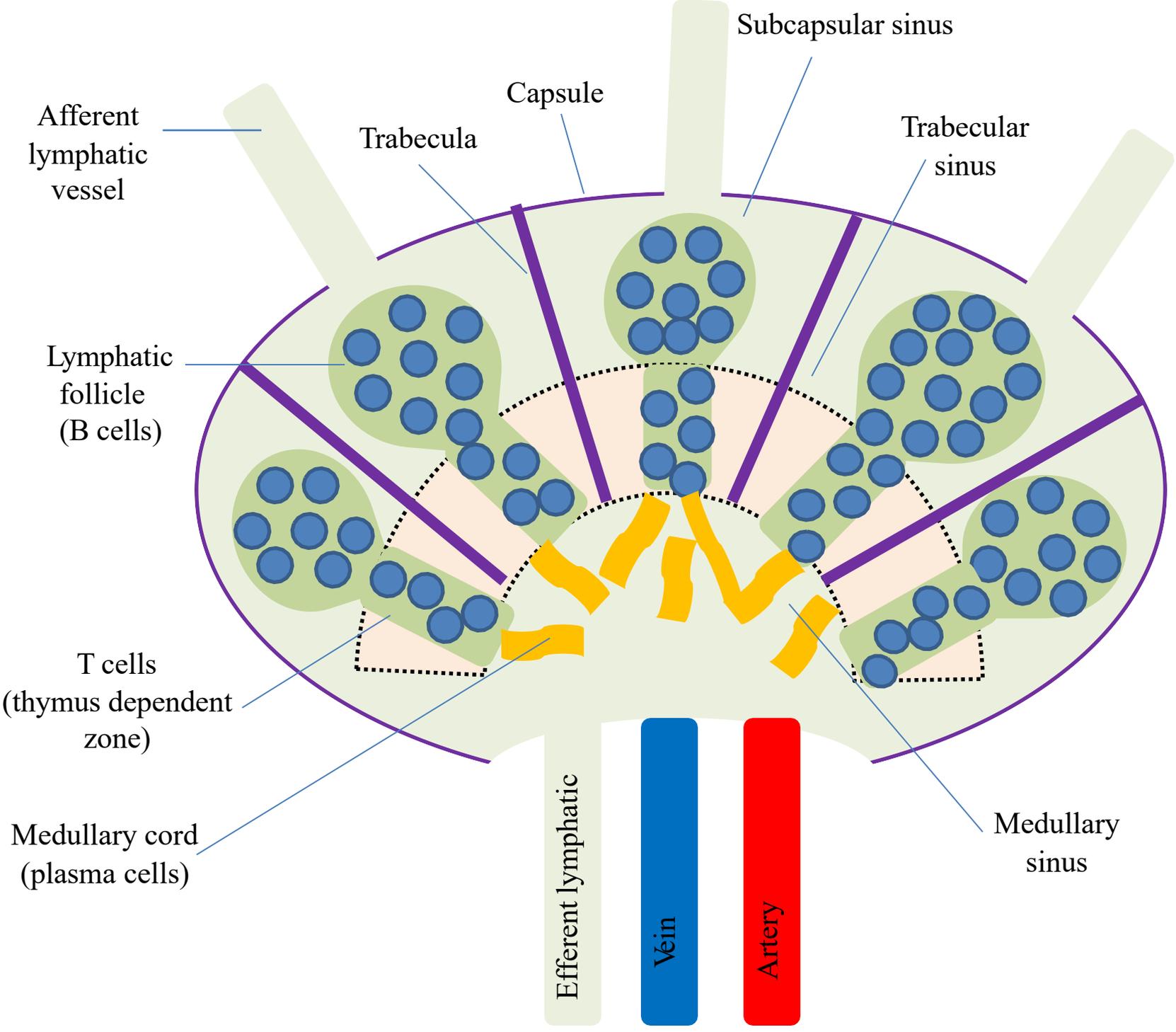
**Efferent lymph** contains lots of activated T-lymphocytes, activated B-lymphocytes, plasma cells and antibodies.

Lymph slows down when it passes in lymph nodes.



