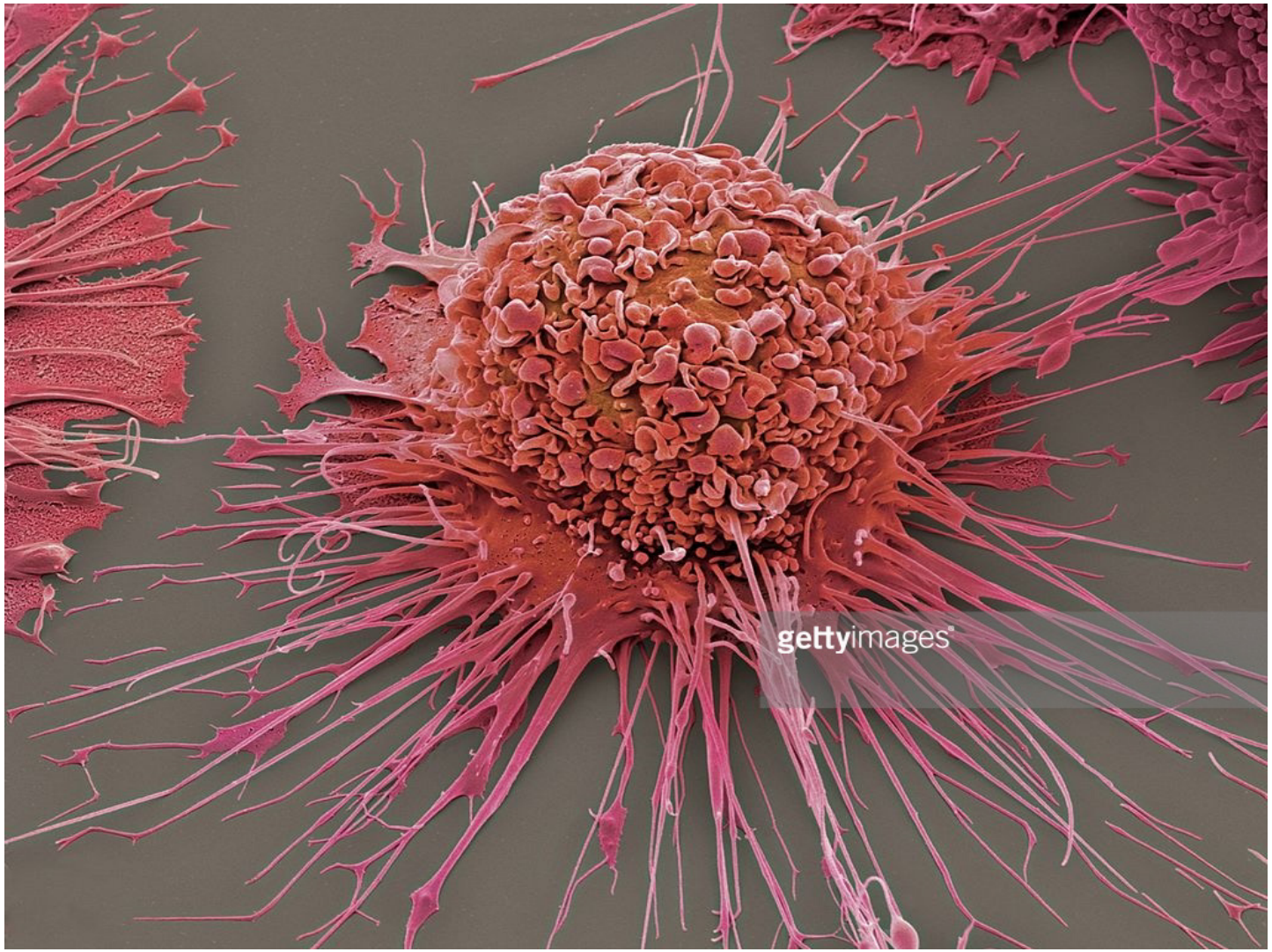
Lab 14 – Lymphoid System

IUSM – 2016

Lymphoid System



SEM of an activated macrophage.

Lab 14 – Lymphoid System

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Introduction

1. The main function of the **immune system** is to protect the body against aberrancy: either foreign pathogens (e.g., bacteria, viruses, and parasites) or abnormal host cells (e.g., cancerous cells).

2. The **lymphoid system** includes all cells, tissues, and organs in the body that contain aggregates (accumulations) of **lymphocytes** (a category of leukocytes including B-cells, T-cells, and natural-killer cells); while the functions of the different types of lymphocytes vary greatly, they generally all appear morphologically similar so cannot be routinely distinguished in light microscopy.

3. Lymphocytes can be found distributed throughout the lymphoid system as: (1) single cells, (2) isolated aggregates of cells, (3) distinct non-encapsulated lymphoid nodules in loose CT associated with epithelium, or (4) encapsulated individual lymphoid organs.

4. **Primary lymphoid organs** are sites where lymphocytes are formed and mature; they include the bone marrow (B-cells) and thymus (T-cells); **secondary lymphoid organs** are sites of lymphocyte monitoring and activation; they include lymph nodes, MALT, and the spleen.

5. **MALT** (**mucosa-associated lymphoid tissue**) consists of collections of lymphocytes and antigen-presenting cells in the lamina propria (loose CT) of the mucosa of the digestive, respiratory, and genitourinary tracts; the cells may be dispersed throughout the mucosa or collected together into aggregates (lymphoid nodules).

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Learning Objectives

1. Describe the cellular organization and functions of the thymus.
2. Describe the structural architecture and cellular composition of lymph nodes, their function(s), and lymph and blood circulation within them.
3. Define the non-encapsulated collections of lymphoid tissue associated with the gastrointestinal tract (GALT): tonsils, Peyer's patches, and appendix.
4. Describe the structural architecture, cellular composition, and function of the spleen.
5. Identify the characteristic structural and cellular components of defined elements of the lymphoid system.
6. Identify the architectural and cellular organization of the thymus.
7. Identify the structural architecture and cellular composition of lymph nodes.
8. Identify the non-encapsulated collections of lymphoid tissue associated with the gastrointestinal tract (GALT): tonsils, Peyer's patches, and appendix.

Learning Objectives (cont.)

9. Identify the connective tissue capsule, trabeculae, white and red pulp in spleen and components of the blood circulation in the spleen.

10. Explain why lymphoid organs contain a network of reticular fibers or epithelial tissue filled with lymphocytes and other cells of the immune system.

11. Compare and contrast the specific unique structural features and regions of lymph nodes, spleen, and thymus and the functional significance of these features.

12. Describe the circulation through the lymph nodes and spleen and how these organs filter lymph and blood, respectively.

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Keywords

Afferent lymphatic vessel
BALT
Central arteriole
Cortex
Efferent lymphatic vessel
Epitheliorecticular cell
GALT
Germinal center
High endothelial venule
Lymph node
Lymphocytes
Lymphoid follicle/nodule
Macrophage
MALT
Mantle zone
Medulla
Medullary cord
Medullary sinus
Paracortex
Periarteriolar lymphoid sheaths
Peyer's patch
Red pulp
Reticular network
Spleen
Splenic cord (of Billroth)
Splenic sinus
Stave cells
Subcapsular sinus
Thymic (Hassal's) corpuscle
Thymic epithelial cell
Thymus
White pulp

