Histology - HLS

Done By

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Lymphatic System

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Spleen

Don't memorize numbers

The lymph is formed inside this organ and drained from this organ by efferent lymphatic vessels (we don't have afferent lymphatic vessels)

✓The spleen is an oval-shaped **intraperitoneal** organ

✓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**

✓Has a notched anterior border.

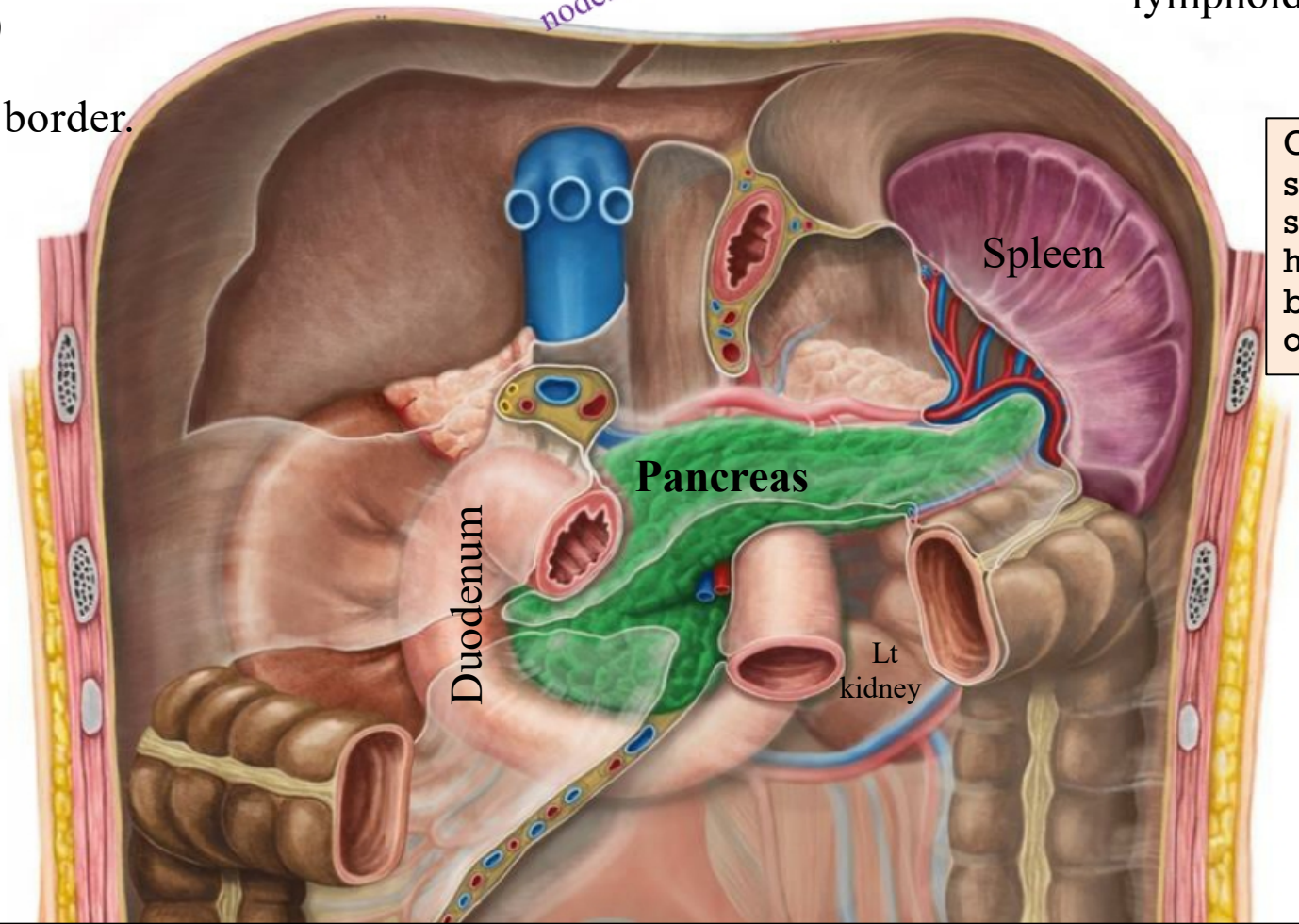
The spleen is the organ of odds number 1, 3, 5, 7, 9 , and11

The spleen resembles a large lymph node

The spleen filters the blood while lymph nodes filter the lymph

✓It lies high on the upper left portion of the abdomen, just beneath the diaphragm, behind the stomach and above the left kidney.

✓It is the largest of the lymphoid organs



On the medial surface of the spleen we have the hilum from where blood vessels enter or leave the spleen

Lymphatic or immunological function

Hematological function

Functions

✓Filtration of blood (defense against blood-borne antigens)

✓The main site of old RBCs destruction.

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

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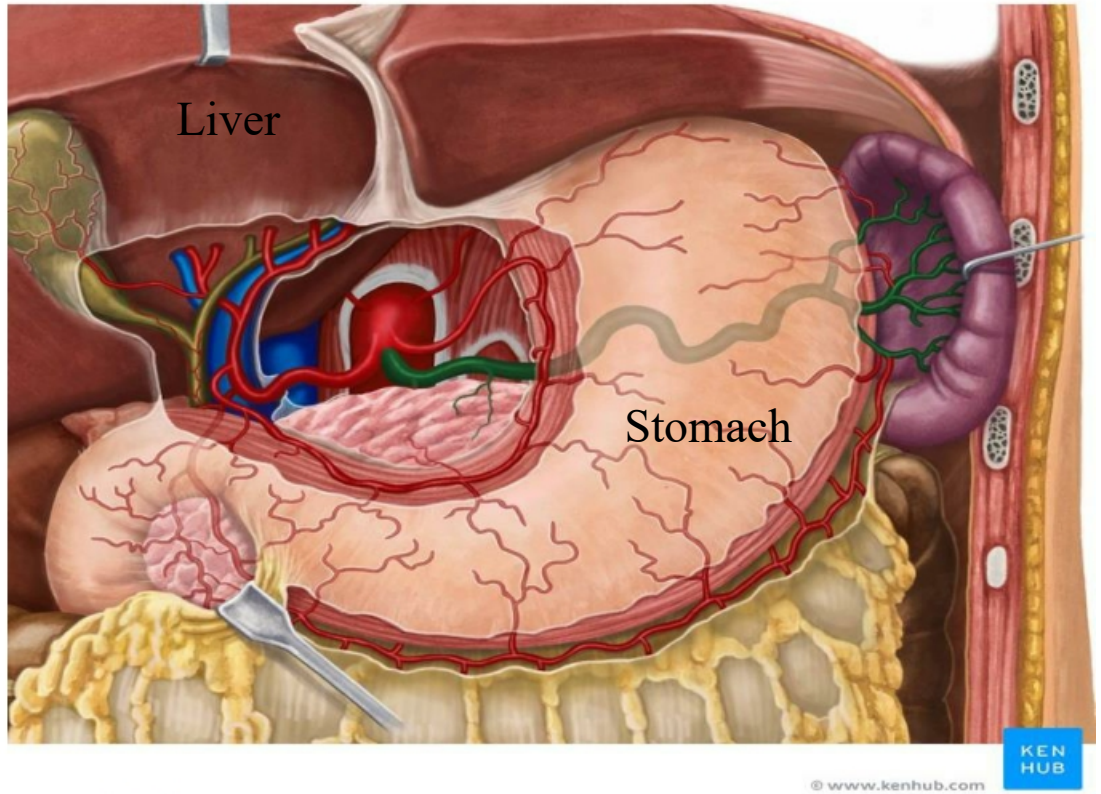
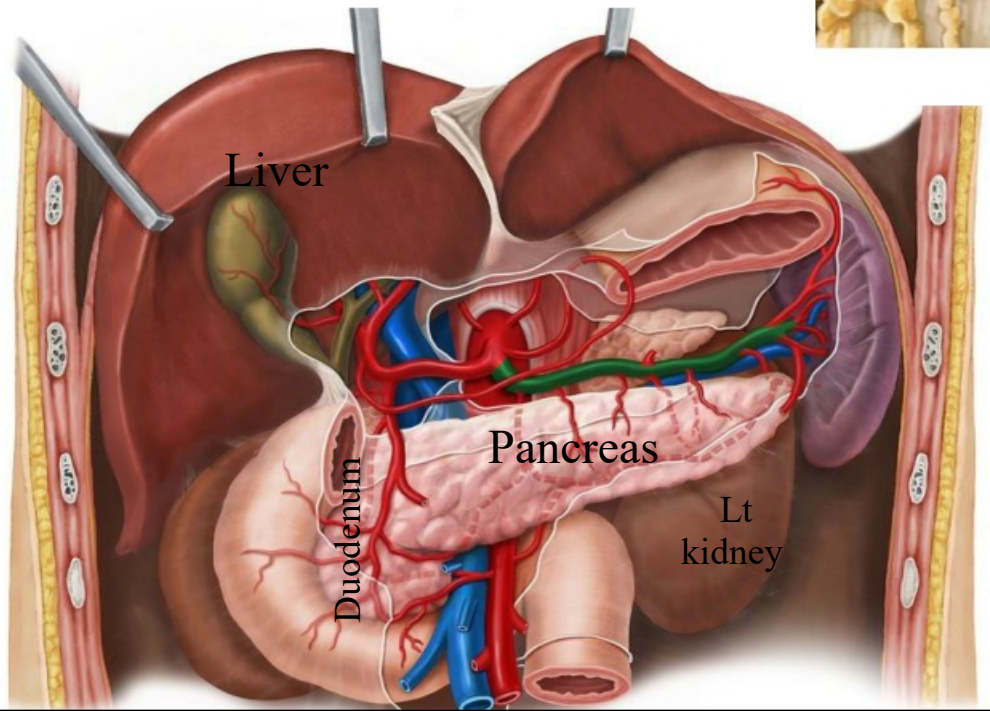
The **splenic artery** is the largest branch of the celiac artery. It has a tortuous course as it runs along the upper border of the pancreas. The splenic artery then divides into about six branches, which enter the spleen at the hilum and here it divides into many branches to supply oxygenated blood into spleen .



