

# SH Lecture - Lymphatic Structure and Organs

From Embryology

## Introduction



This lecture will provide an overview of the lymphoid structure and histology of key cells, vessels, structures and organs lymphoid organs, including the lymph nodes, spleen and thymus, as well as extranodal lymphoid tissues including mucosal associated lymphoid tissues (MALT).

In this lecture I will go through the structures in sequence from cells through to organs, immunity itself is covered in detail elsewhere in the course.

### Textbook References

[Collapse]

Hill, M.A. (2016). *UNSW Embryology* (16th ed.) Retrieved February 26, 2016, from <https://embryology.med.unsw.edu.au>

- SH Laboratory Support | Movie - AIDS related lymphoma | Student Lecture Feedback
- Lymphatic Quiz



**Virtual Slides - Lymphatic** (<http://moodle.telt.unsw.edu.au/mod/book/view.php?id=828270>): Human Blood Smear (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=794799>) | Bone Marrow Smear (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=802056>) | Thymus (infant)

(<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=804049>) | Thymus (adult 1) (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=794807>) | Thymus (adult 2) (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=802962>) | Spleen (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=804048>) | Spleen (silver stain) (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=804648>) | Lymph Node (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=804046>) | Lymph Node (silver stain) (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=804042>) | Lingual tonsil (tongue} (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=804051>) | Pharyngeal tonsil (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=804050>) | Appendix (<http://moodle.telt.unsw.edu.au/mod/lti/view.php?id=804637>) (slide access requires Zpass login)

- Additional background information:

**Immune Links:** Introduction | Blood | Spleen | Thymus | Lymphatic | Lymph Node | Antibody | **Med Lecture - Lymphatic Structure** | Med Practical | Immune Movies | Vaccination | Bacterial Infection | Abnormalities | Category:Immune

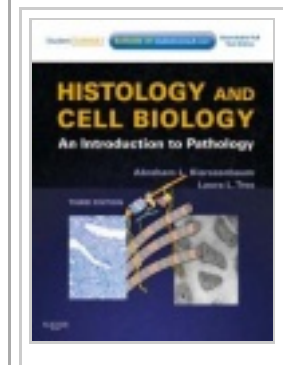
### Historic Embryology[Expand]

[Expand]  
Previous  
Lectures

**Janeway's Immunobiology** (see in additional information) NCBI Bookshelf (<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=imm.TOC&depth=2>) A good detailed textbook on the lymphatic system.

**Nature Immunology** - These are short (5-10 min) animations showing how the immune system monitors the epithelial and environment interface at different anatomical locations.

- Immunology of the skin (<http://www.nature.com/ni/multimedia/skin/index.html>)
- Immunology of the lung (<http://www.nature.com/ni/multimedia/lung/index.html>)
- Immunology in the gut mucosa (<http://www.nature.com/ni/multimedia/mucosal/index.html>)



UNSW Students have online access to the current 3rd edn. through the UNSW Library subscription (<http://www.unsw.ebib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=2074364>).

- Chapter 6. Blood And Hematopoiesis (<http://www.unsw.ebib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430108&pg=186>)
- Chapter 10. Immune-Lymphatic System (<http://www.unsw.ebib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430108&pg=320>)
  - Lymph Node (<http://www.unsw.ebib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430108&pg=335>)
  - Thymus (<http://www.unsw.ebib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430108&pg=339>)
  - Spleen (<http://www.unsw.ebib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430108&pg=345>)
- Chapter 16. Lower Digestive Segment Protection of the small intestine (<http://www.unsw.ebib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430108&pg=501>)
- Blood Chapter Page 169 - Blood development information. Page 191 - Myeloid lineage histology.

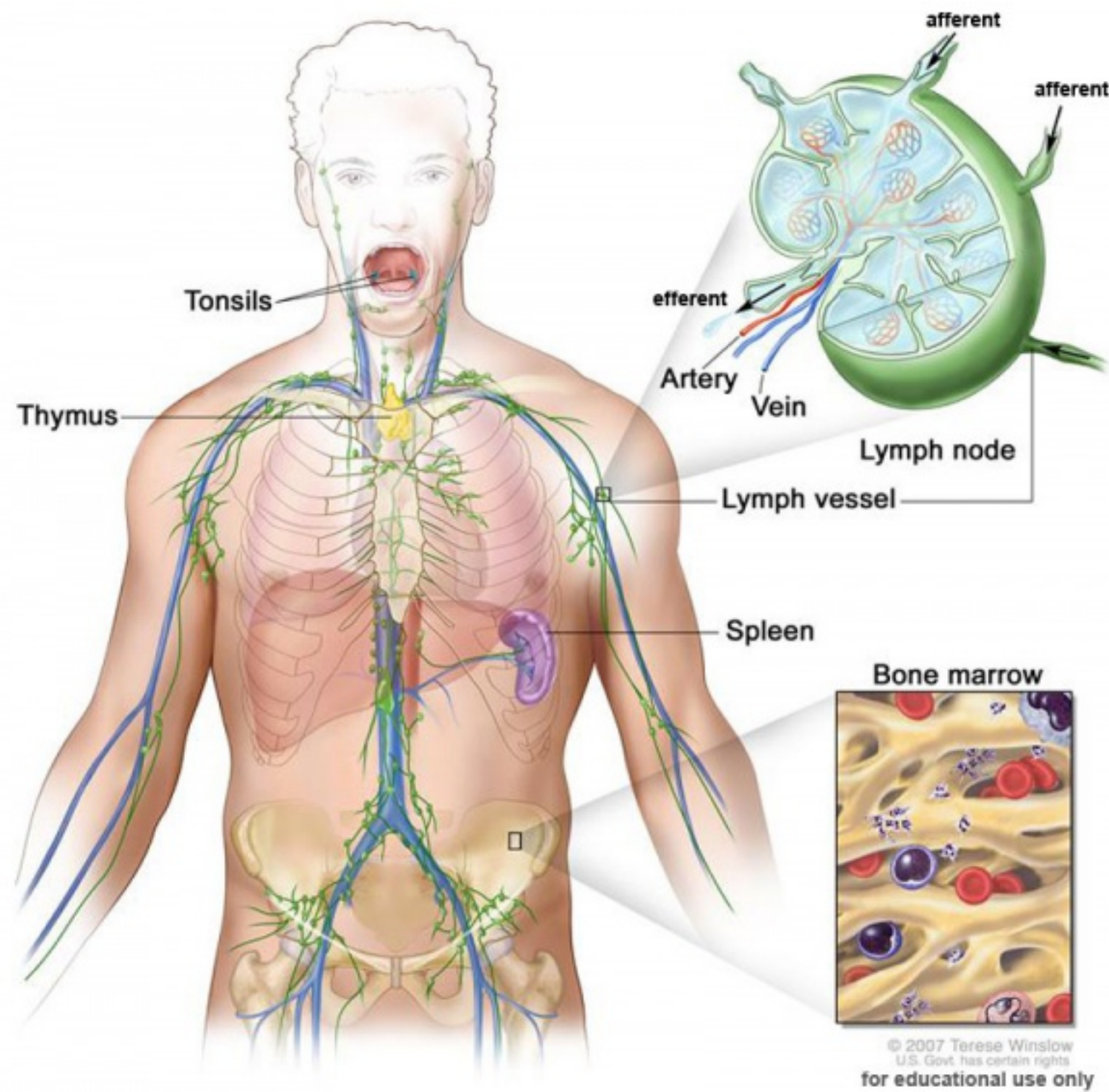


## Structure

## Function

1. **Cells** - blood cells (parenchyma), connective tissue (stroma)
2. **Vessels** - lymphatic vessels
3. **Diffuse** - (extra-nodal tissue) nodules, Mucosal Associated Lymphoid Tissues (MALT)
4. **Nodes** - (historic, "glands")
5. **Organs** - thymus, spleen

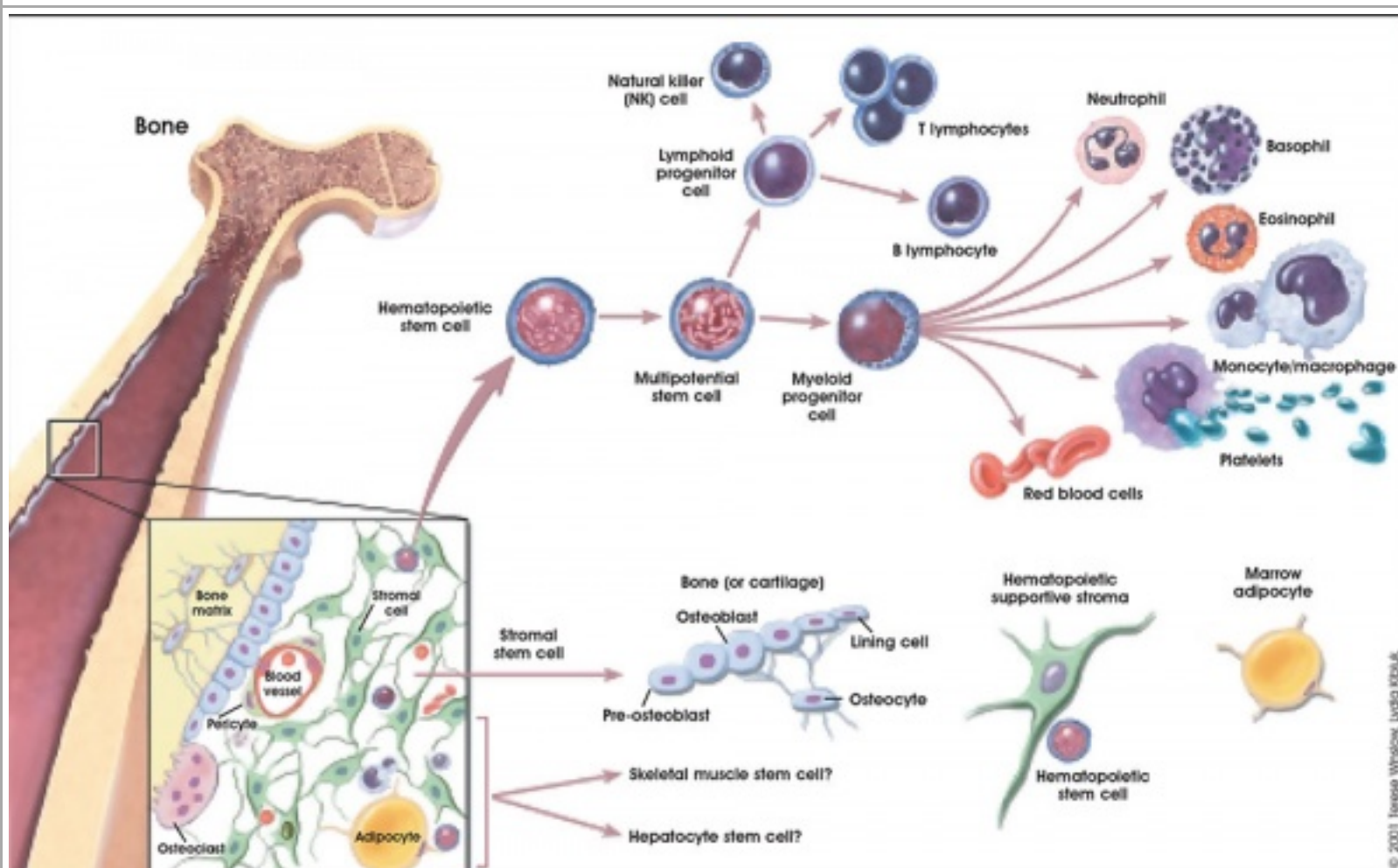
1. **Immune** - “monitor” of body surfaces, internal fluids
2. **Extracellular fluid** - returns interstitial fluid to circulation
3. **Gastrointestinal tract** - carries fat and fat-soluble vitamins



## Blood Cells

### Blood Cell Development

[Collapse]



### Two Blood Cell Systems

1. **Mononuclear Phagocytic System** - circulating monocytes of peripheral blood and non-circulating (fixed) tissue macrophages found throughout the body.



2. **Lymphoid System** - lymphocytes, three major types of T, B, and NK.

Lymphoid Organs

- Central - (primary) Lymphocytes develop from precursor cells in bone marrow and thymus. (see blood marrow image)
- Peripheral - (secondary) Lymphocytes respond to antigen lymph nodes or spleen.

<b>Blood Cells</b>	<b>[Collapse]</b>
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The blood cell information shown below in the table is shown to identify the relative proportions of different cell types in the circulating blood. This information is provided in the lecture as additional information for reference purposes only.

**Blood Cell Numbers**

The adult ranges of cells / 1 litre (l), total blood volume is about 4.7 to 5 litres. Blood Development | Blood Histology

**Red Blood Cells**

- Male: 4.32 - 5.66 x 10<sup>12</sup>/l
- Female: 3.88 - 4.99 x 10<sup>12</sup>/l

**Leukocytes (white blood cells)**

- Male: 3.7 - 9.5 x 10<sup>9</sup>/l
- Female: 3.9 - 11.1 x 10<sup>9</sup>/l

**Granulocytes**

- 1.8 - 8.9 x 10<sup>9</sup>/l
  - Neutrophils: 1.5 - 7.4 x 10<sup>9</sup>/l
  - Eosinophils: 0.02 - 0.67 x 10<sup>9</sup>/l
  - Basophils: 0 - 0.13 x 10<sup>9</sup>/l

**Non-Granulocytes**

- **Monocytes** 0.21 - 0.92 x 10<sup>9</sup>/l

**Lymphocytes**

- 1.1 - 3.5 x 10<sup>9</sup>/l
  - B-cells: 0.06 - 0.66 x 10<sup>9</sup>/l
  - T-cells: 0.77 - 2.68 x 10<sup>9</sup>/l
    - CD4+: 0.53 - 1.76 x 10<sup>9</sup>/l
    - CD8+: 0.30 - 1.03 x 10<sup>9</sup>/l
    - NK cells: 0.20 - 0.40 x 10<sup>9</sup>/l

**Platelets**

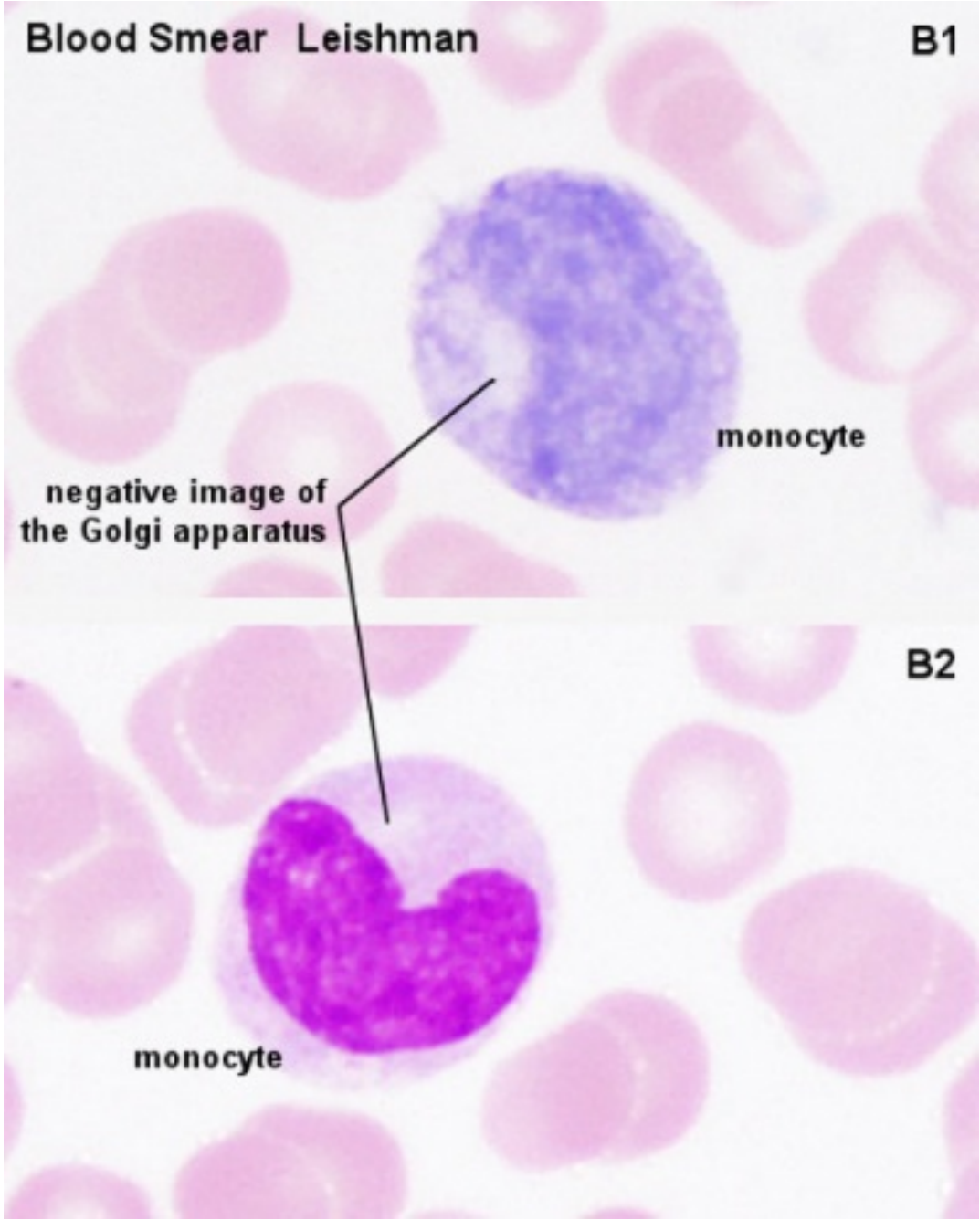
- 140 - 440 x 10<sup>9</sup>/l
  - not a cell, a cell fragment.





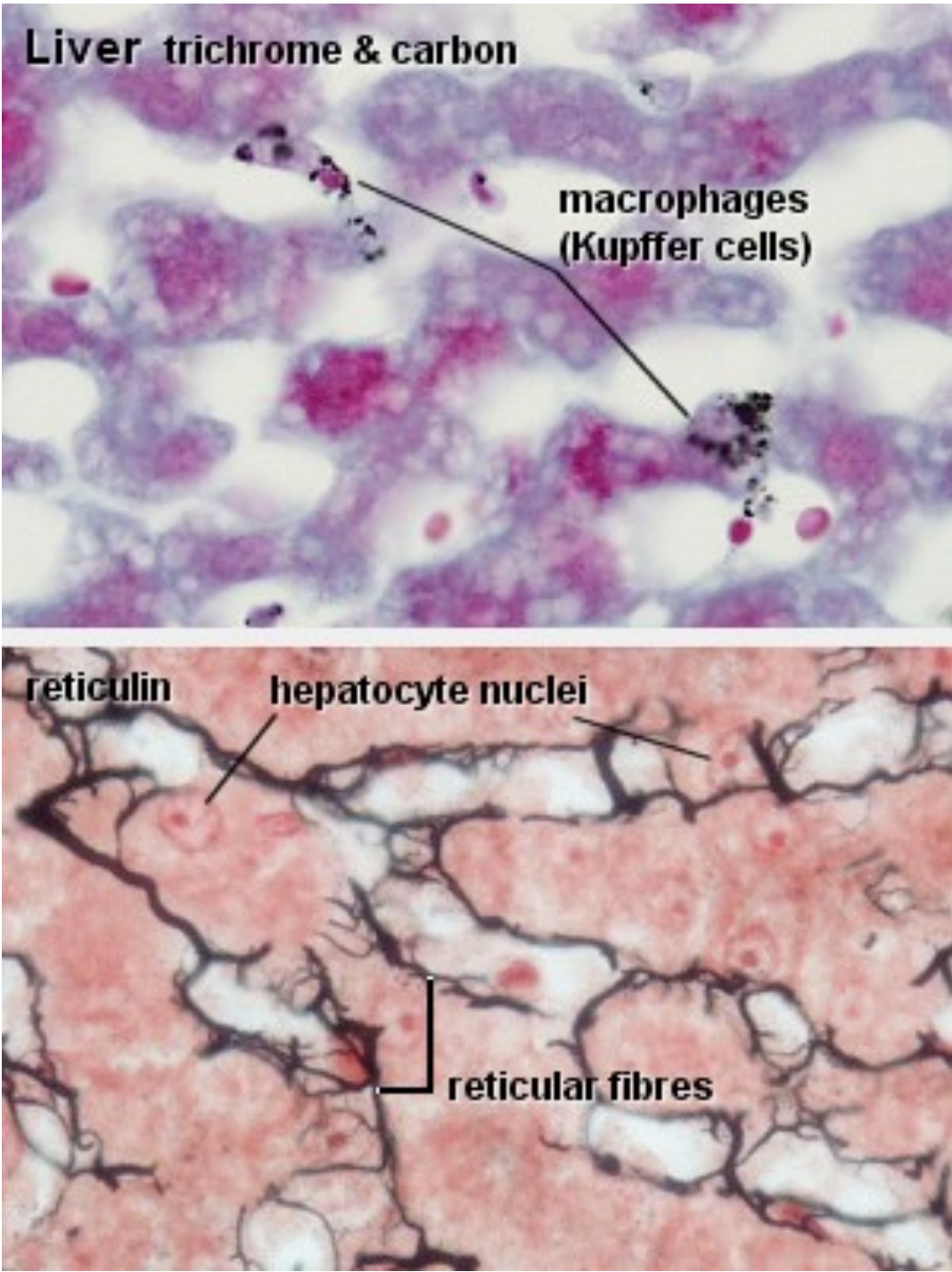


Mononuclear Phagocytic System (MPS, also called Lymphoreticular System or Reticuloendothelial System, RES)



Circulating **monocytes** of peripheral blood.