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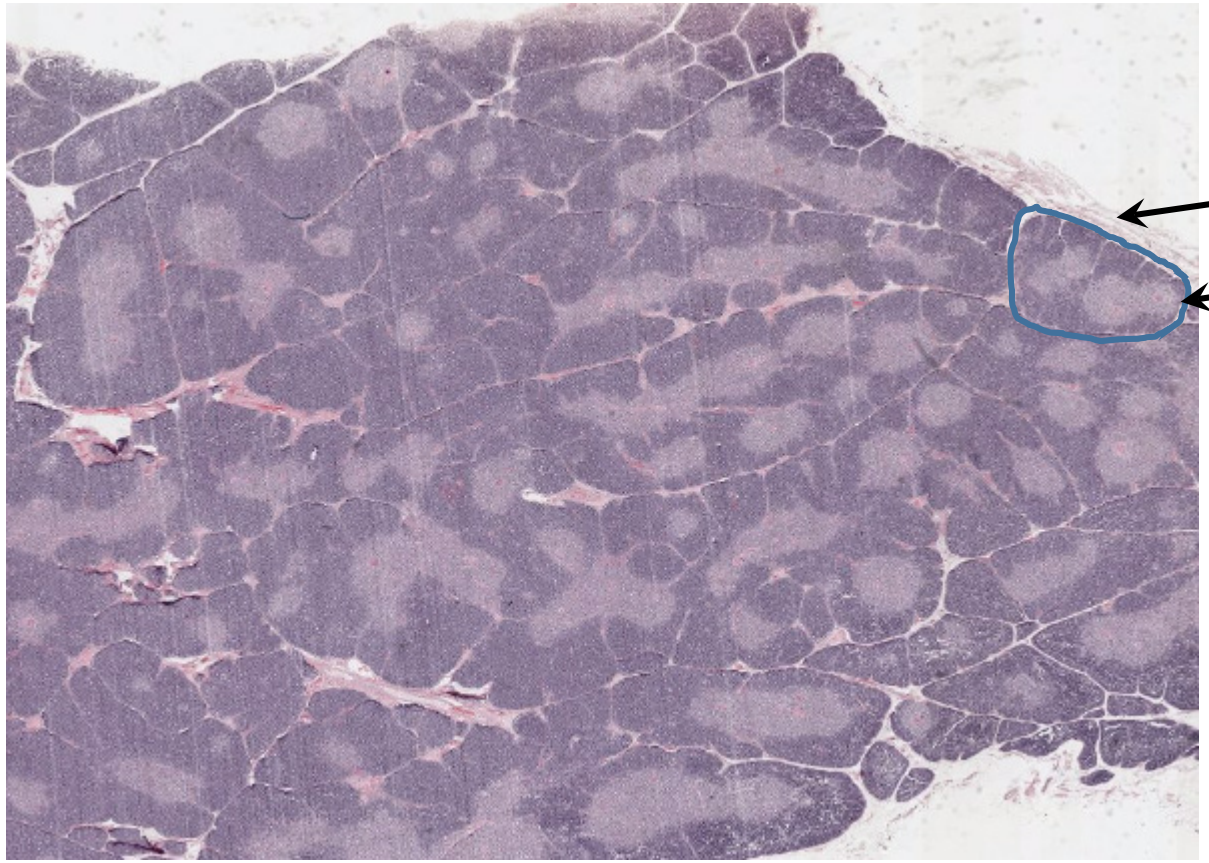
Slide 126: Thymus, H&E



the **thymus** is the site of T-cell (lymphocyte) maturation; it is bi-lobed (seen at the gross level) and surrounded by a vascularized dense CT **capsule**; **trabeculae/septa** arise from the capsule and divide the lobes into incompletely-separated lobules; each lobule has a dark-staining **cortex** and a light-staining **medulla**

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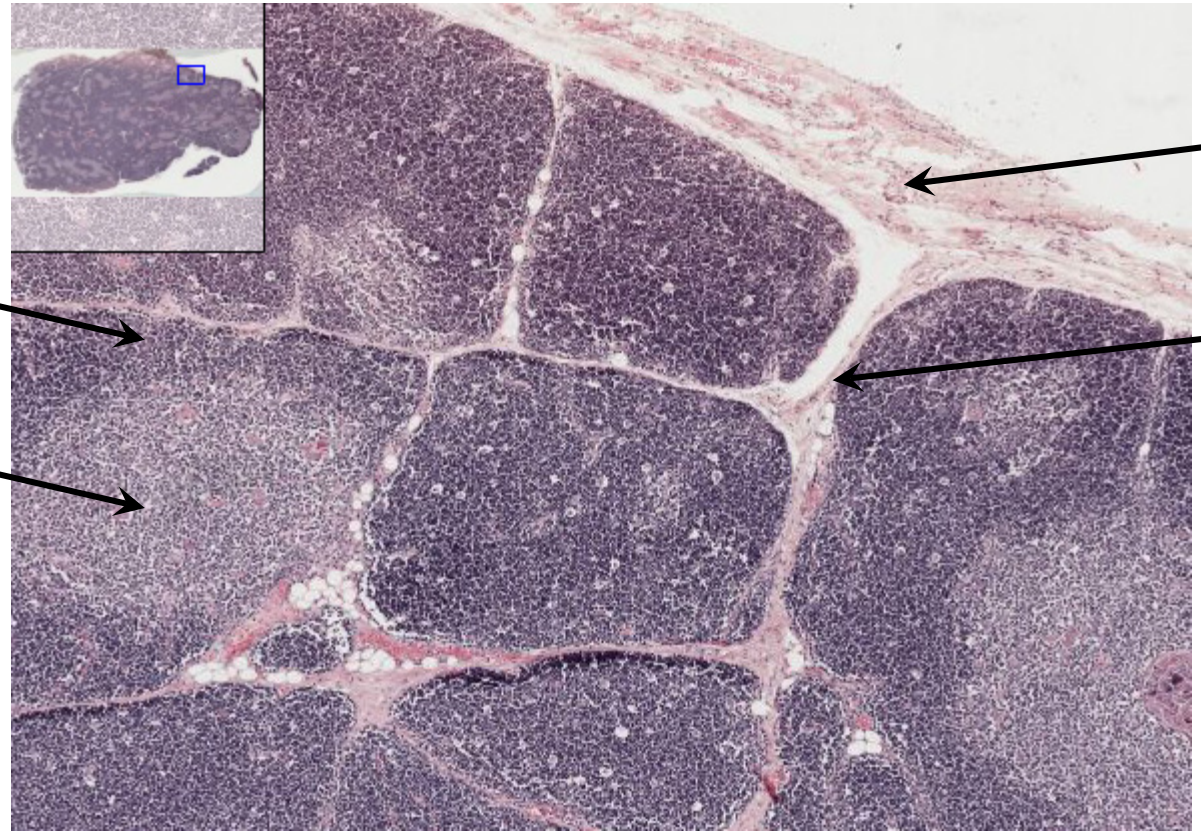
Slide 126: Thymus, H&E



capsule

cortex of lobule (basophilic)

medulla of lobule (eosinophilic)

septum of CT extending from the capsule, separating the parenchyma of the gland into lobules

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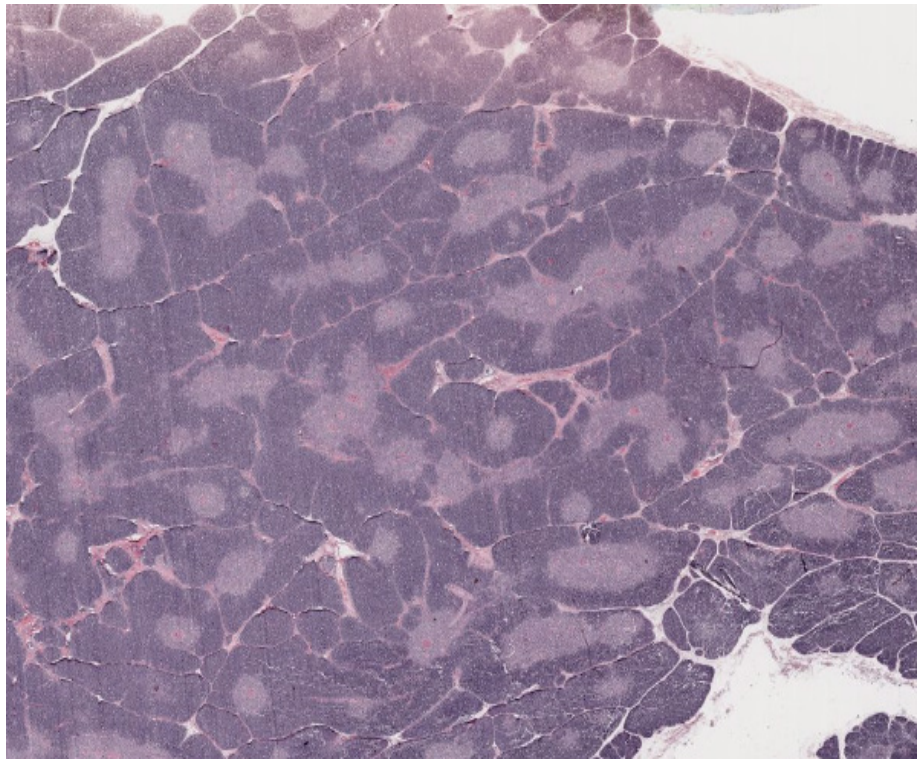
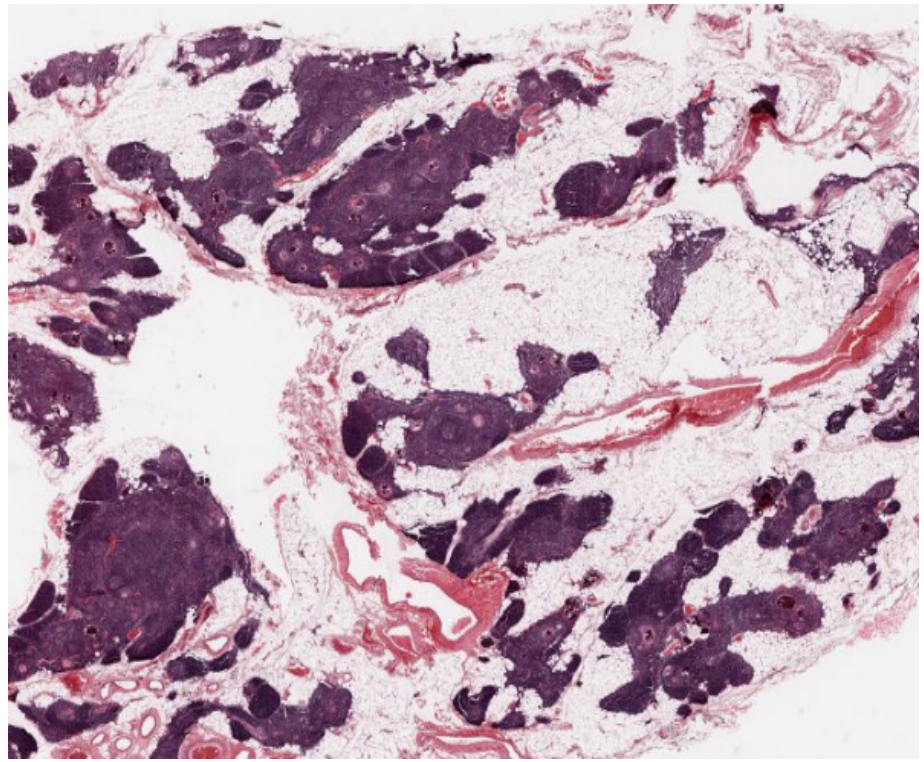
Slide 126: Thymus, H&E