The **splenic artery** supplies the spleen as well as large parts of the stomach and pancreas



Abdominal Aorta

⇩

Celiac Trunk

⇩

Splenic artery

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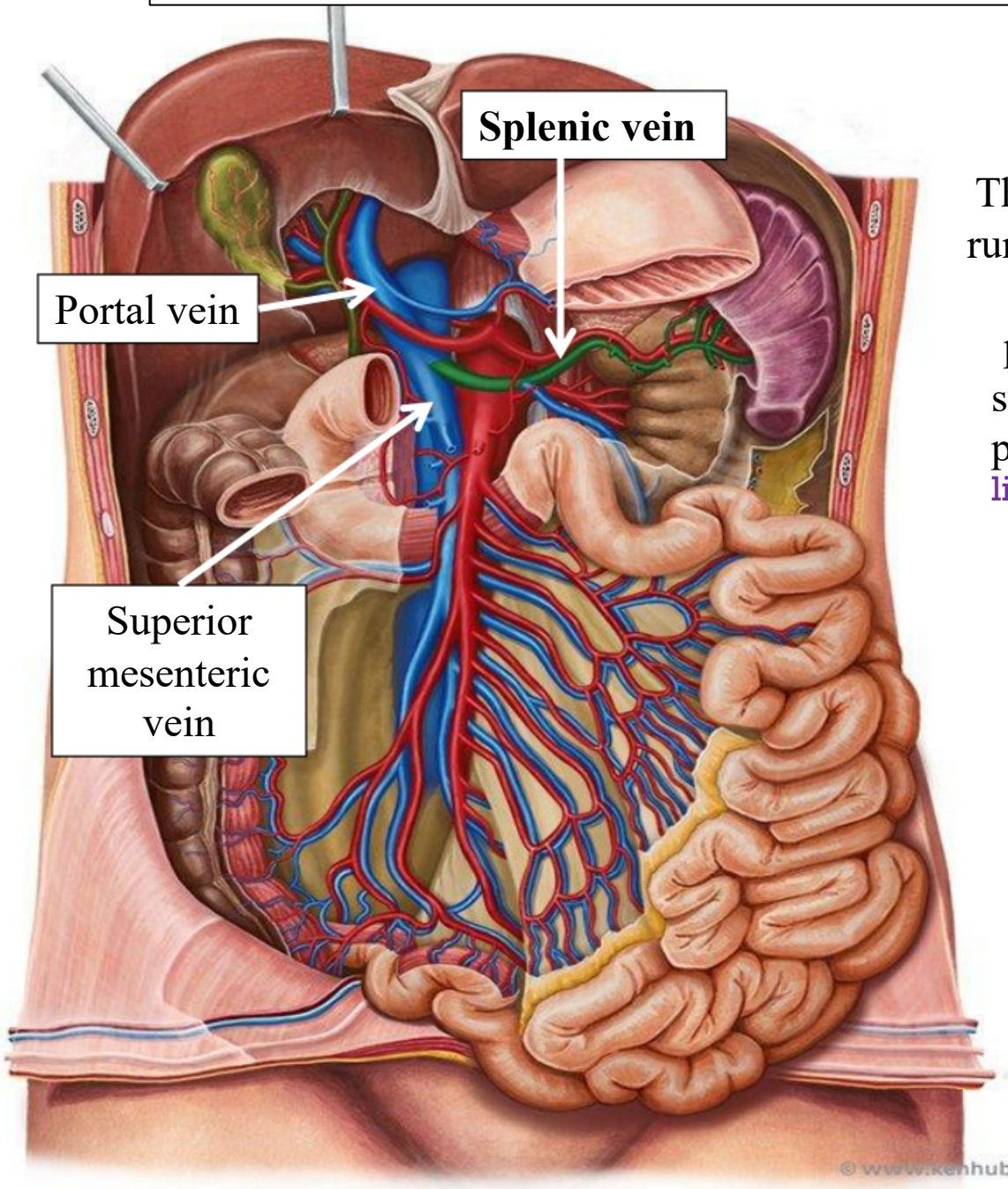
Inferior mesenteric vein drains into splenic vein



The **splenic vein** leaves the hilum and runs behind the tail and the body of the pancreas. Behind the neck of the pancreas, the splenic vein joins the superior mesenteric vein to form the portal vein (portal vein enters the liver through porta hepatis)

In cases of portal hypertension, spleen often enlarges from venous congestion.

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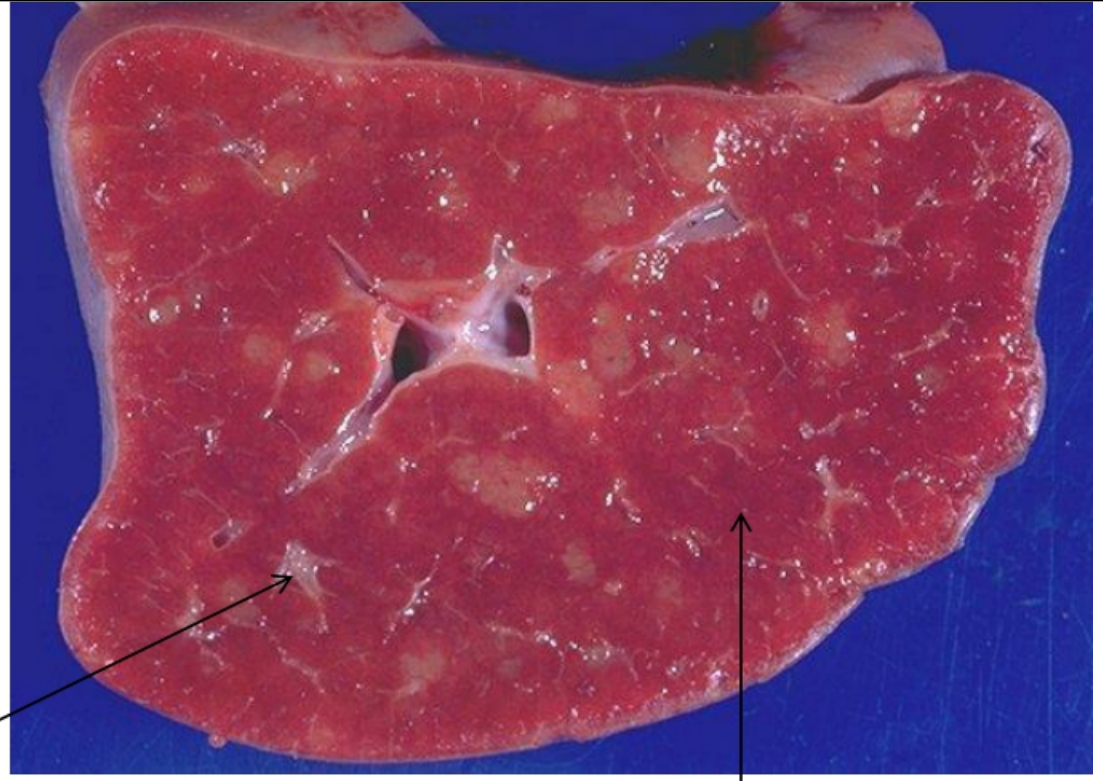
The parenchyma of the spleen appears in fresh specimen as:

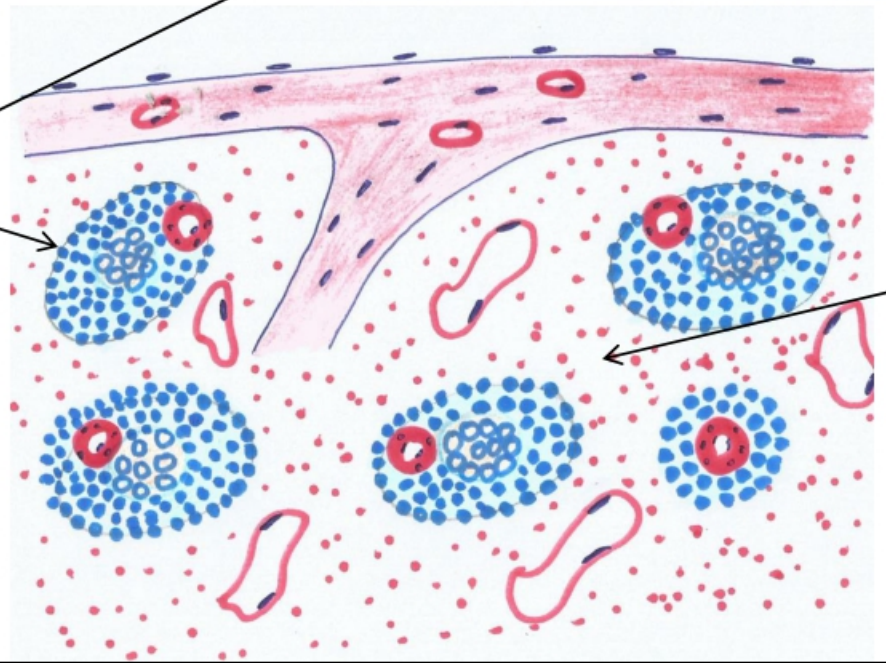
Condensation of WBCs in particular lymphocytes

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)



Stroma of spleen is formed by reticular tissue



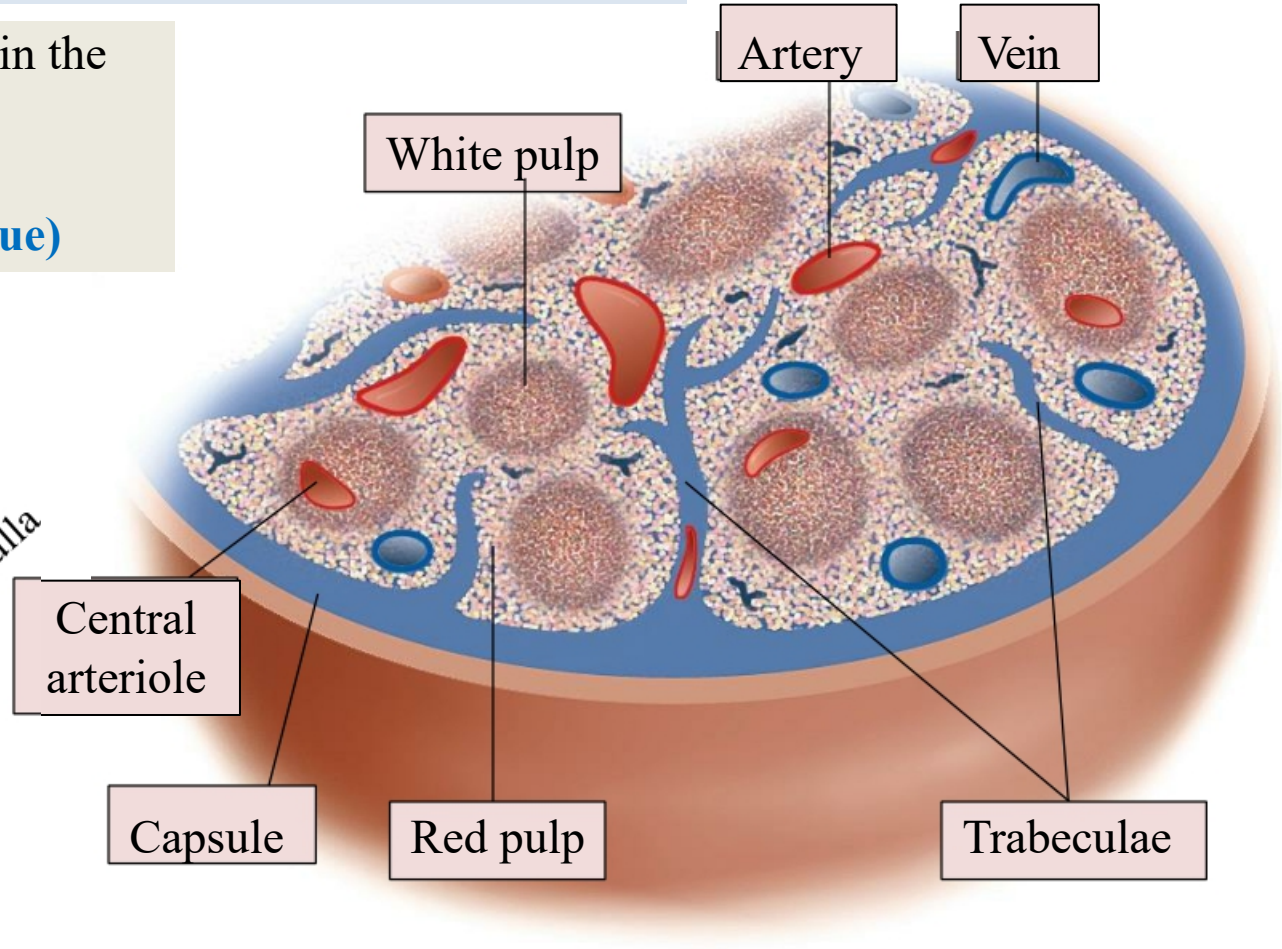
The spleen is covered by a **capsule** of dense connective tissue, and have capsular extensions called the **trabeculae** (to divide the spleen into smaller compartments)

Large trabeculae originate at the hilum, on the medial surface of the spleen, and carry branches of the splenic artery, vein, lymphatics, and nerves into the spleen

The spleen is composed of parenchyma and stroma
Parenchyma: Splenic pulps
Stroma: Reticular tissue (reticular fibers and reticular cells)

There are two types of pulp in the spleen:
Red pulp (rich in blood)
White pulp (lymphatic tissue)

Unlike lymph nodes, the spleen:
1- Has no afferent lymphatics
2- Has no lymphatic sinus system
3- Its lymphatic tissue is not arranged into cortex and medulla



Splenic artery
Divides into trabecular arteries as it enters the hilum

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. (Aggregation of T lymphocytes) >> so central arteriole locates at the center of the sheath

Penicillar arterioles The morphology is like penicillus
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.

Terminal capillaries (Sheathed capillaries)
Some of these terminal capillaries are sheathed with APCs (macrophages) for additional immune surveillance of blood

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

Most of the RBCs pass through this route

Closed circulation: the capillaries open directly into the splenic sinusoids (blood is enclosed by endothelium)

Splenic sinusoids
↓
Trabecular veins
↓
Splenic vein

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White pulp (lymphoid tissue)

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

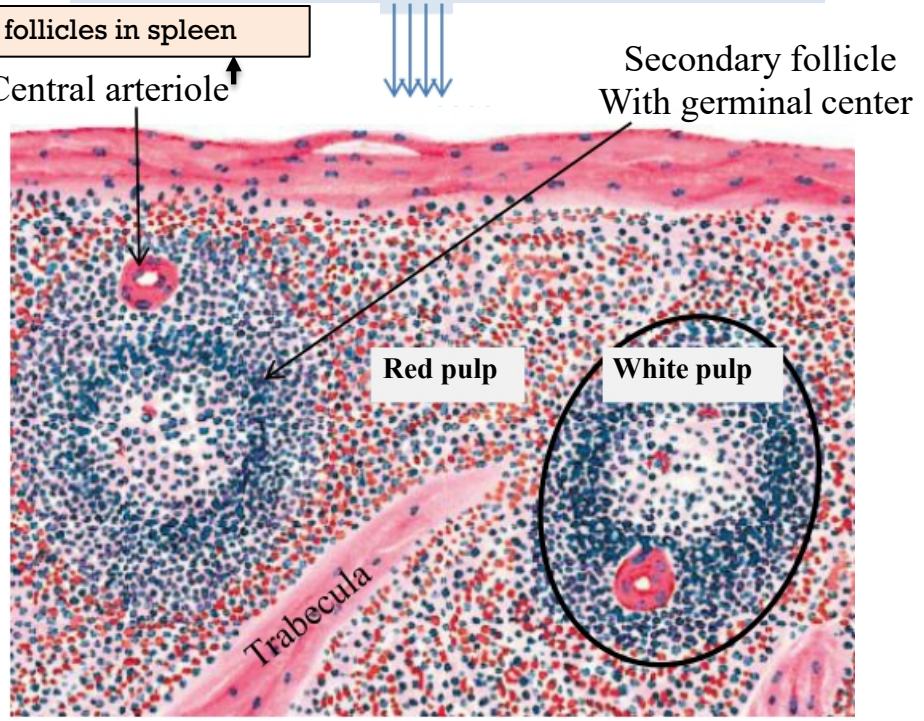
✓The white pulp contains:

Periarteriolar lymphatic sheaths (PALS):

tightly packed T cells arranged in cylindrical sheaths around central arterioles

- PALS is equivalent to paracortex of the lymph node so it's thymus dependent zone , the presence of mature immunocompetent T lymphocytes depends on the normal development of thymus
- Along the pathway of the central arteriole , a lymphatic follicle appears displacing the central arteriole into more peripheral location but still called central or in some books it's called follicular arteriole

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).



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)

If you section the spleen and you see all lymphatic follicles are stimulated so you know that this patient is infected , in particular with an infection caused by blood borne antigens such as capsulated bacteria causing septicemia

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.

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

Red pulp (blood filled)

✓Constituting 75% of the spleen, the red pulp is responsible for the hematological (circulatory) function of the spleen.

✓The red pulp contains :

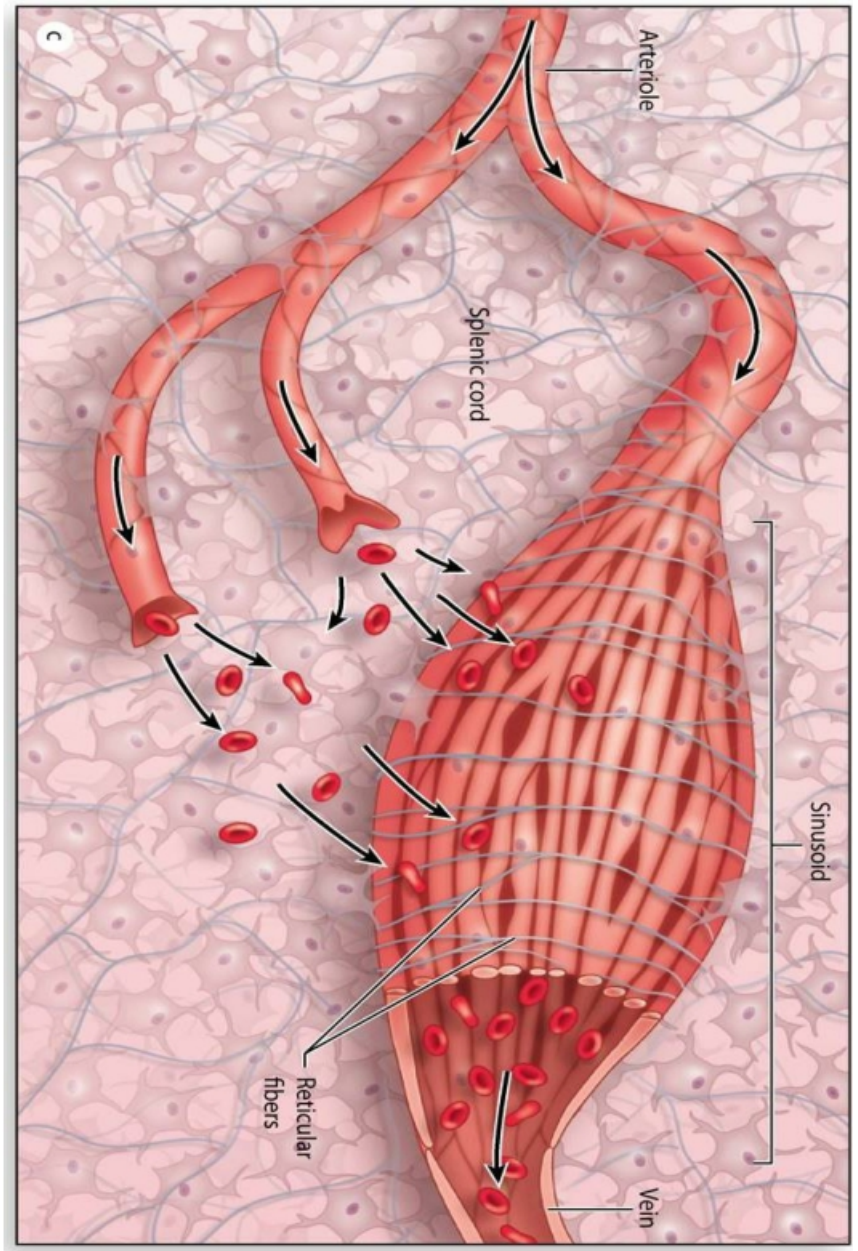
Splenic cords (Billroth's cords): consist of all cells between the sinusoids in the red pulp (reticular cells, macrophages, plasma cells, lymphocytes, RBCs, platelets, other leukocytes)

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

↓↓**Red pulp**



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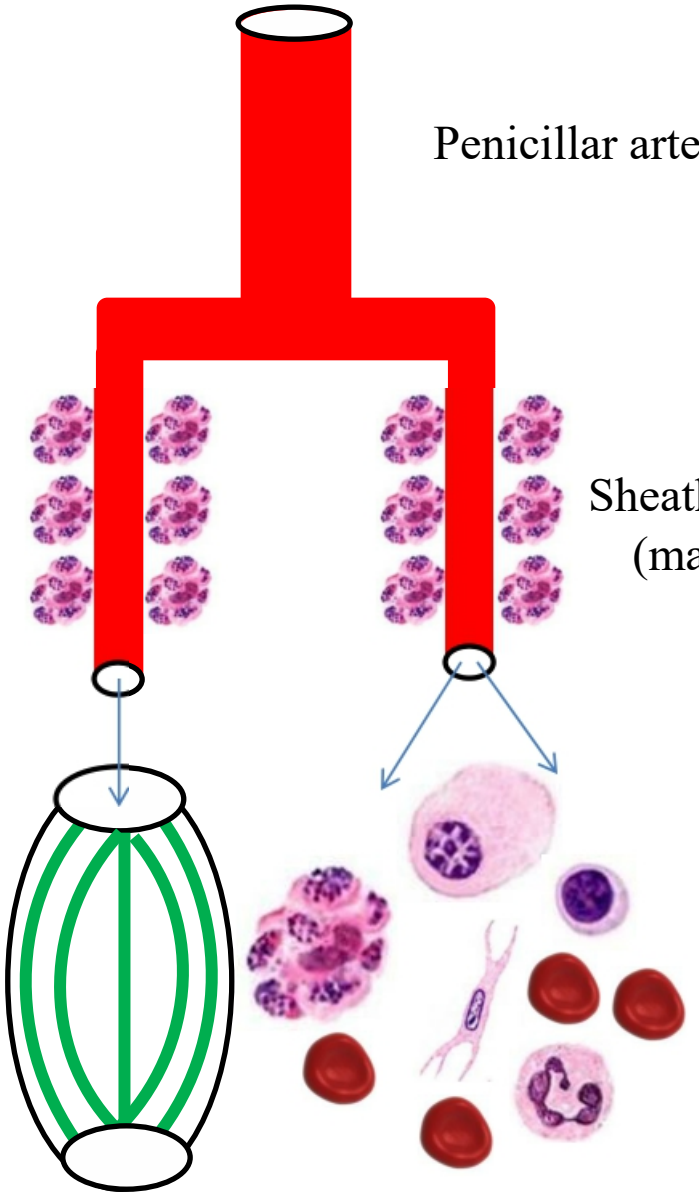

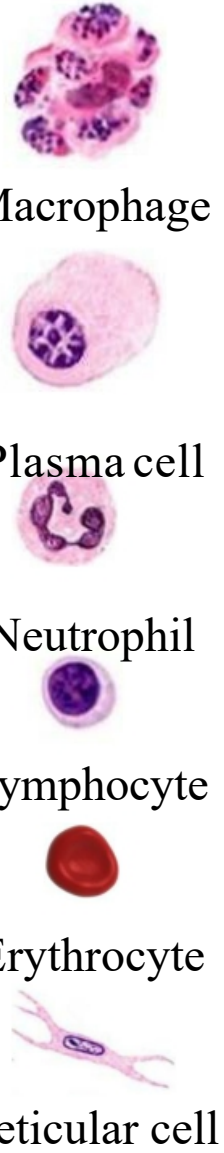

Note: When B cells in the primary follicles are exposed to Antigen, they proliferate and differentiate to plasma cells and move toward the red pulp.