- monocytes entering the connective tissue differentiate into **macrophages**)



Non-circulating (fixed) tissue **macrophages** (MΦ)

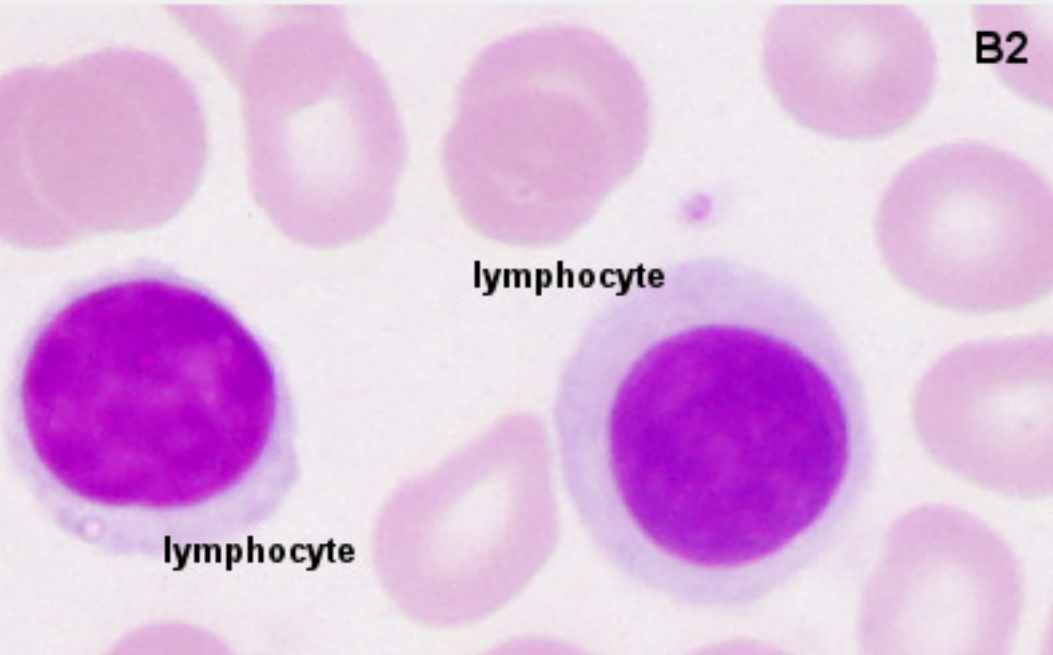
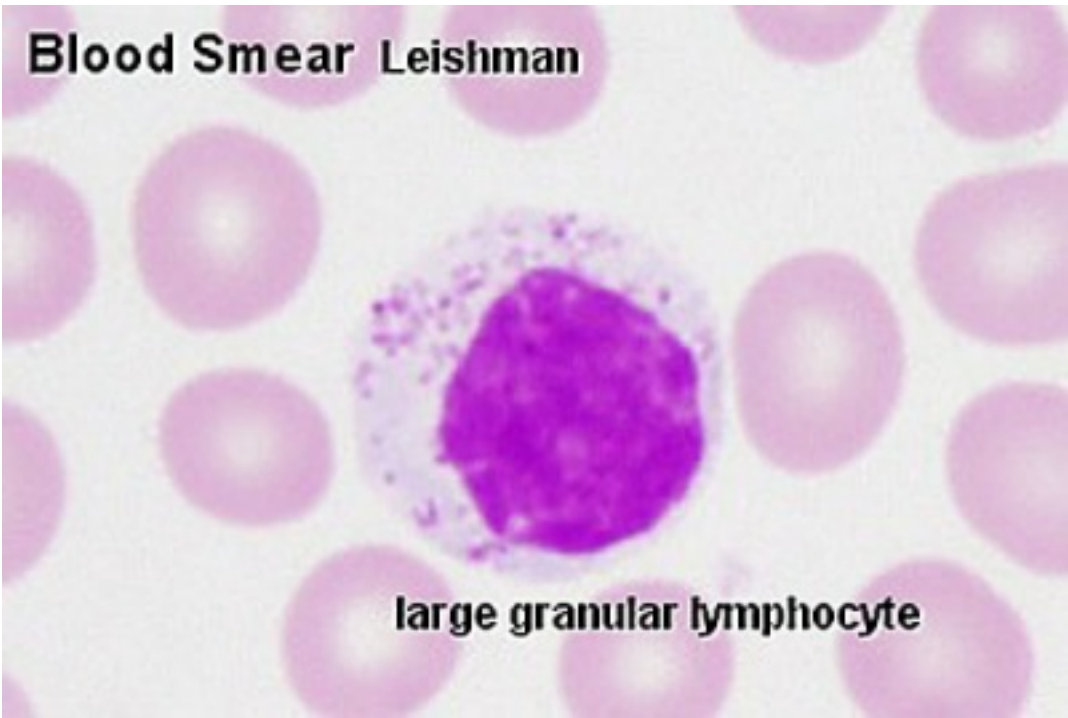
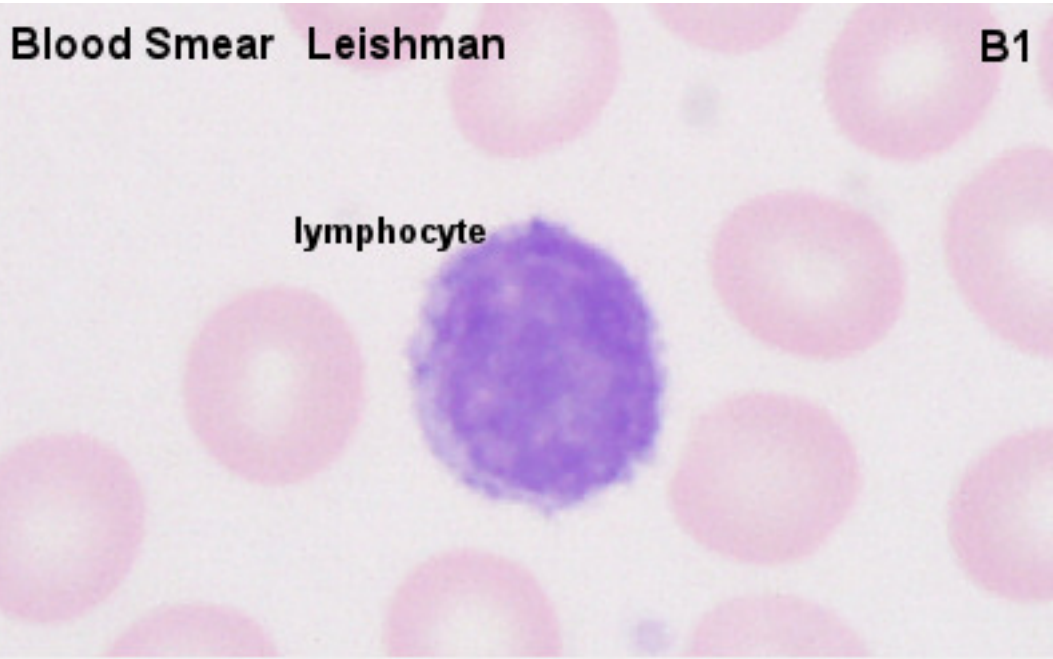
- found throughout the body (Liver, Kuffer cells), spleen, nodes and other tissues.

2. Lymphoid System

Adaptive immunity functional cells are the **lymphocytes** (B, T, NK) and **dendritic cells** (process antigen and present it on their surface, monocyte precursor derived).

- Antibody-mediated** - B Lymphocyte secreting antibody = **Plasma Cell**
- Cell-mediated** - T Lymphocytes form **memory cell**, Cytotoxic T cells, T helper cell





**B Cell Development**

- Bone marrow
- blood
- Lymph node, nodule
- Lymphatic vessel
- Bone marrow

**Germinal Centres**

- Bone Marrow
- Medullary cords contain plasma cells



**Plasma cells**

- Activated B cell, plasma B cells, plasmocytes, effector B cells and B cell that is secreting antibody.
- secrete antibody directly into blood for distribution to all body
- in local extrafollicular sites are short lived 2–4 days
- longer-lived plasma cells in bone marrow 3 weeks to 3 months+
- "clockface" nucleus
  - Nucleus has darker (heterochromatin) regions around periphery of nucleus separated by lighter (euchromatin) regions.

**Lymphocyte Electron Micrographs[Expand]**

**Lymphocyte Circulation**

- Microbial **antigens** are carried into a lymph node by **dendritic cells**, which enter via afferent lymphatic vessels draining an infected tissue.
- **T and B cells** enter the lymph node via an artery and migrate out of the bloodstream through postcapillary venules.
  - Unless they encounter their antigen, the T and B cells leave the lymph node via efferent lymphatic vessels, which eventually join



- the thoracic duct.
- The thoracic duct empties into a large vein carrying blood to the heart.
- A typical circulation cycle takes about 12–24 hours.

**Links:** MBoC Chapter 24 - The Adaptive Immune System (<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=mboc4&part=A4419>) | MBoC Figure 24-14. The path followed by lymphocytes as they continuously circulate between the lymph and blood (<http://www.ncbi.nlm.nih.gov/books/NBK26921/figure/A4442>) | Immunobiology (<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=imm>)

## Diffuse Lymphatic Tissue

### Diffuse Lymphatic Tissue Locations

Alimentary canal, respiratory passage and urogenital tract.

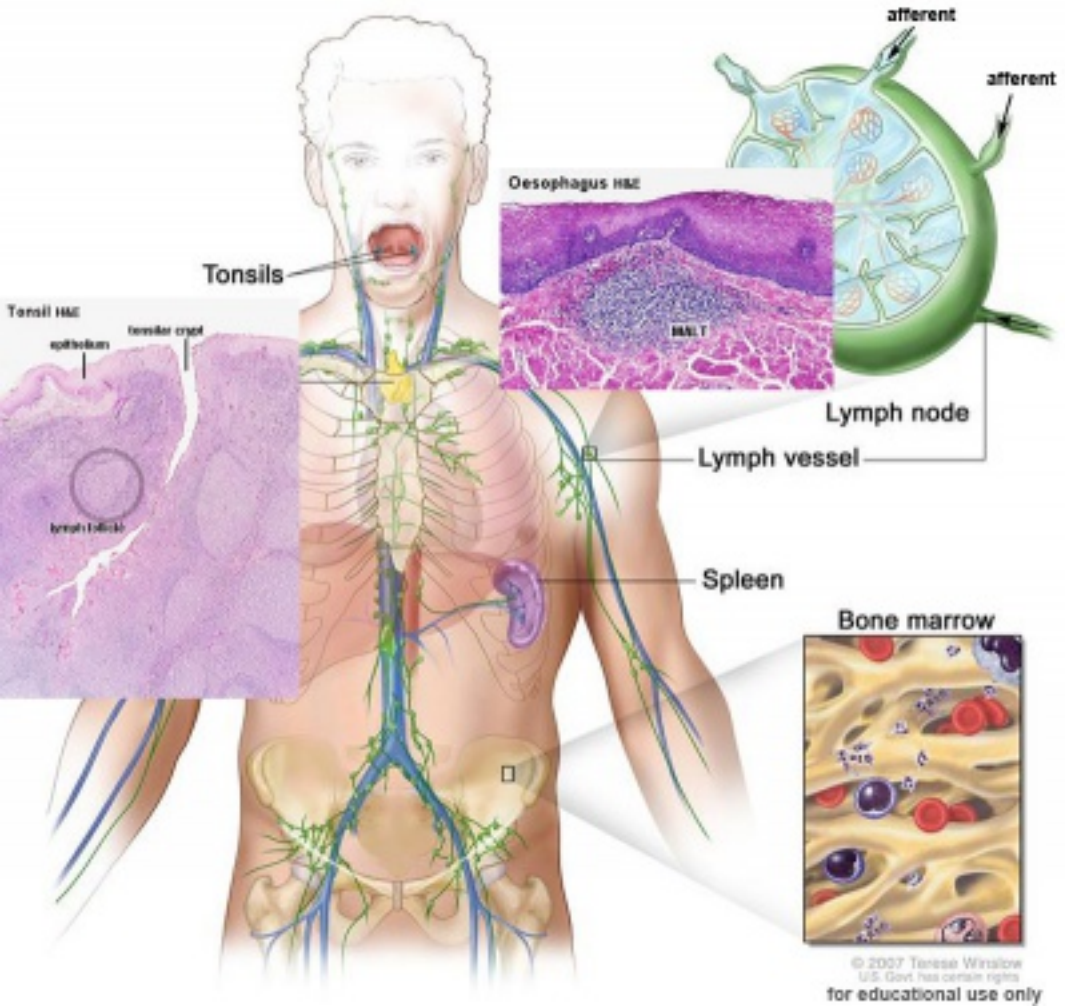
- BALT** - **B**ronchus **A**ssociated **L**ymphoid Tissue or **GALT** - **G**ut Associated **L**ymphatic Tissue
- Not enclosed by a connective tissue capsule**
- Located in subepithelial tissue - **lamina propria**
- Diffuse lymphatic tissue + nodules
- Reactive - enlarge when activated (by antigen)

### Lymphocytes

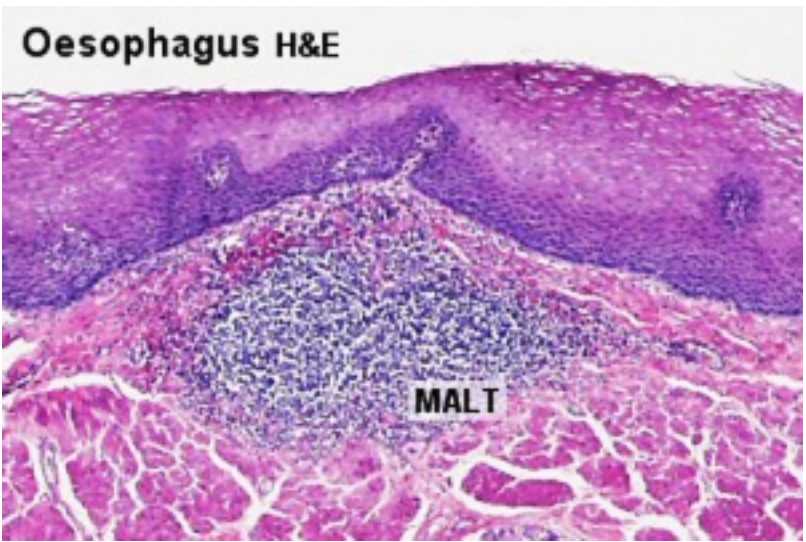
- travel to nodes and back again
- proliferation and differentiation

### Gastrointestinal Tract

- Oropharynx - Tonsils
- Distal small intestine (ilieum) - Peyer’s Patches
- Appendix, cecum

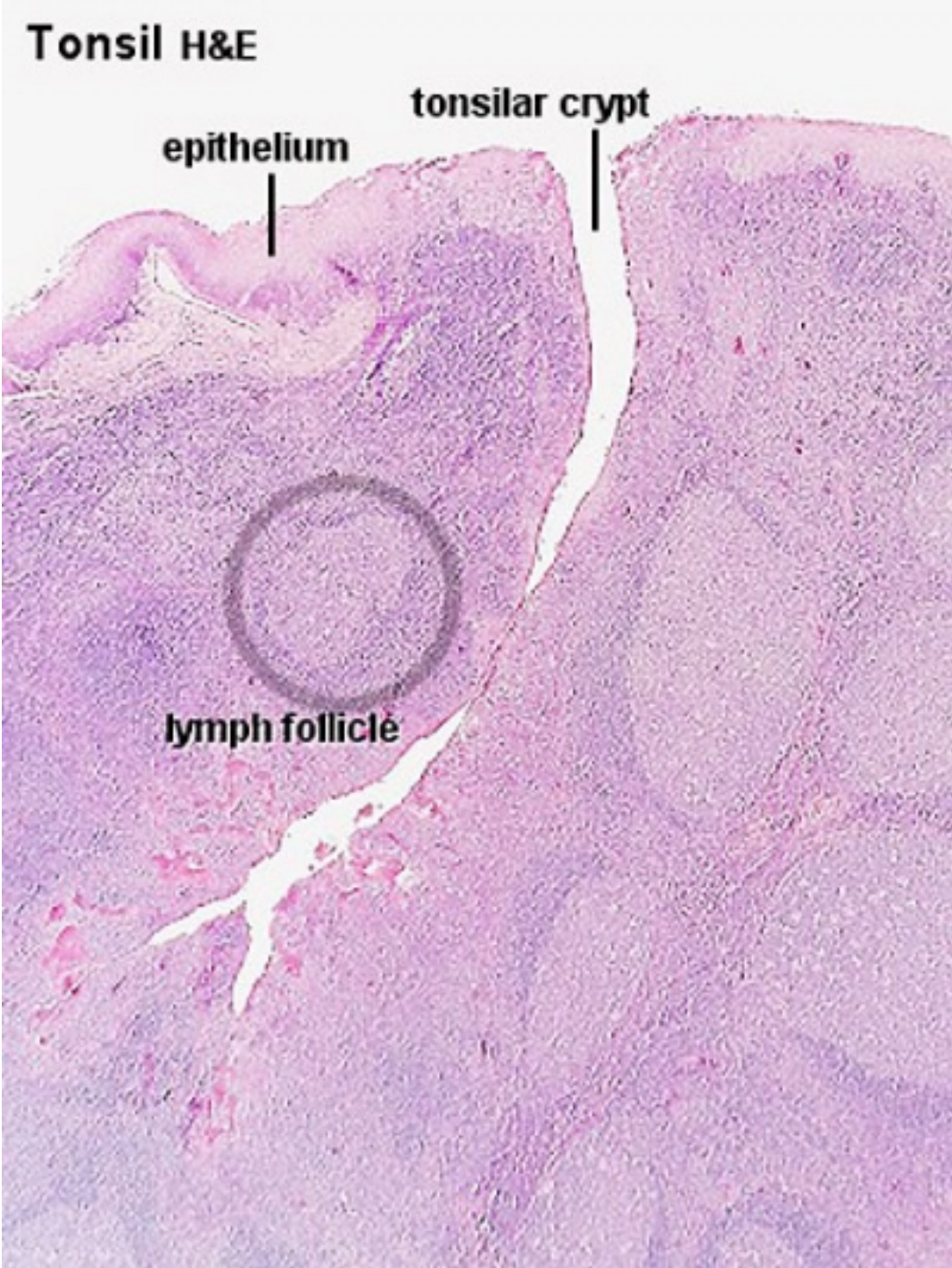
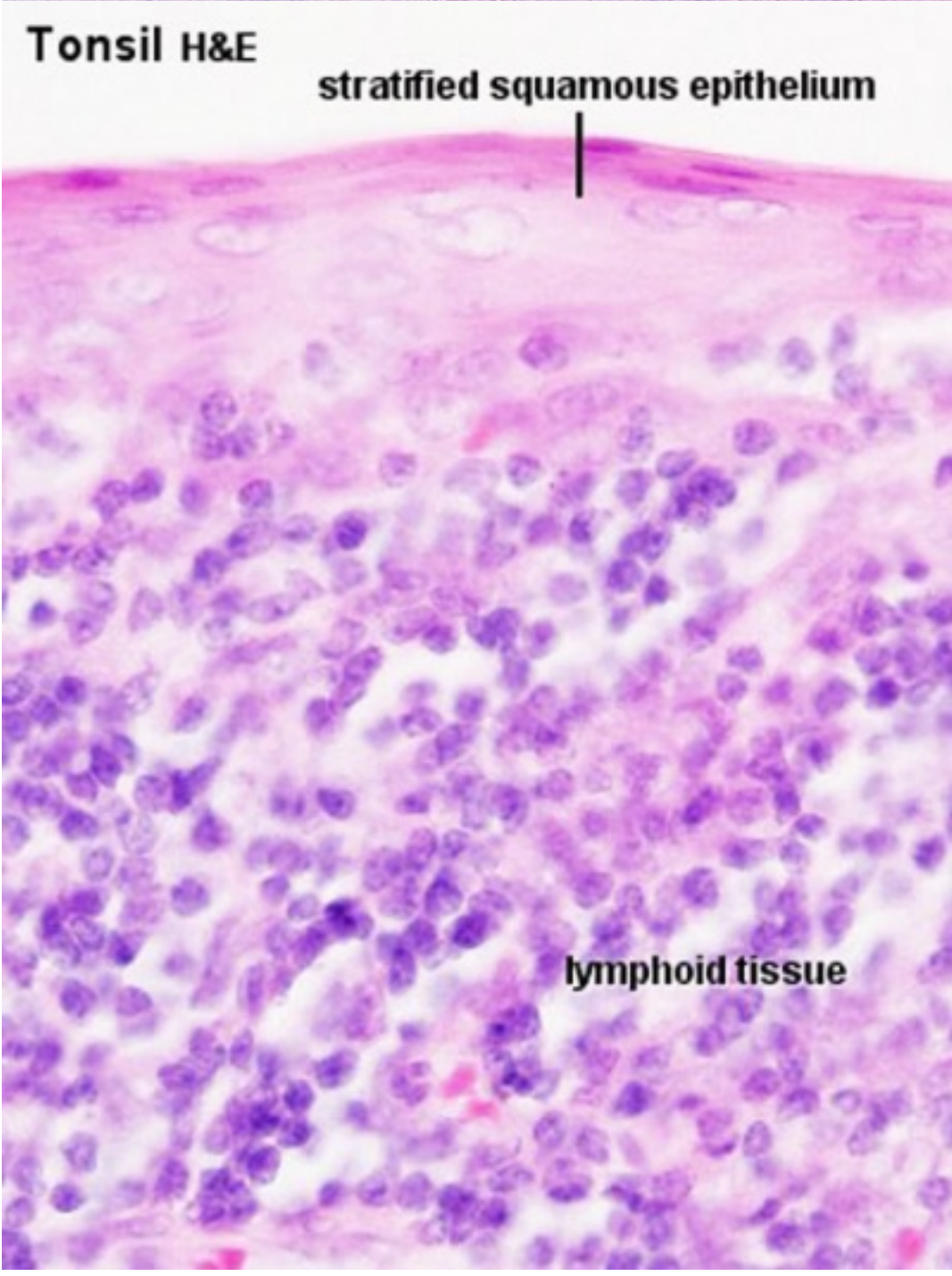


Tonsil and MALT

Mucosal Associated Lymphoid Tissues		[Collapse]
Anatomical location - Palatine ( <b>tonsils</b> ), Lingual and Pharyngeal ( <b>adenoids</b> )		
Ring of oral adenoid tissue: <ul style="list-style-type: none"><li>anterior - <b>lingual tonsil</b> formed by the submucous adenoid collections.</li><li>lateral - <b>palatine tonsils</b> and adenoid collections near the auditory tubes.</li><li>posterior - <b>pharyngeal tonsil</b> on the posterior wall of the pharynx.</li><li>between main masses are smaller collections of adenoid tissue.</li></ul>		