non-involuted thymus has clear thymic architecture with distinctive lobules with divisions into cortex and medulla regions

Slide 123: Thymus, H&E



involuted thymus lacks distinction between cortex and medulla of lobules and has an abundance of adipose tissue

by puberty, the thymus has begun to undergo **involution** (degeneration) with a drop in lymphocyte production; thymic corpuscles (in the medulla) become more prominent and the parenchyma of the gland is replaced with loose CT and adipose tissue

Lab 14 – Lymphoid System

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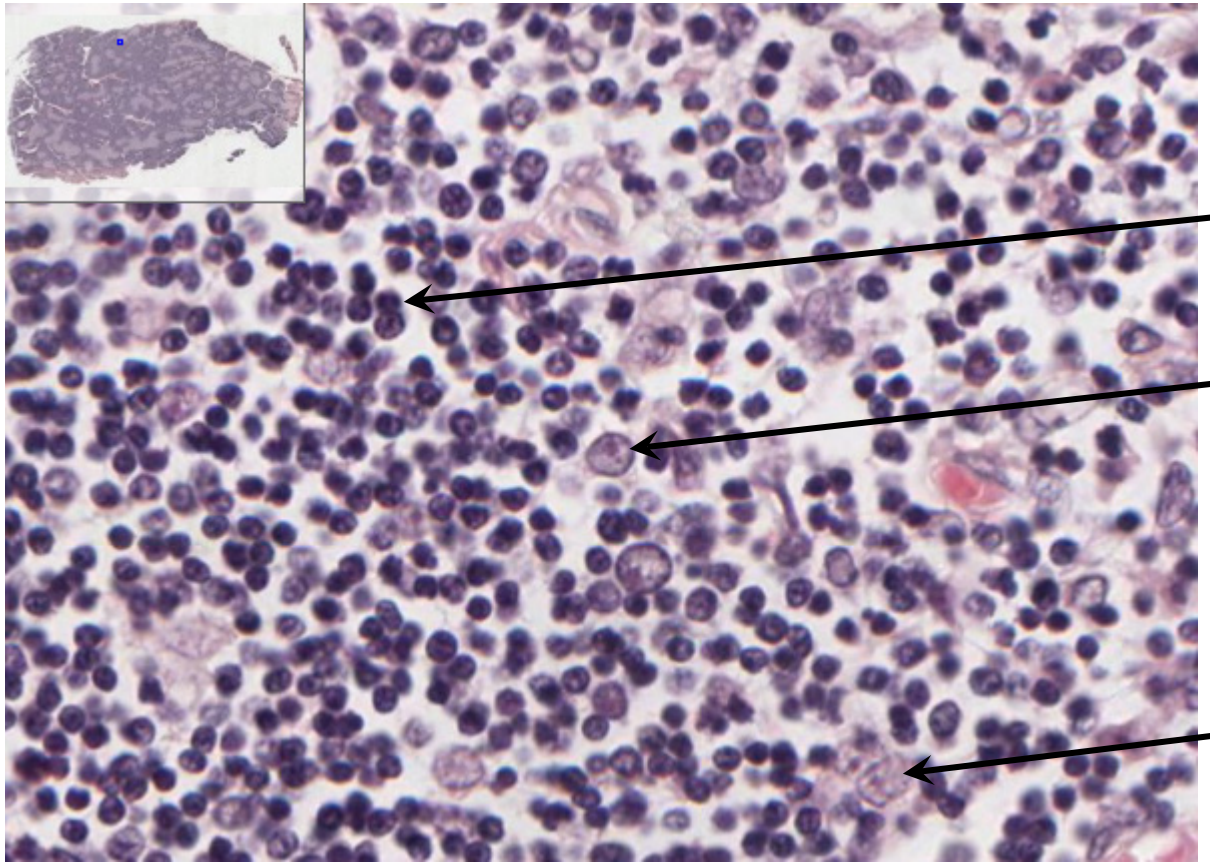
Slide 126: Thymus, H&E



the basophilic **cortex** of each lobule is the site of positive T-cell selection; it contains an extensive population of T-cell precursor **lymphocytes** (thymocytes), with basophilic nuclei with little cytoplasm, as well as **macrophages** and a few cortical **thymic epithelial cells** (**epithelioreticular cells**); ERCs have large round/oval euchromatic nuclei; they around found both in the cortex and medulla and perform a variety of functions, including compartmentalizing the cortex, creating a blood-thymus barrier, and thymocyte education

Lab 14 – Lymphoid System

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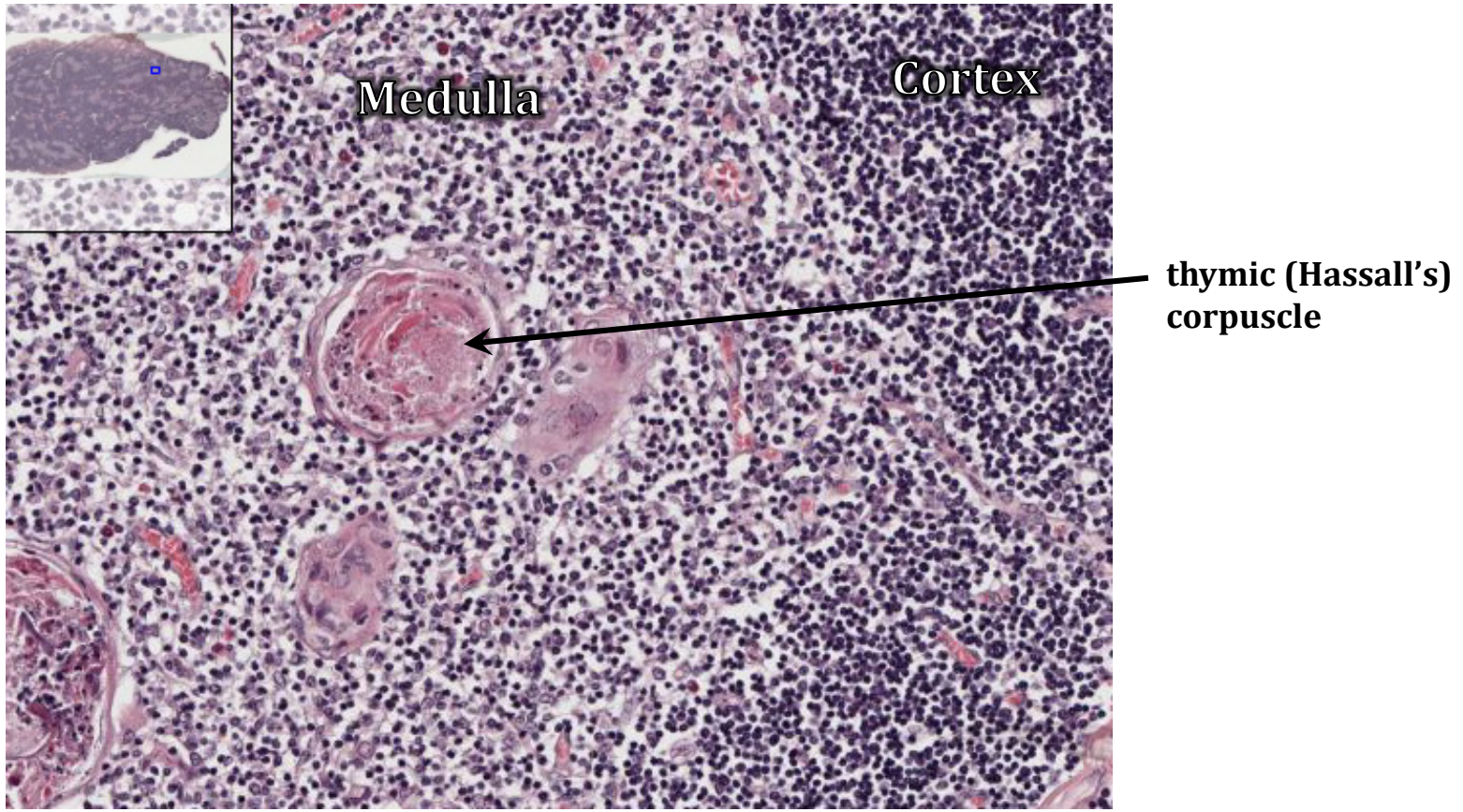
Slide 126: Thymus, H&E