All the **lymphatic sinuses** are lined by a discontinuous layer of simple squamous endothelium





## Lymphocytes can enter lymphoid tissues in two ways:

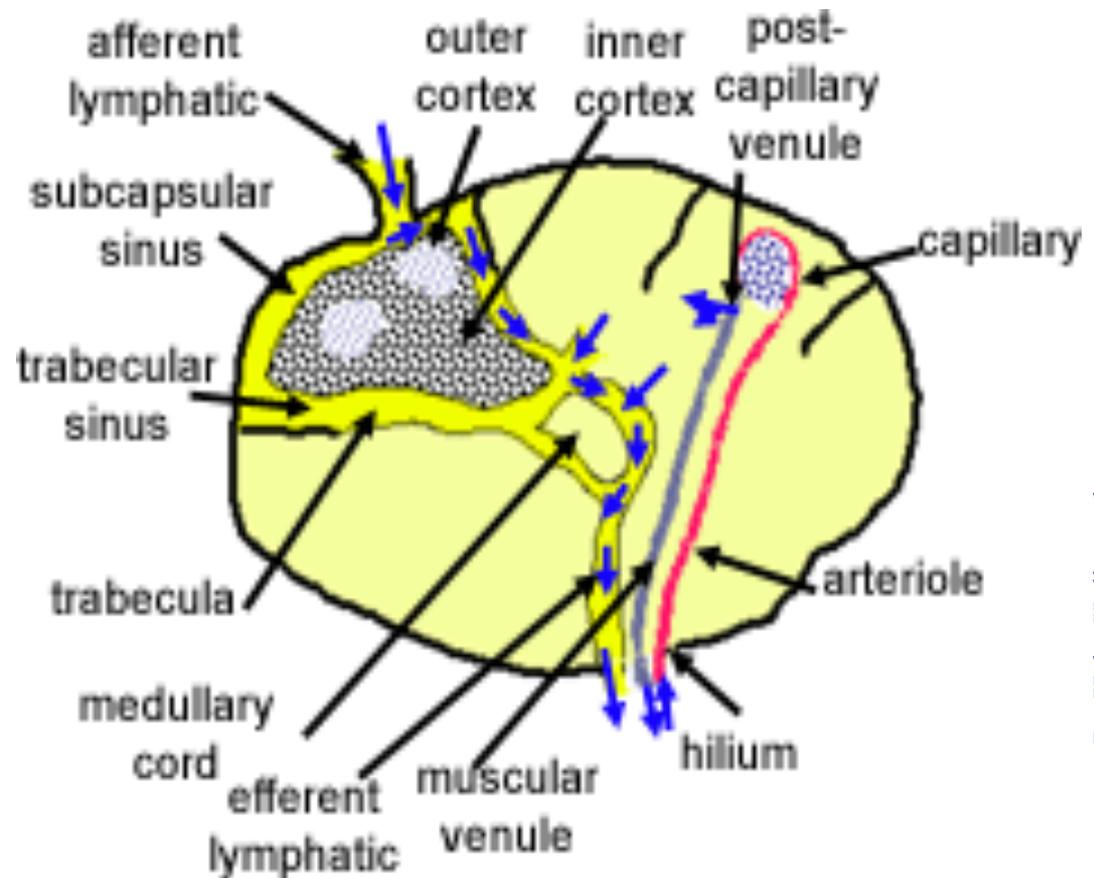
- 1) Direct entry into lymph nodes via afferent lymphatics
- 2) Entry from blood capillaries across specialized endothelial cells present in the postcapillary venules (High Endothelial Venules= HEV) within the **paracortex** of the lymph node