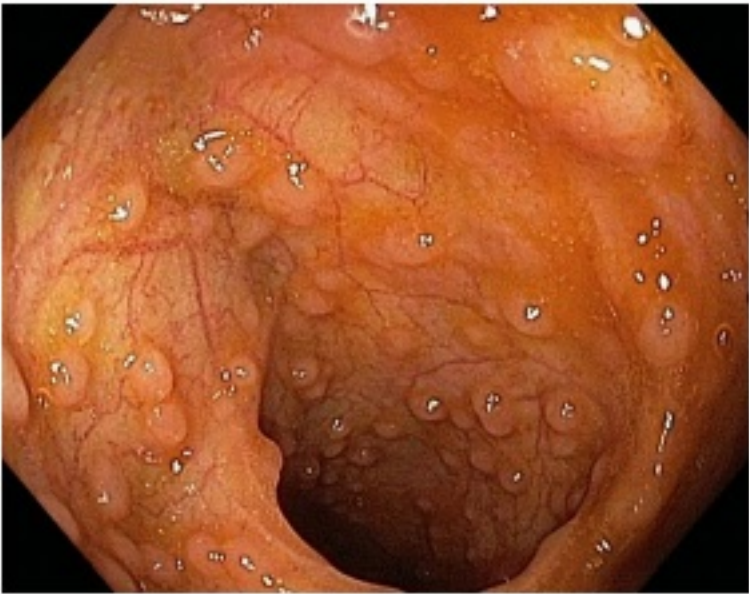
Tonsils		[Collapse]



<p><b>Palatine Tonsils</b></p> <ul style="list-style-type: none"> <li>the "tonsils", lateral wall of oropharynx</li> <li>covered by <b>stratified squamous epithelium</b></li> <li>numerous crypts (10-20) infolds of surface epithelium</li> <li>Afferent lymph vessels absent</li> <li>Efferent lymph vessels are present</li> </ul>	<div data-bbox="716 0 1627 1225"> <p><b>Tonsil H&amp;E</b></p>  </div> <div data-bbox="716 1225 1627 2457"> <p><b>Tonsil H&amp;E</b></p>  </div>
<p><b>Lingual Tonsils</b></p> <ul style="list-style-type: none"> <li>lamina propria root of tongue</li> <li>covered by <b>stratified squamous epithelium</b></li> <li>salivary glands and skeletal muscle are directly adjacent</li> </ul>	<p><b>Pharyngeal Tonsils</b></p> <ul style="list-style-type: none"> <li><b>adenoids</b> or nasopharyngeal tonsils, upper posterior part of throat</li> <li>covered by a <b>pseudostratified ciliated epithelium</b> with goblet cells</li> </ul>



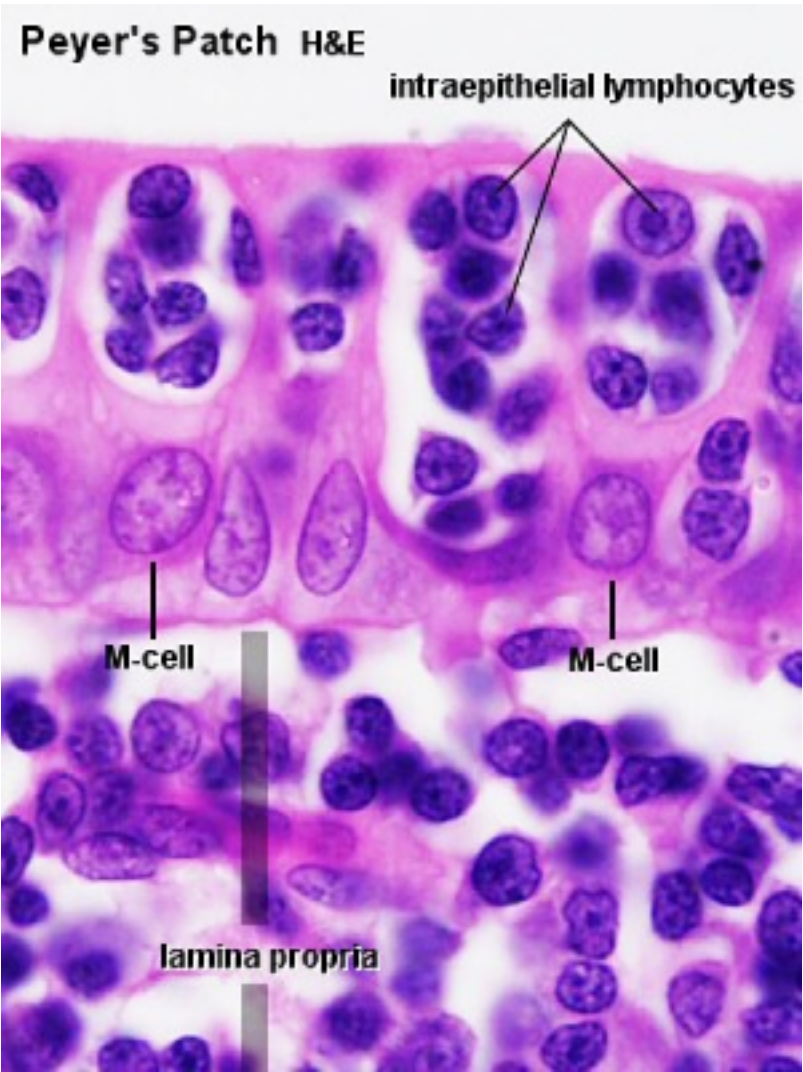
Located in the ileum



Peyers patches (ileocolonoscopy)



Peyer's Patch (histology)



microfold cells or M-cells  
(transport gut lumen organisms and particles to immune cells across the epithelial barrier).

About Peyer's Patch

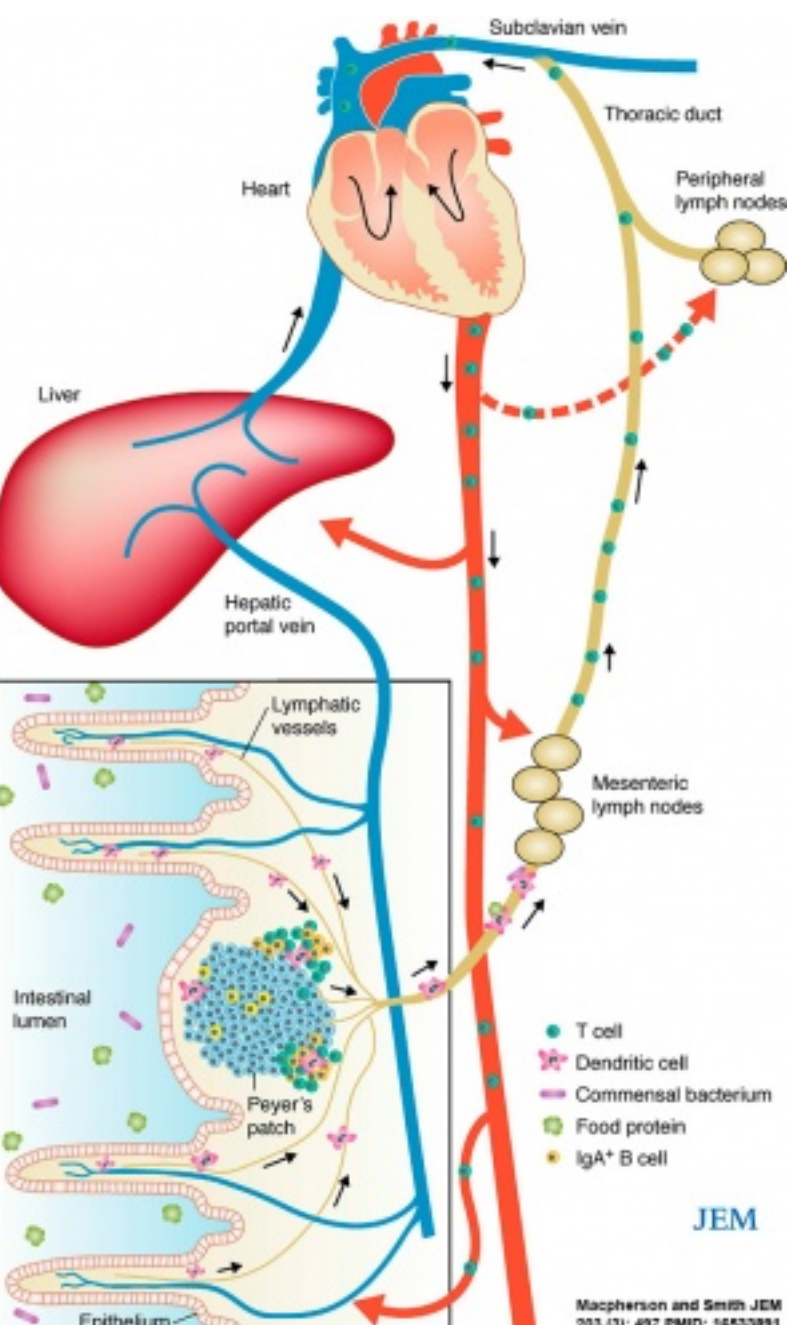
**External Links Notice** - The dynamic nature of the internet may mean that some of these listed links may no longer function. If the link no longer works search the web with the link text or name.

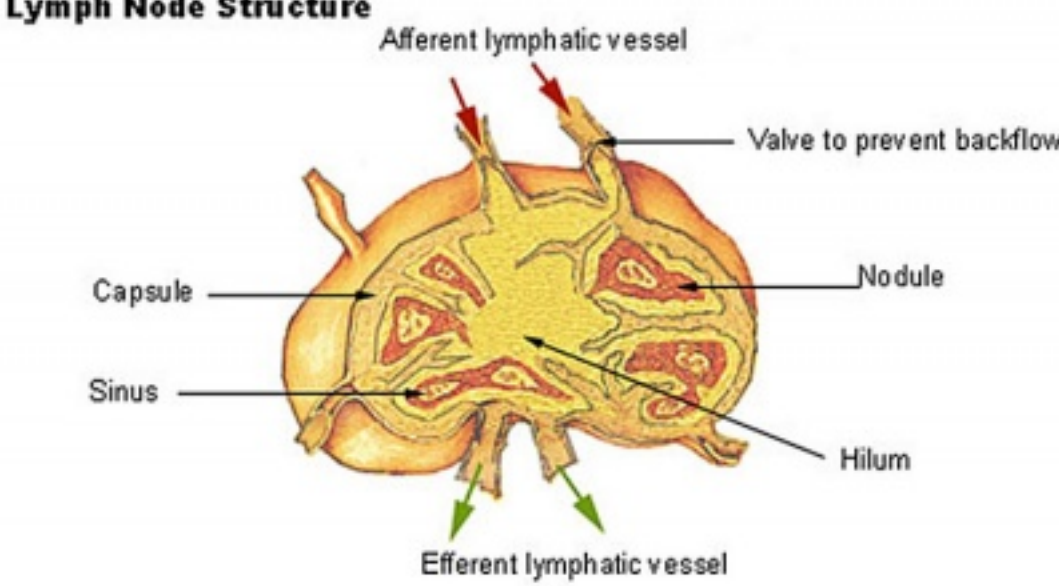
- Learn how the Peyer's Patches function in the Gut Mucosa immune function in this Nature Immunology Animation - Immunology in the Gut Mucosa (<http://www.nature.com/ni/multimedia/mucosal/animation/index.html>)
- Peyer's Patches are named after Johann Conrad Peyer (1653 – 1712) a Swiss anatomist who first described these specialised structures.

Lymph Nodes

Lymph Node Anatomy



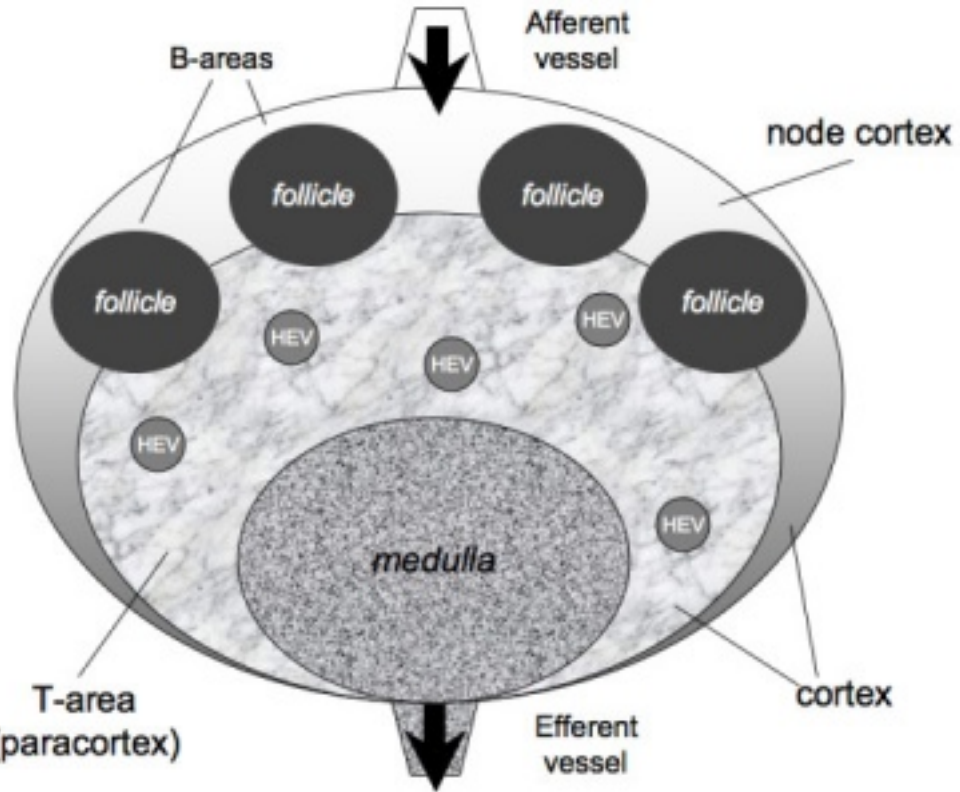
Lymph Node Anatomy [Collapse]	
<ul style="list-style-type: none"> <li>Location throughout the entire body - concentrated in axilla, groin, lung, gastrointestinal tract mesenteries</li> <li>Small (1 mm - 2 cm) encapsulated organ (diffuse lymphoid tissue - no capsule)</li> <li>Antigen transformed lymphocytes from the blood</li> <li>In lymph vessel pathways “filter” lymph <ul style="list-style-type: none"> <li><b>Afferent</b> - towards node (A - arrives at the node)</li> <li><b>Efferent</b> - away from node (E - exits the node)</li> </ul> </li> </ul>	
 <p>Mesenteric lymph nodes</p>	

Lymph Node Functions [Collapse]	
<ul style="list-style-type: none"> <li>In lymph vessel pathways “filter” (surveillance) lymph</li> <li><b>Immune</b> - detect infections from peripheral tissues <ul style="list-style-type: none"> <li>skin, respiratory tract, gastrointestinal tract, etc.</li> </ul> </li> <li>secondary lymphoid organ</li> <li>return extracellular fluid to circulation</li> </ul>	
	

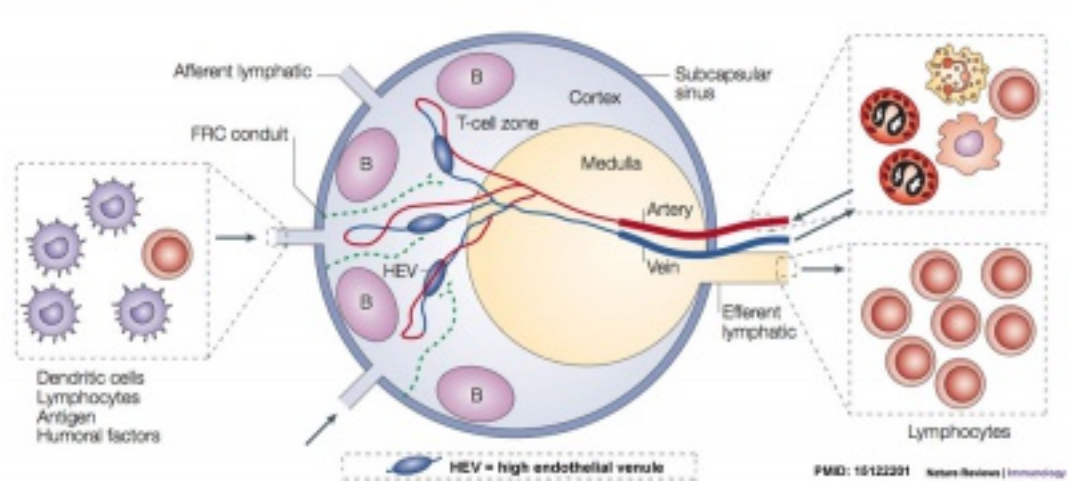
## Lymph Node Structure

Lymph Node Structure [Collapse]	



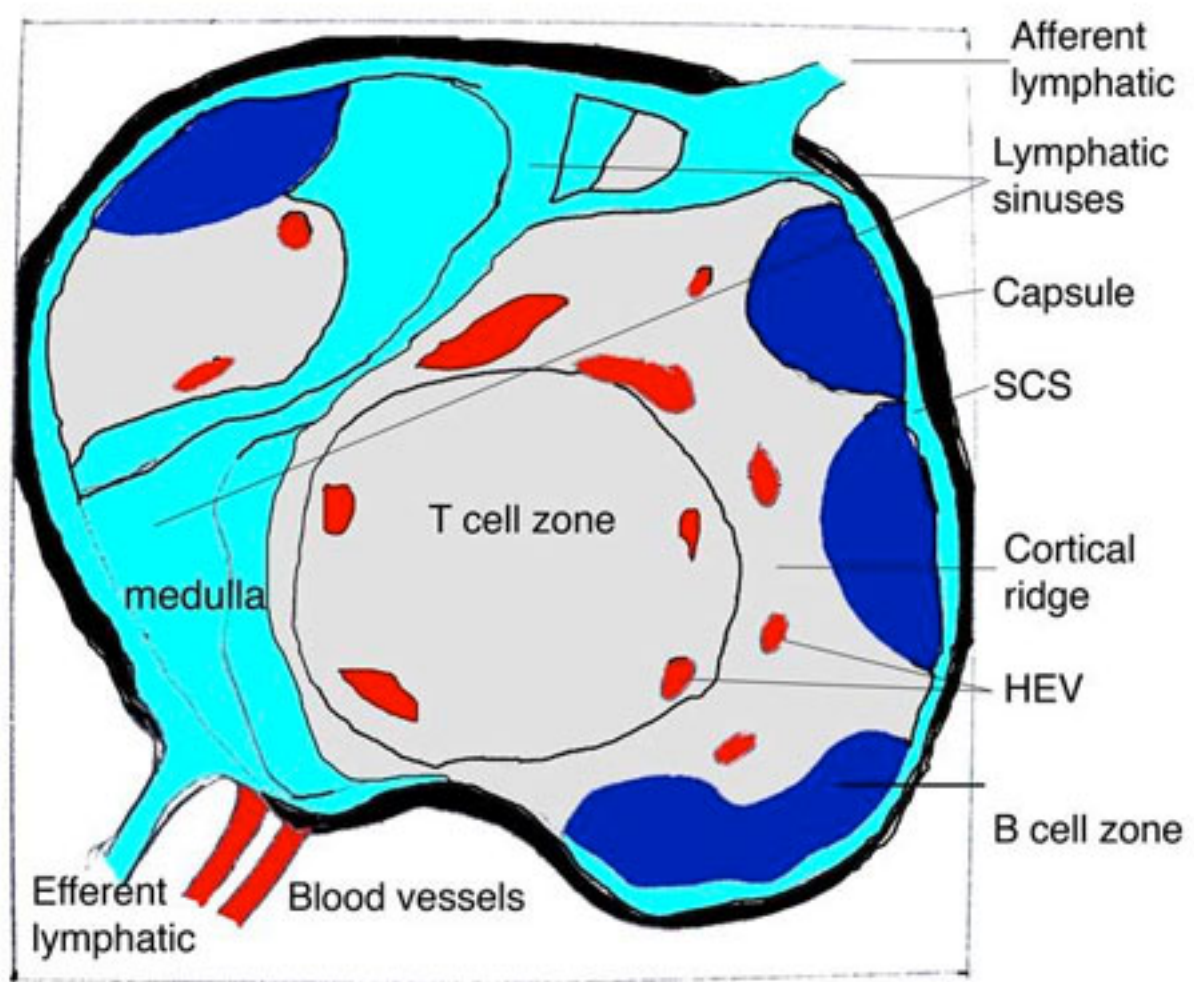


Simplified structure



### Lymphocyte (T and B) Traffic

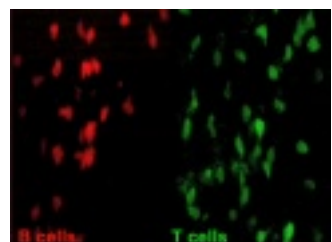
1. Enter from high endothelial venules (HEVs also called post-capillary venules)
2. Spend 8 to 24 h in the lymph node interstitium.
3. Enter a network of medullary sinuses.
4. Drain from sinuses into efferent lymphatic vessels.