the **medulla** of each lobule is the site of negative T-cell selection; it is characterized by a more eosinophilic appereance due to fewer and larger lymphocytes (thymocytes) and the presence of **thymic corpuscles** which are large, oval structures with whorls of keratinized, flattened cells; the corpuscles are thought to play a role in regulatory T-cell development, though their significance remains unknown; their presence is a defining characteristic of the medulla and the thymus in general

Lab 14 – Lymphoid System

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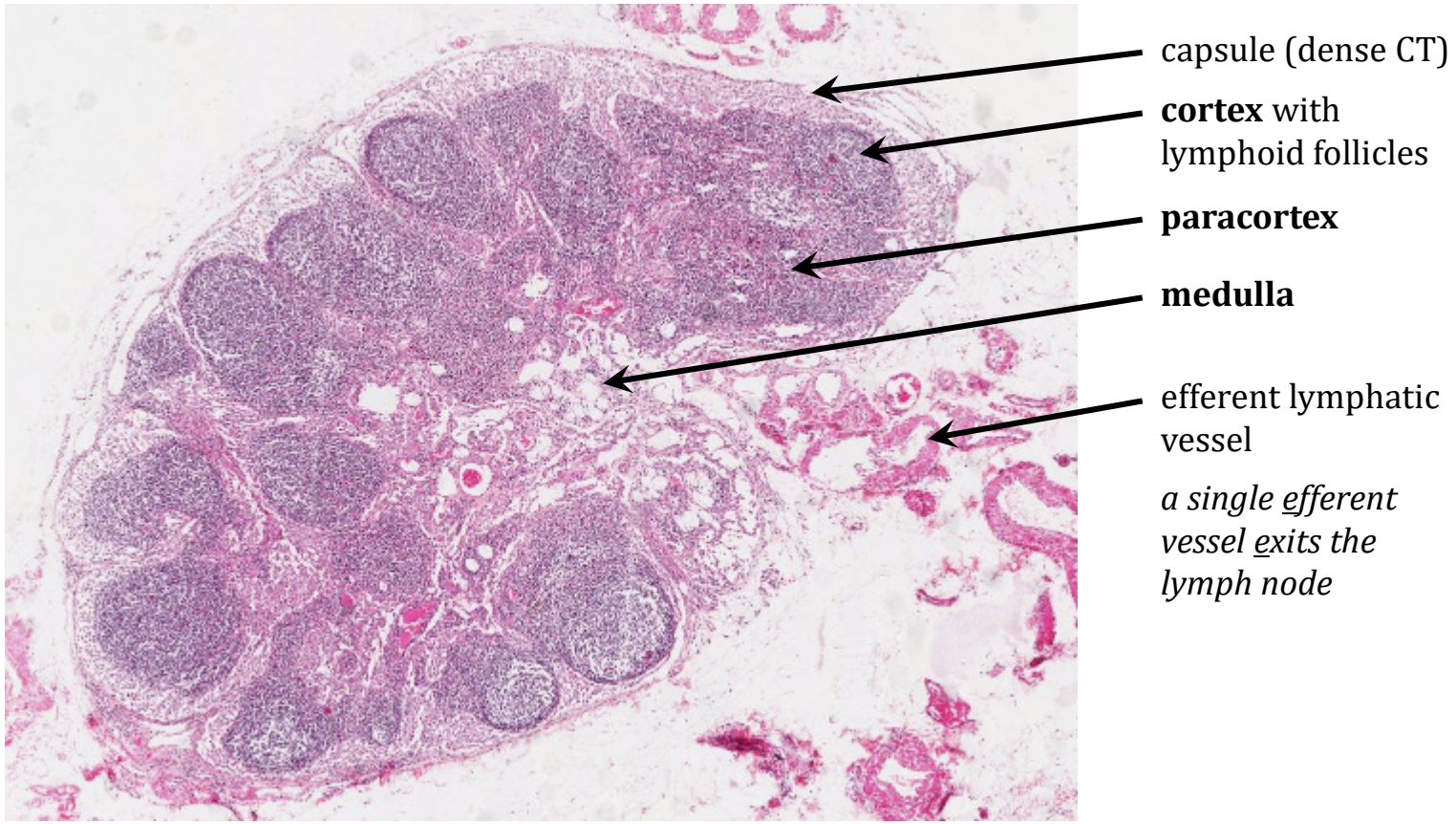
Slide 42: Lymph Node, H&E



lymph nodes are bean-shaped, encapsulated "lymph filters" situated periodically along the length of lymphatic vessels (generally 400-450 total in the body); they contain lymphocytes (B-cells and T-cells) and macrophages contained in a reticulin-fiber scaffold; all lymph passes through at least one node before returning to the venous circulation; unlike the thymus, lymph nodes do not have lobules; instead, the entire lymph node is organized into an outer **cortex** and inner **medulla**

Lab 14 – Lymphoid System

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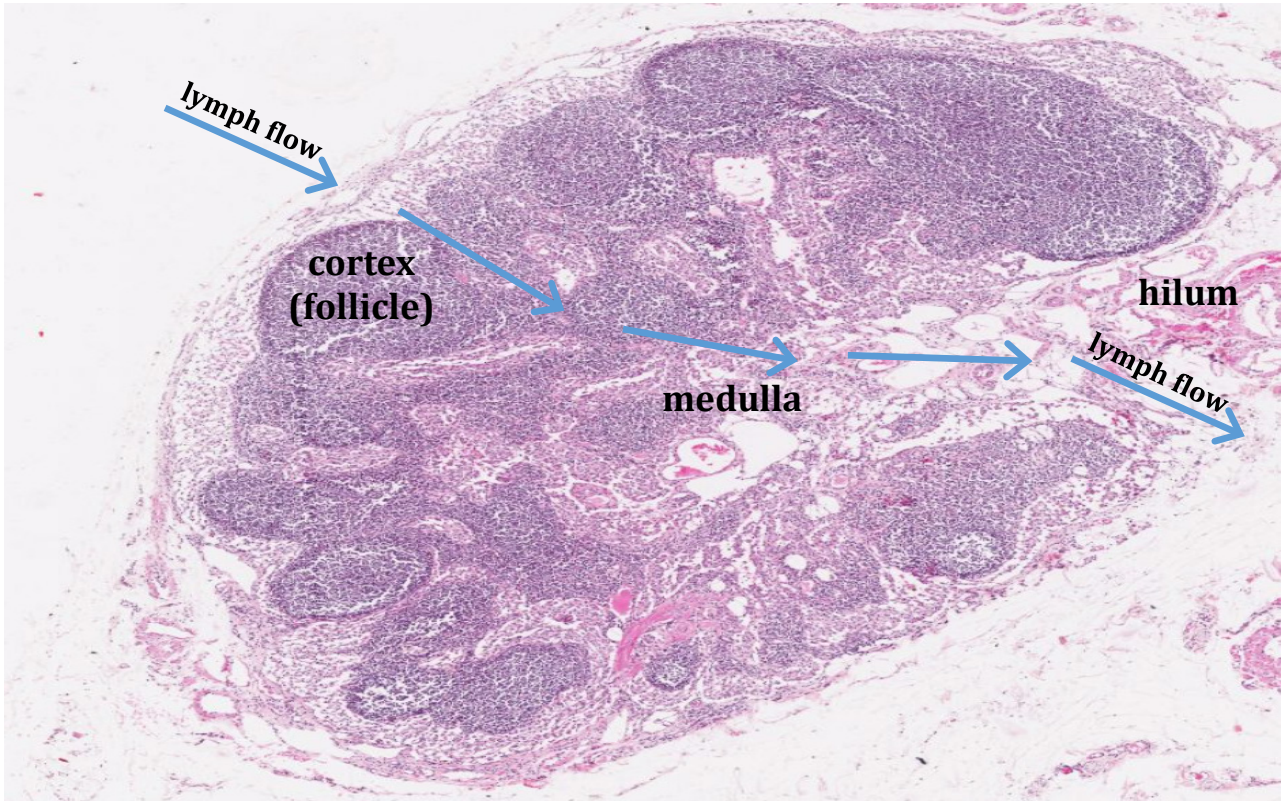
Slide 42: Lymph Node, H&E



lymph enters through any of the multiple afferent lymphatic vessels draining into the lymph node; the lymph passes through a series of sinuses (subcapsular → cortical → medullary) before exiting through the single efferent lymphatic vessel (in the hilum); as the lymph passes through the sinuses, it contacts macrophage pseudopods which engulf antigen and present it to lymphocytes in the lymphoid follicles in the cortex; antigen may also escape the sinuses and directly contact lymphocytes

