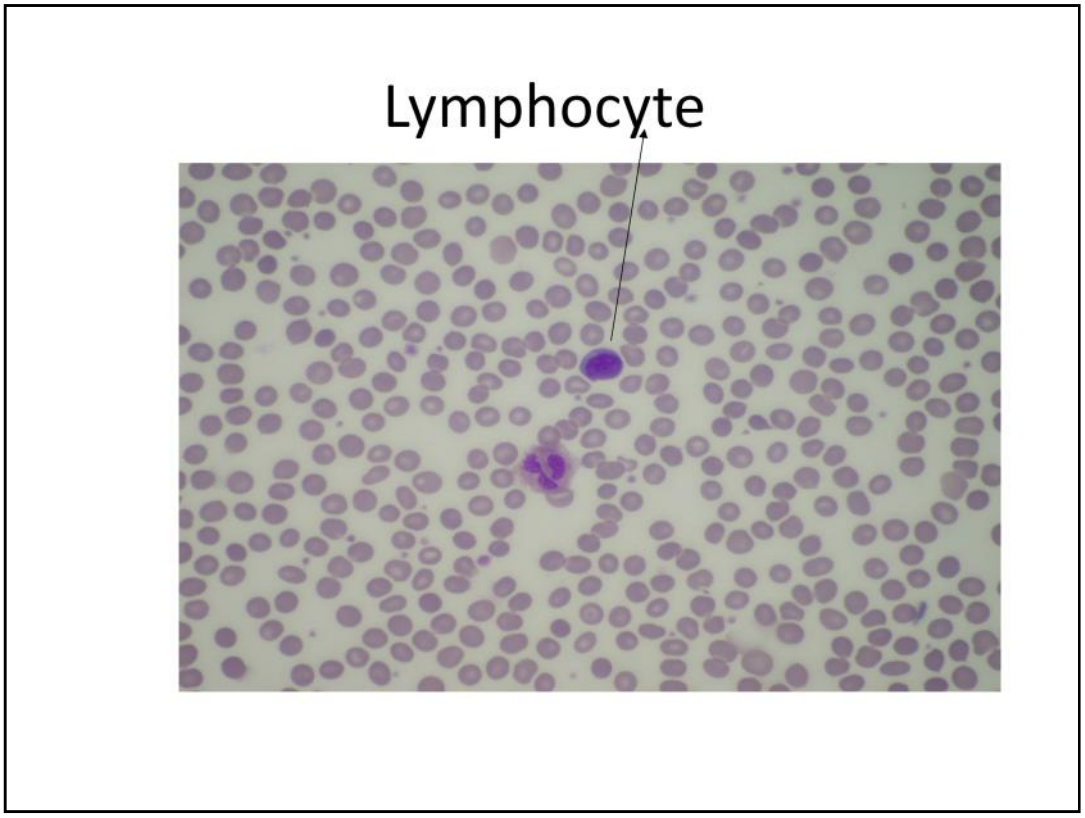
Lymphatic system



Pointing at the lymphocyte :•

• where does this cell come from ? from the bone marrow

•Where does it go then ? to the peripheral lymphoid organs i.e to the lymph nodes , spleen & MALT .

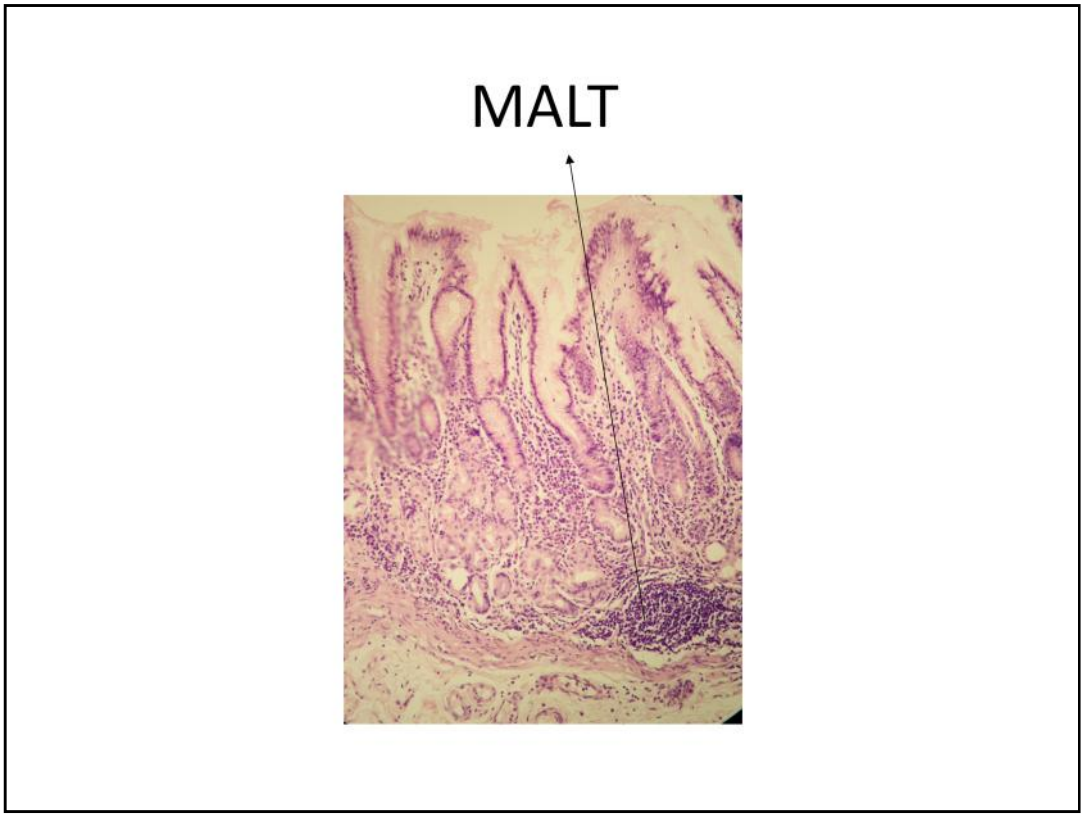
•This cell is responsible for what type of immune reactions ? specific.

•This cell can be an activated B cell ? True .

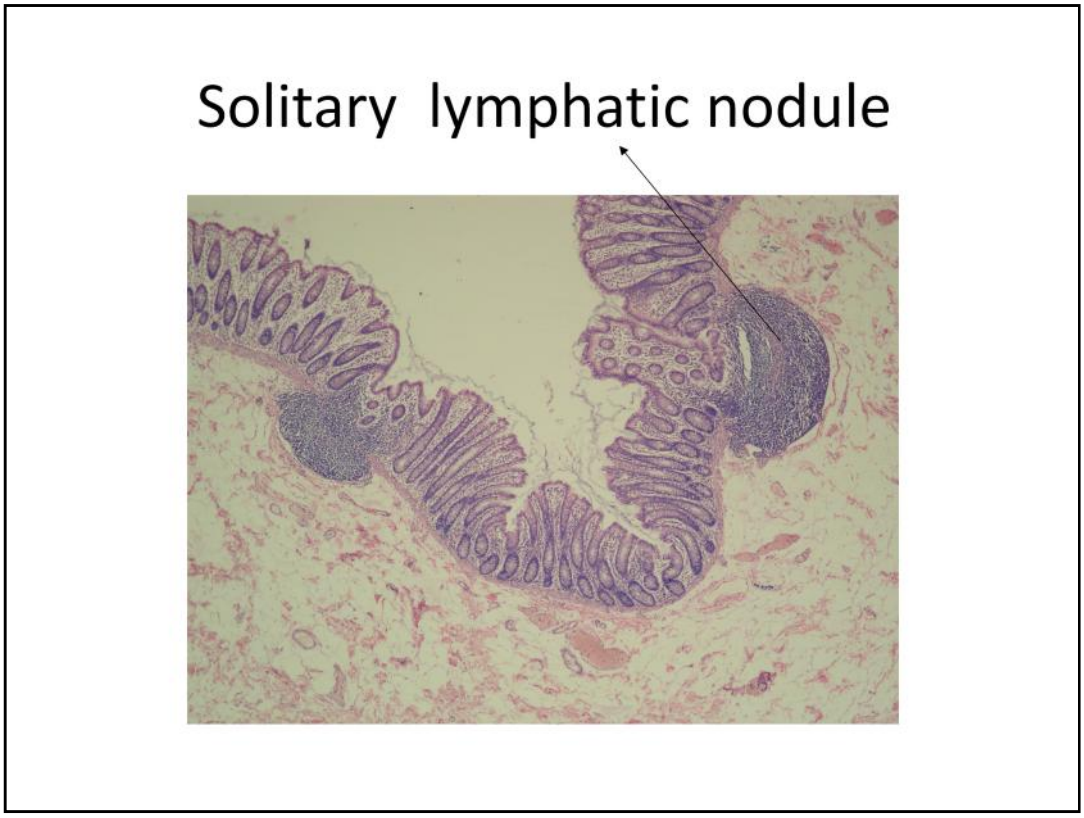
•This cell can be identified if being B or T cell morphologically ? False .

•Most of the circulating cells of this type are in the activated form ? False , most of the circulating lymphocytes are small inactive virgin cells and only 3% are in the activated large form

• A question that was asked last year : is the naïve cell a mature cell ? YES , it is mature or with the same meaning it is immunocompetent , but it is not yet activated , it hasn't yet been exposed to an antigen .



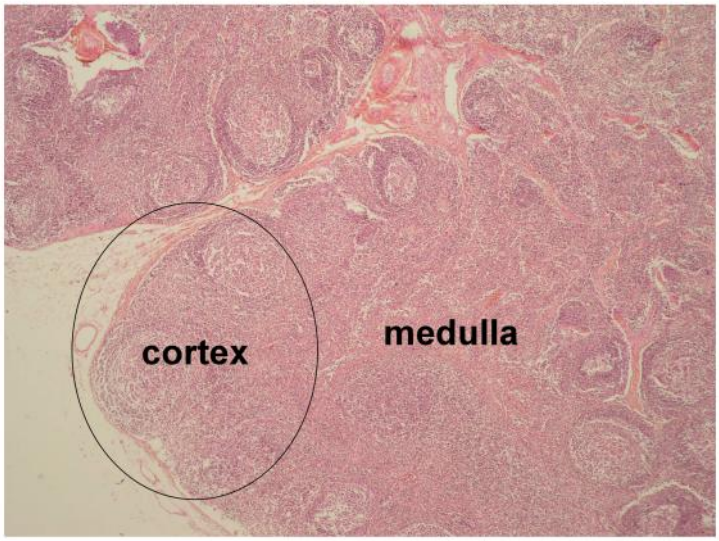
MALT : mucosa – associated lymphatic tissue .
Is the diffuse lymphatic tissue & is **not encapsulated** .
This section is from the gastric mucosa .
Might be in the form of single nodules or aggregations of many lymphatic nodules , the latter can be seen in peyer's patches which are usually found in the ileum .
An inmmune reaction can take place here as a result of the exposure of the activated lymphocyte to the antigen and hence more & more effector (activated) T & B lymphocytes are produced.
Again , **aggregations** of lymphatic nodules can be seen in Peyer's patches in the ileum , why ? because it acts as a defense weapon in a critical region seperates between two mediums ; a clean one that's free of bacteria & this is the small intestine & the colon which is a dirty medium full of bacteria , so peyer's patches along with the appendix act to defense the zone and prevent the entry of the microbes from the large intestine (colon) to the small intestine



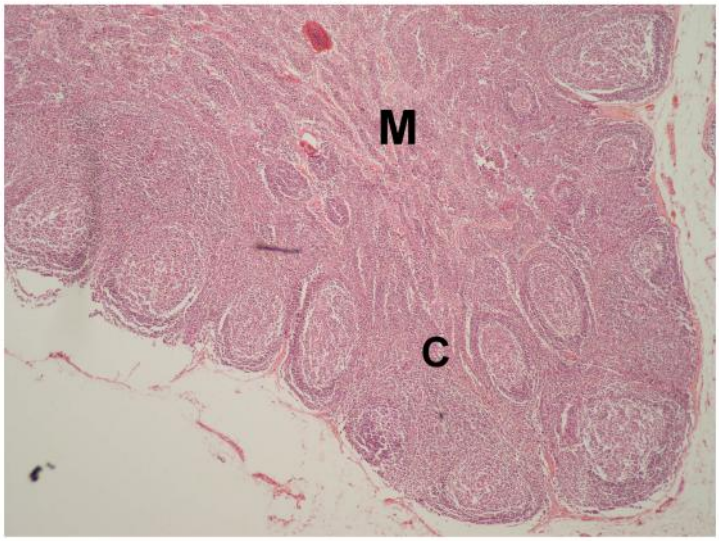
Solitary lymphatic nodule .
This is part of MALT , for example , in the gut .
it has all the contents of the lymphatic system i.e T cells , B cells , macrophages …etc .