### Lymph pathway

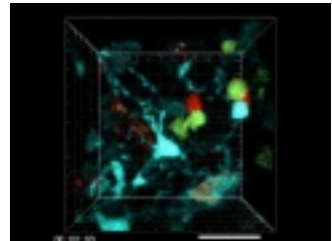
1. Afferent vessel
2. Subcapsular sinus
3. Paratrabeular sinus
4. Medullary sinus
5. Efferent vessel

### Watch T and B Lymphocytes Move



Lymph Node 7

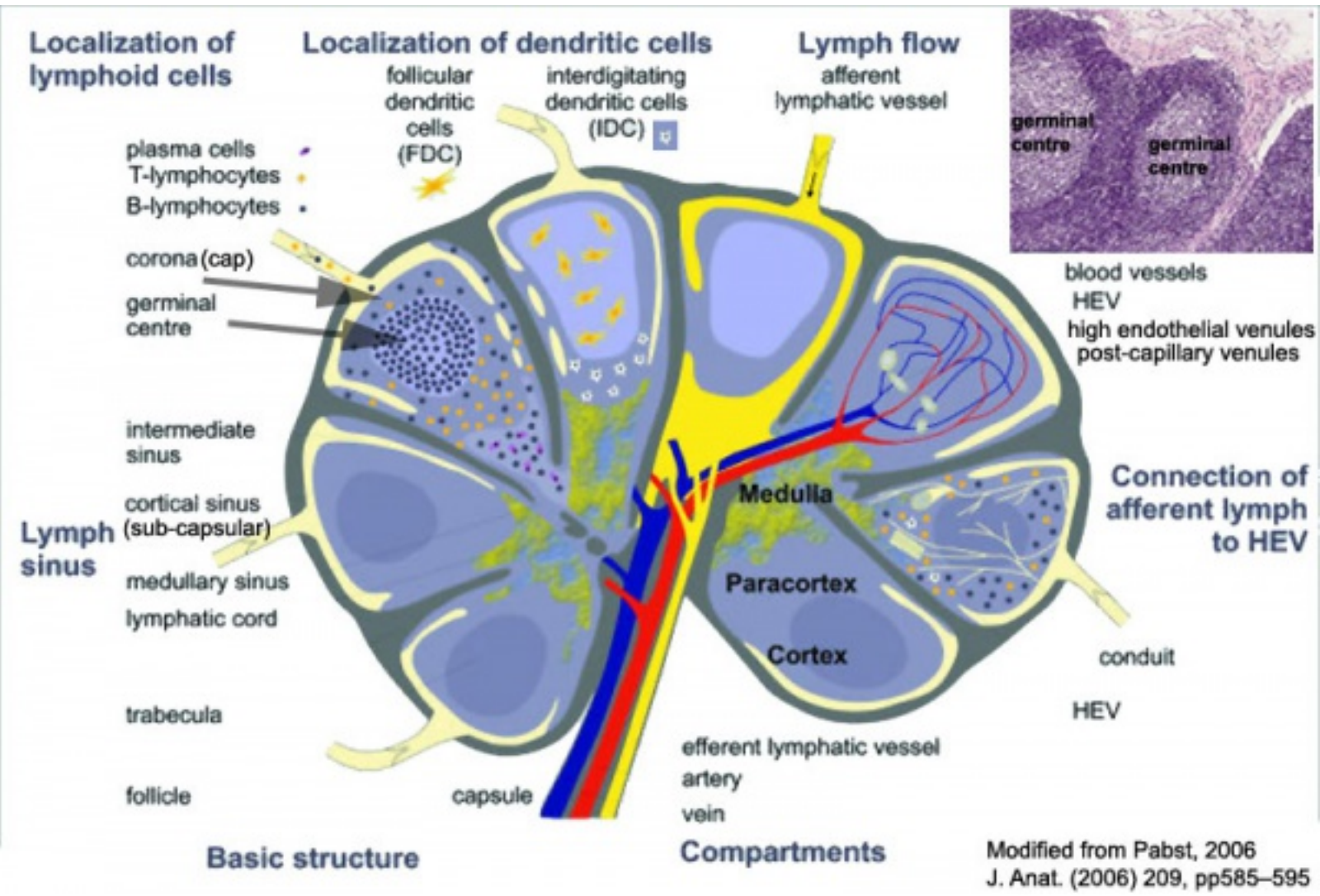
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Lymph Node 8

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## Lymph Node



blood vessels  
HEV  
high endothelial venules  
post-capillary venules

Connection of afferent lymph to HEV

conduit  
HEV

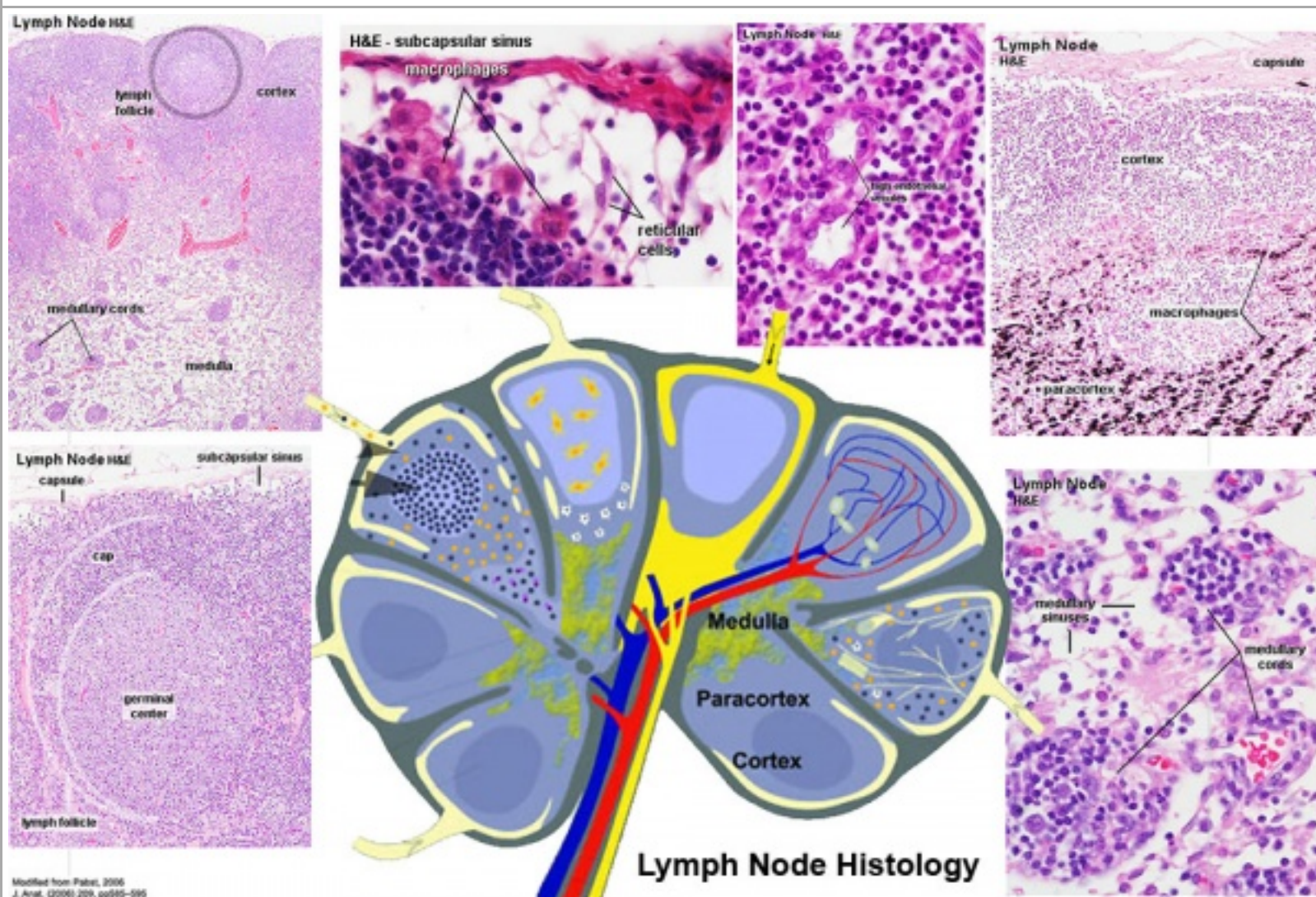
Modified from Pabst, 2006  
J. Anat. (2006) 209, pp585–595



## Lymph Node Histology

## Lymph Node Histology

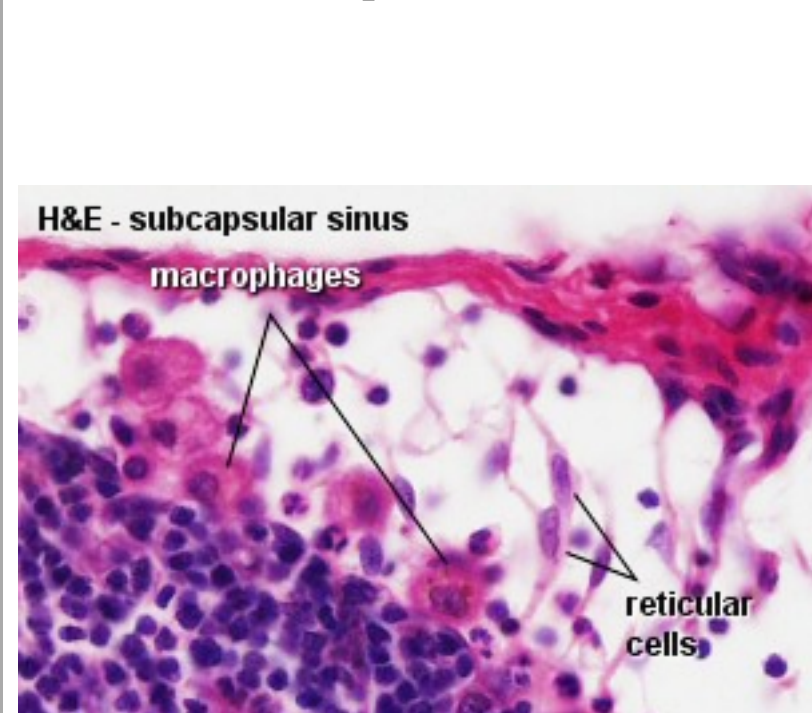
**[Collapse]**



## Connective Tissue

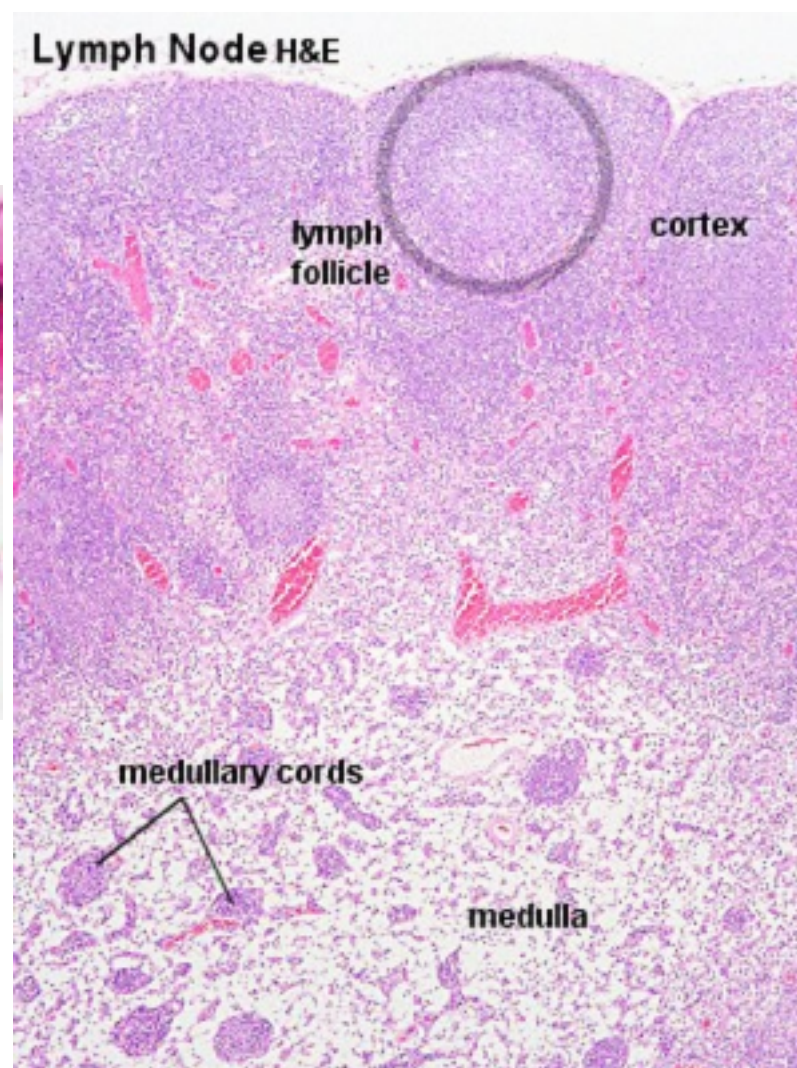
- **Capsule** - dense connective tissue (irregular CT, some adipocytes))
- **Trabeculae** - dense connective tissue
- **Reticular Tissue** - Reticular cells and fibers, supporting meshwork (collagen type III)
  - Reticular cell produces reticular fibers (**collagen type III**) and surrounds the fibers with its cytoplasm
  - reticular fibres can also be produced by fibroblasts

## Subcapsular Sinus

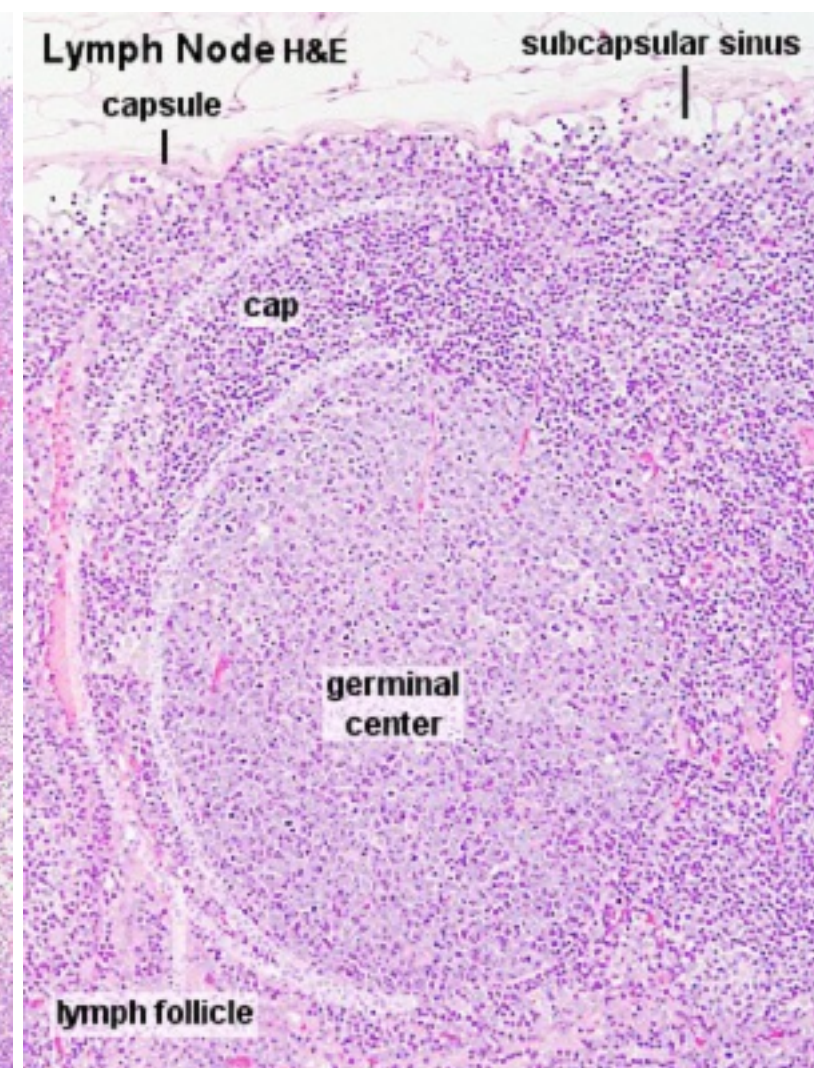


(marginal sinus, continuation of trabecular sinus)

## Follicle



## Germinal Centre

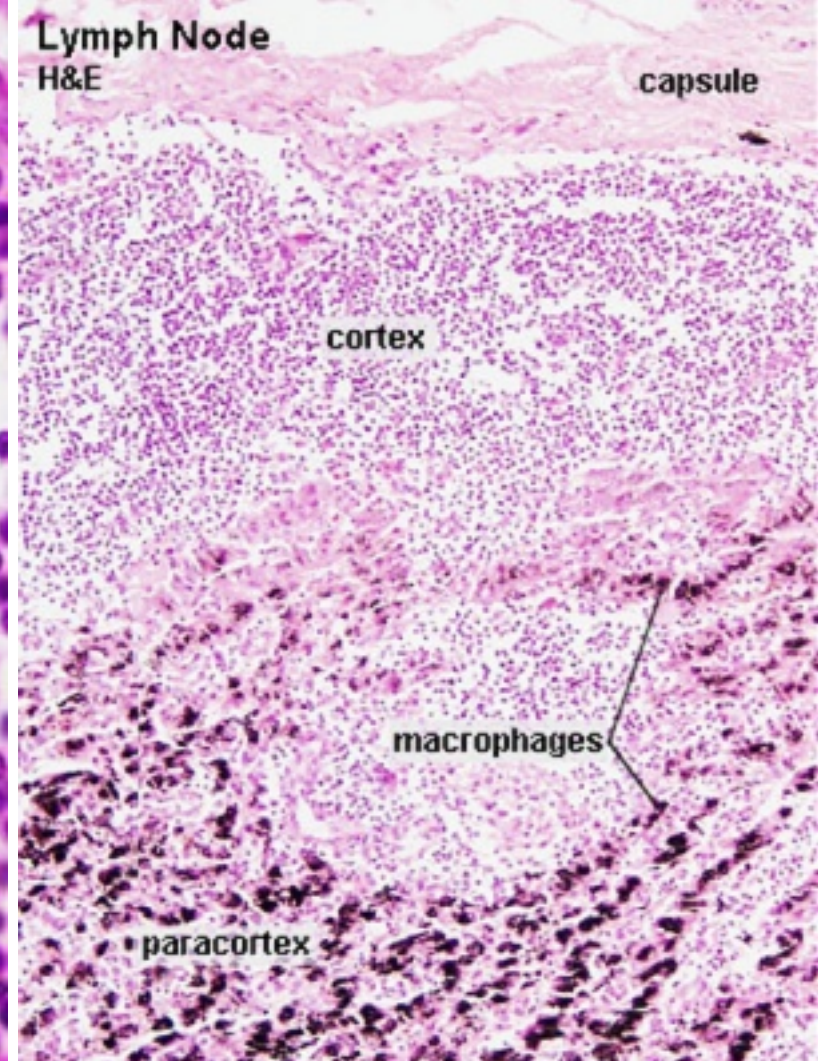
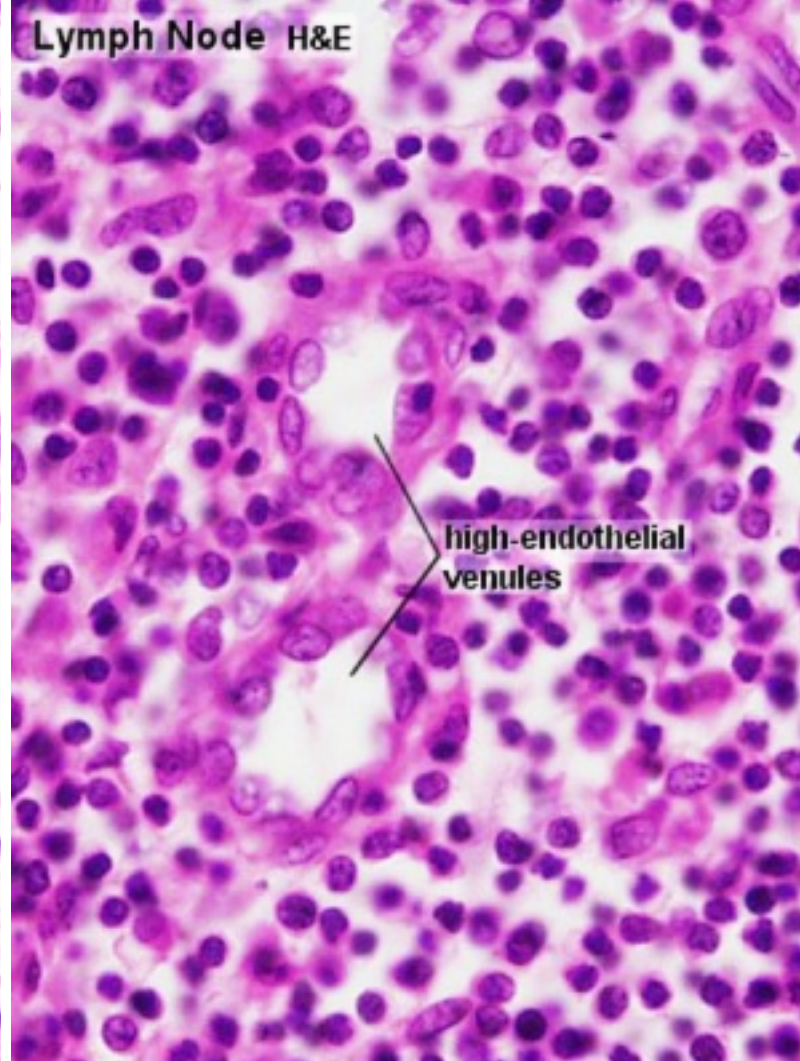
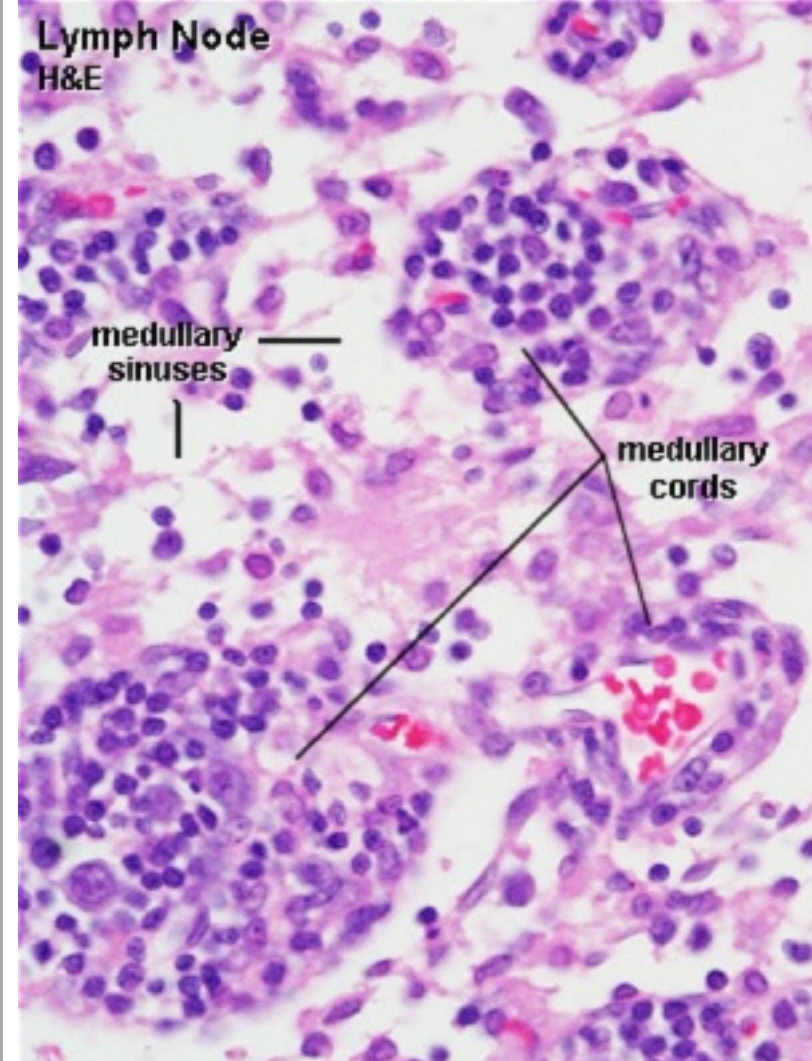