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



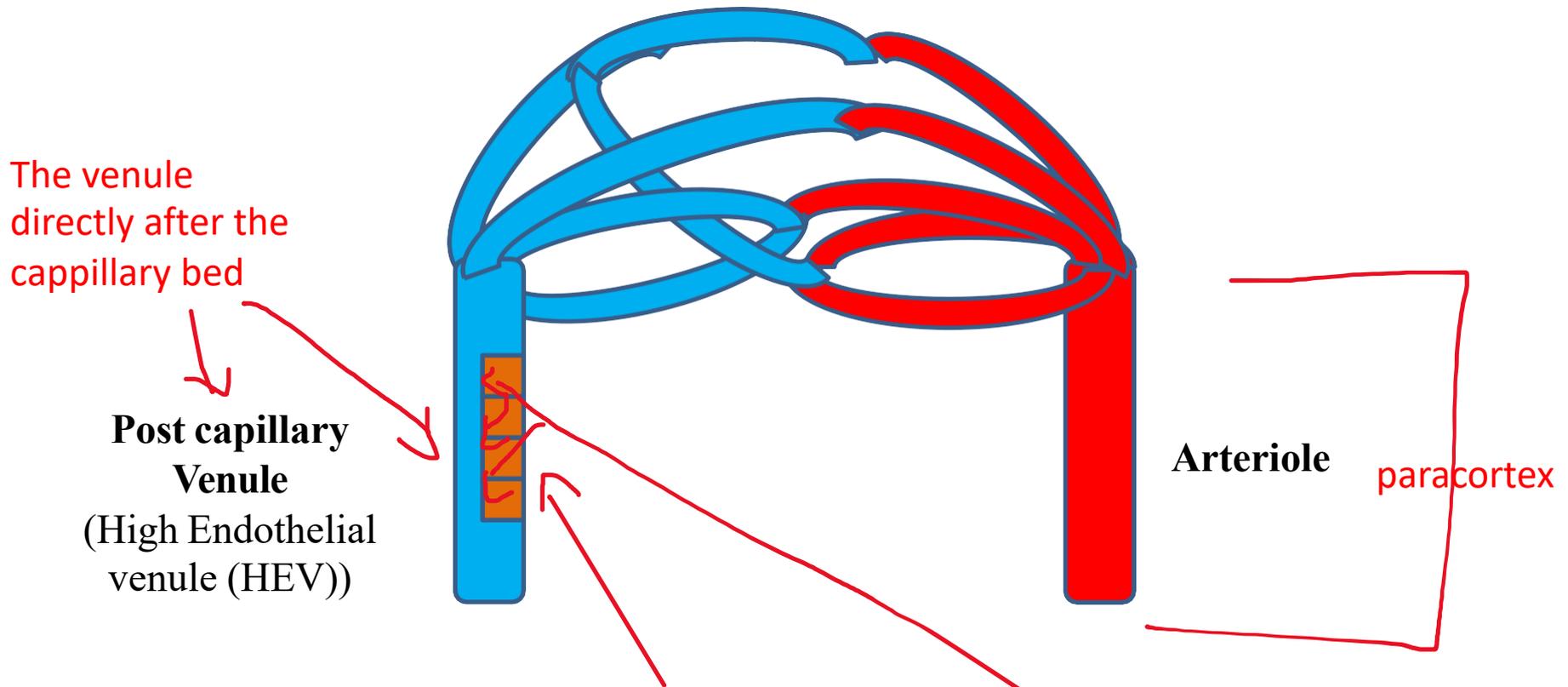
The structure of the post-capillary venule, in the paracortex is unusual in that it is not lined by simple squamous epithelium, but by a **simple cuboidal epithelium**. These are called high endothelial venules (HEVs) Lymphocytes recognize and adhere to these endothelial cells, and squeeze through them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

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



The venule directly after the capillary bed

**Post capillary Venule**  
(High Endothelial venule (HEV))

**Arteriole** paracortex

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The lining epithelium is simple cuboidal epithelium instead of simple squamous epithelium so we call them high endothelial venules

Adressins (ligand on the apical surface) that attach to the homing receptors on lymphocytes

T cells enter through the HEV and stay there because it is in the paracortex, but B cells migrate to the primary follicle

## Lymphatic trunks and ducts

All lymphatic vessels coalesce to form larger trunks which eventually converge to form the right lymphatic duct and the thoracic duct