Lymphoid Organs:
Lymph node

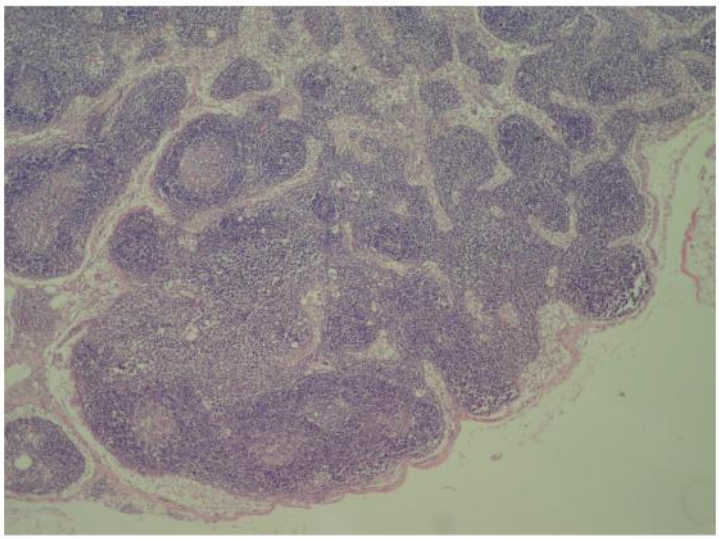
Lymph node



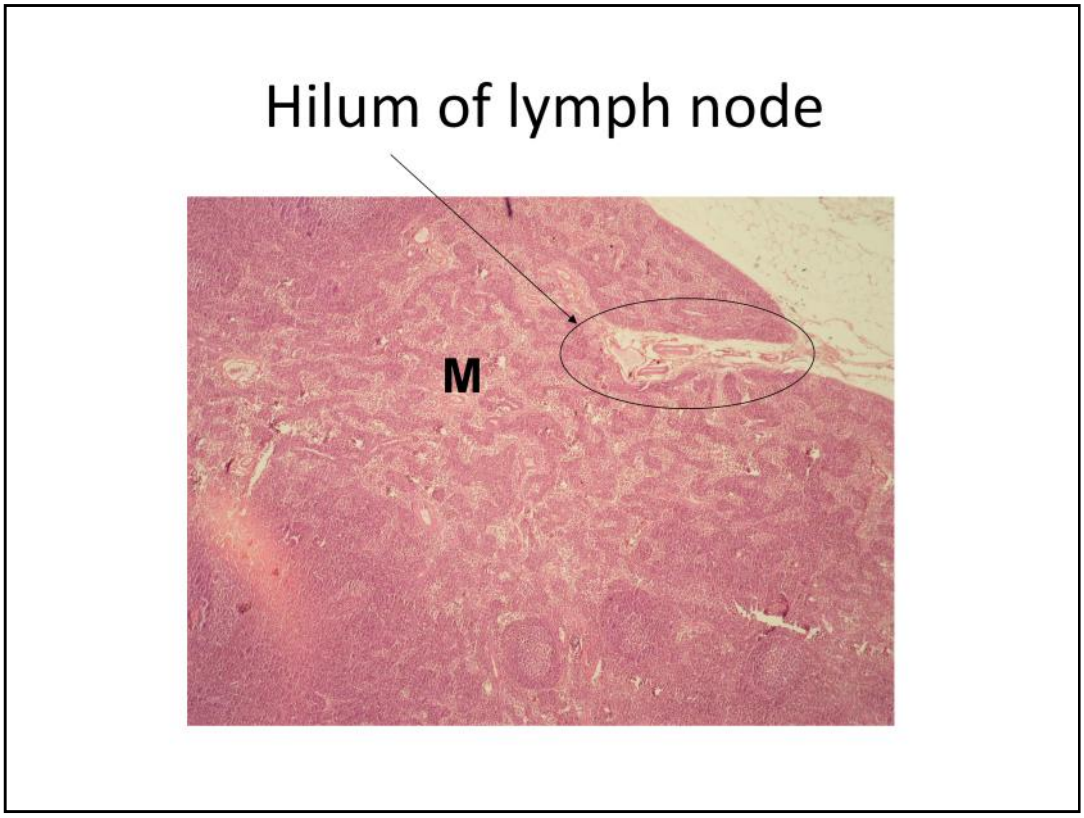
a lymph node section .
is composed of :
an outer part → has follicles → the cortex .
& of inner part → has cords → the medulla .



You can see the follicular nodules in the cortex " C ".
You need to identify whether the follicle is a primary or a secondary one :
The secondary follicle → outer dark part full with cells & inner pale part has few cells and is called the germinal center .
The primary follicle → all of it is dark .
The pale center or the **germinal center** in the 2ry follicle **represents** the **proliferation of the activated B cells** which move then towards the margins that appear dark in color , then theses cells (the products of the proliferation of B cell ; the plasma & the memory cells) leave **the cortex** entering the **medulla** forming the medullary cords to be ***temporarily*** **stored there** , as 90% of **the plasma cells leave the medulla to the bone marrow** & only 10% remains there , & **the memory cells leave the medulla to the circulation** where they can then enter the spleen or another lymph node or some keep circulating in the blood .
** the medullary cords can have some few activated B lymphocytes as well .
** memory cells live months to years .
Q : Is there a functional relationship between the cortex & the medulla ?
A : YES , because what is produced in the cortex (the plasma cells & the memory cells) are **temporarily** stored in the medulla .
Q : **The primary source of antibodies (Ab) comes from the bone marrow** *more* than lymph nodes or spleen? A : True , as 90% of the plasma cells which produce the Abs are in the bone marrow .
Contents of the follicles :
In the 1ry follicle : resting (inactive) B lymphocytes with its servant ; the follicular dendritic cells.
In the 2ry follicle : activated B cells undergoing enlargement , proliferation & differentiation at the pale center . { you need to well memorize these 3 words }
B cells within the follicle can be exposed to the antigens that are either :
Processed by APC elsewhere ; like Langerhans cells in the skin , and are ready to be presented to the B cells in the follicles , **or**
Free antigens , which will be processed & presented to the B cells by the follicular dendritic cells .
** processing of the antigen is the digestion of it and its conversion from proteins to smaller polypeptides.
** B cells can interact with free antigens that are not bound to MHC molecules , but if the antigen is conjugated with MHC II , then the interaction will be stronger .
In any lymph node section , most nodules or follicles that can be seen in the cortex are the 2ry follicles with pale centers , it's rare to see the 1ry ones .



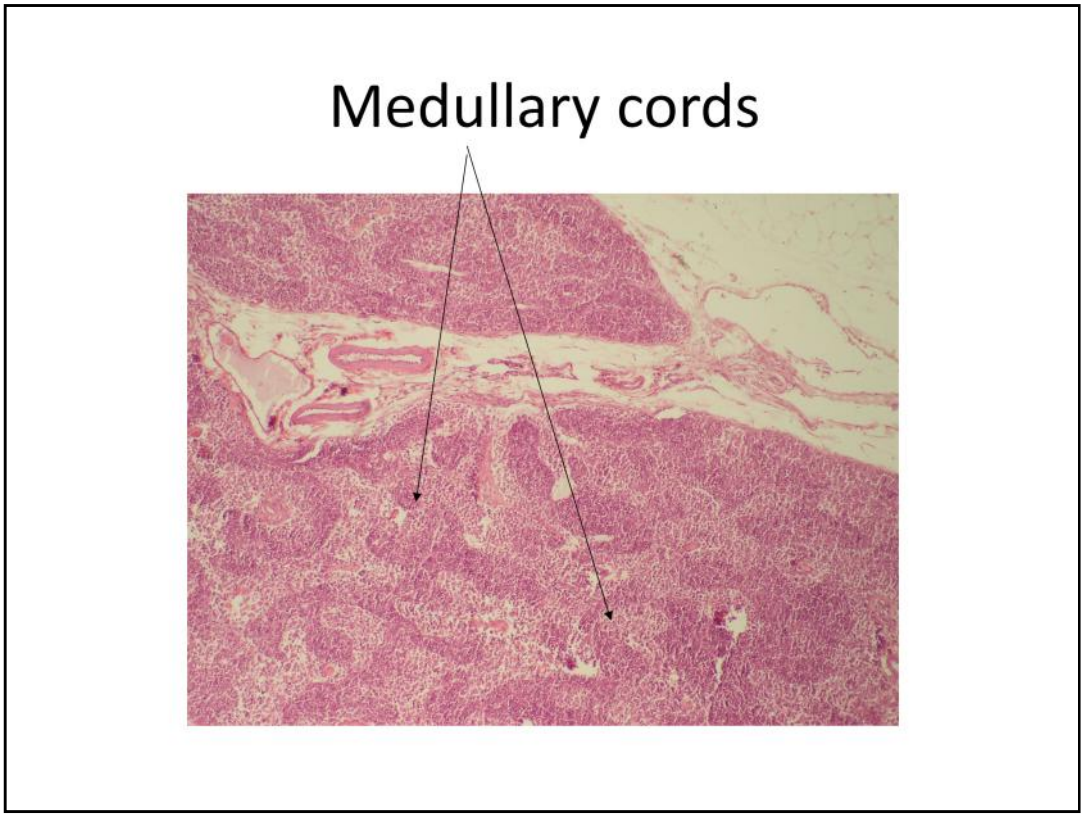
We can see follicles , so this part is the cortex .
In the follicles , we can recognize a pale center & dark margins , so it’s a 2ry follicle.



Hilum of lymph node .
Entering at the hilum is the artery , and leaving is the vein & the efferent { Hint : **e**fferent : **e**xit } , but **the afferent enters at other side rather than the hilum** .

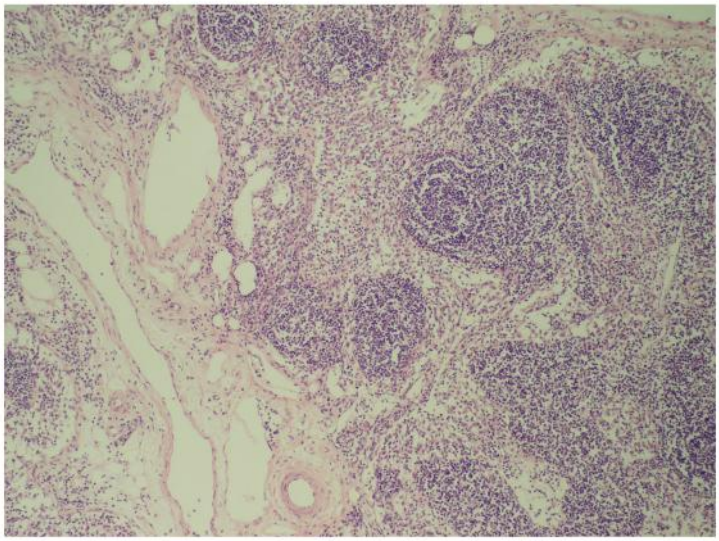
A special feature of the lymph nodes that is not found in the spleen & thymus is that the lymph nodes have *both* efferent & afferent lymphatics .

A fact knowing is a must :
Eventually , lymph from all over the body accumulate & drain to the Thoracic duct , to the venous circulation .
Thoracic duct :
Is a lymphatic duct , 45 cm in length , it starts from the abdomen entering the thorax as cistern chyli , moving along the thorax to drain finally at the junction between the left internal jagular vein & the left subclavian vein to be opened to the venous circulation .
Q : why do lymph should go back to the venous circulation ? **A** : because it has vital substances; like proteins that our body needs .
Before lymph go back to blood , at least it should pass through one lymph node to be filtered there , but unfortunately , not all bad contents are filtered , for example , the metastatic cancer cells entering the lymph node can't be simpely engulfed & cleared by the macrophages there .
Cancer metastasis can be
lymphatic metastasis : via which cancer cells can enter the lymph node , or
blood metastasis .
a clinical case : if you checked a patient with enlarged axillary lymph nodes , what are the possibilities ?
if the node is tender (hurting) the enlargement will be as a result of infection .
if the node is tough & not tendering , it then might be a result of other diseases like malignancy .
** the enlargement here is due to immune reactions which result in the proliferation of the lymphocytes .
M : refers to the medulla which has the medullary cords .