## Medullary Cords and Sinuses

## High Endothelial Venues

## Macrophages





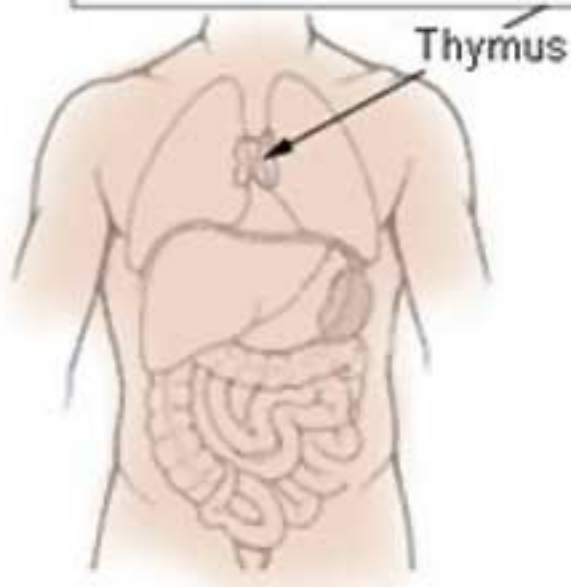
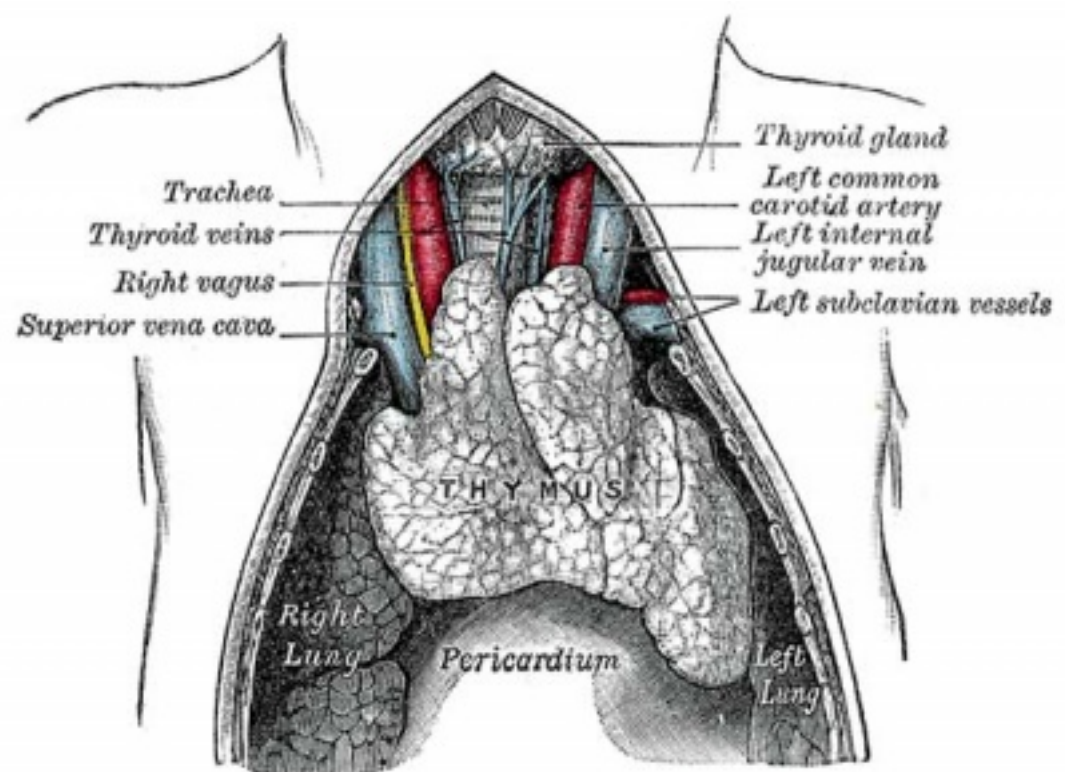
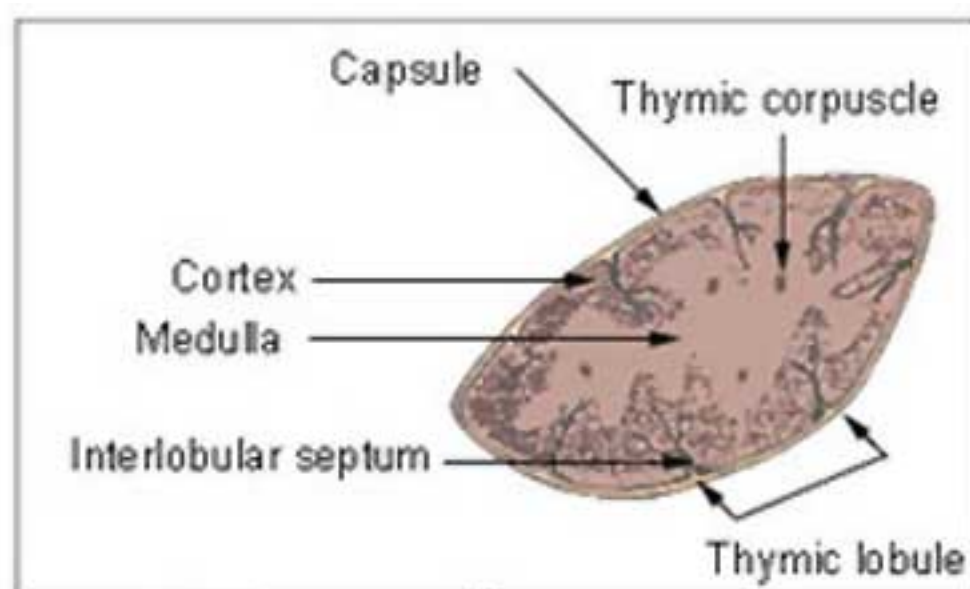
**Lymph Node Cartoons:** Detailed structure | Cartoon with Histology | Lymphocyte traffic | Simple structure | Simple node anatomy | Wiki node image | Internal structure | Mesenteric lymph node | Histology | Gallery | Lymph Node Development

**Links:** Immunobiology - Figure 1.8. Organization of a lymph node (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A47>)

# Thymus

## Thymus Anatomy

### Thymus Anatomy



### Thymus

adult thymus - bilobed, superior mediastinum, anterior to heart infant thymus - large

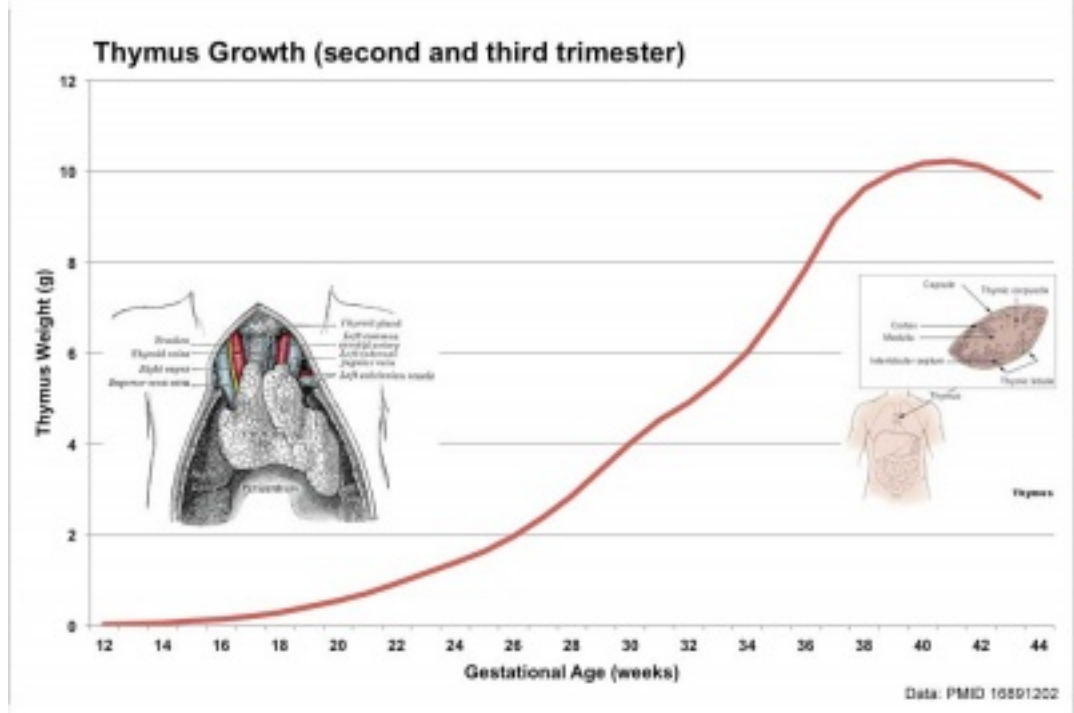
### Thymus Involution

### Overall Size Changes with age

- birth 10-15 g
- puberty 30-40 g
- after puberty - involution
  - replaced by adipose tissue



- middle-aged 10 g



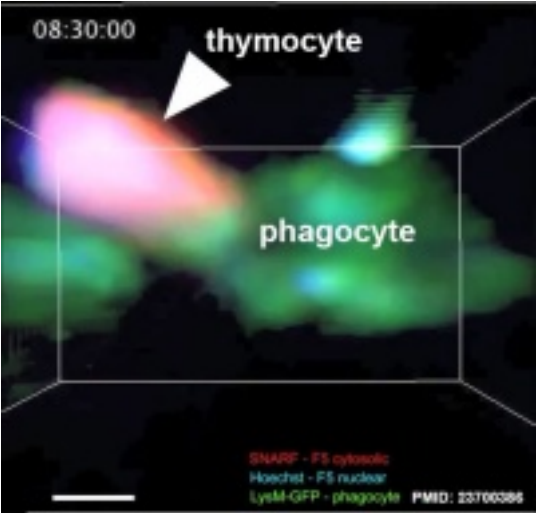
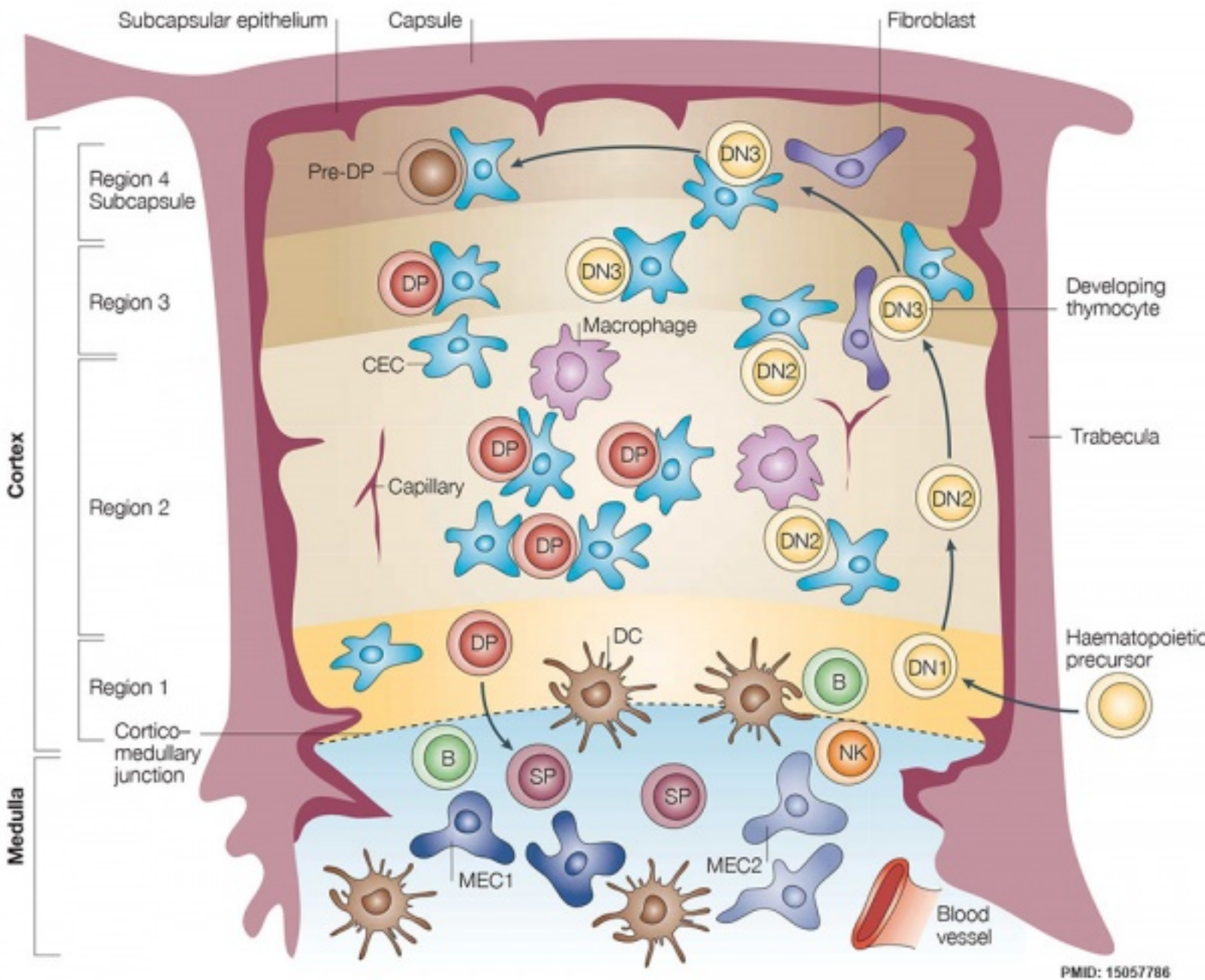
## Thymus Functions



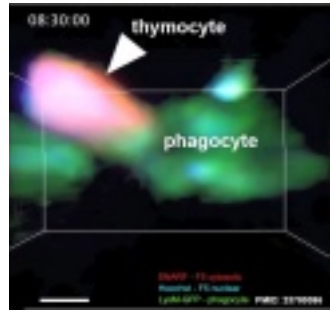
- specialised thymus microenvironments allow the production of self-tolerant T-cells (T lymphocytes) from immature precursors.
  - immature precursors enter the thymus
  - differentiate and undergo selection by thymic epithelial cell (TEC) subtypes
  - mature release into circulation of these cells
- destruction of cells that recognise self antigens
- T-cells kill infected and oncogenic cells

T Cells maturation within the thymus

1. **T cell progenitors** enter the thymus at the cortex/medulla border via post-capillary venules
2. **migrate** toward the capsule in response to chemokine signalling.
3. **cortex** - thymocytes undergo positive selection by cTECs then migrate to the medulla
4. **medulla** - thymocytes are screened for reactivity to tissue-restricted self antigens expressed by mTECs.
5. **Mature T cells** exit the thymus via blood or lymphatic vessels in response to a sphingosine-1-phosphate (S1P) gradient.

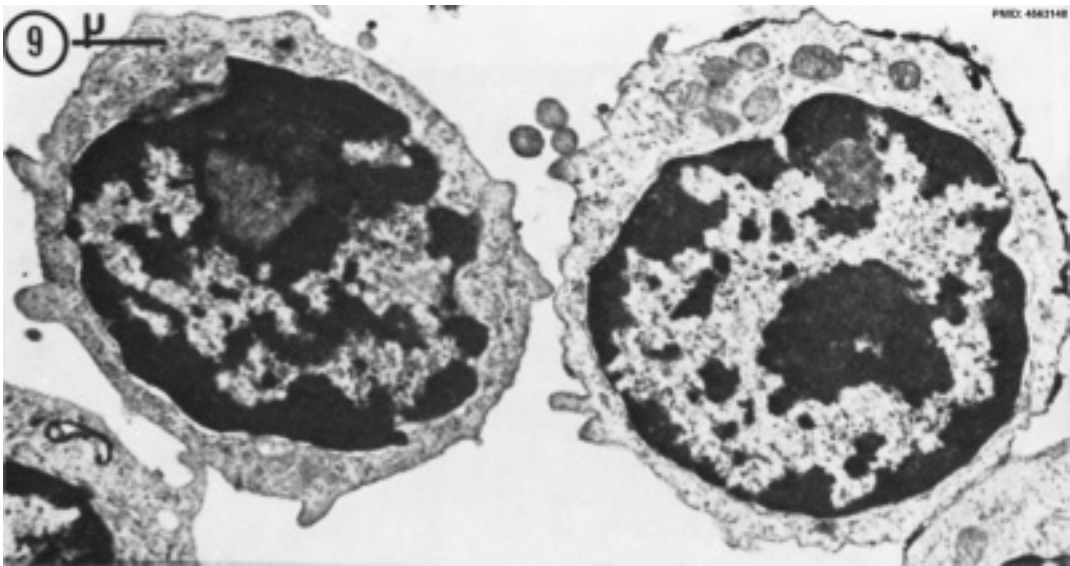


Macrophages phagocytosis of T cells



Thymus 1

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EM - T and B lymphocytes (look the same)

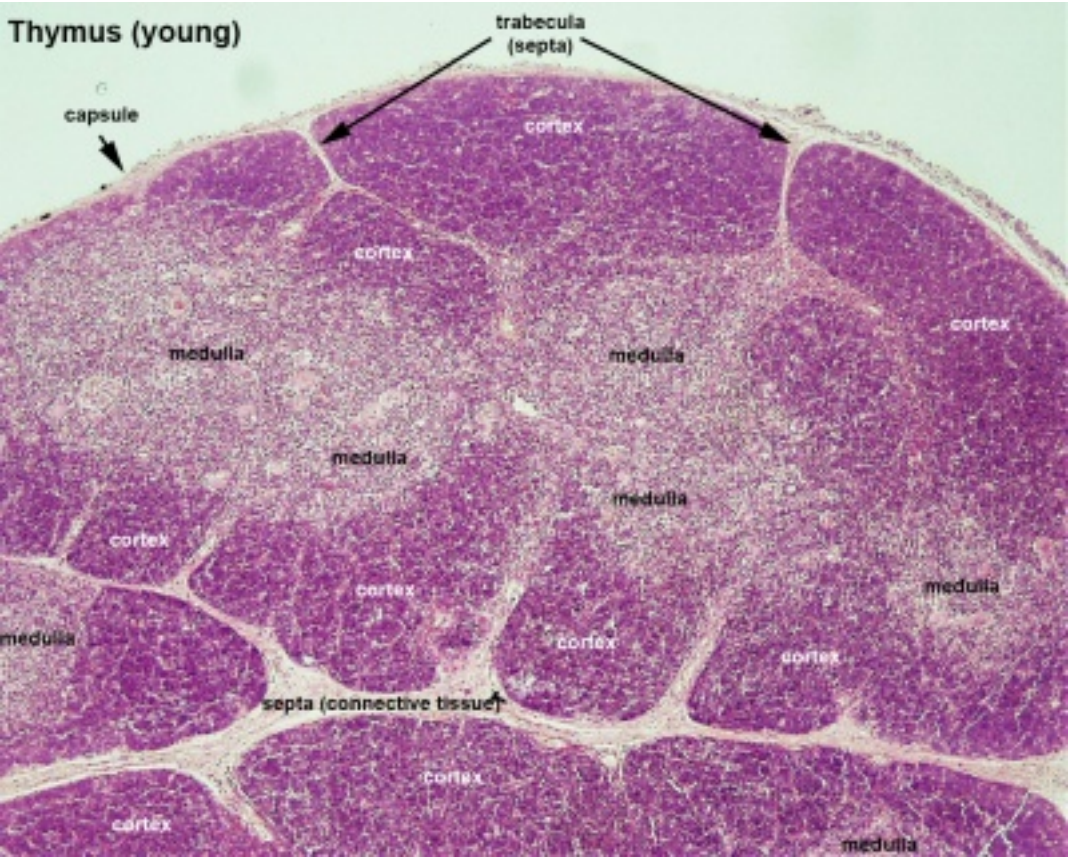


Structure Overview

- Connective tissue capsule (thin) with numerous trabeculae (septa)
  - major blood vessels run in CT
- Lobules containing **cortex** and **medulla** regions
  - medullary regions are continuous (connected together)
- NOT supplied by afferent lymph vessels

Blood-Thymic Barrier

- Blood vessels are separated from thymus cortex by epithelioreticular cells.
- impermeable to most macromolecules.
- Barrier layers: capillary endothelium - endothelial basal lamina- perivascular CT sheath - basal lamina of epithelioreticular cells - epithelioreticular cell sheath