Lab 14 – Lymphoid System

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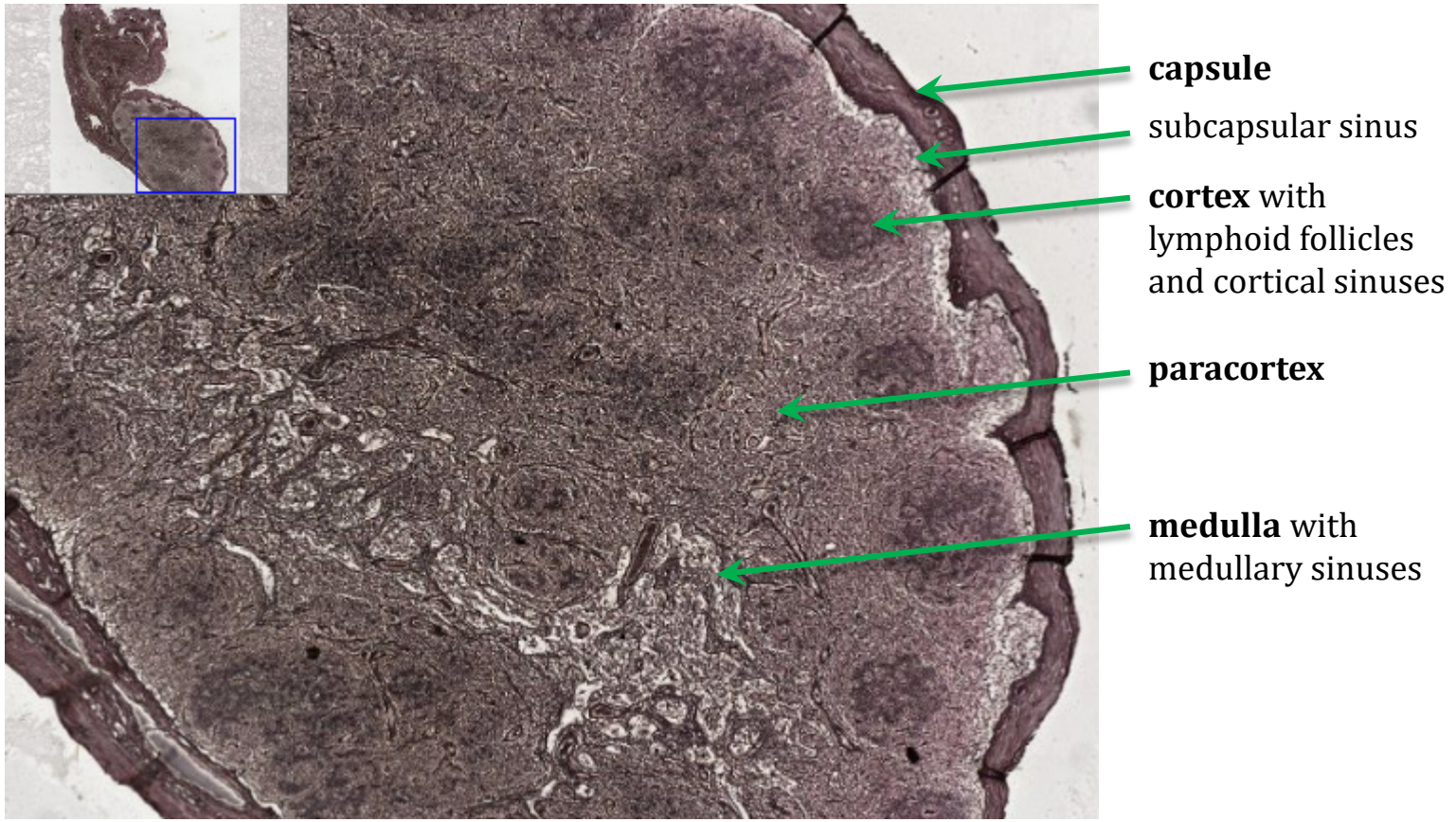
Slide 99: Lymph Node, Silver



Lab 14 – Lymphoid System

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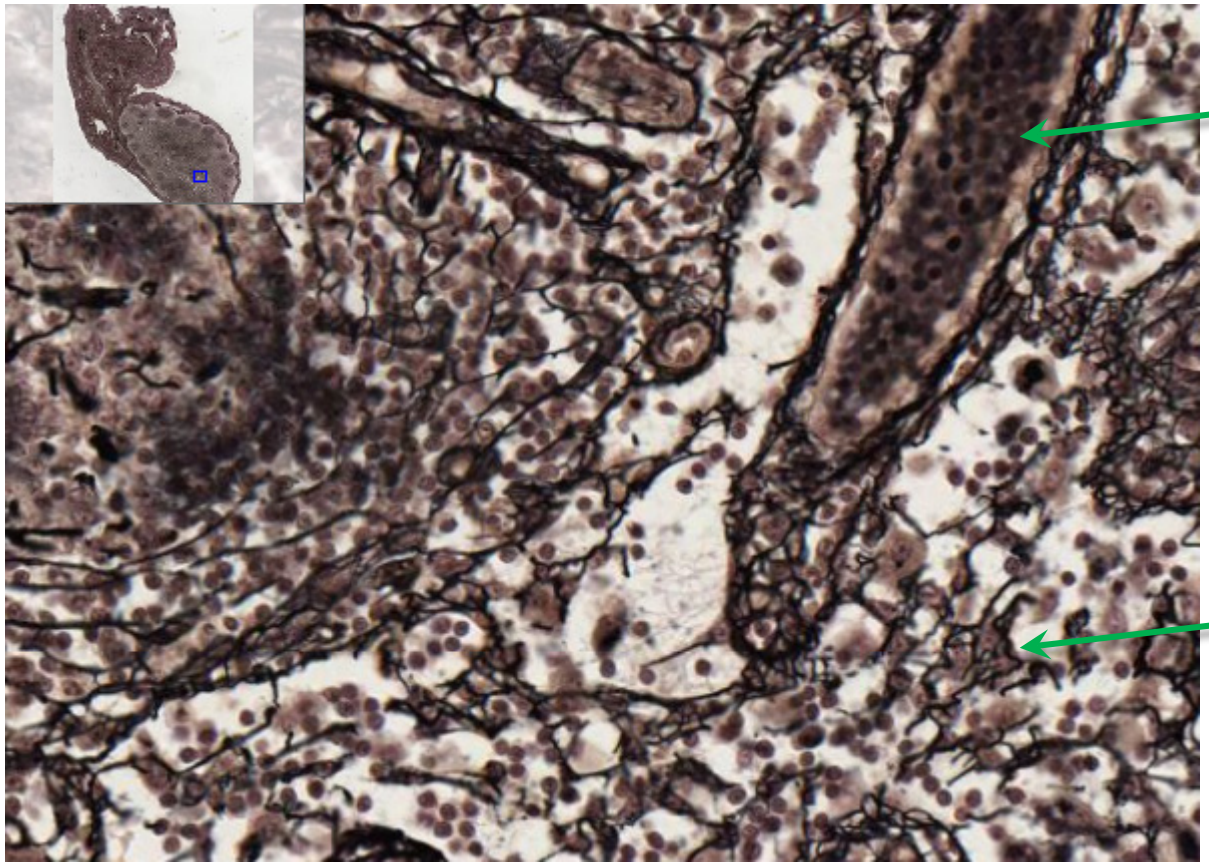
Slide 99: Lymph Node, Silver



silver staining shows clearly the abundant reticular fibers (type III collagen), made by reticular cells, composing the **reticular network** within the lymph node (and other lymphoid organs except the thymus); beyond the reticular cells, macrophages and dendritic cells are also present within the network but can be difficult to identify in normal slide preparations