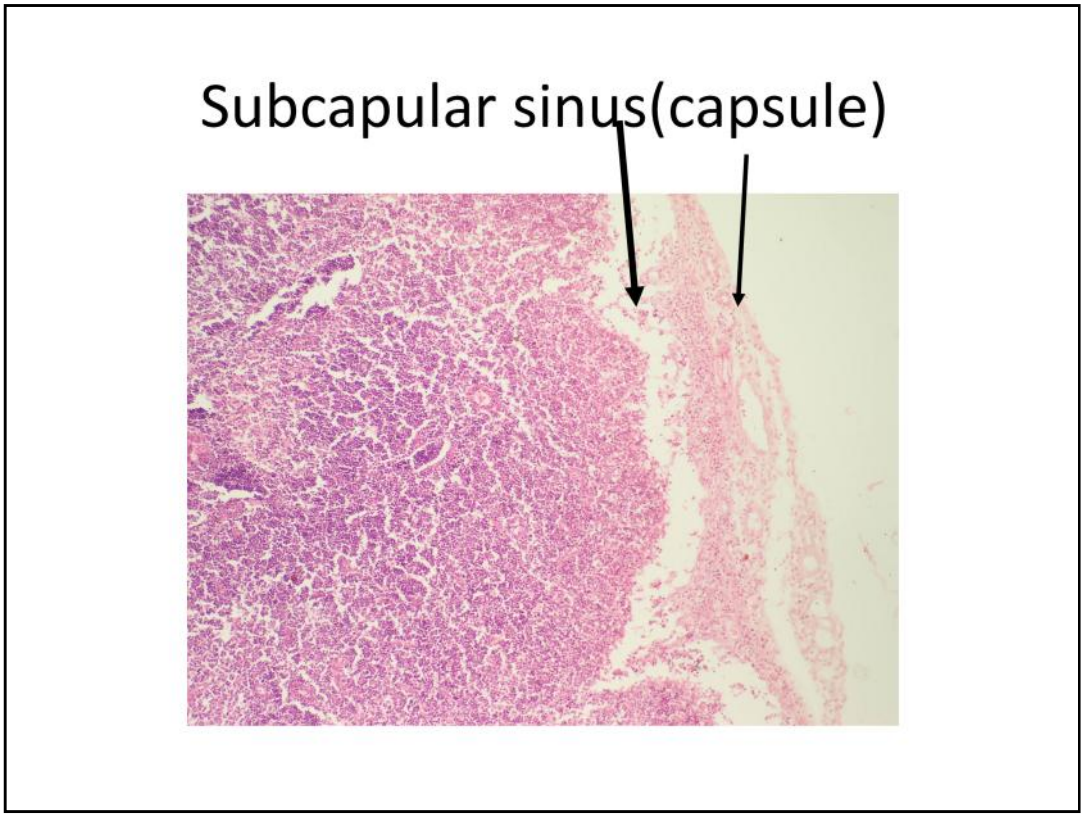


Medullary cords.

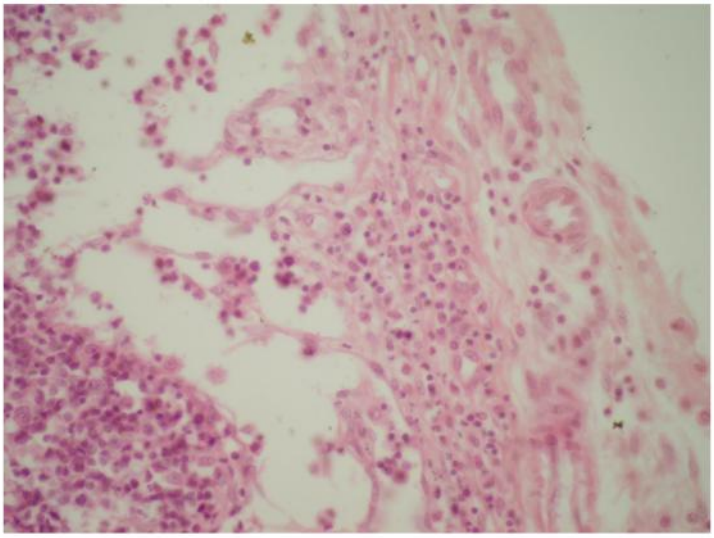
Possible exam questions on this slide :
Knowing that this is a section in a lymph node :
What is this area ? Medulla .
The pointed structure is ? medullary cords .
The spaces seen here are ? medullary sinuses .



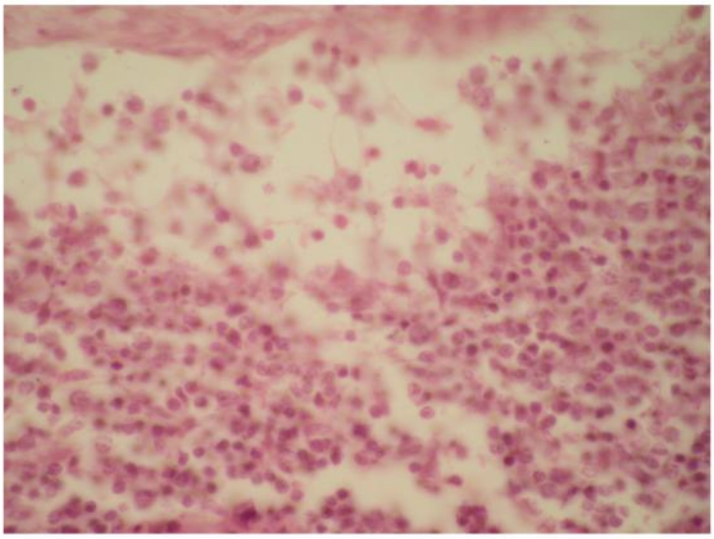
Medullary sinuses can be seen here .
For a vessel if it has :
thick wall → it will be a blood vessel , either artery or vein .
thin wall → it will be a lymphatic vessel .

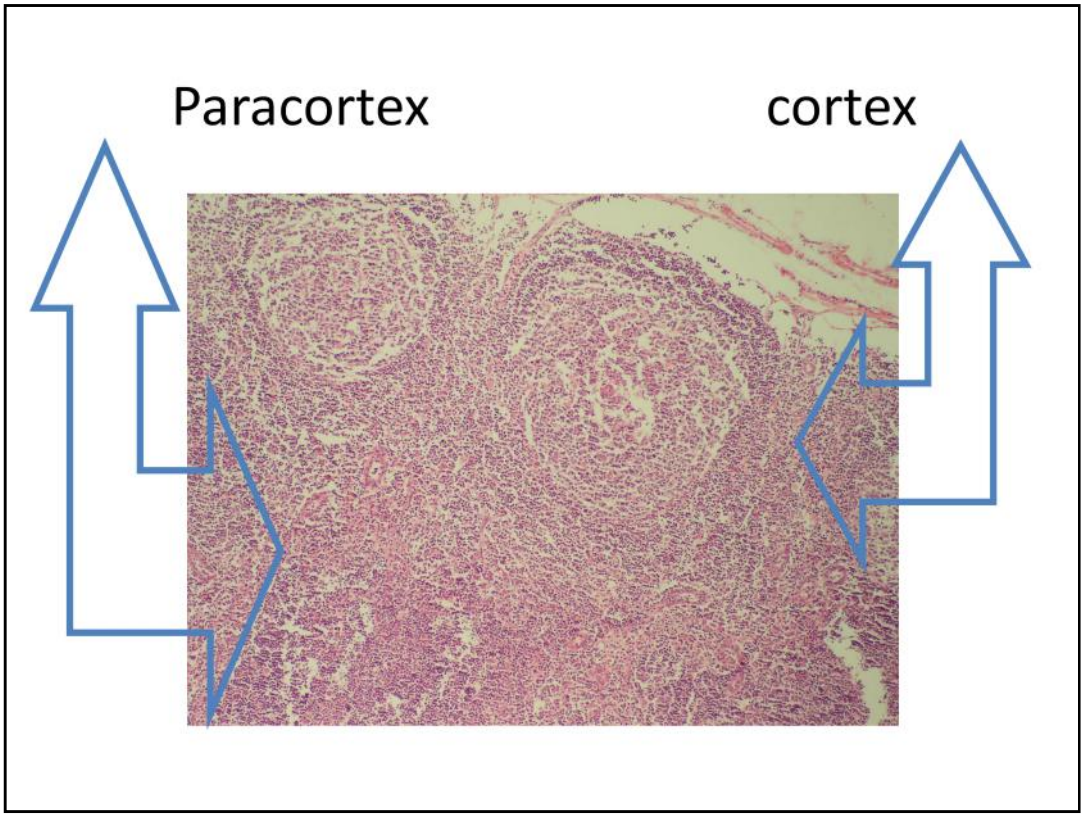


subcapsular sinuses (capsule) , The capsule is dense connective tissue that sends many trabeculae.
directly beneath the capsule is a space → the subcapsular lymph sinus .
Q : what phenomenon takes place here ? & what for ?
A : slowing of lymph flow rate , to give chance for the macrophages here to contact the antigens & get rid of them (99 % of antigens , bacteria & foreign particles entering the lymph node are engulfed by macrophages present here) .
Flow of lymph within the lymph node happens in this sequence :
Afferent → subcapsular lymph sinus → trabecular lymph sinus → medullary sinus → to the efferent



Subcapsular lymph sinus full with macrophages .





We can see follicular nodules so this is cortex
Inner pale centers with outer dark margins → so this is 2ry follicle .

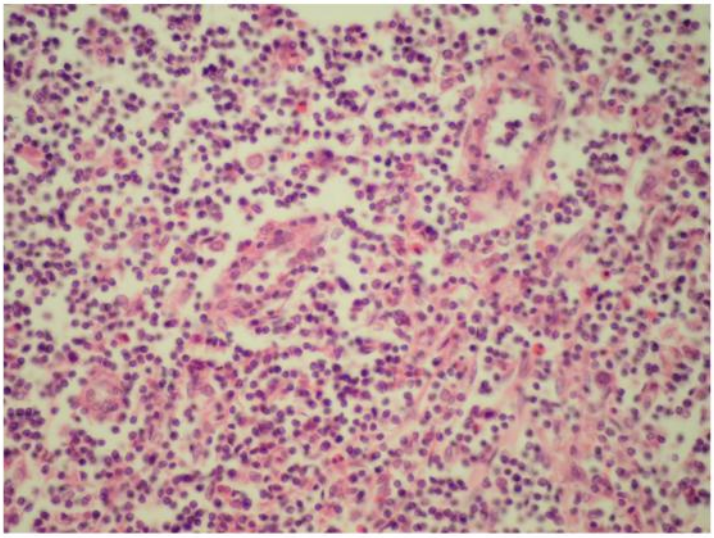
Q : within this follicle , what type of immune reaction may occur ?
A: antibody – mediated immune reaction , coz the cells here are the activated B cells .
Activation of B cells requires two signals :
Recognition of the antigen .

Costimulatory signal : this signal can occur by many methods one being the following :
T helper cells in the paracortex can migrate & get closer to the site of B cells in the follicles & secrete many cytokines , most important one is the interlukin 2 (IL-2) .

We can see in this slide the paracortex or the deep cortex or the thymus dependent zone because it depends on hormones produced by the thymus , so if the thymus is surgically removed or get involuted in old ages , this zone will undergo atrophy .
In the paracortex there are the T cells & their servant(خدامتها) ; the interdigitating dendritic cells .
The type of immune reaction here is : cell- mediated immune reaction , T cells become activated upon antigen processing & presentation by the interdigitating dendritic cells .