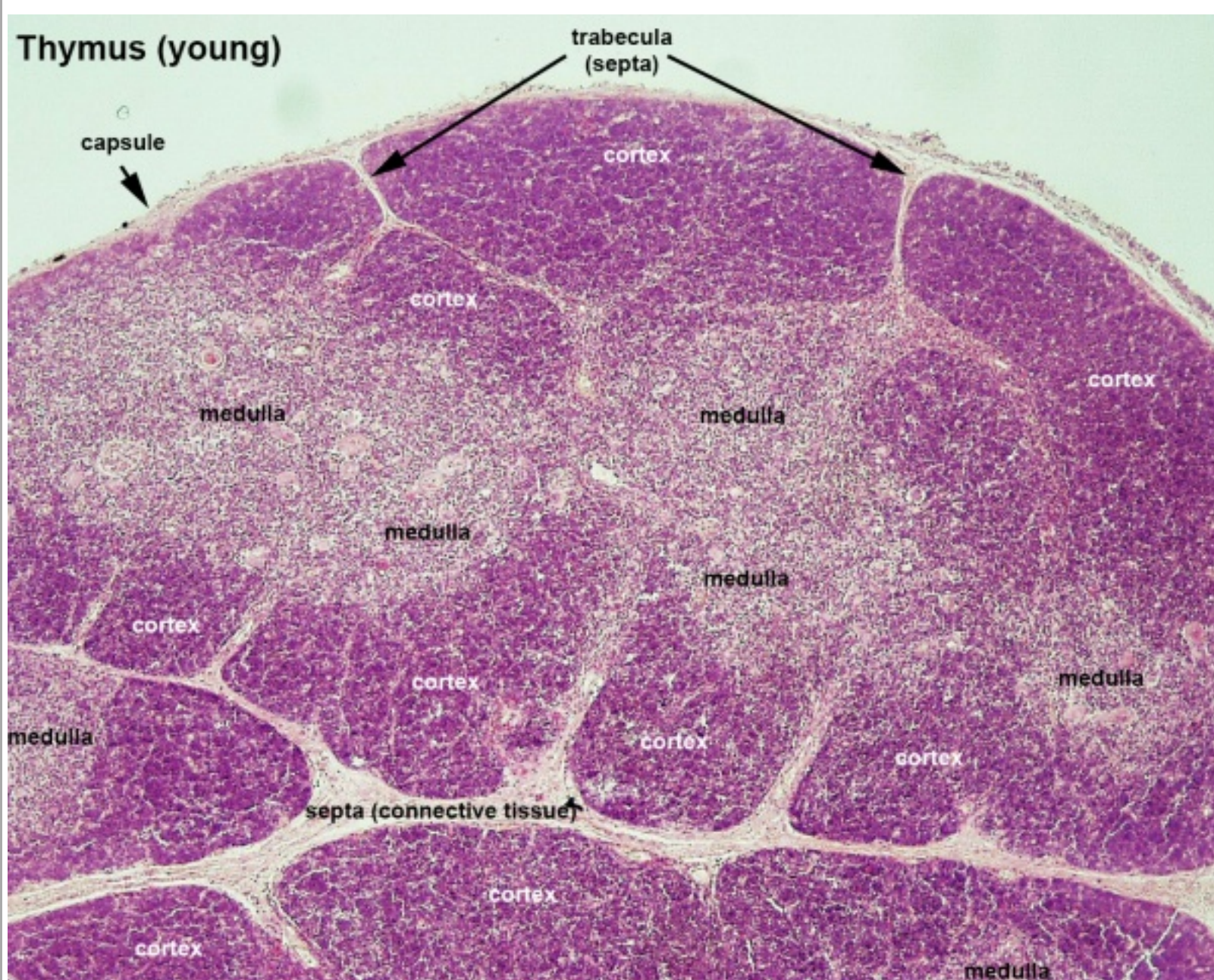
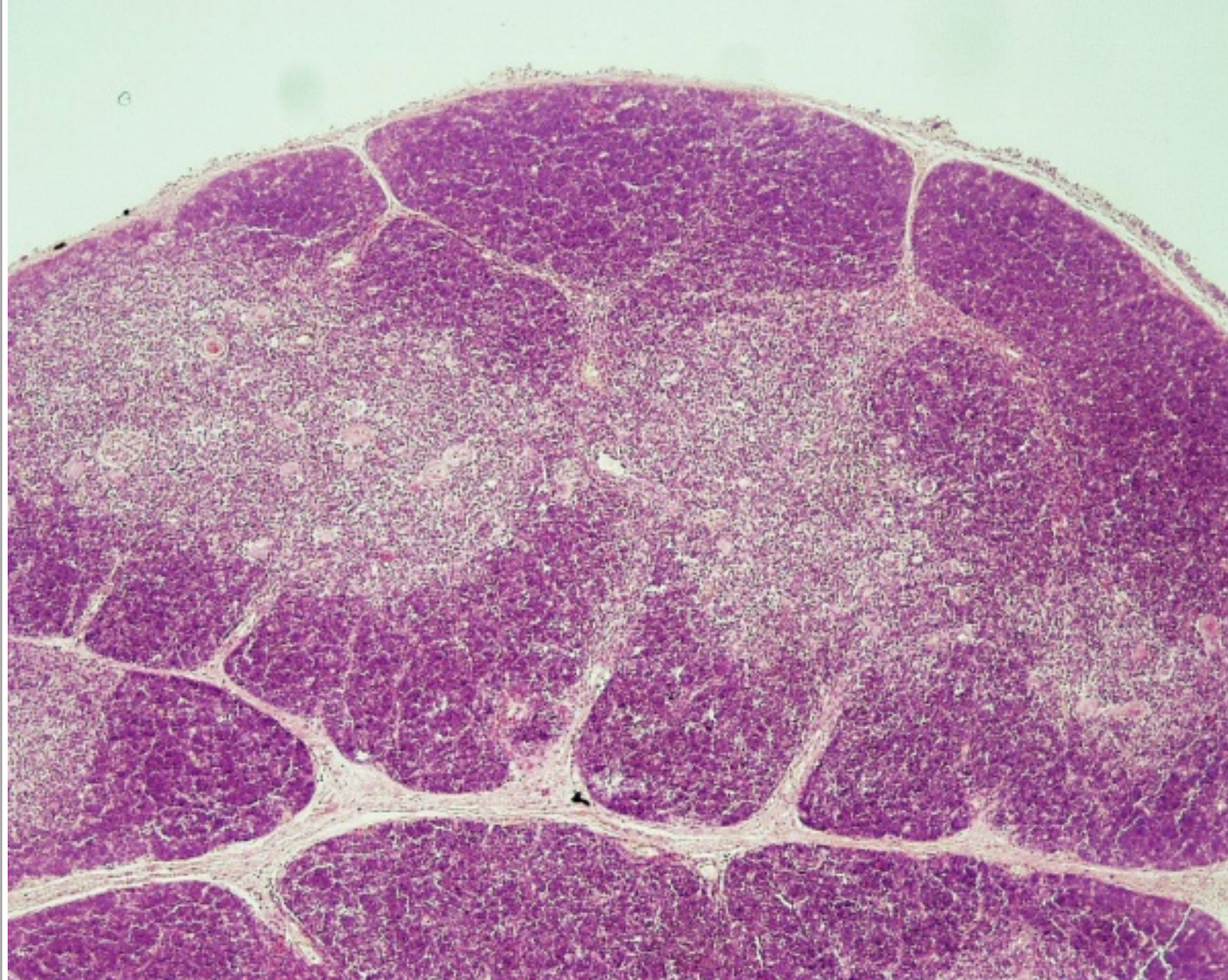


Thymus Epithelioreticular cells (TEC)	Macrophages	Lymphocytes
<ul style="list-style-type: none"><li>■ Abundant, eosinophilic, large, ovoid and light nucleus 1-2 nucleoli</li><li>■ sheathe cortical capillaries</li><li>■ form an epitheloid layer</li><li>■ maintain microenvironment for development of T-lymphocytes in cortex (thymic epitheliocytes)</li></ul>	<ul style="list-style-type: none"><li>■ cortex and medulla</li><li>■ difficult to distinguish from reticular cells in (Stain - Haematoxylin Eosin)</li><li>■ remove auto-reactive T-lymphocytes</li></ul>	<ul style="list-style-type: none"><li>■ located in cortex and medulla</li><li>■ more numerous (denser) in cortex</li><li>■ majority are developing T-lymphocytes (= thymic lymphocytes or thymocytes)</li></ul>

Thymus Histology

- Capsule (thin) with trabecular or septa (dense connective tissue)





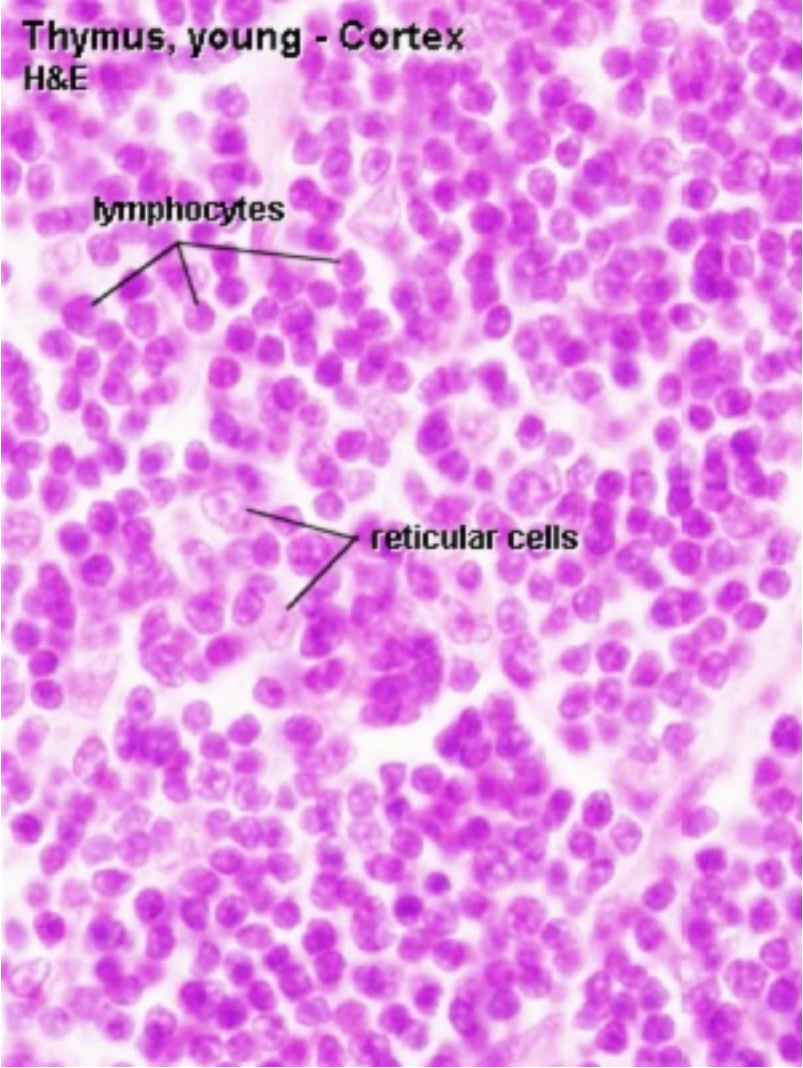
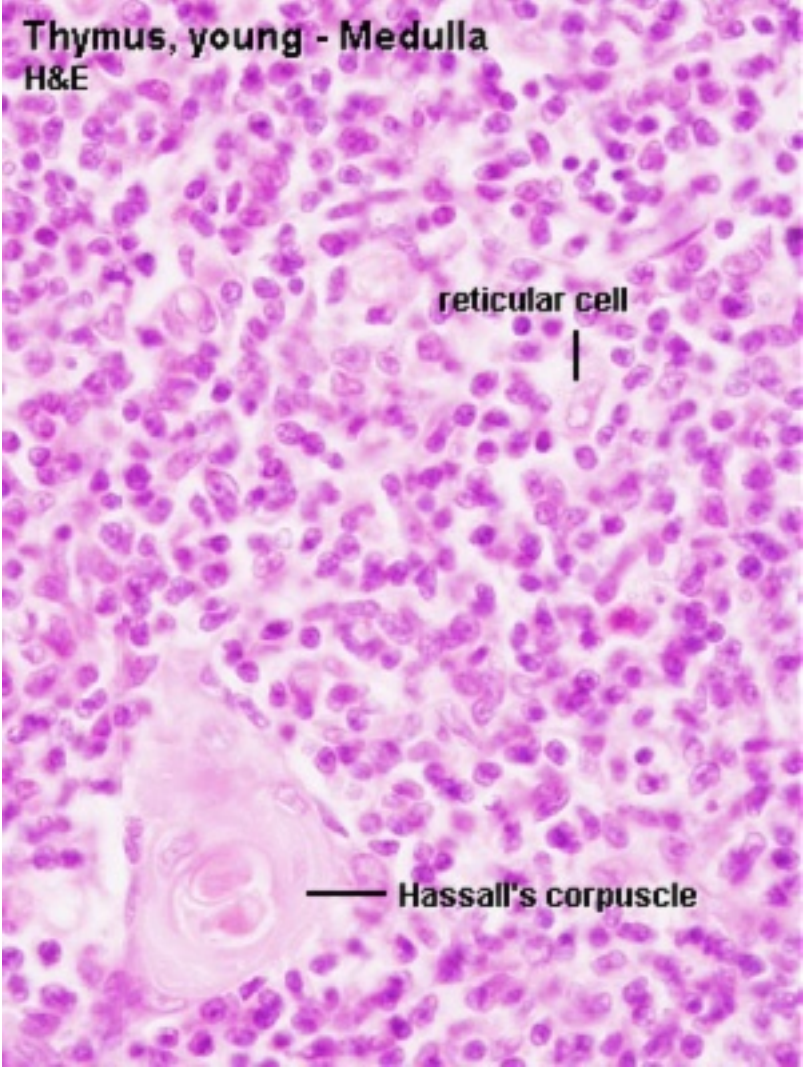
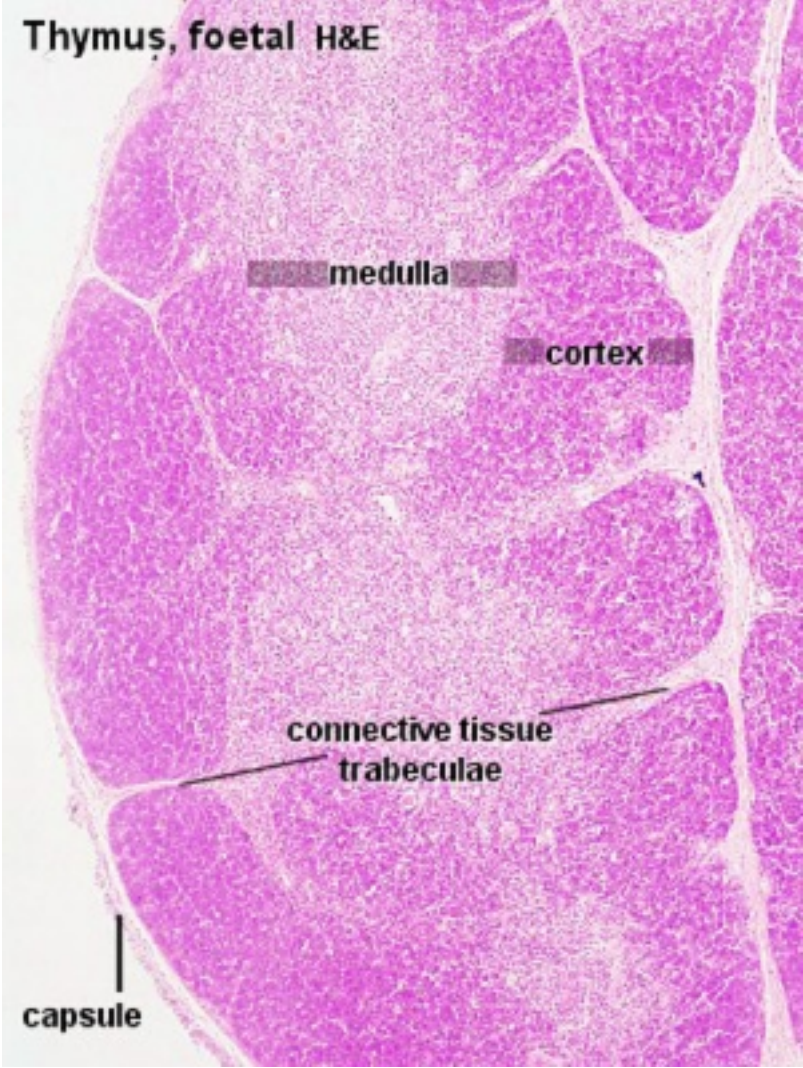
Infant thymus

Fetal thymus

Young medulla

Young cortex





- Cortical lymphoid tissue is replaced by adipose tissue (involution)
- Increase in size of thymic corpuscles
- **Thymic corpuscle** - (Hassall's corpuscle) mass of concentric epithelioreticular cells.

**Thymus Histology:** Fetal Thymus overview | Fetal Thymus Medulla | Fetal Thymus Cortex | Adult Thymus | unlabeled fetal overview | unlabeled fetal medulla | unlabeled fetal thymic corpuscle | unlabeled fetal cortex | unlabeled adult overview | Category:Thymus | Immune System Development

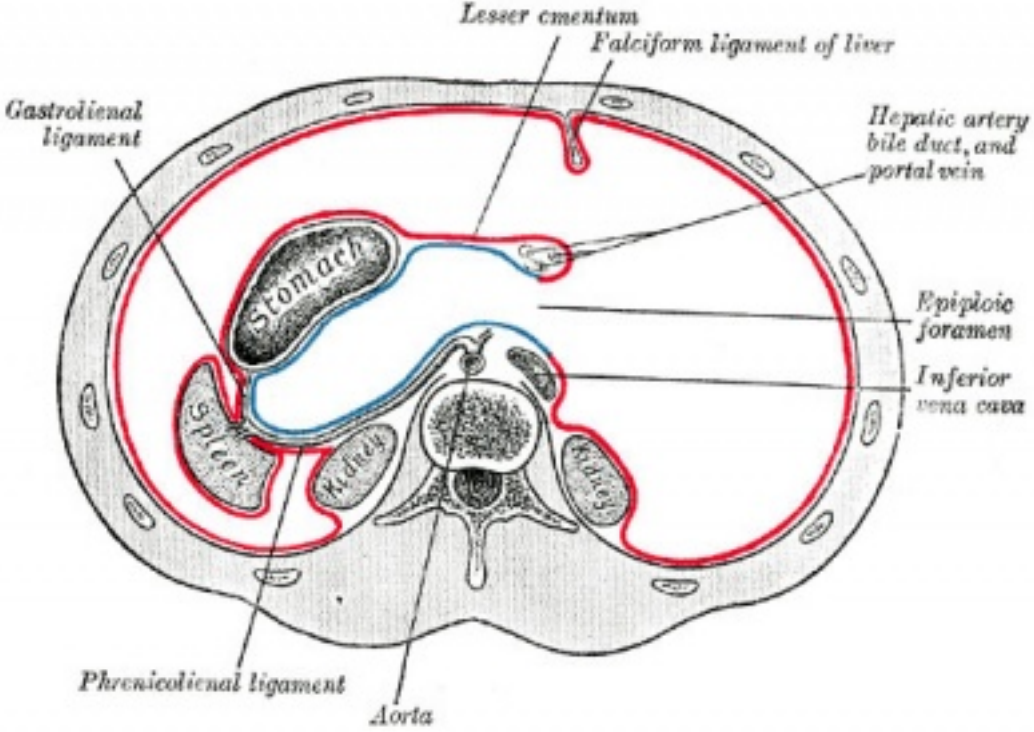
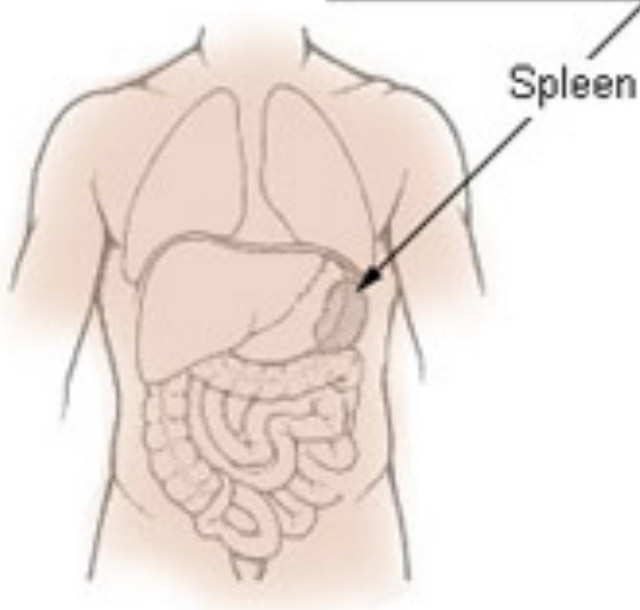
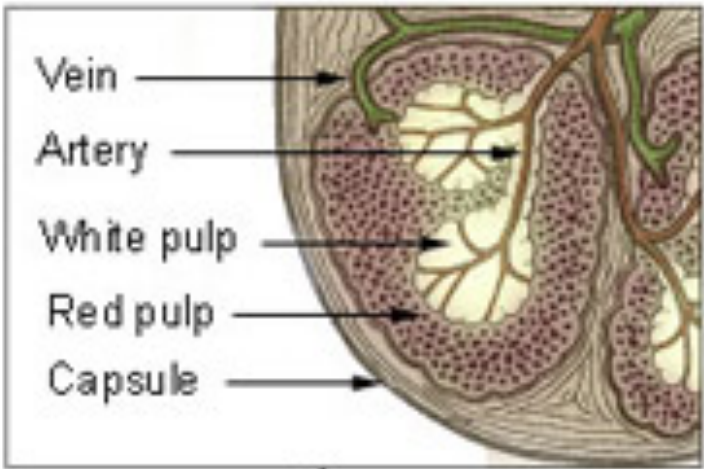
# Spleen