Lab 14 – Lymphoid System

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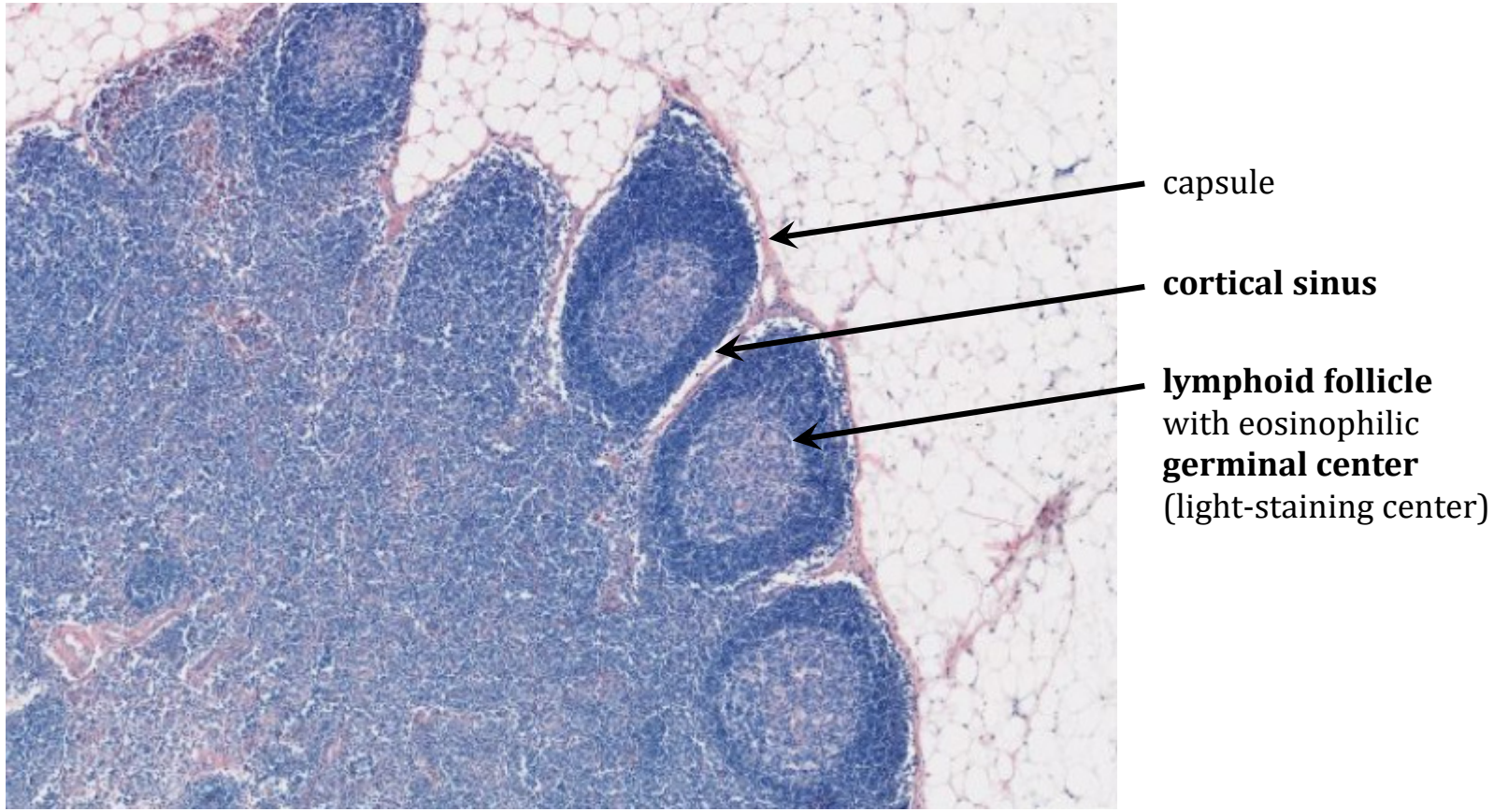
Slide 28 (464): Lymph Node, Giemsa



the **cortex** contains a dense collection of lymphocytes (primarily B cells) organized into **lymphoid follicles/nodules**; the follicles can be classified as either *primary* or *secondary* based upon lymphocyte activation; upon B cells activation, a **germinal center** forms within the follicle (a *secondary follicle*); the **cortical sinsues** conduct lymph from the subcapsular sinuses to the medullary sinuses

Lab 14 – Lymphoid System

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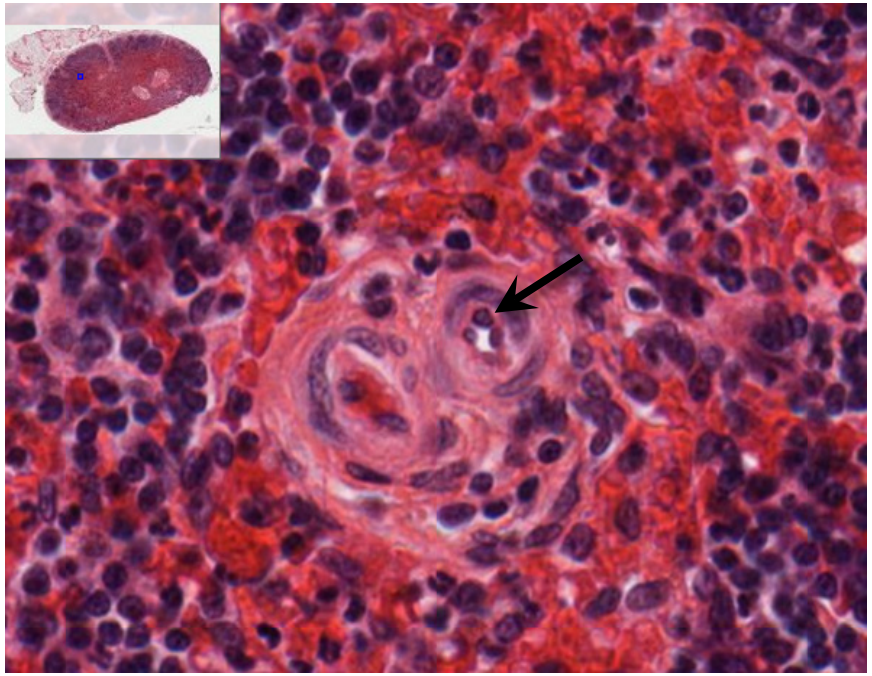
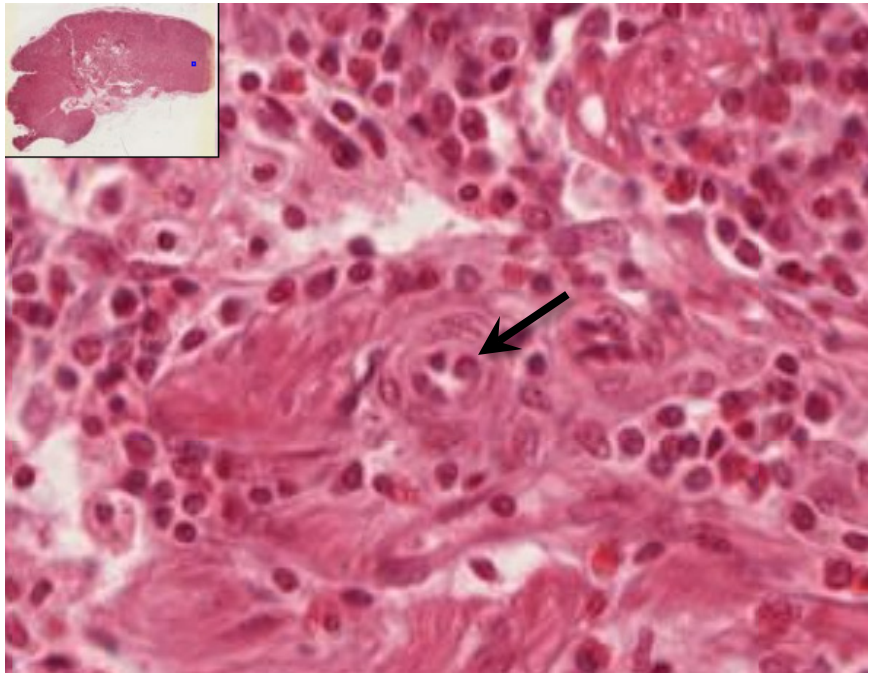
Slide 104 (NW): Lymph Node