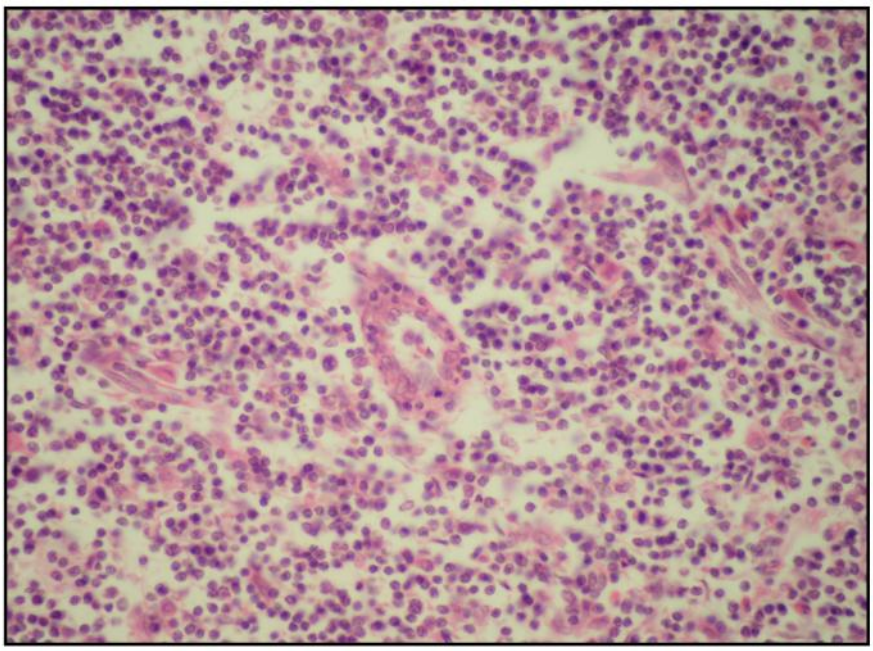
Q : is there a functional relationship between the cortex & the paracortex ?
A : YES , because the activation of B cells in the cortex requires a costimulatory signal which is provided by T helper cells present in the paracortex .

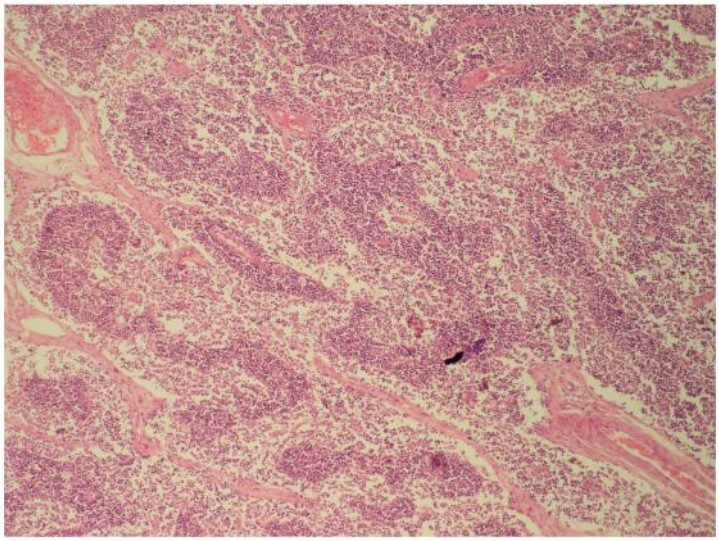
Post capillary venule



Post capillary venule .
Post capillary venules present in the paracortical region
Large artery → elastic artery → muscular artery → arteriole → capillaries → venule → vein→ large vein.
Normally , the epithelium of the venule is simple squamous , but here , **the epithelium is cuboidal & this type of epithelium is called high epithelium** .
The epithelial cells here have a chemotactic activity i.e they release chemotactic factors that can attract the T & B lymphocytes from the blood within the venule to the lymph node , so that T cells can enter from blood to the paracortex & B cells to the cortex.

Post capillary venule

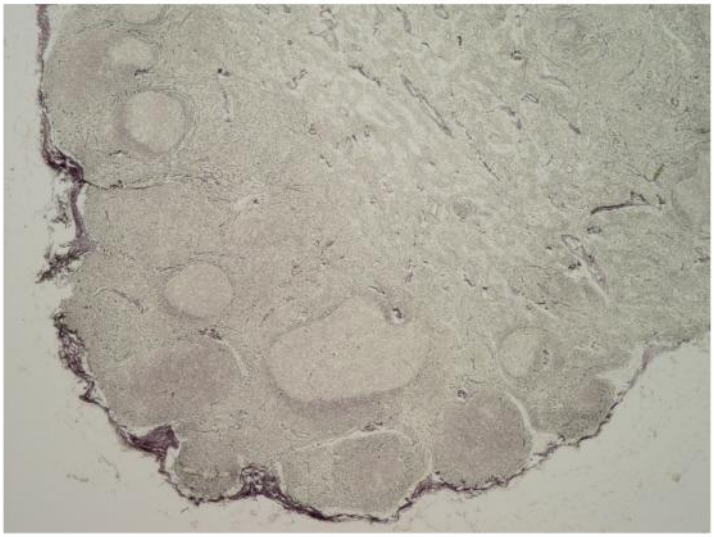




Medullary cords surrounded by spaces which are the **medullary sinuses** : This is the medulla .
Q : the pointed section contains the following :
Plasma cells permenantely ? False

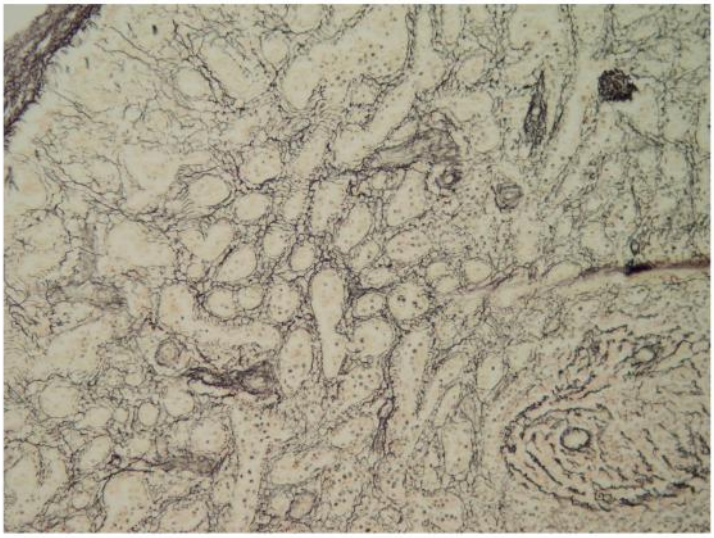
90% of the produced plasma cells ? False , it's 10% .
Memory cells temporarily ? True .

Macrophages & activated B lymphocytes ? True .
T lymphocytes ? False .



No nuclei can be seen here , in another words , no lymphatic cells can be seen.
The shadow here represents **the parenchyma of the lymph node having reticular fibers** , and the spaces in between are filled with lymphocyte that we cannot see at the level of the stain used here which is **argirophilic stain** interact with **silver salts** , but to examine lymphocytes we stain them by H & E .

Argyrophilic reticular fibers



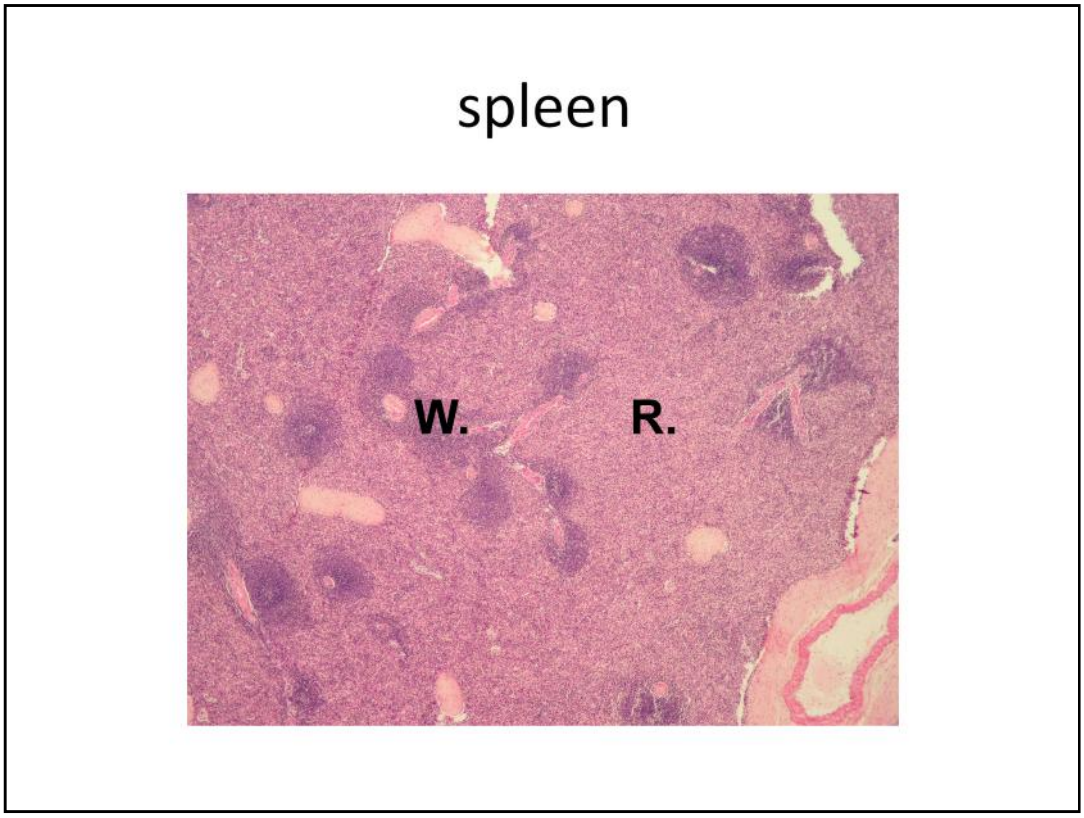
Argirophilic reticular fibers .
This is a meshwork of reticular fibers produced by reticular cells .

Important to notice that : reticular cells in lymph nodes & spleen ***differ*** from the reticular cells in the thymus in terms of : Function & Origin
Function : reticular cells in lymph nodes & spleen produce reticular fibers but in the thymus they don't , **so NO reticular fibers in the thymus** but the

reticular cells in the **thymus** serve the following 3 functions :
Formation of the blood – thymus barrier .
Act as APC (antigen presenting cells) .
Some secrete thymic hormones .

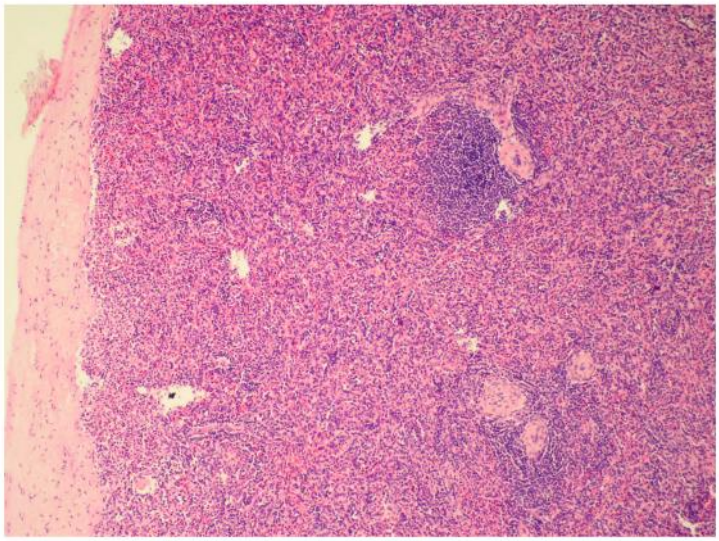
Origin : reticular cells in the thymus originate from the 3rd pharyngeal pouch .

spleen

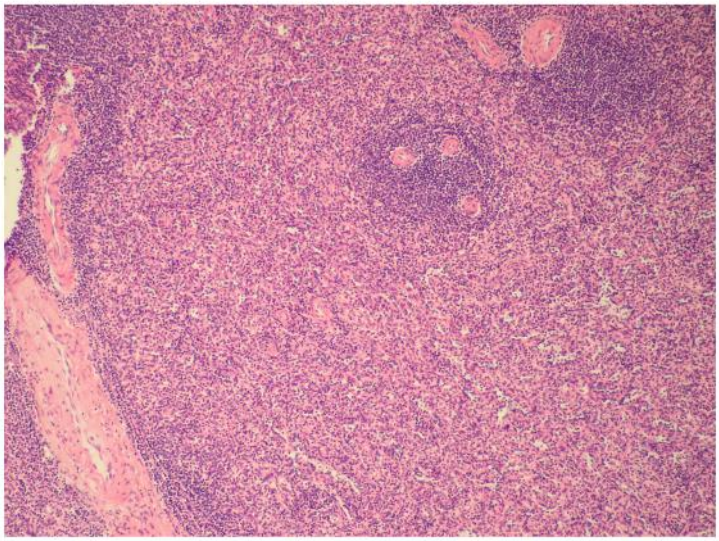


Spleen has its hilum at the medial surface .
Three important facts about spleen :
It doesn't have afferent , it has only efferent .
No lymph sinuses .
It's not arranged in cortex & medulla , it's divided instead into white pulp & red pulp .