## Spleen Anatomy

### Spleen Anatomy



Spleen



left hypochondriac region

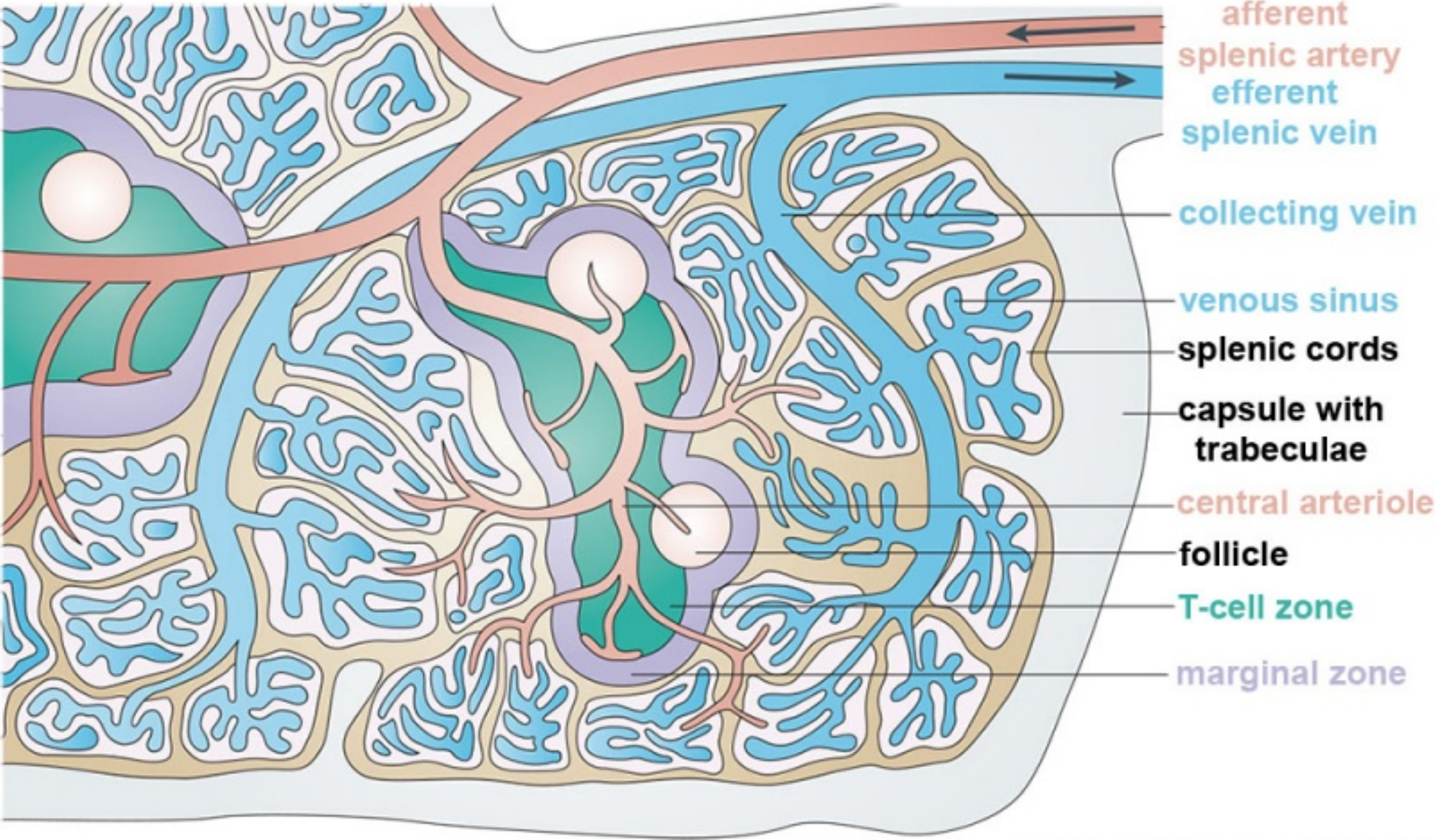
almost entirely surrounded by peritoneum adherent to its capsule

Spleen Functions

Spleen Functions	[Collapse]
<div>1. <b>Immune</b> - filters blood in much the way that the lymph nodes filter lymph.<div>1. <b>Lymphocytes</b> in the spleen react to pathogens in the blood and attempt to destroy them.</div><div>2. <b>Macrophages</b> then engulf the resulting debris, the damaged cells, and the other large particles.</div></div> <div>2. <b>Red Blood Cell Removal</b> - spleen (and liver) removes old and damaged erythrocytes from the circulating blood.</div> <div>3. <b>Blood Reservoir</b> - The sinuses in the spleen also act as a reservoir for blood. In emergencies (haemorrhage) smooth muscle in the vessel walls and in the capsule of the spleen contracts, squeezes blood out of the spleen into the general circulation.</div>	

Spleen Structure





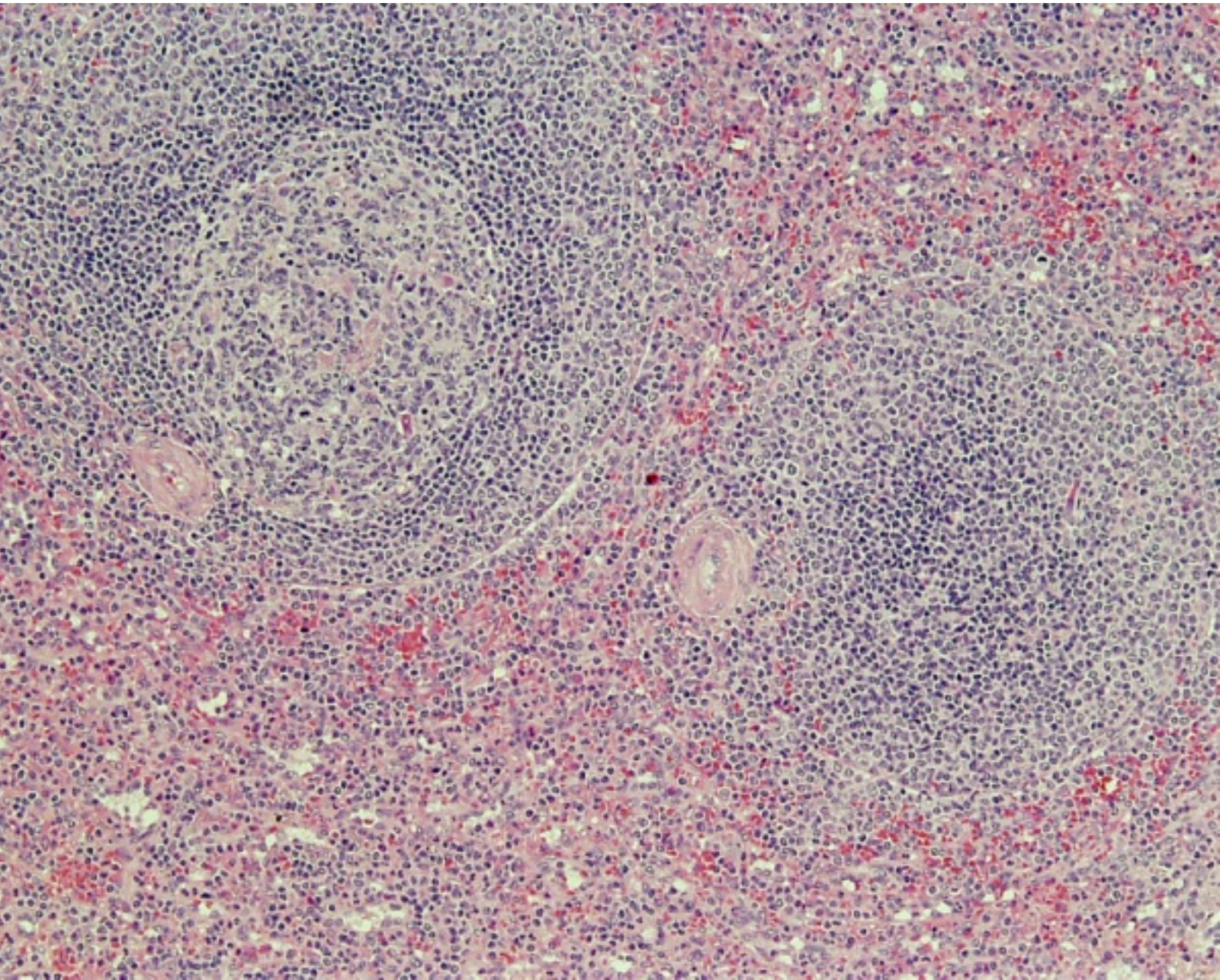
Nat Rev Immunol. 2005 Aug;5(8):606-16. PMID: 16056254

- **afferent splenic artery** branches into central arterioles, which are sheathed by white pulp areas.
- **white pulp** areas consist of the T-cell zone (also known as the periarteriolar lymphoid sheath, PALS), arterioles and B-cell follicles.
- arterioles end in cords in the **red pulp**, from where the blood runs into venous sinuses that collect into the **efferent splenic vein**.
- larger arteries and veins run together in connective-tissue trabeculae, which are continuous with the capsule that surrounds the spleen.

Spleen Histology

Spleen Histology

- Capsule with trabeculae (dense connective tissue)
- Reticular fibroblasts - reticular fibres (Type III collagen)





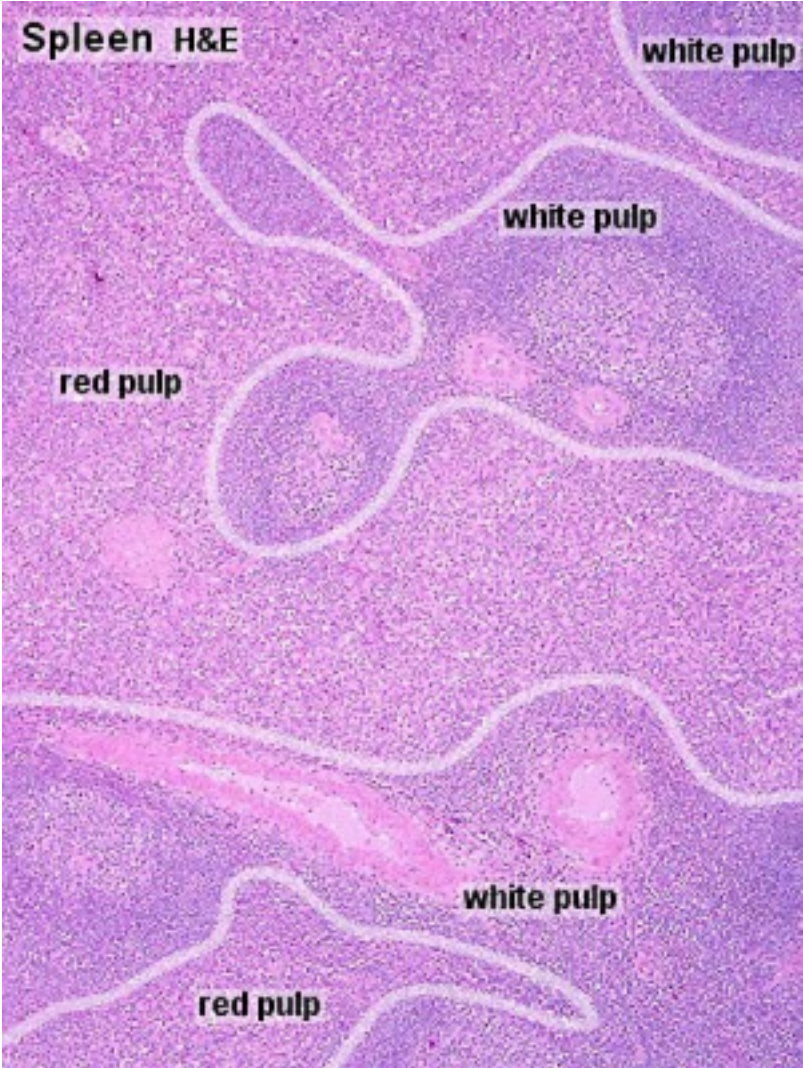
## White Pulp

- lymph follicle
- germinal center
- central artery
  - periarterial lymphoid sheath (PALS)

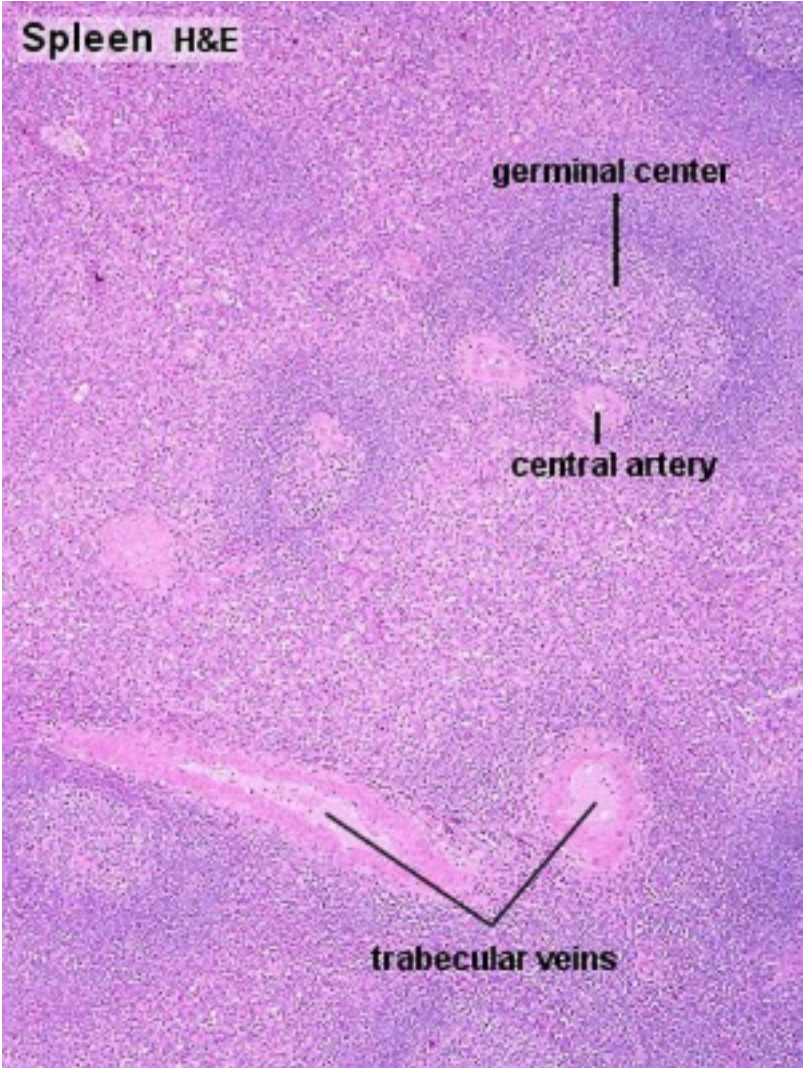
## Red Pulp

- splenic cords
  - macrophages
  - reticular fibroblasts
- splenic sinuses
  - endothelium (discontinuous structure)

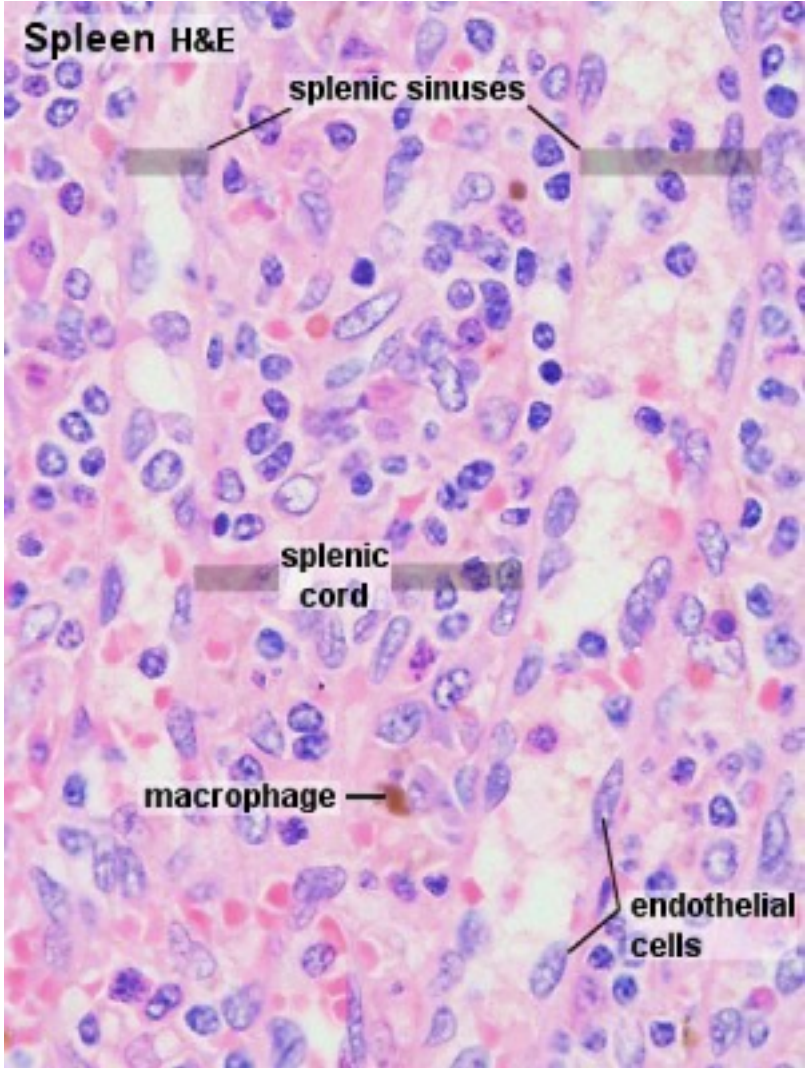
### Overview - red and white pulp



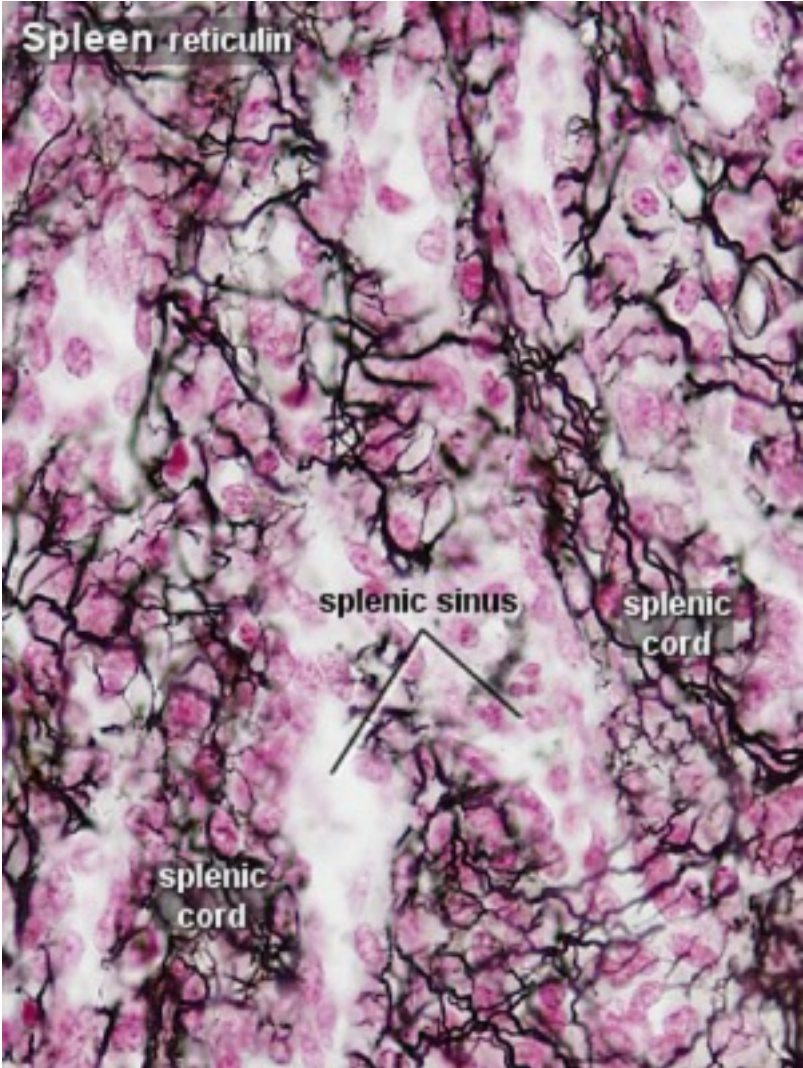
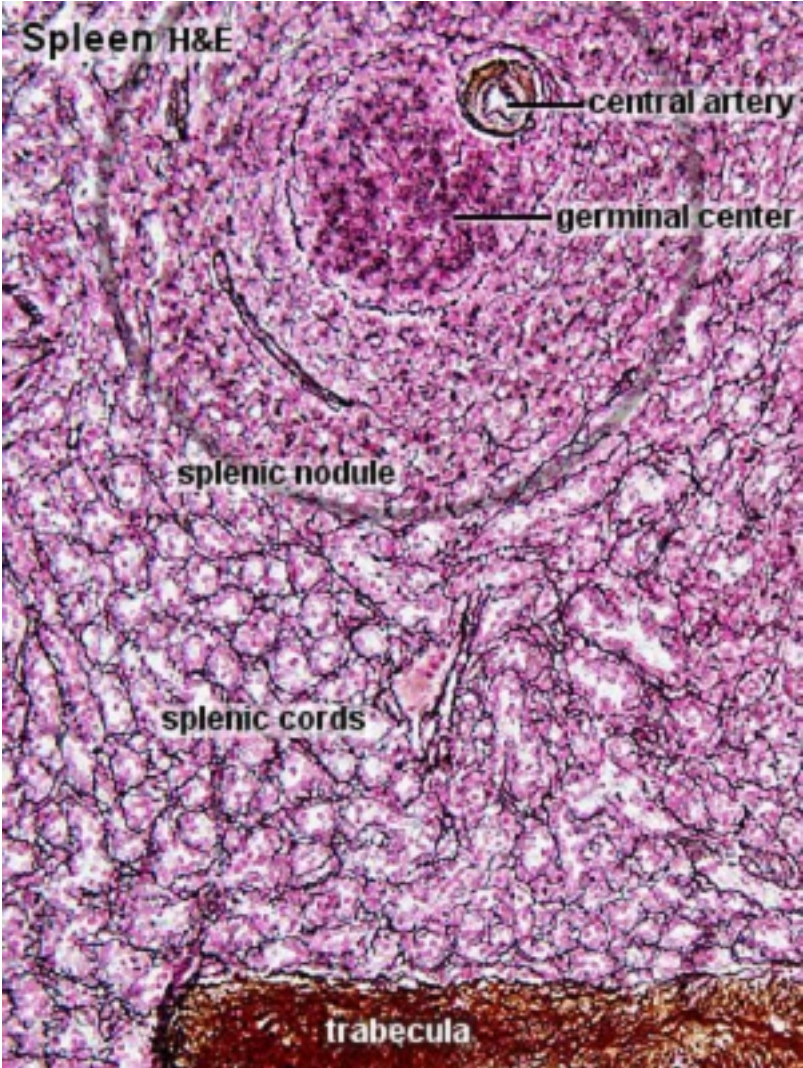
### Overview - blood vessels



### Red pulp



**Reticular Fibers** (type III collagen) act as supporting meshwork (can be seen in Silver stained preparations)



**Spleen Development:** Adult Histology | Overview Red and White Pulp | Overview Red and White Pulp | Cords and Sinuses | Reticular Fibre overview | Reticular Fibre detail | unlabeled red and white pulp | unlabeled red pulp and macrophages | unlabeled white pulp germinal centre | unlabeled reticular fibre | unlabeled white pulp reticular | unlabeled red pulp reticular | Structure cartoon | Cartoon and stain | Category:Spleen | Histology Stains | Immune System Development

## Additional Information

*Content shown under this heading is not part of the material covered in this class. It is provided for those students who would like to know about some concepts or current research in topics related to the current class page.*



# Janeway's Immunobiology



A useful resource textbook for further reading on **Lymphatic Structure and Organs** is Immunobiology (<http://www.ncbi.nlm.nih.gov/books/NBK10757/>) 5th edition The Immune System in Health and Disease Charles A Janeway, Jr, Paul Travers, Mark Walport, and Mark J Shlomchik. Open links in a new tab if you wish to refer back to this lecture page.