Slide 28a (464): Lymph Node



the **paracortex** (or deep cortex) is located between the cortex and medulla; most of the T cells within the lymph node are localized to the paracortex; additionally, a defining characteristic of the paracortex is the presence of **high endothelial venules** (**HEVs**) (shown with arrows above); the aptly-named HEVs differ from regular venules by having a simple cuboidal or columnar endothelium; the majority of lymphocytes enter into the tissue of the lymph node by exiting the blood through the HEVs – T cells then remain in the paracortex while B cells migrate to the cortex; HEVs are also found in other lymphoid organs, except the thymus and spleen

Lab 14 – Lymphoid System

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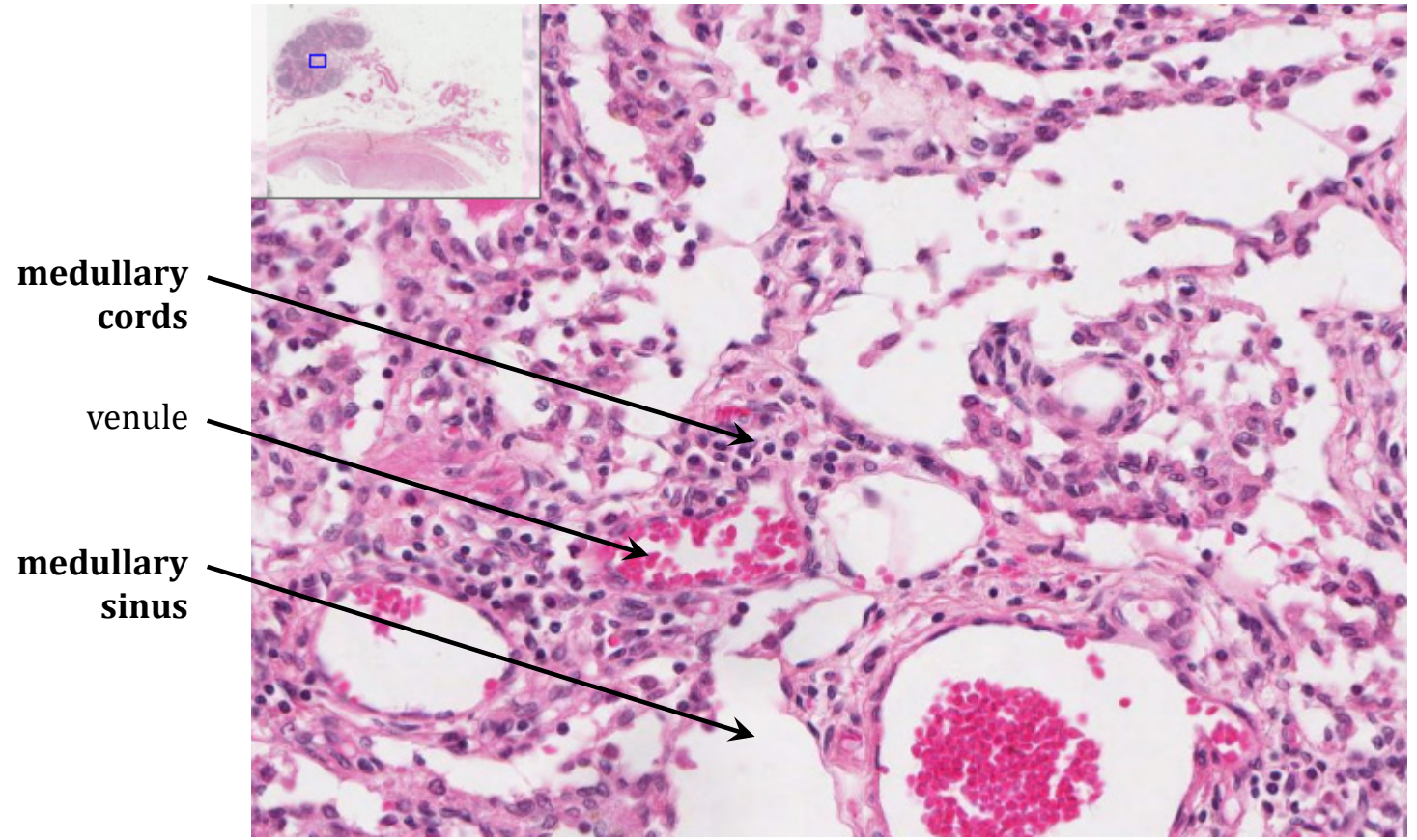
Slide 42: Lymph Node, H&E



medullary cords are elongated organizations of lymphocytes surrounding the lymphatic **medullary sinuses**; from the medullary sinuses, lymph will leave the node through the efferent lymphatic vessel exiting the hilum; within the cords, plasma cells (migrated from germinal centers in secondary follicles in cortex) secrete antibodies into the lymph which leaves the node to eventually return to the systemic circulation

Lab 14 – Lymphoid System

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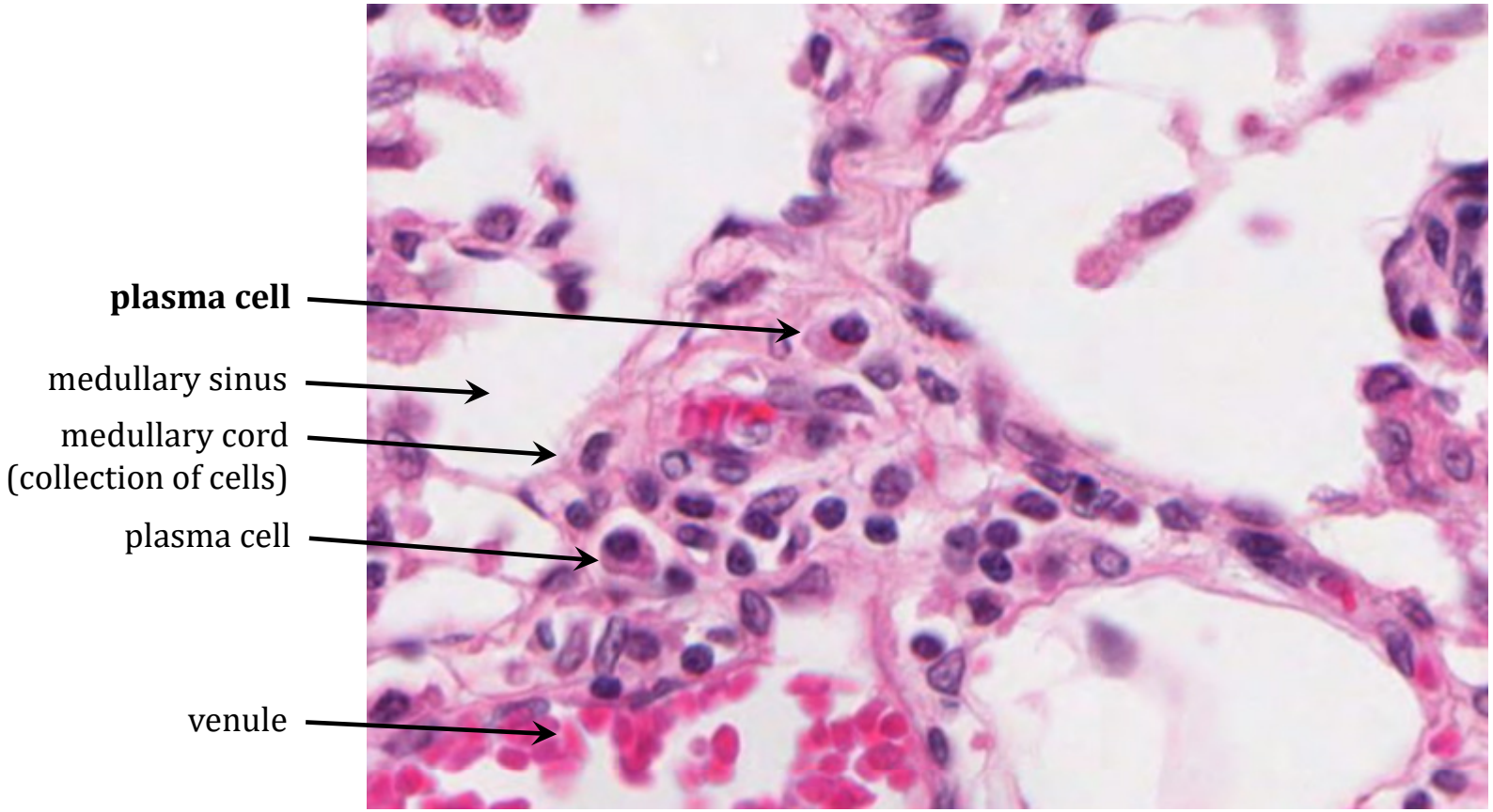
Slide 42: Lymph Node, H&E



plasma cells are activated B-cells that actively secrete antibodies (thousands per second); they generally have spherical nuclei (chromatin may have a "clock face" appearance) displaced to the periphery of the cell by the cytoplasm full of protein-producing machinery, including abundant rER and Golgi apparatus; the abundant rER (basophilic) and proteins (eosinophilic) within the cytoplasm result in an *amphophilic* (Gr. "both loving") staining pattern; plasma cells may reside in the medulla or exit the node to take up residences in other organs