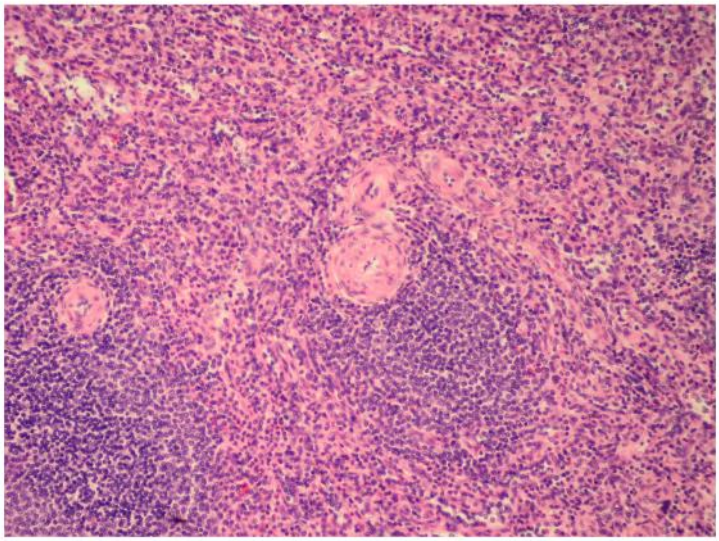
The white pulp → the periarteriolar sheath (PAS) & splenic follicles or the malpighian corpuscle .
The red pulp → dispersed between the white pulp & is composed of : capillary sinusoids surrounded by splenic cords .
In the splenic cords we have " kol ma haba o dab " → RBCs , WBCs , macrophages , platelets & plasma cells .
Q : why are there macrophages in the splenic cords near the blood sinusoids ?
A : to engulf the old RBCs , old platelets & blood borne antigens .



Here we can see the **splenic follicle which has the central artery <u>located peripherally</u>**, although the artery is eccentric in position , it's still called central artery as its centrally located originally within the periarteriolar sheath .The red pulp can be seen also filling in between the follicles , and the spaces here are blood sinusoids surrounded by splenic cords .



Here we can see the follicle with the central artery located peripherally .
Splenic artery → trabecular arteries → central artery → penicillar artery ,Then pencillar artery ends either :
Directly in the blood sinusoid : closed circulation , or
To the tissue surrounding the sinusoids : opened circulation .
Eventually , all blood drains to the sinusoids then forming the splenic vein .
Surrounding the splenic follicle is the marginal zone which has the marginal sinuses & it acts as a gate for T & B cells entry from the circulation to spleen similar in this to the post capillary venules function in lymph nodes , & here we can find macrophages (so **macrophages can be in both the red pulp & white pulp in the marginal zone**)



T cells & the interdigitating dendritic cells surround the central artery forming the periarteriolar sheath , then the central artery continues to be surrounded by B cells forming the follicle in where it is located peripherally .

So in the periarteriolar sheath : cell – mediated immune reaction via the T cells .

& in the follicle : Ab – mediated immune reaction via the B cells .

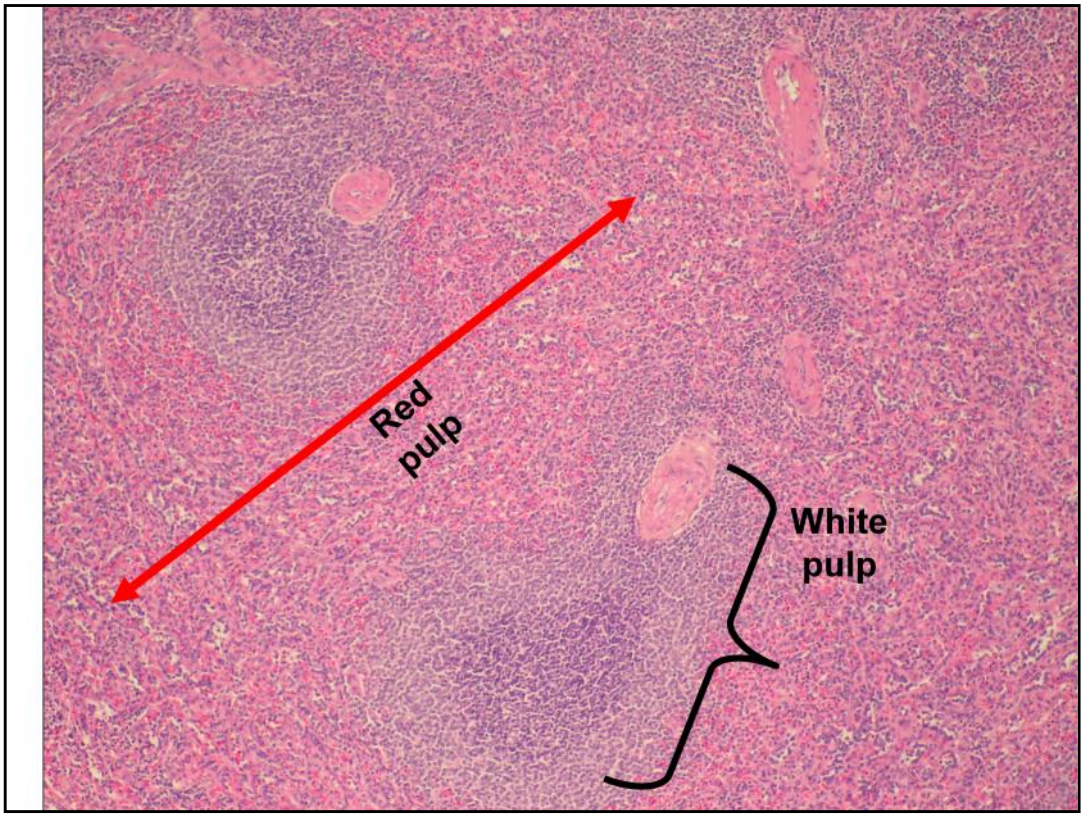
Functions of spleen :

Cemetery of the RBCs , via the macrophages that engulf the old ones .

Production of WBCs & RBCs in the fetus .

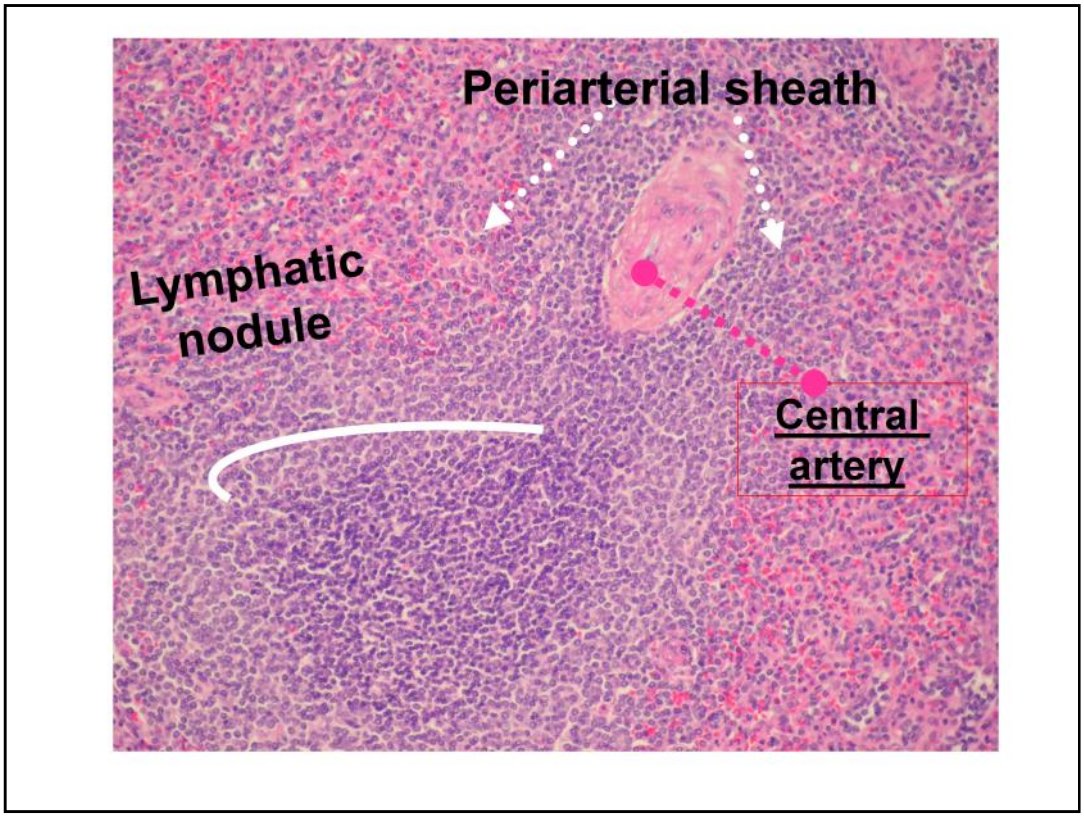
Production of lymphocytes during the process of proliferation in the immune reactions .

Q :The only source of lymphocyets is the bone marrow ?False, because spleen & lymph nodes aid as well .

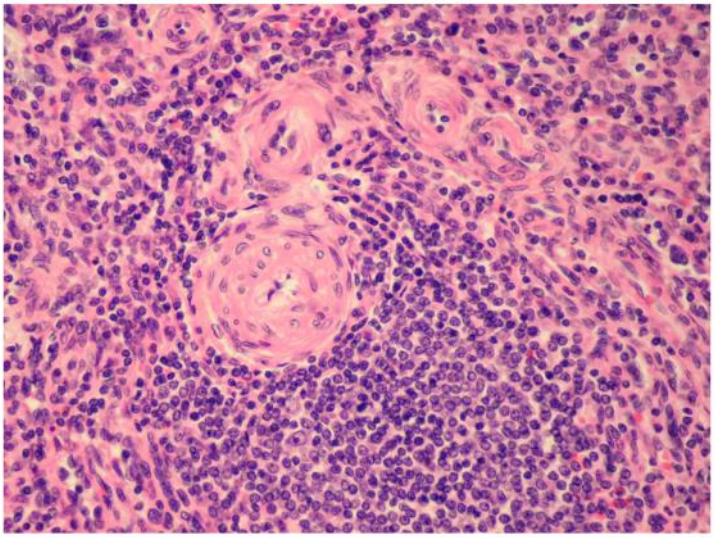


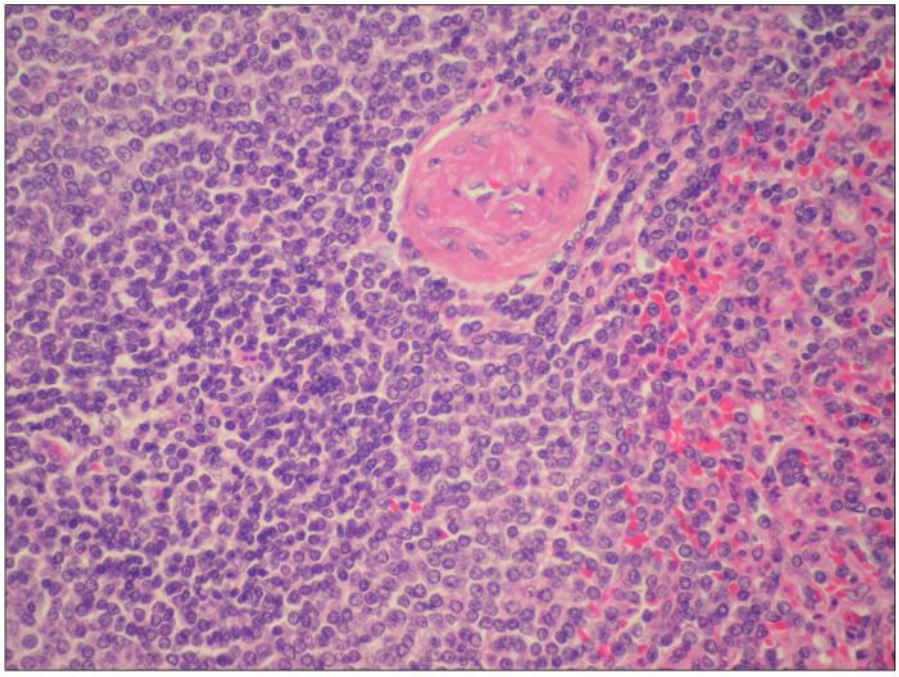
Here we can see the red & white pulps
Q : the central artery is branch of the trabecular artery ? True .