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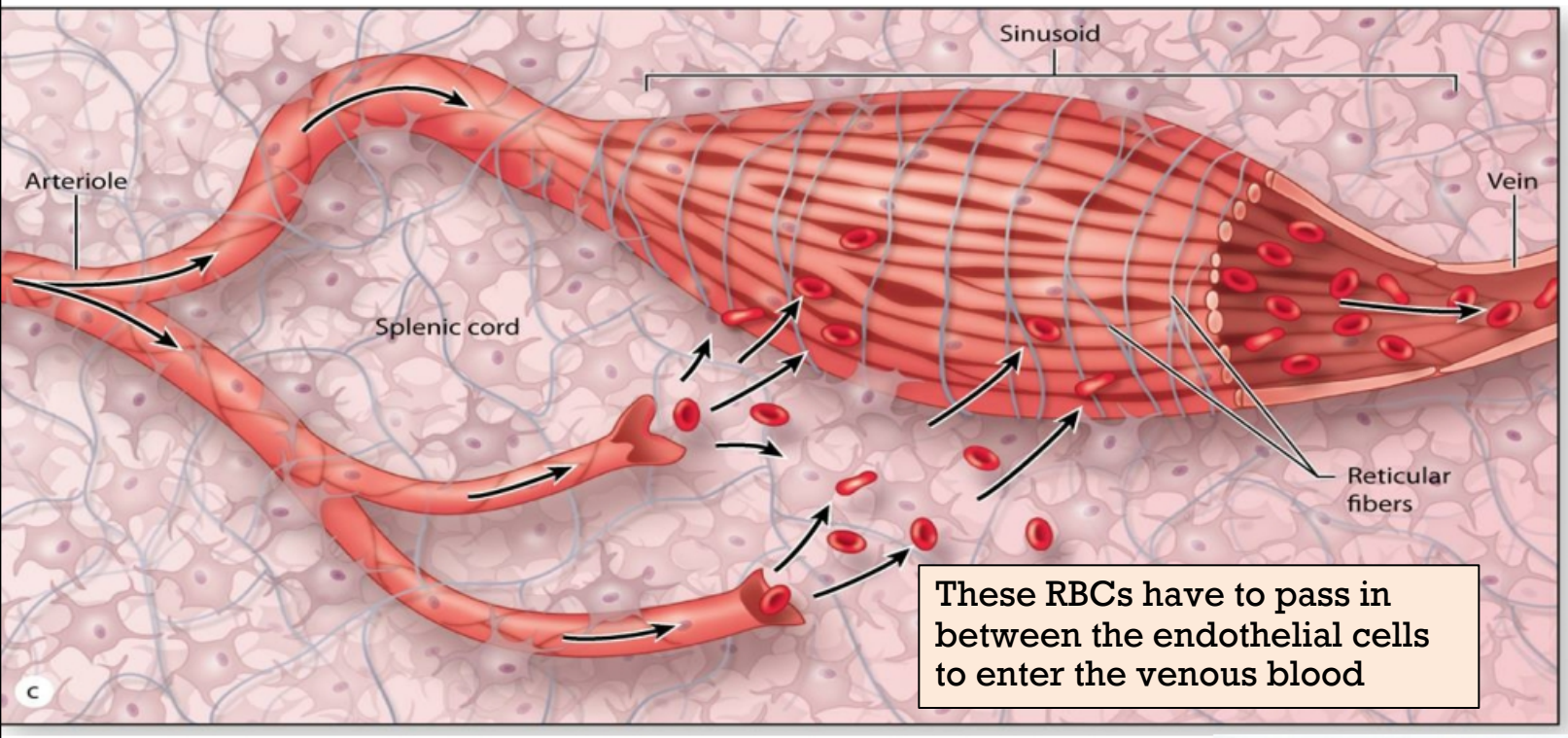
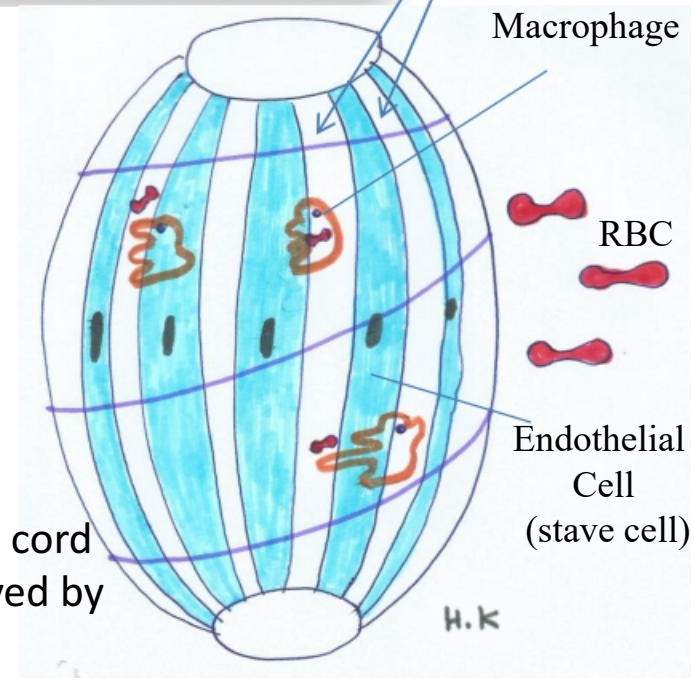


Note the wide gaps between endothelial cells which allow for movement of entire cells from cords to sinuses

- Splenic sinusoid : Large space filled with blood , lined with endothelial cells and these special endothelial cells are arranged longitudinally, and they don't have cell junctions (desmosomes, tight junctions),and in between theses cells we have large intercellular clefts , these endothelial cells are supported by a discontinues layer of basement membrane forming bars, also we have many macrophages that extend their cytoplasmic processes into the lumen to recognize any foreign antigens inside the blood
- Spaces in between sinusoids where we have blood are called splenic cords which are cords of cells supported by reticular tissue

In this route plasma and all the formed elements of blood must reenter 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)

As RBC is getting older or abnormal It will have denaturation of its plasma membrane proteins or sub membranous proteins (RBCs don't have organelles , so can't regenerate new proteins) , so this old cell will be less flexible (squeezing or twisting is less) ,it will be slow and undergo membranous fragmentation then this cell will be identified by macrophages and getting eaten

We call this test when RBC pass in between the endothelial cells to enter the venous blood twisting or flexibility test

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

Hemoglobin is broken into **Heme** and **Globin**

amino acids pool of blood

Iron: carried by transferrin to bone marrow (used again)