### Right lymphatic duct

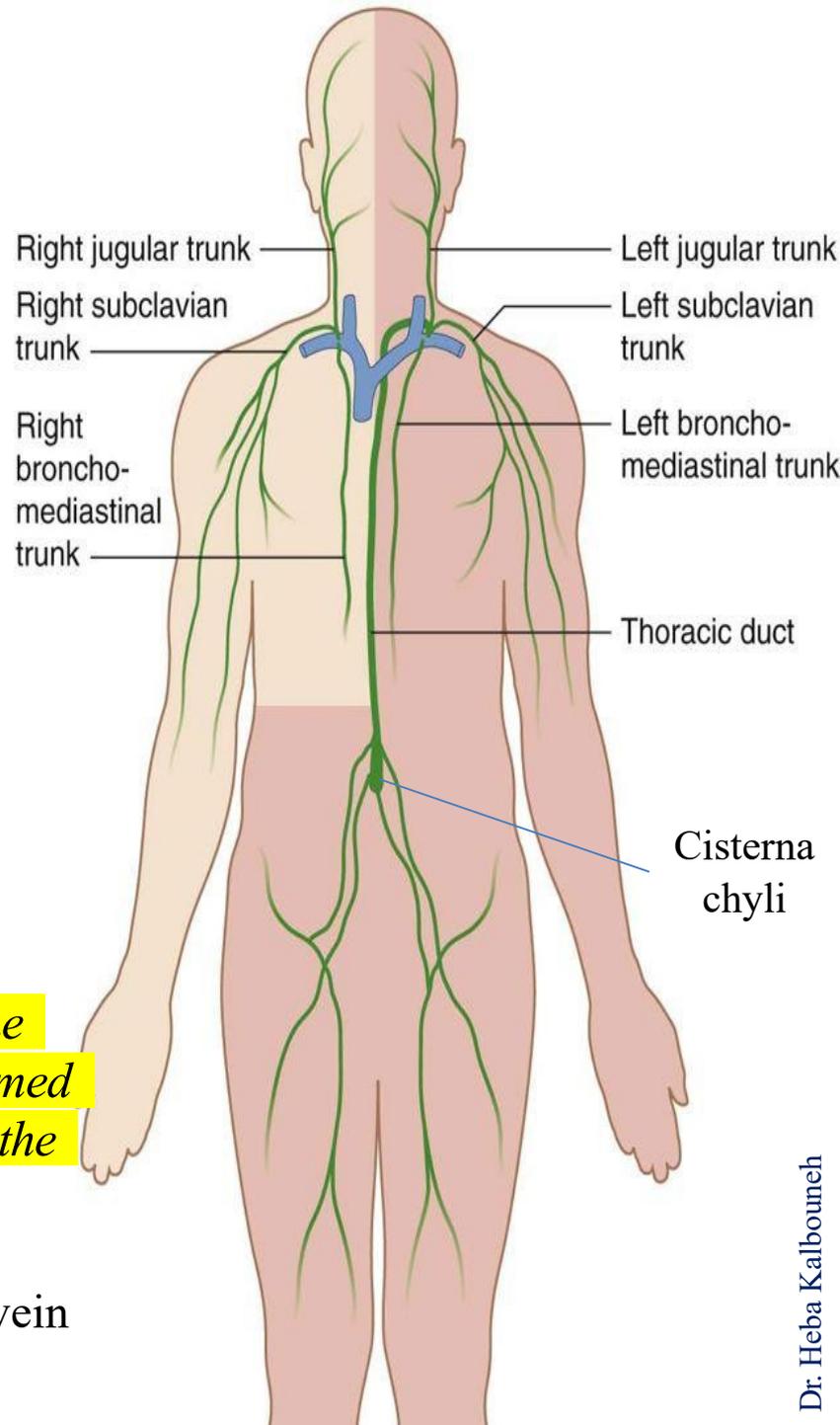
- ✓ Is formed by right jugular and right subclavian trunks
- ✓ Drains lymph from the upper right quadrant of the body (the right side of the head and neck, the right side of the thorax and the right upper limb)
- ✓ Empties into the junction where right internal jugular vein joins the right subclavian vein (Rt venous angle)