Structure of the spleen is built around its blood supply .
The white pulp is built around the artery .
The red pulp is built around the sinusoids

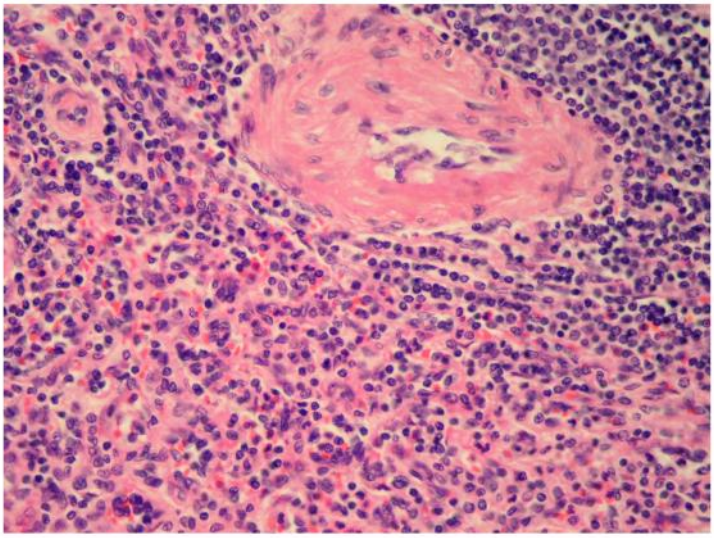


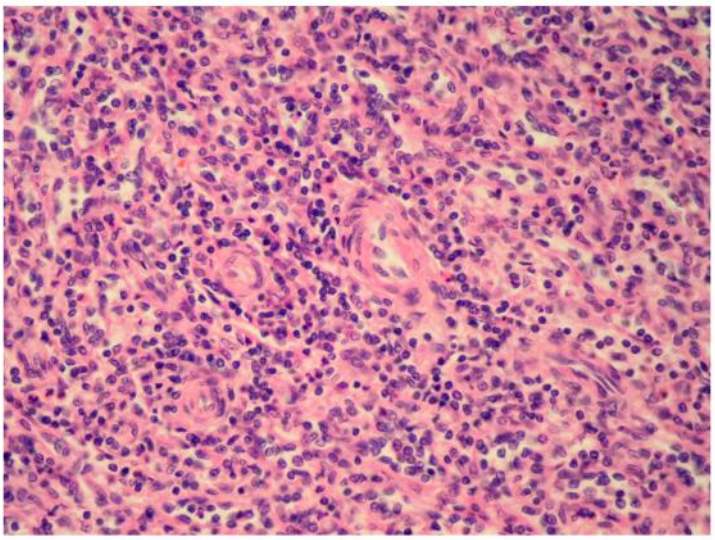
The white pulp with the PAS & the follicle
The follicle has B cells & follicular dendritic cells .



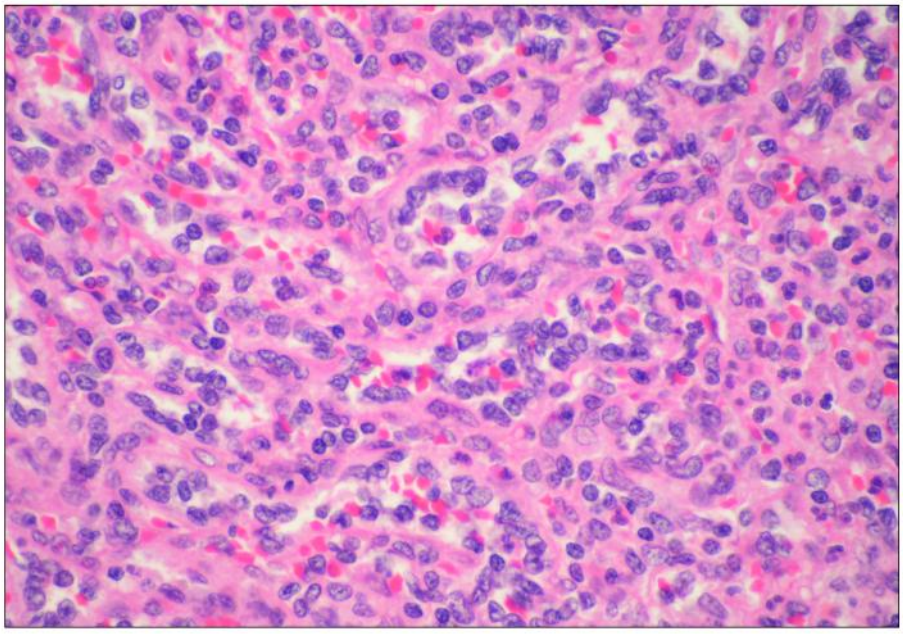


This is the central artery , once we see it , then sure this is the white pulp
The artery is composed of many layers of smooth muscles that we can recognize their nuclei & not their boundaries

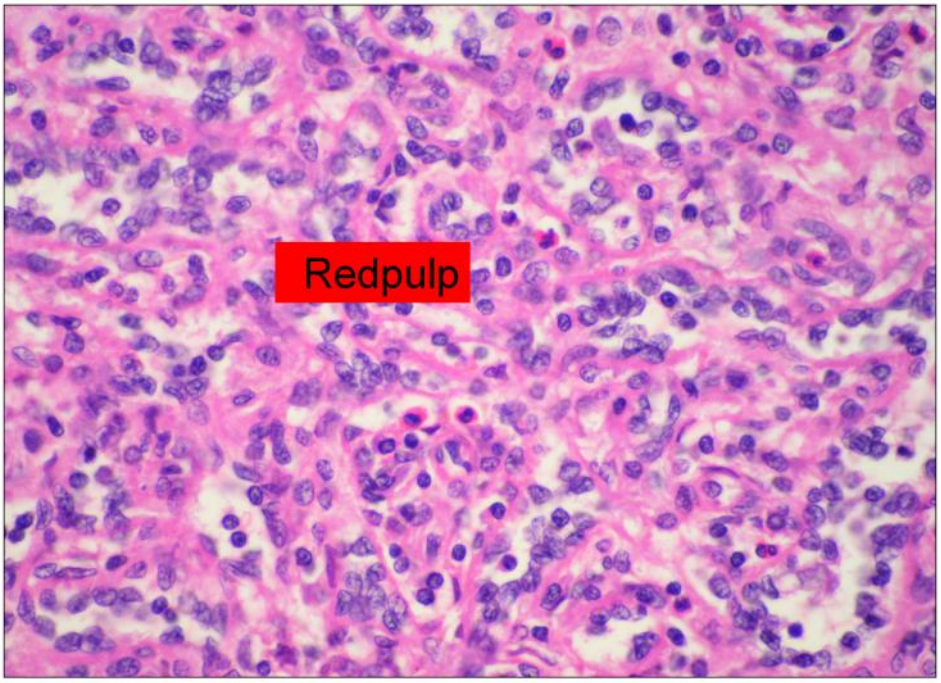




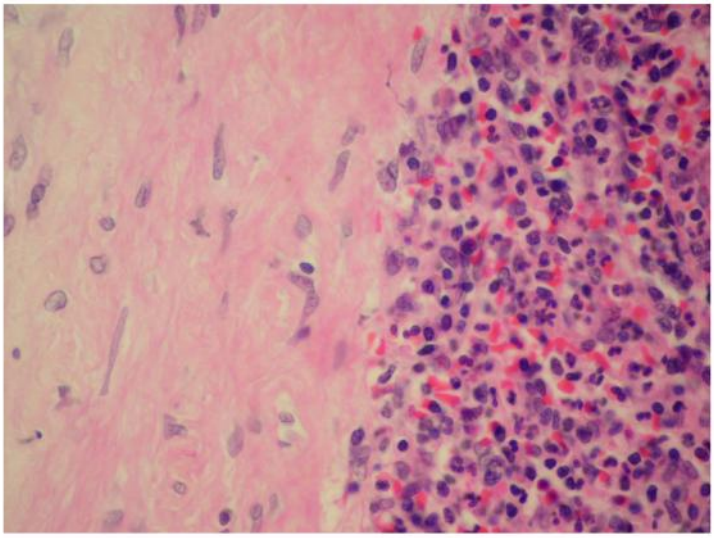
No central artery , no nodules , so this is **red pulp** .
the question stem here comes like this :
This slide shows *a section in spleen* , & then you will be asked questions depend on your identification of the slide being a red pulp , for example :
Q. No platelets present in this section ? <u>False</u> , " remember that the red pulp has kol ma haba o dab "



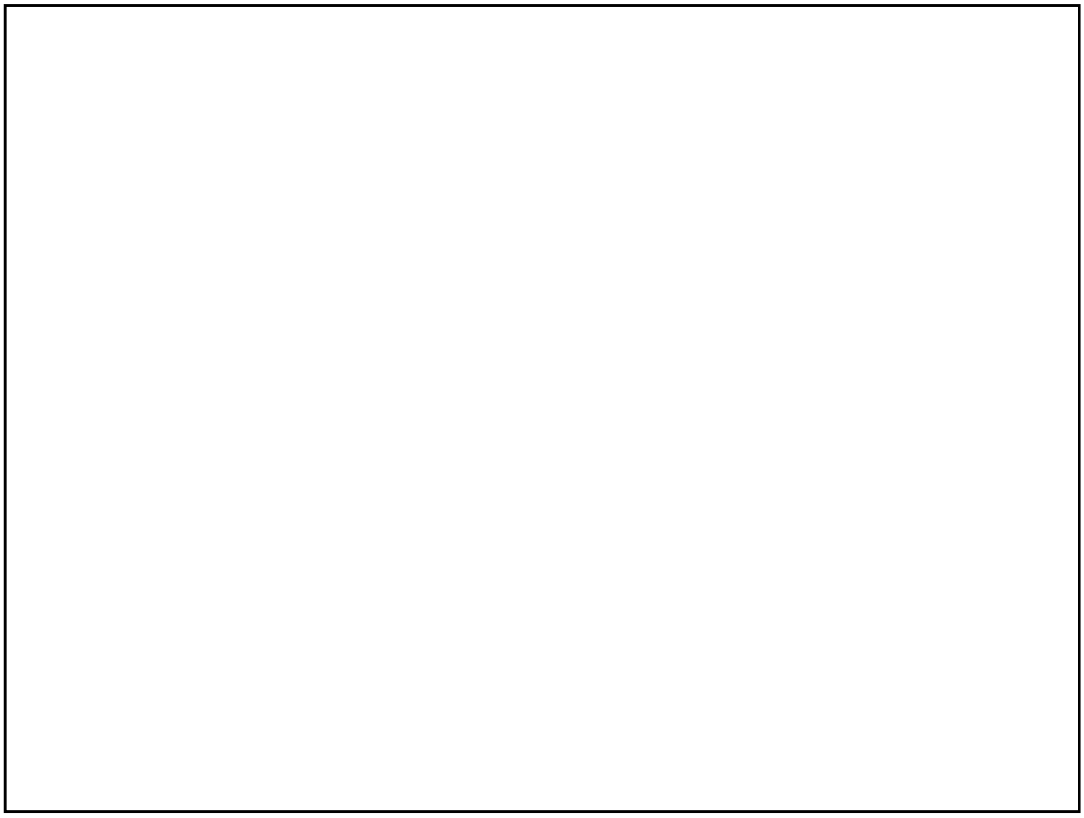
Red pulp ,Spaces here are sinusoids surrounded by splenic cords .


Redpulp

Capsule of spleen



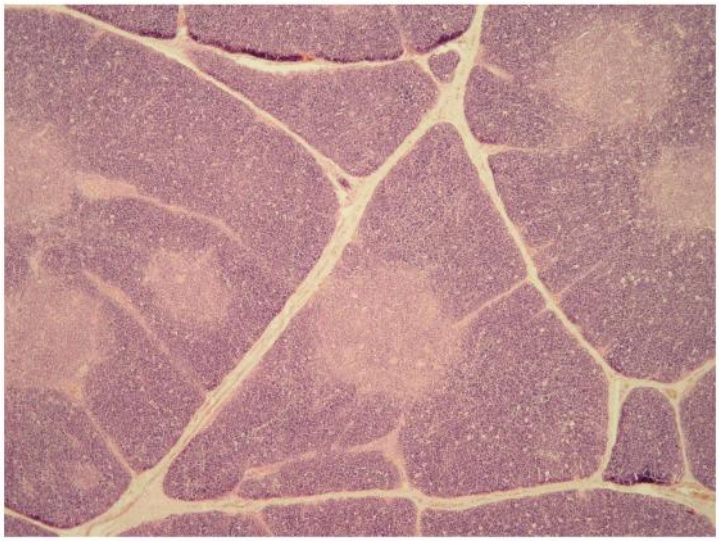
Capsule of spleen .
Within the capsule we can recognize nuclei of smooth muscles .
Q : why do we have smooth muscles in the spleen ?
A : spleen in human stores little amount of blood , while in animals like dogs & camels they store much more amount of blood in their larger spleen , anyway , in human , when we lose a lot of blood as in case of severe hemorrhage then the sympathetic system is on , so these smooth muscles become activated 'coz they are sympathetically innervated and as a result they will contract squeezing the spleen to evacuate blood into the circulation in compensation for the blood loss , although it's a minimal amount (30 – 70ml) but still helpful .
Q : in secondary lymphoid organs there is concentration of antigens ? True , because the 2ry lymphoid organs trap the antigens whether blood borne Ags (in spleen via the sinusoids of marginal zone) or lymph borne Ags (in lymph nodes) , then presenting them by APCs to the lymphocytes which become activated & thus immune reactions proceed .