Bilirubin: excreted by liver bile

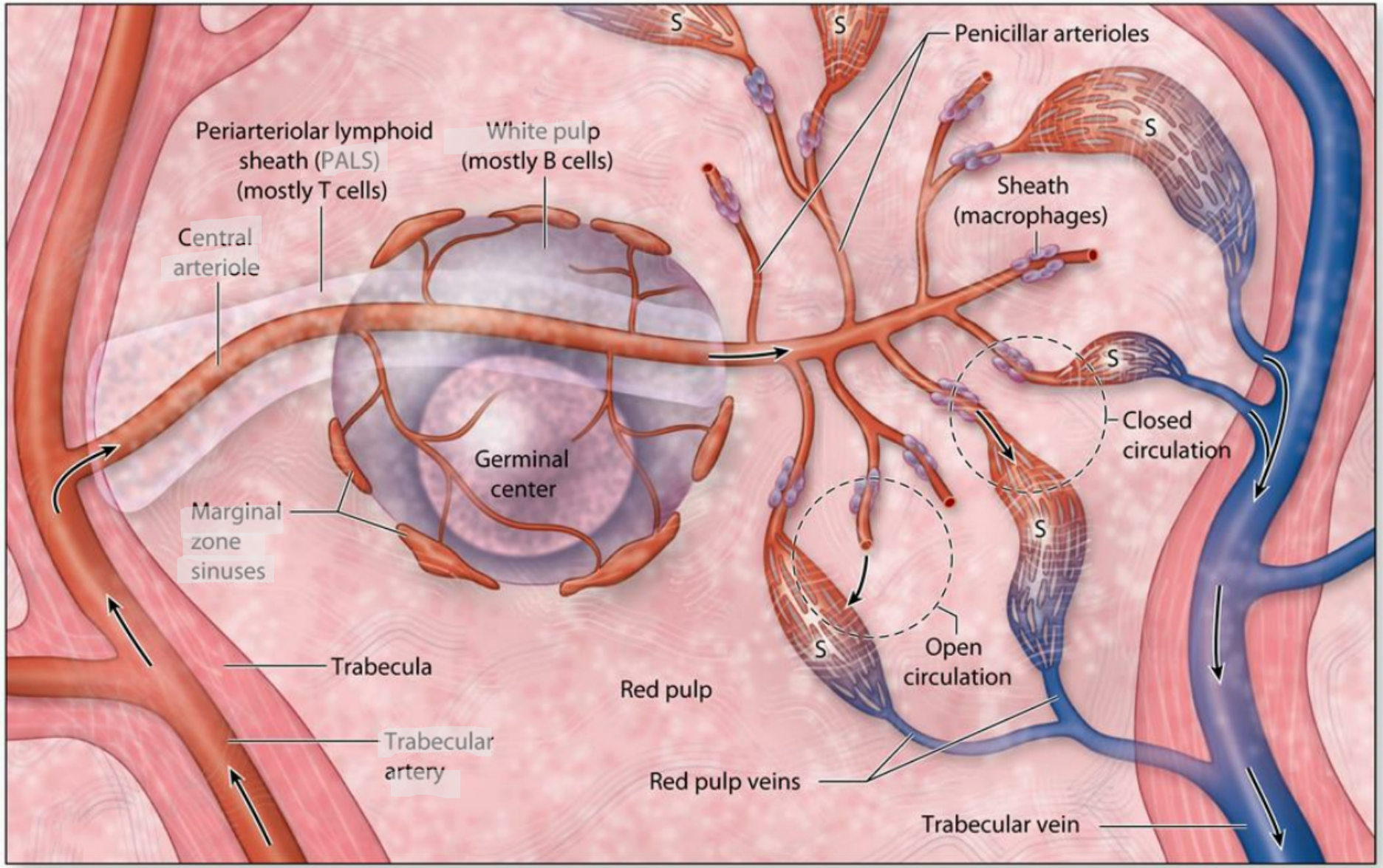
After surgical removal of the spleen (splenectomy), the number of abnormal erythrocytes in the circulation increases although most such cells are then removed by macrophages in sinusoids of the bone marrow and liver.

Fresh and young RBC will pass quickly with high flexibility in between endothelial cells to the venous blood and will not be captured by macrophages

More brone to have septicemia

Some RBCs need more than one circulation to be eliminated (enter the spleen >> not eliminated, then renter until it will be captured and eliminated)

Schematic view of the blood circulation and the structure of the spleen, from the trabecular artery to the trabecular vein.



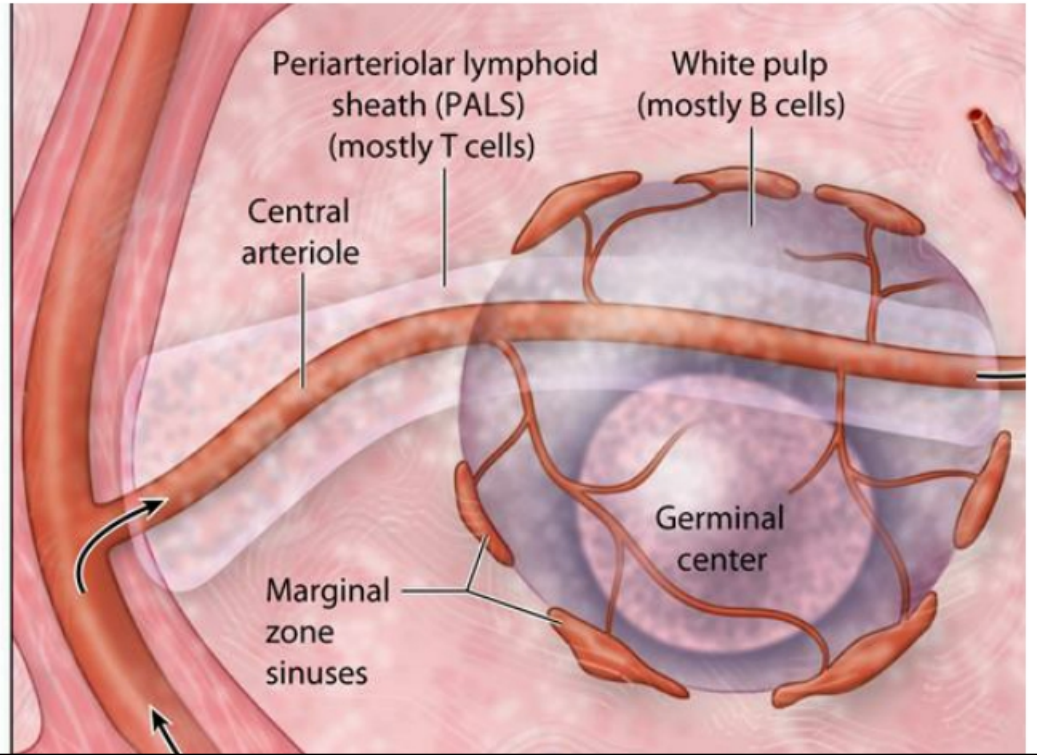
The area between white pulp and red pulp is called marginal zone

Marginal zone sinuses

✓Located between the white and the red pulp

✓The spaces between these sinuses are wide (2-3um)

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

Lymphocytes come into contact with APCs, if they recognize their Ag-MHC complex, the lymphocytes initiate immune response within the white pulp

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

- While the blood is passing through the white pulp it's going to be screened for any antigens or microbes, if there's an antigen, APC will phagocytose it presenting it on MHC to T lymphocytes which in order will activate B cells and the B cells will become activated and move in the center of the follicle to form germinal center
- Activated B cells form plasma cells , these plasma cells move from the germinal center (white pulp) to populate inside red pulp (splenic cords)

- Inside the capsule of the spleen, inside the trabeculae we have smooth muscle cells or myofibroblasts, these cells are contractile and stimulated by sympathetic nervous system, if we have stimulation of smooth muscle cells we will get contraction of the spleen, then the blood will move from splenic cords into splenic sinusoids and this increases the volume of blood

Functions of the spleen:
It has circulatory as well as lymphatic functions

To summarize

Is more prominent in lower animals

Blood cell production: During the fetal life, blood cells are produced in the spleen

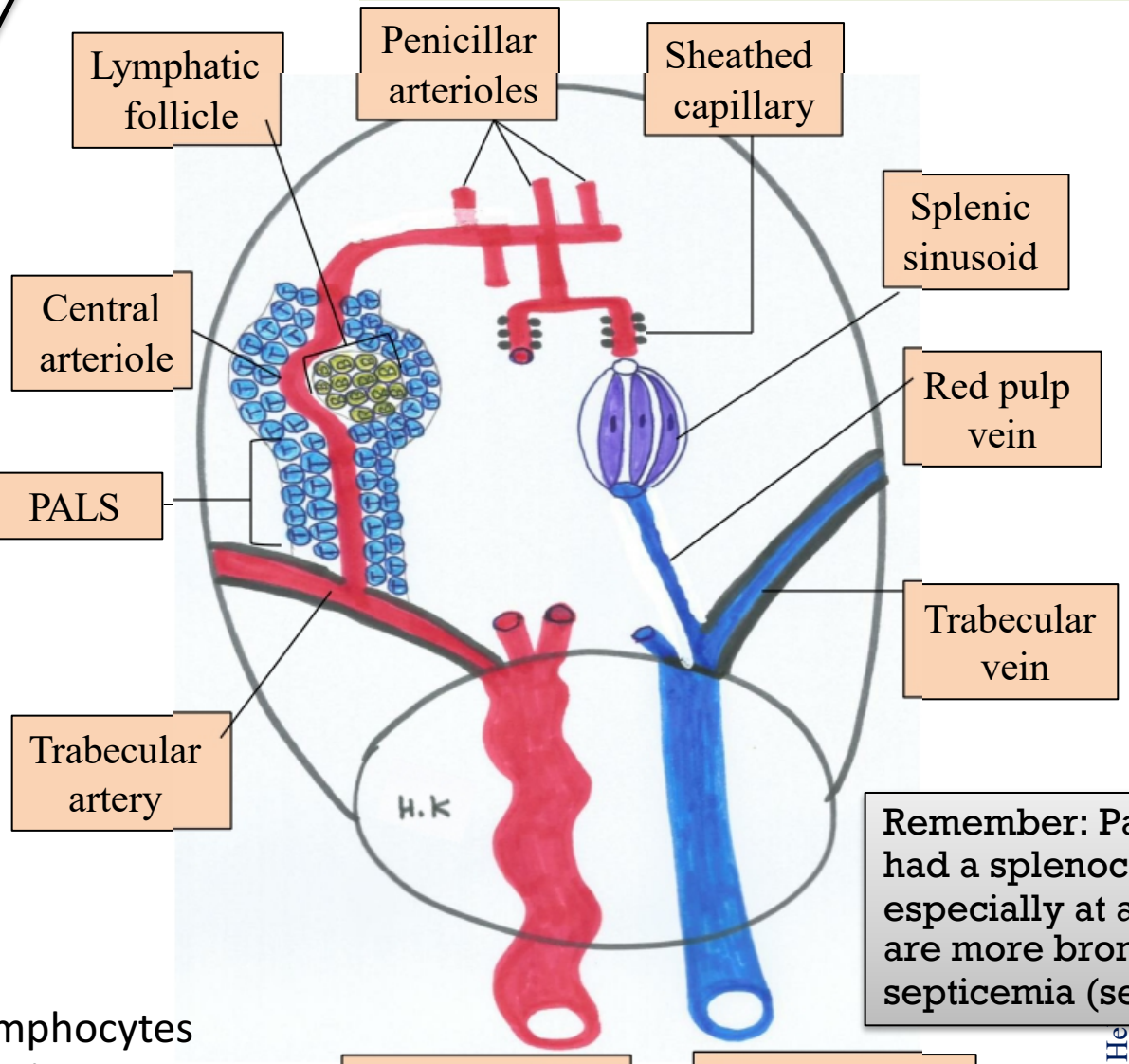
Blood storage: A small quantity of blood is stored in the sinusoids of the red pulp