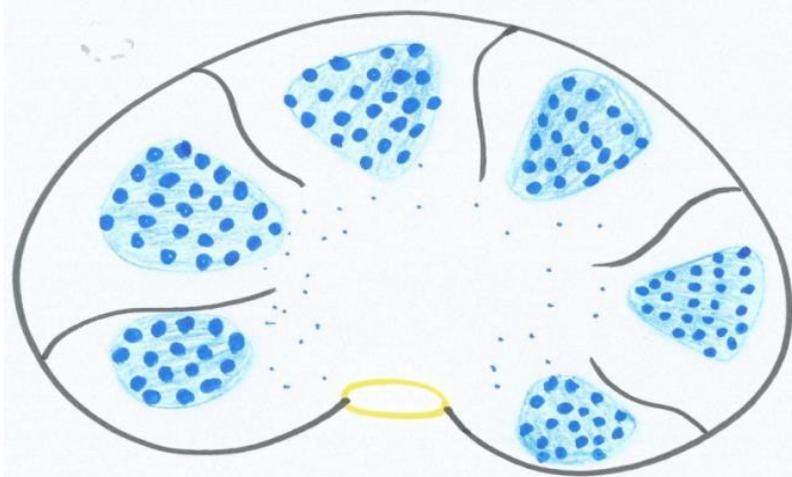
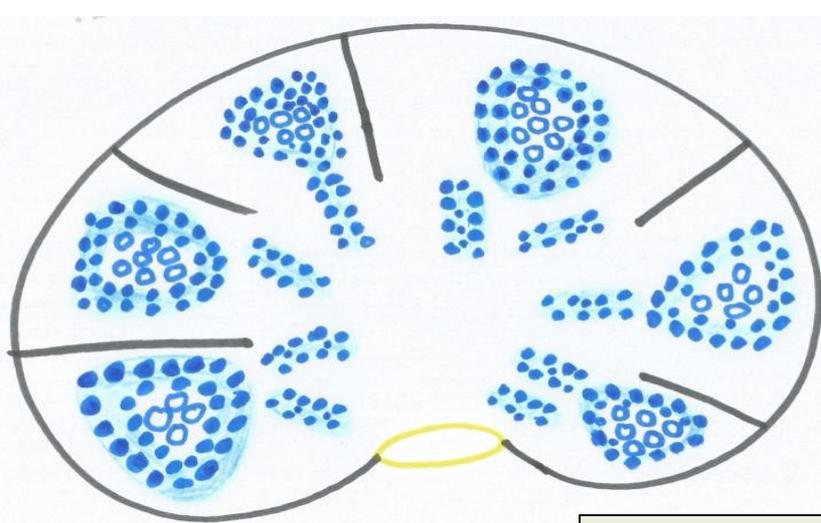
### Thoracic duct (Left lymphatic duct)

- ✓ Is larger and drains lymph from the rest of the body.
- ✓ Originates in the abdomen as cisterna chyli

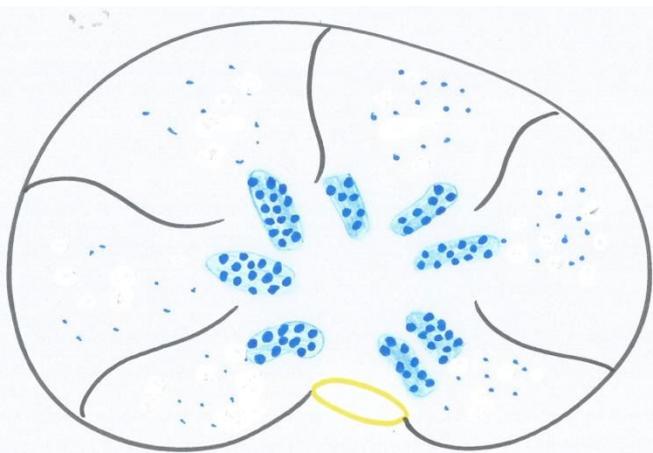
*Cisterna chyli is a dilated sac at the lower end of the thoracic duct (anterior to the bodies of L1 and L2) formed by confluence of the right and left lumbar trunks and the intestinal trunk*

- ✓ Passes through the diaphragm at the aortic aperture
- ✓ Empties into the junction where left internal jugular vein joins the left subclavian vein (Lt venous angle)





Try to describe these histological sections and the clinical picture a patient would have in each case



Answered in the next lecture