It’s said that antibody – mediated immune reactions are more effective & rapid in spleen than in lymph nodes , and this is due to the fact that the T helper cells which are needed for the activation of B cells are closer in location to the B cells in the spleen than in lymph nodes i.e in spleen ,the T cells are in the periartelioar sheath & B cells are in the splenic follicles which are all located within the white pulp , but in lymph nodes , the T cells are in the paracortex & B cells are in the cortex ; in two different regions , so it takes time for the T helper cells to reach the B cells and activate them .

Thymus

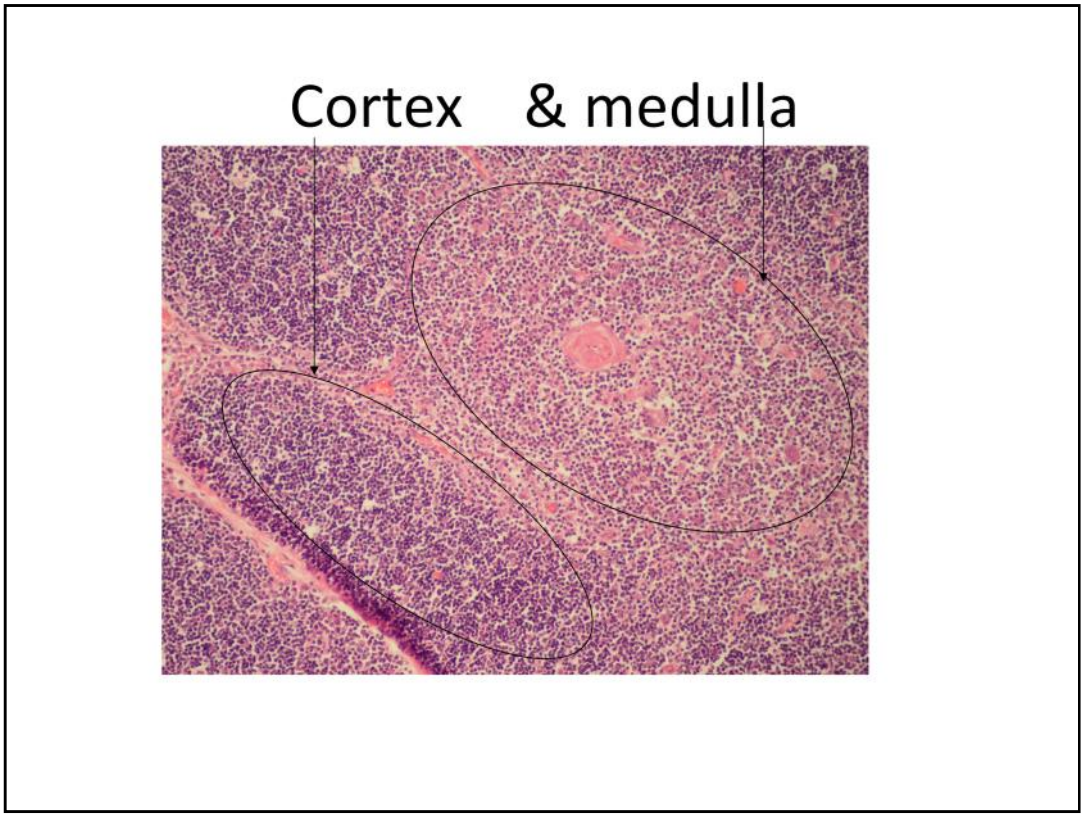
Lobules of Thymus



Lobules of thymus .

Location of the thymus : behind the upper part of the sternum , at birth it's 15 g , then at puberty it becomes 30 g then involutes to become 15g at old ages where most of its tissue is replaced by adipose tissue.

Capsulated organs , with trabeculae dividing the thymus into lobules, each of which has a cortex & a medulla .



The cortex has more cells which are **im**mature T lymphocytes , ***while*** the **m**ature/naïve/ immunocompetent T cells present in the **m**edulla from where they leave to reach their specific sites in the periphery lymphoid organs i.e in the paracortex in lymph nodes & the the periarteriolar sheath in spleen .

Thymus has only efferent lymphatics no afferent lymphatics so no lymph sinuses. { both afferent & efferent together present only in the lymph nodes }.

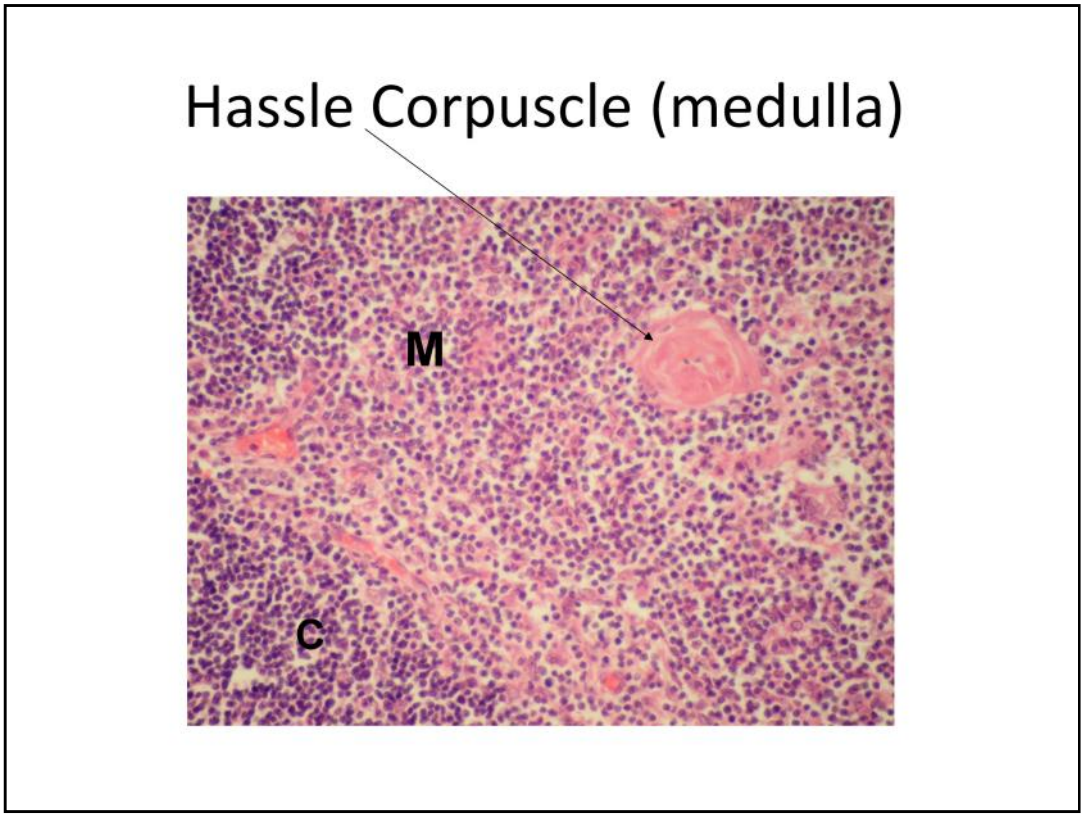
in the cortex : immature T cells , 3 types of epithelial reticular cells & macrophages .

98 % of T lymphocytes die by apoptosis due to :

Inability to recognize MHC I & II , or

The recognition of self proteins .

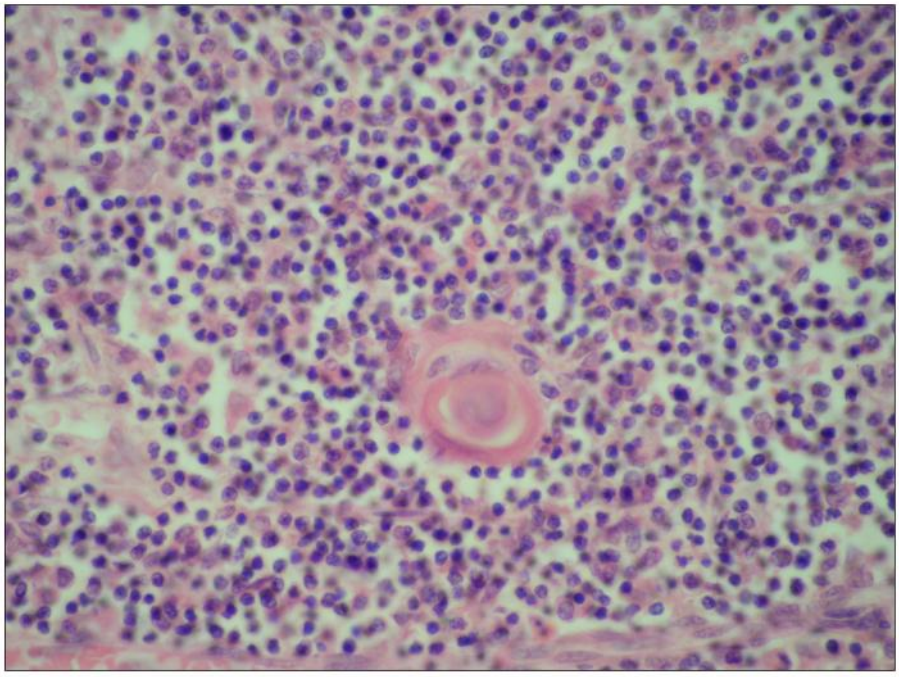
So surviving T cells can recognize MHCI & II via CD4 & 8, & don't interact with self antigens

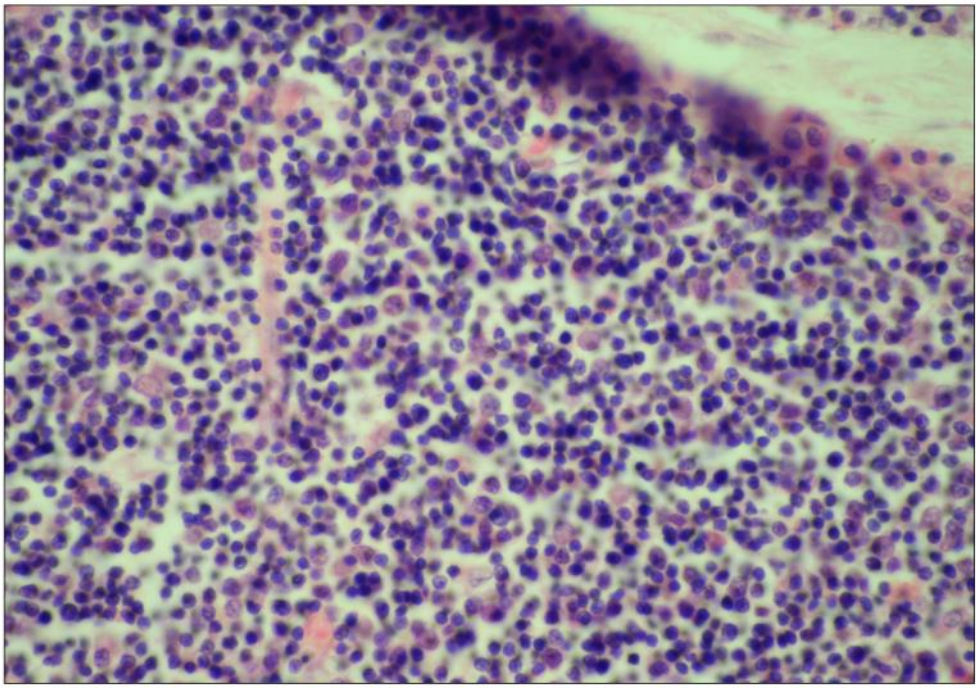


Hassle corpuscle (medulla) .

They are degenerated reticular cells that don’t produce any thymic hormones .