I have included some links in this table below to specific notes and there is also available a complete list of contents.

**External Links Notice** - The dynamic nature of the internet may mean that some of these listed links may no longer function. If the link no longer works search the web with the link text or name.

Immunobiology (<http://www.ncbi.nlm.nih.gov/books/NBK10757/>) 5th edition The Immune System in Health and Disease Charles A Janeway, Jr, Paul Travers, Mark Walport, and Mark J Shlomchik.

## Part I. An Introduction to Immunobiology and Innate Immunity Chapter 1. Basic Concepts in Immunology

- The components of the immune system (<http://www.ncbi.nlm.nih.gov/books/NBK27092/>)
  - Figure 1.3 All the cellular elements of blood, including the lymphocytes of the adaptive immune system, arise from hematopoietic stem cells in the bone marrow (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A40>)
  - Figure 1.4 Myeloid cells in innate and adaptive immunity (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A41>)
  - Figure 1.5 Lymphocytes are mostly small and inactive cells (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A42>)
  - Figure 1.6 Natural killer (NK) cells (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A43>)
  - Figure 1.7 The distribution of lymphoid tissues in the body (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A45>)
  - Figure 1.8 Organization of a lymph node (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A47>)
  - Figure 1.9 Organization of the lymphoid tissues of the spleen (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A48>)
  - Figure 1.10 Organization of typical gut-associated lymphoid tissue (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A49>)
  - Figure 1.11 Circulating lymphocytes encounter antigen in peripheral lymphoid organs (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A51>)
- Summary to Chapter 1 (<http://www.ncbi.nlm.nih.gov/books/NBK27092/#A52>)

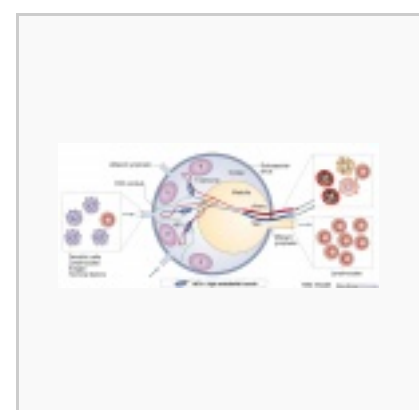
## Part III. The Development of Mature Lymphocyte Receptor Repertoires Chapter 7. The Development and Survival of Lymphocytes

- Generation of lymphocytes in bone marrow and thymus (<http://www.ncbi.nlm.nih.gov/books/NBK27123/>)
  - Figure 7.3 The early stages of B-cell development are dependent on bone marrow stromal cells (<http://www.ncbi.nlm.nih.gov/books/NBK27123/figure/A803>)
  - Figure 7.5 The development of a B-lineage cell proceeds through several stages marked by the rearrangement and expression of the immunoglobulin genes (<http://www.ncbi.nlm.nih.gov/books/NBK27123/figure/A806>)
  - Figure 7.7 The cellular organization of the human thymus (<http://www.ncbi.nlm.nih.gov/books/NBK27123/figure/A809>)
  - Figure 7.13 Thymocytes at different developmental stages are found in distinct parts of the thymus (<http://www.ncbi.nlm.nih.gov/books/NBK27123/figure/A818>)
- Survival and maturation of lymphocytes in peripheral lymphoid tissues (<http://www.ncbi.nlm.nih.gov/books/NBK27150/>)
- Summary to Chapter 7 (<http://www.ncbi.nlm.nih.gov/books/NBK27123/#A819>)

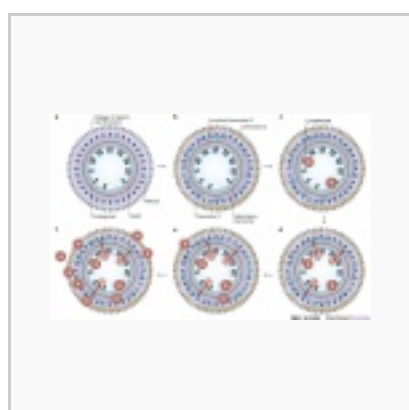


**SH Practical - Lymphatic Structure and Organs** associated practical support page. Note that virtual slides will be used in the associated practical class and this linked page is provided for student self-directed learning of concepts from the virtual slides.

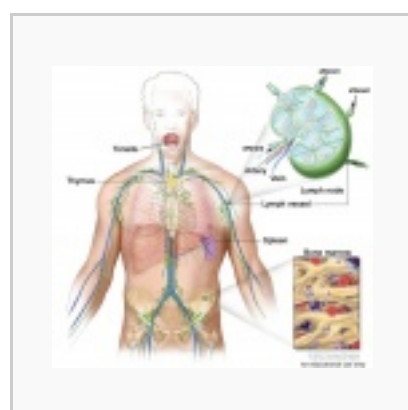
**Lymphatic cartoon links:** Overview | Tonsil | Tonsil and MALT | Thymus | Spleen | Bone marrow | **Lecture - Lymphatics** | Immune System Development



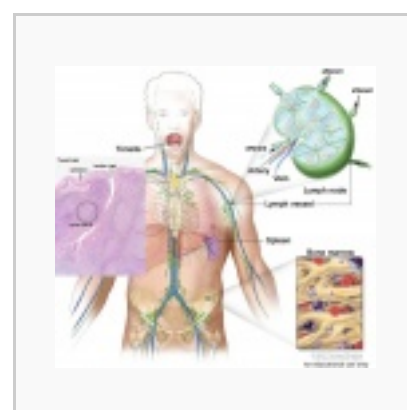
Cell Trafficking into and out of Lymph Nodes



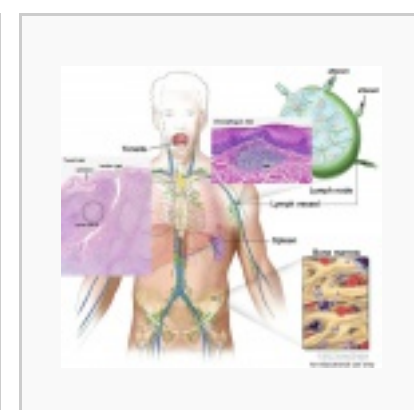
Lymphocyte Migration at High Endothelial Venule Model



Overview

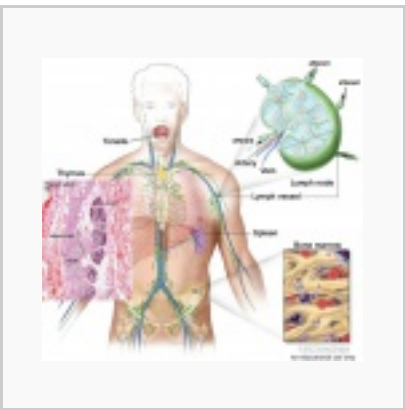


Tonsil



Tonsil and MALT

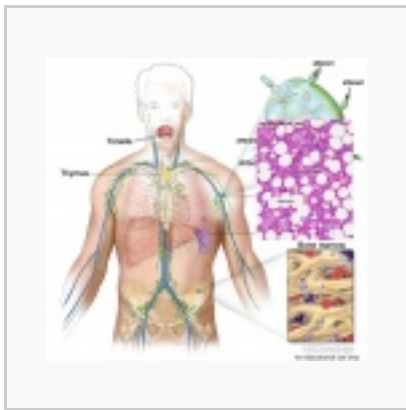




Thymus



Spleen



Bone marrow

**Mouse Lymphocyte Motility Movies[Expand]**

**Additional Images[Expand]**

- Figure - Gut associated lymphoid tissue (GALT) and systemic mucosal immunity (<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3144400/figure/F1/>)

**Nature Immunology - Videos**

These are short (5-10 min) animations showing how the immune system monitors the epithelial and environment interface at different anatomical locations.

- Immunology of the skin (<http://www.nature.com/ni/multimedia/skin/index.html>)
- Immunology of the lung (<http://www.nature.com/ni/multimedia/lung/index.html>)
- Immunology in the gut mucosa (<http://www.nature.com/ni/multimedia/mucosal/index.html>)

**Government Sources**

These information pages provide general information to the public. See how the biology concepts have been simplified to make them more understandable.

**USA**

- Basic AIDS and Immune System Information (<https://www.aids.gov/hiv-aids-basics/just-diagnosed-with-hiv-aids/hiv-in-your-body/immune-system-101>)
- NIAD - Immune System (<http://www.niaid.nih.gov/topics/immunesystem/Pages/default.aspx>)

**Australia**

- Healthdirect HIV/AIDS (<http://www.healthdirect.gov.au/hiv-infection-and-aids>)

**Blood Cells[Expand]**

**Anatomy of the Human Body (1918) - Lymphatics[Expand]**

Textbook Links: MBoC Figure 24-6. The development and activation of T and B cells | <http://www.ncbi.nlm.nih.gov/books/NBK26921/figure/A4430/> Figure 24-7. Electron micrographs of nonactivated and activated lymphocytes (<http://www.ncbi.nlm.nih.gov/books/NBK26921/figure/A4429>) | Immunobiology - Figure 1.9. Organization of the lymphoid tissues of the spleen (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A48>)

**Structure** - Cells, Vessels, Diffuse (extra-nodal tissue), Nodes, Organs.

- Cells
- Vessels
- Diffuse
  - Mucosal Associated Lymphoid Tissues (MALT)
  - Extranodal Lymphoid Tissues
  - Nodules
- Lymph Nodes
  - Position
  - Structure
  - Function
- Organs
  - Position, Structure, Function
  - Thymus
  - Spleen

**Terms**



A few key terms associated with the Lymphoid system.

## Immune System Development

- **adenoid** - (Greek " + *-oeides* = in form of) in the form of a gland, glandular; the pharyngeal tonsil.
- **Afferent lymph** - vessel carrying lymph towards a node.
- **anastomose** - joining of two tubes or structures together.
- **Antibody mediated immunity** - the immune function of plasma cells (active B lymphocytes) secreting antibody which binds antigen.
- **antibodies** - mammals have five classes (IgA, IgD, IgE, IgG, and IgM)
- **antigen** - any substance that is recognised by the immune system and stimulates antibody production.
- **appendix** - is a gut-associated lymphoid tissue (GALT) located at the beginning of the colon. The anatomy is as a finger-like structure that arises from the cecum. The length (2.5-13 cm) is longer in both infants and children and also has more abundant lymphatic tissue in early life. The wall structure is similar to the small intestine (though with no villi), nor plicae circularis. Lymph nodules surround the lumen of the gastrointestinal tract and extend from the mucosa into the submucosa.
- **B lymphocyte** - (B-cell) historically named after a structure called the **bursa** of Fabricius in birds, a source of antibody-producing lymphocytes. These cells develop in the bone marrow. (More? Electron micrographs of nonactivate and activated lymphocytes)
- **BALT** - Bronchus Associated Lymphoid Tissue
- **band cell** - (band neutrophil or stab cell) seen in bone marrow smear, a cell undergoing granulopoiesis, derived from a metamyelocyte, and leading to a mature granulocyte. Also occasionally seen in circulating blood.
- **cecum** - (caecum, Latin, *caecus* = "blind") within the gastrointestinal tract a pouch that connects the ileum with the ascending colon of the large intestine.
- **cell** - has a specific cell biology definition, but is often used instead of "lymphocyte" when describing B and T cells.
- **Cell-mediated immunity** - the immune function of T lymphocytes.
- **"clockface"** - a term used to describe the appearance of plasma cell nuclei due to the clumping of the chromatin at the nucleus periphery. More clearly seen in tissue plasma cells than the bone marrow smear, where they are sometimes confused with the basophilic erythroblasts. Image - plasma cell
- **CD** - (cluster of differentiation) identifies immunological surface markers on cells.
- **CD4+** - (T helper cells) refers to T lymphocytes that express CD4 (glycoprotein of the immunoglobulin superfamily) on their surface. These cells can be infected by human immunodeficiency virus (HIV).
- **CD8+** - (cytotoxic T cells) refers to T lymphocytes that express CD8 (glycoprotein of the immunoglobulin superfamily) on their surface.
- **"clockface"** - a term used to describe the appearance of plasma cell nuclei due to the clumping of the chromatin at the nucleus periphery. More clearly seen in tissue plasma cells than the bone marrow smear, where they are sometimes confused with the basophilic erythroblasts.
- **cords of Billroth** - spleen cellular columns located in red pulp. surrounded by splenic sinusoids. Cords contain reticular cells, macrophages, lymphocytes, plasma cells and erythrocytes.
- **cortex** - outer layer, used in association with medulla (inner layer or core) a general description that can be applied to describing an organ with a layered structure.
- **dendritic cell** - (DC, antigen-presenting cell, APC) cells that present antigens and induce a primary immune response in resting naïve T lymphocytes. Originate from the same common progenitor as monocytes (PMID 20193011). In 2011 Ralph M. Steinman received half the Nobel Prize ([http://www.nobelprize.org/nobel\\_prizes/medicine/laureates/2011/](http://www.nobelprize.org/nobel_prizes/medicine/laureates/2011/)) half of the award to to Ralph M. Steinman *for his discovery of the dendritic cell and its role in adaptive immunity*.
- **Effector cells** - the immune functioning (active) B and T lymphocytes.
- **Efferent lymph** - vessel carrying lymph away from a node.
- **GALT** - Gut Associated Lymphatic Tissue consisting of Peyer's patches, isolated lymphoid follicles and mesenteric lymph nodes.
- **haemopoiesis** (hemopoiesis) formation of blood cells.
- **Hassall's corpuscle** - thymic corpuscle.
- **high endothelial venule** - (HEV) the specialised post-capillary venous region that enables blood lymphocytes to enter a lymph node. These specialised post-capillary venules enables blood lymphocytes to enter a lymph node. Their endothelial cells express ligands that bind lymphocytes, aiding their adhesion and subsequent transmigration into the lymph node.
- **IEL** - Intraepithelial Lymphocyte are T lymphocytes located in the gastrointestinal tract epithelium. Natural IELs (previously 'type b' IELs) acquire activated phenotype during development in the thymus in the presence of self antigens. Induced IELs (previously 'type a' IELs) progeny of conventional T cells activated post-thymically in response to peripheral antigens.
- **IgA** - the main class of antibody in secretions (saliva, tears, milk, and respiratory and intestinal secretions).
- **IgD** - the immunoglobulin B cell starts to produce as a cell-surface molecule after leaving the bone marrow.
- **IgE** - bind Fc receptors (surface of mast cells in tissues and basophils in the blood) release of potent pro inflammatory molecules mediators of allergic reactions.
- **IgG** - the major class of immunoglobulin in the blood.
- **IgM** - the first class of antibody made by a developing B cell, which may switch to making other classes of antibody.
- **immunodeficiency** - when one or more components of the immune system is defective. (More? Immunobiology - immunodeficiency (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Search&db=books&rid=imm.section.1494>))
- **intraepithelial lymphocyte** (IEL) immune cells residing in the gastrointestinal tract epithelium. image - Intraepithelial lymphocyte differentiation
- **involution** - in the thymus refers to the replacement, mainly in the cortex, of cells by adipose tissue. (More? PubMed- thymus involution (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=Search&term=thymus+involution&doptcmdl=Books>)) | Cancer Medicine - Thymomas and Thymic Tumors (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Search&db=books&rid=cmed6.section.23856#23857>))
- **Kupffer cells** - stellate macrophage cells located in the liver sinusoids, named after Karl Wilhelm von Kupffer (1829 - 1902) a German anatomist who originally identified these cells. (More? Liver Development)
- **lacteal** - term used to describe the lymphatic vessels of the small intestine.
- **lamina propria** - a layer of loose connective tissue found underneath the epithelium of mucosa.
- **Langerhans cell** - (LC, dendritic cell) Antigen-presenting immune cell found mainly in the basal/suprabasal layers of adult skin and



- mucosa. Cells lie in the basal/suprabasal layers of stratified epidermal and mucosal tissues. First in the innate antiviral immune defines and can migrate to lymph nodes and induce a T cell–mediated adaptive immune response. (More? Integumentary | Immune System Development)
- **Leukocyte** - (Greek, *lukos* = clear, white) white blood cell.
  - **lingual** - related to the tongue.
  - **lymph node** - connective tissue encapsulated lymphoid organ (1mm - 2cm in size), positioned in the pathway of lymph vessels. (More? Lymph Node Development)
  - **lymphangion** - the functional unit of a lymph vessel that lies between two semilunar (half moon-shaped) valves.
  - **M cell** - (microfold cell) found in the follicle-associated epithelium of the Peyer's patch. Function to transport gut lumen organisms and particles to immune cells across the epithelial barrier.
  - **macrophage** - a large highly motile white blood cell which engulfs foreign material (bacteria etc) and both degenerating cells and cell fragments. Differentiates from a monocyte and found in many different tissues and locations. Current theory suggests tissue macrophage is also derived from resident stem cell population in many tissues. More? Immunobiology - Defects in phagocytic cells are associated with persistence of bacterial infection (<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=imm.figgrp.1508>))
  - **MALT** - Mucosa Associated Lymphoid Tissue
  - **medulla** - inner layer or core, used in association with cortex (outer layer) a general description that can be applied to describing an organ with a layered structure.
  - **Memory Cell** - effector T cell (lymphocyte)
  - **mesenteric lymph nodes** - Part of GALT as well as being involved in gut-draining. 
  - **Mononuclear Phagocytic System** - (MPS, Lymphoreticular System, Reticuloendothelial System, RES) Consists of circulating monocytes in the peripheral blood and non-circulating (fixed) tissue macrophages ( $M\Phi$ ) located in tissues and organs.
  - **negative selection** - T cells bearing autoreactive T cell antigen receptors (TCRs) are eliminated during their development in the thymus, protects against autoimmunity.
  - **normoblast** - seen in bone marrow smear, a developing erythroblast (red blood cell) that still retains a nucleus.
  - **parenchyma** - (Greek = *enkeim* "to pour in") cells forming the functional cells of an organ or tissue. These cells carry out the function of the organ at a cellular level, and are not the structural cells, connective tissue, extracellular matrix (stromal).
  - **periarterial lymphoid sheath** - (PALS) in the spleen the white pulp that surrounds the central arteries. (T-lymphocytes, macrophages and plasma cells)
  - **Plasma Cell** - active B cell (lymphocyte) which is secreting antibody. Located in either bone marrow or peripheral lymphoid tissues, these cells have and increased cytoplasmic volume (due to increase rough endoplasmic reticulum) in comparison to the inactive (non-secreting) lymphocyte.
  - **sentinel lymph node** - the hypothetical first lymph node or group of nodes reached by metastasizing cancer cells from a primary tumour.
  - **splenic sinusoids** - enlarged spleen capillary spaces located in red pulp and surrounding cords of Billroth.
  - **stroma** - (Greek = "a cover, table-cloth, bedding") tissue forming the framework/support of an organ or tissue. That is the structural cells which form connective tissue and secrete extracellular matrix, rather than the functional cells (parenchymal). All organs can therefore be functionally divided into these 2 components, stromal/parenchymal.
  - **Subcapsular sinus** (=marginal sinus) space lying under the connective tissue capsule which receives lymph from afferent lymphatic vessels.
  - **Thymic corpuscle** (=Hassall's corpuscle) a mass of concentric epithelioreticular cells found in the thymus. The number present and size tend to increase with thymus age. (see classical description of Hammar, J. A. 1903 Zur Histogenese und Involution der Thymusdrüsi. Anat. Anz., 27: 1909 Fiinfzig Jahre Thymusforschung. Ergebn. Anat. Entwickl-gesch. 19: 1-274.)
  - **thymic epitheliocytes** - reticular cells located in the thymus cortex that ensheath the cortical capillaries, creating and maintain the microenvironment necessary for the development of T-lymphocytes in the cortex.
  - **T helper cells** - (helper T-cells) ( $T_h$  cells, CD4+) refers to T lymphocytes that when mature express CD4 (glycoprotein of the immunoglobulin superfamily) on their surface.
  - **T lymphocyte** - (T-cell) named after thymus, where they develop, the active cell is responsible for cell-mediated immunity (killer T cells and helper T cells). Cells express T-cell receptor on surface and directly kill virally or bacterially infected cells. These cells can themselves be infected by HIV. (More? Electron micrographs of nonactivate and activated lymphocytes)
  - **thymus** - an immune/endocrine (thymic hormone) organ involved in the maturation of T lymphocytes (T-cells). Thymus Development
  - **tonsils** - lymph nodules embedded in the mucus membranes located at the back of the mouth and top of the throat. The overlying epithelium helps identify the location.
  - **vermiform appendix** - see appendix, anatomical region containing gut-associated lymphoid tissue located within the gastrointestinal tract at the beginning of the colon. The anatomy is as a finger-like structure that arises from the cecum. The length (2.5-13 cm) is longer in both infants and children and also has more abundant lymphatic tissue in early life. The wall structure is similar to the small intestine (though with no villi), nor plicae circularis. Lymph nodules surround the lumen of the gastrointestinal tract and extend from the mucosa into the submucosa.
  - **white pulp** - (Malpighian bodies of the spleen, splenic lymphoid nodules) spleen lymphoid region, organized as lymphoid sheaths with both T-cell and B-cell compartments, around the branching arterial vessels (resembles lymph node structure).

## Glossary Links

A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z | Numbers | Symbols



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