RBC destruction: Most worn-out or damaged red blood cells are destroyed in the spleen (some in the liver and bone marrow). They are phagocytized by macrophages

Defense mechanism:
Macrophages phagocytize microbes that have penetrated the blood. Antigens in the blood activate B and T cells residing in the spleen, triggering immune response

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

The blood flow in the spleen goes from splenic artery to trabecular artery to central arteriole, and upon leaving the white pulp, the blood flows through penicillar arterioles and terminal sheathed capillaries to the splenic sinusoids, and back to veins of the pulp, trabecular veins and the splenic vein



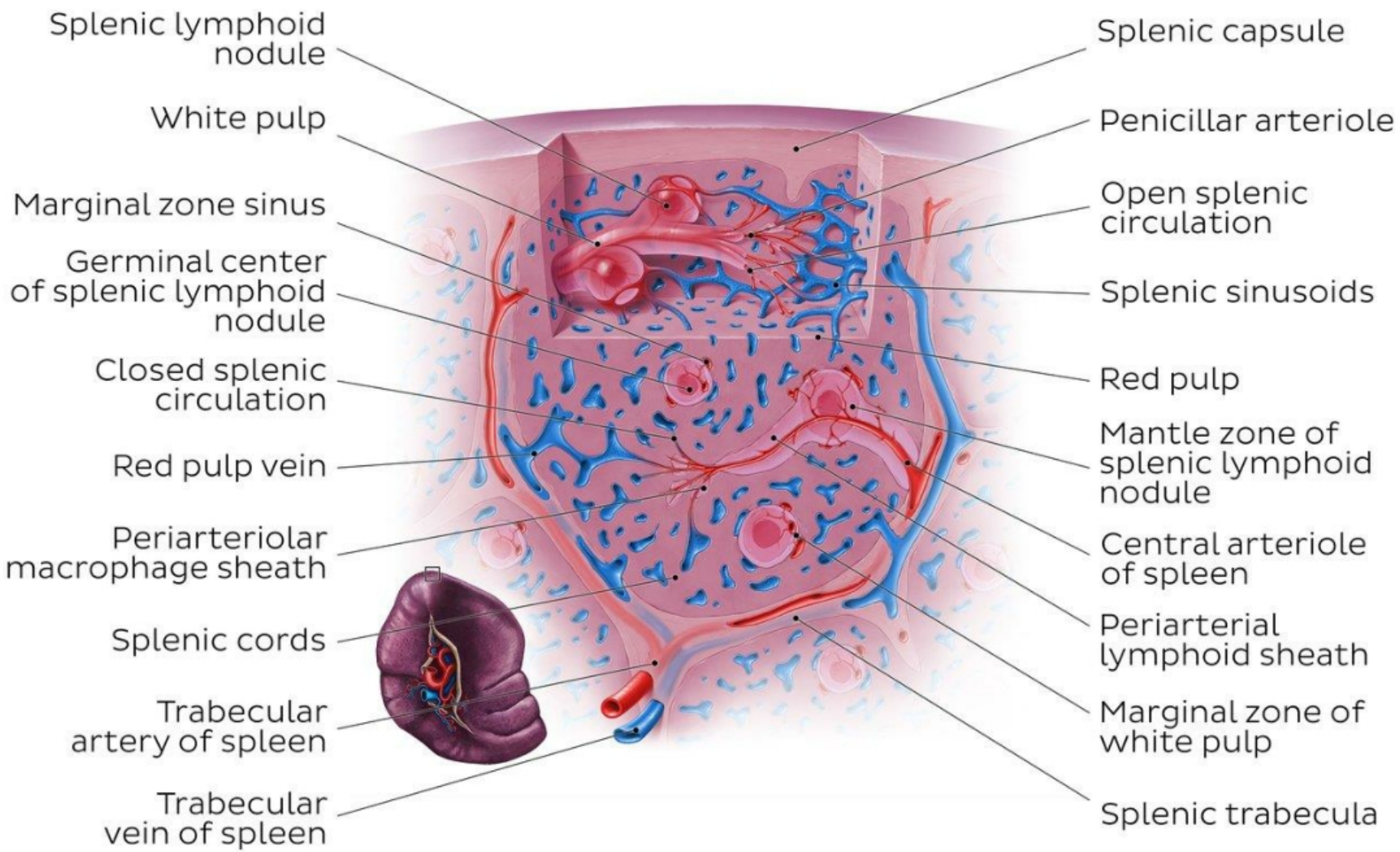
Remember: Patients who had a splenoctomy especially at a young age are more brone to septicemia (sepsis)

Dr. He

Under LM we can't differentiate between T and B cells, so how we differentiate PALS area and lymphoid area under LM ?

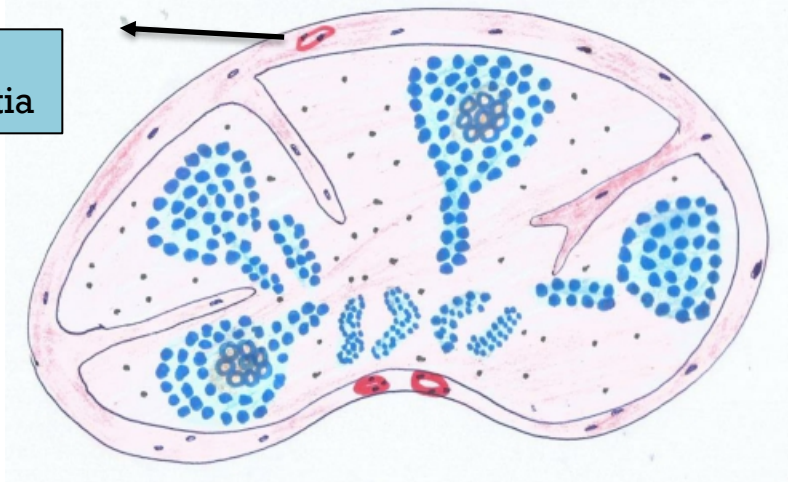
- If you see in the cross section that the central arteriole is located centrally and surrounded by basophilic nuclei >> PALS area
- But if you see aggregations of Lymphocytes and you find an arteriole peripherally located >> area of lymphatic follicle of white pulp