Contents : Mature T cells & few macrophages .



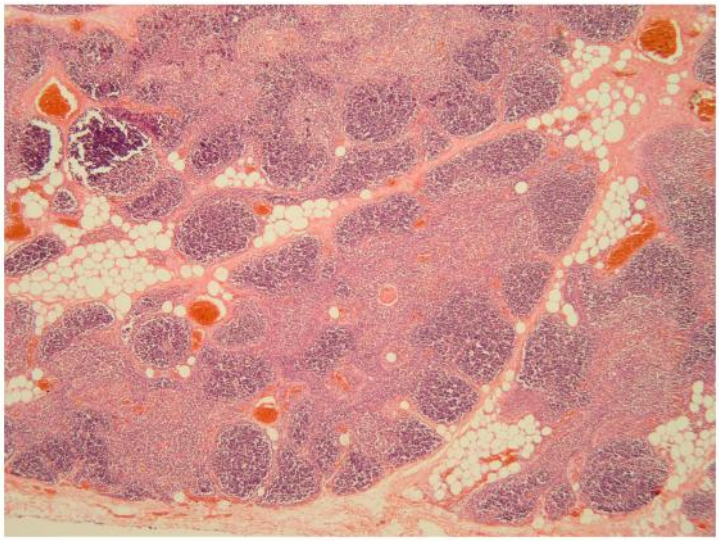


This is **the cortex**, In it we **have the thymus – blood barrier**.

Blood supply reaches the cortex at the level of capillaries not artery or arterioles , why ?

The capillaries have tight junctions between the cells ,continuous basal lamina , outer sheath of connective tissue & epithelial cells with desmosmes all together prevent blood borne antigens entry to the cortex where the **developing T lymphocytes present which need to be not exposed to Ags** at the stage of development , but some self proteins can pass .

Involuted thymus



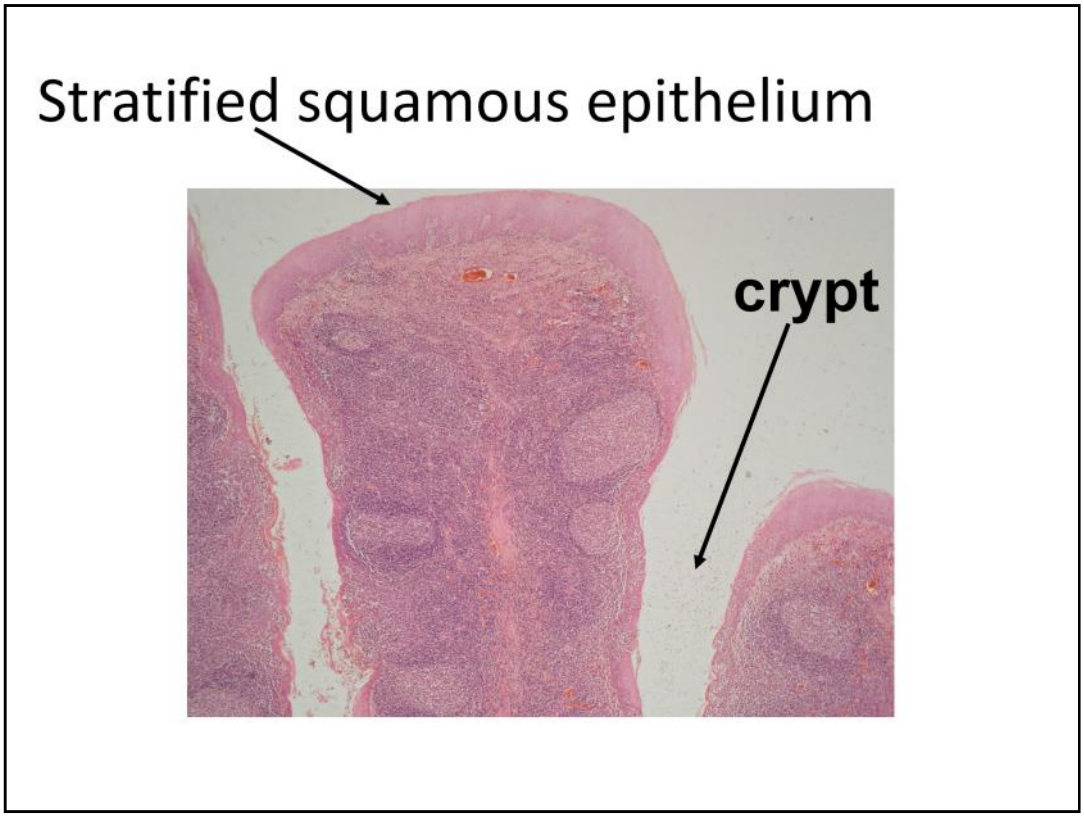
Involuted thymus .

Adipocytes can be seen here.

The removal of thymus at old ages has minmal effects but at younger ages it has greater effects on the body immunity , in another words , T cells in the periarteriolar sheath in spleen & the paracortex in lymph nodes are less dependent on the thymus hormones at old ages than at younger ages .

Thymus hormones act locally & peripherally where they reach the spleen & lymph nodes .

Palatine Tonsils



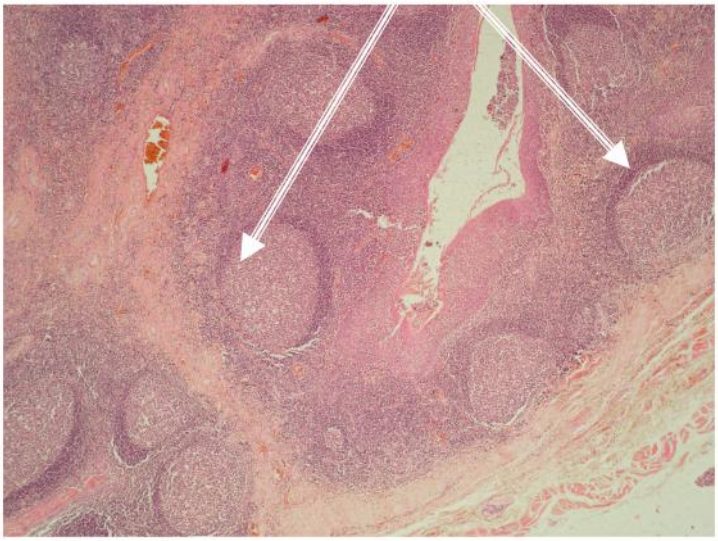
Section from palatine tonsils .

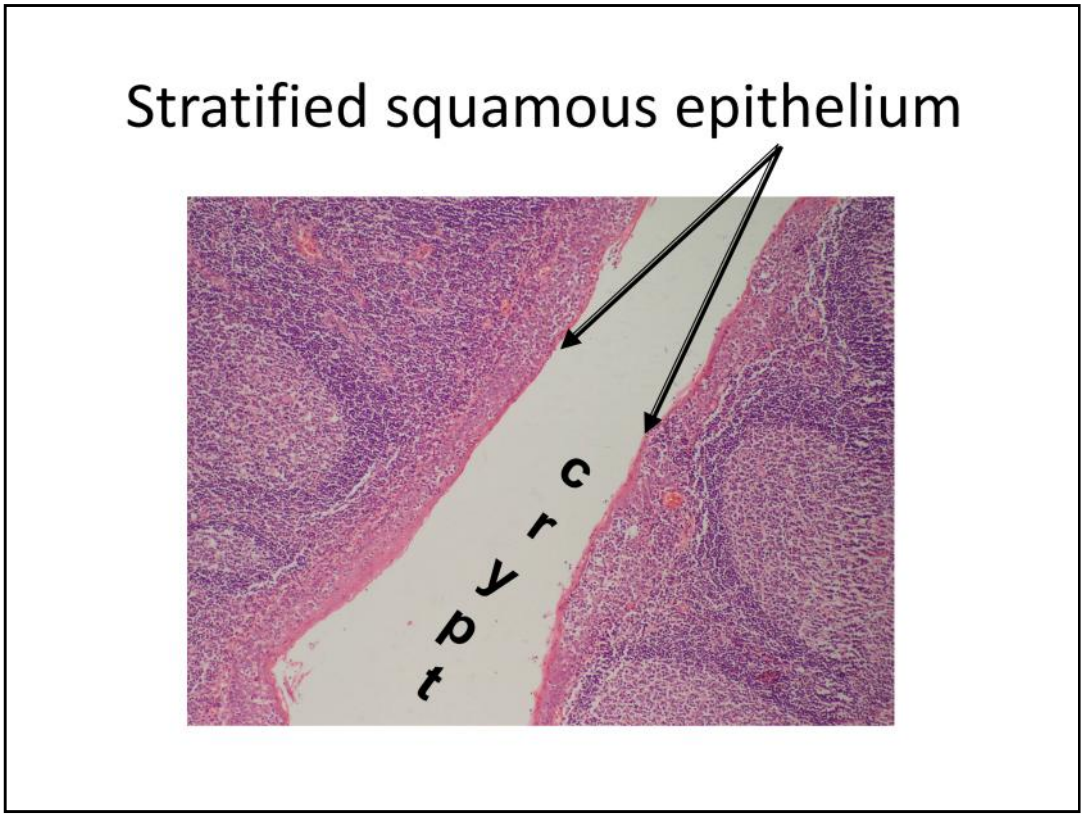
Has a lot of lymphatic nodules , and we can notice the pale centers , so they are 2ry lymphatic nodules .

Covered with stratified squamous epithelium .

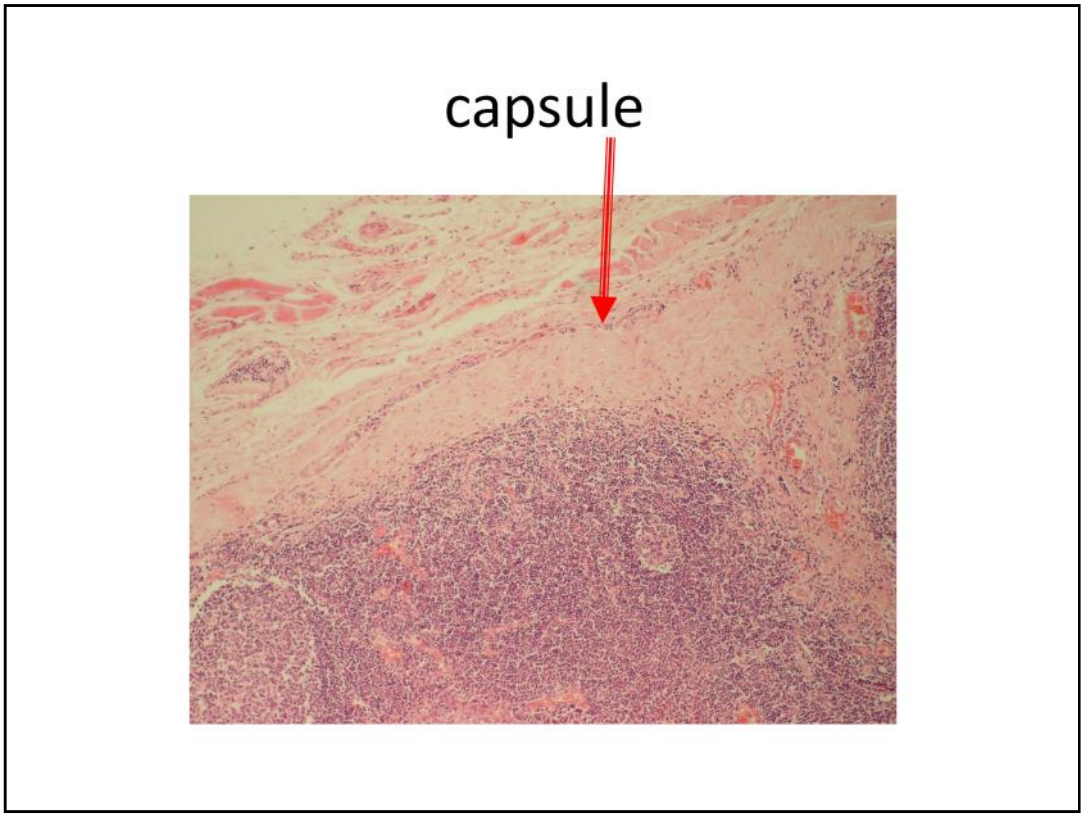
There are crypts , which in case of infection become wider with white fluid getting out from them .

Lymphatic nodules





The stratified squamous epithelium covers the crypts as well.



The carotid artery is a vital structure located close to the palatine tonsils , so we need to be careful.
When the palatine tonsils are to be surgically removed