If we have germinal center it's easy to determine the lymphatic follicle

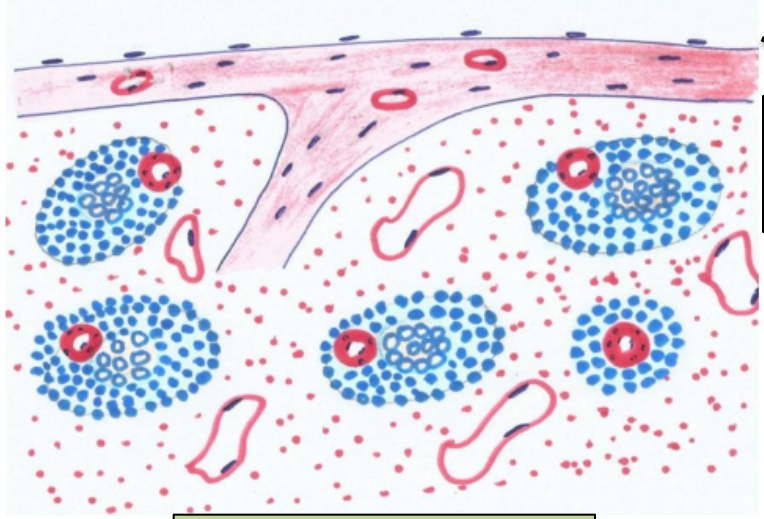


Refer to the video to identify the structure of spleen and lymph nodes

The outermost layer is adventitia



Histology of lymph node



The outermost layer is serosa

Histology of spleen

Lymph node	Spleen
Multiple, small	Single, large
Along the course of lymphatic vessels	Intra-abdominal Upper left quadrant
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

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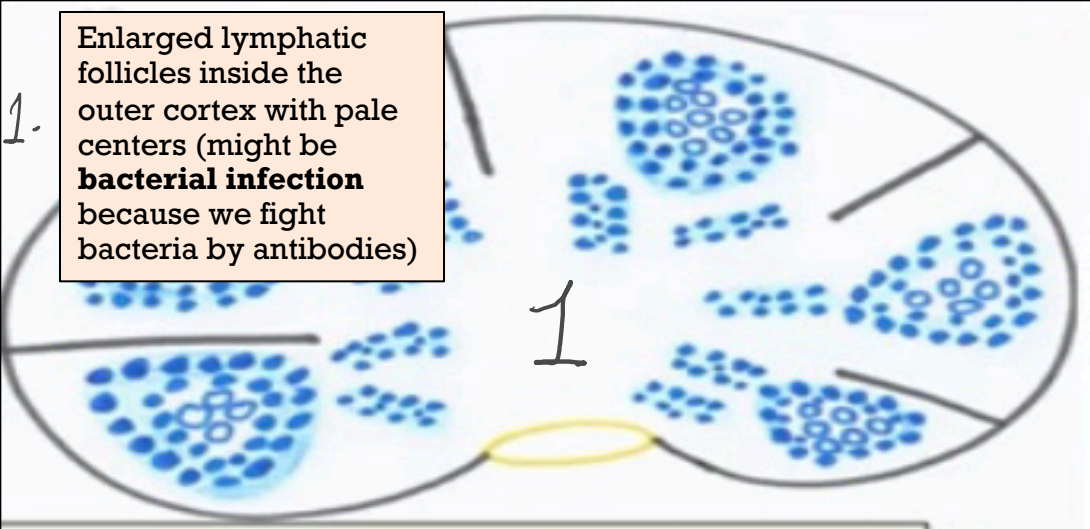
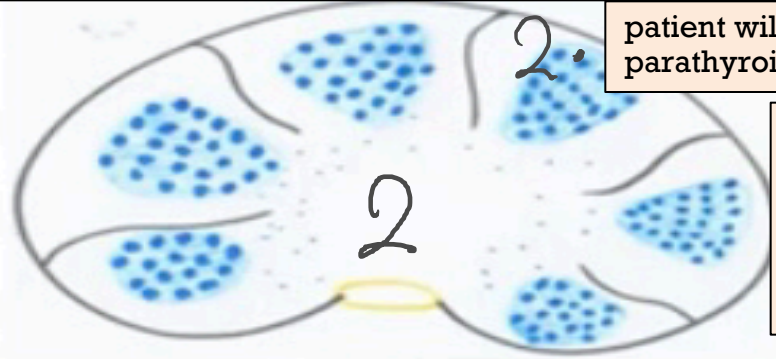
1. Enlarged lymphatic follicles inside the outer cortex with pale centers (might be **bacterial infection** because we fight bacteria by antibodies)



Germinal centers, enlarged follicles: bacterial infection

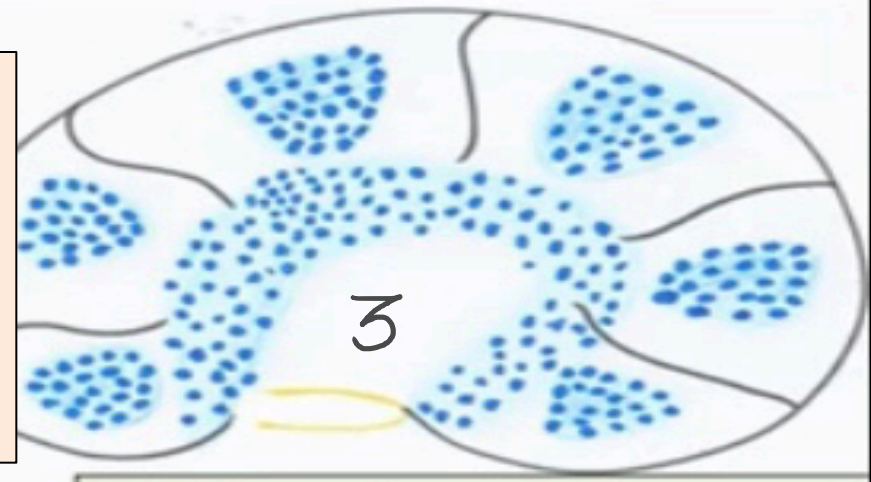
2. patient will suffer from underdeveloped parathyroid glands which lead to hypocalcemia

Normal follicles inside the outer cortex and the area. Of the paracortex is underdeveloped (abnormal or absence of thymus) >>the patient will have problems in cell mediated immunity



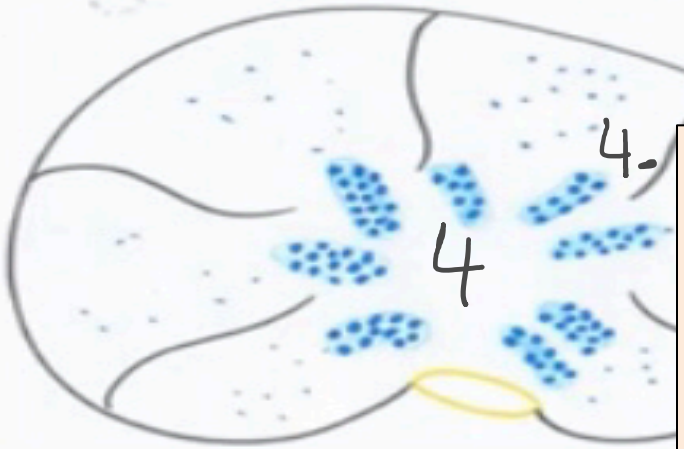
Underdeveloped paracortex: DiGeorge syndrome

3. Normal lymphoid follicles inside the outer cortex but the area of the inner cortex is over developed (might be **viral infection** because we fight viruses by cell mediated immunity)
It also could be an Intracellular microbes

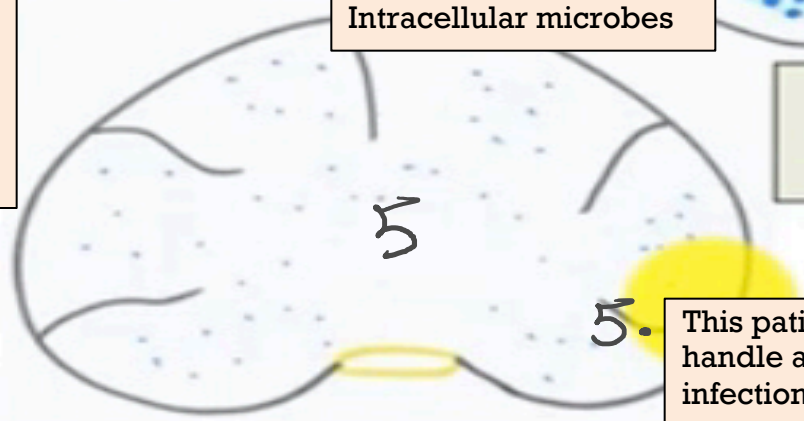


Enlarged paracortex: ex. Viral infection

4. Underdeveloped lymphoid follicles with normal paracortex >> indicates a problem in B cells >>Can't produce antibodies and fight bacteria



Underdeveloped outer cortex: Bruton's immunodeficiency disease



5. This patient can't handle any type of infection

Both B and T areas are underdeveloped