Lab 14 – Lymphoid System

IUSM – 2016

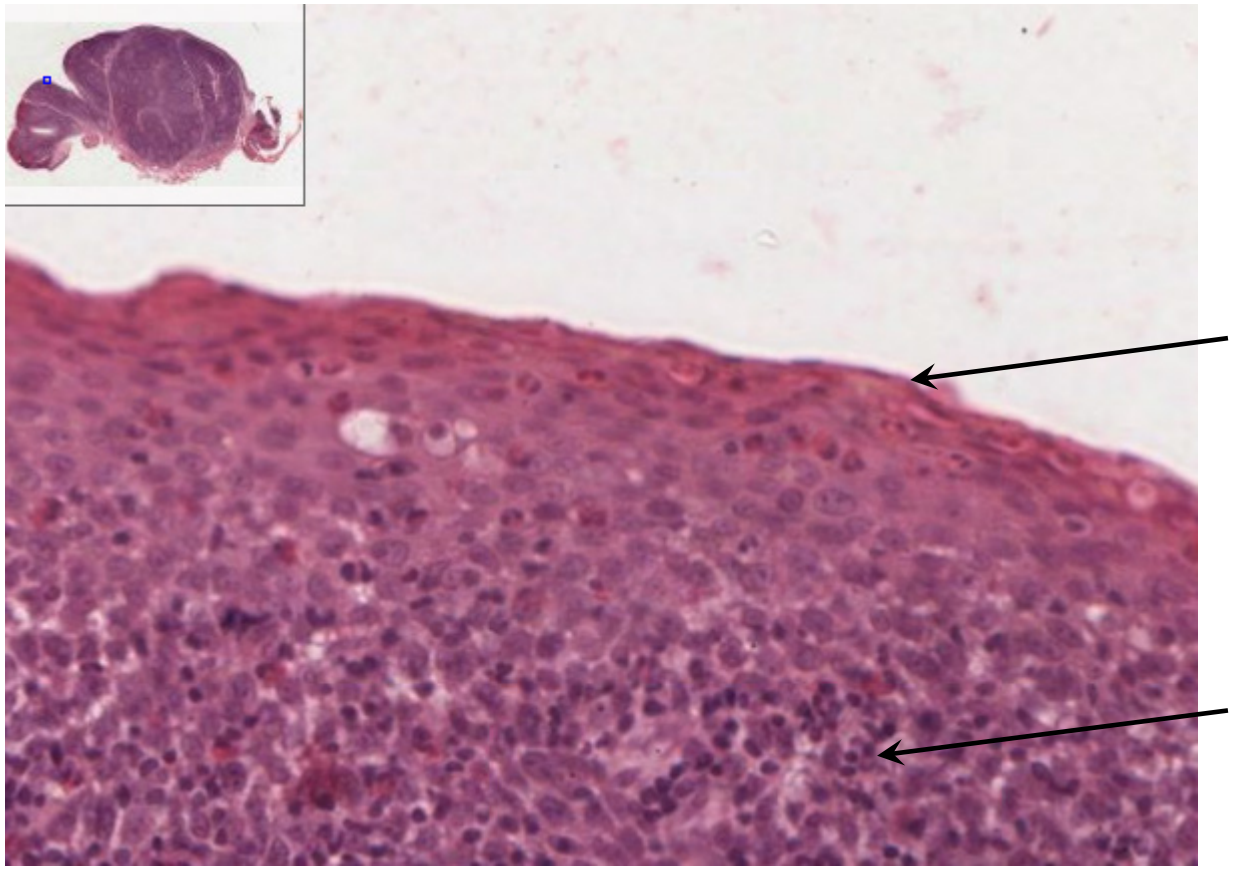
Slide 136: Palatine Tonsil, H&E

tonsils are located at the entrance of the pharynx; they are specialized **MALT** structures composed of aggregates of **lymphoid nodules** within the CT of the lamina propria, under the epithelium, of the mucosa; they lack afferent lymphatic vessels and the cortex/medulla architecture of lymph nodes, but they do have efferent lymphatic vessels and high endothelial venules; the **palatine tonsils** are a pair of tonsils in the wall of the oropharynx

Lab 14 – Lymphoid System

IUSM – 2016

Slide 136: Palatine Tonsil, H&E



some parts of the palatine tonsil have such extensive infiltration of lymphocytes into the mucosa that it is difficult to still appreciate the stratified squamous appearance of the overlying epithelium

lymphocytes

Lab 14 – Lymphoid System

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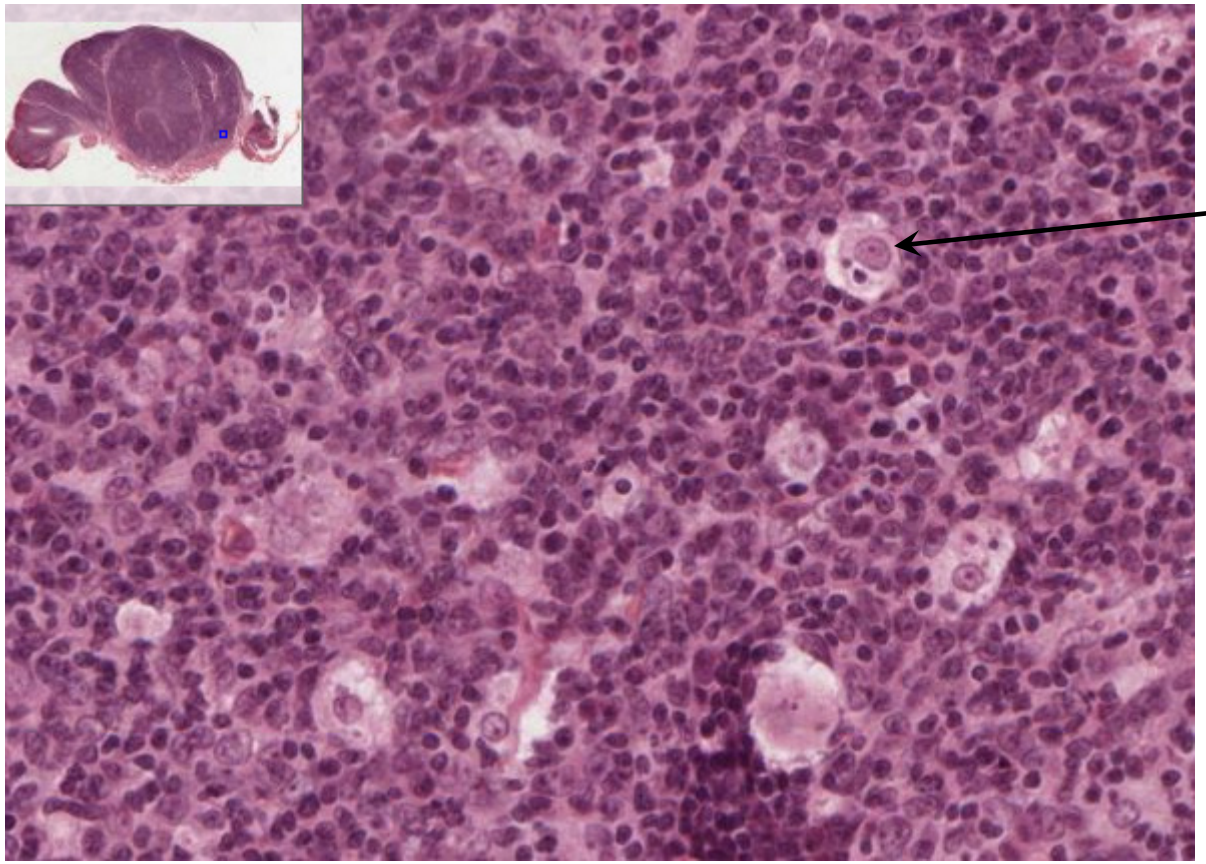
Slide 136: Palatine Tonsil, H&E



macrophages are common within the lymphoid nodules of tonsils; their presence amongst the darker-staining lymphocytes gives a "starry night" appearance to the nodule and can be helpful in distinguishing tonsils from other lymphoid structures

look within the germinal centers of the nodules to find examples of mitotic figures representing the proliferating lymphocytes

Lab 14 – Lymphoid System

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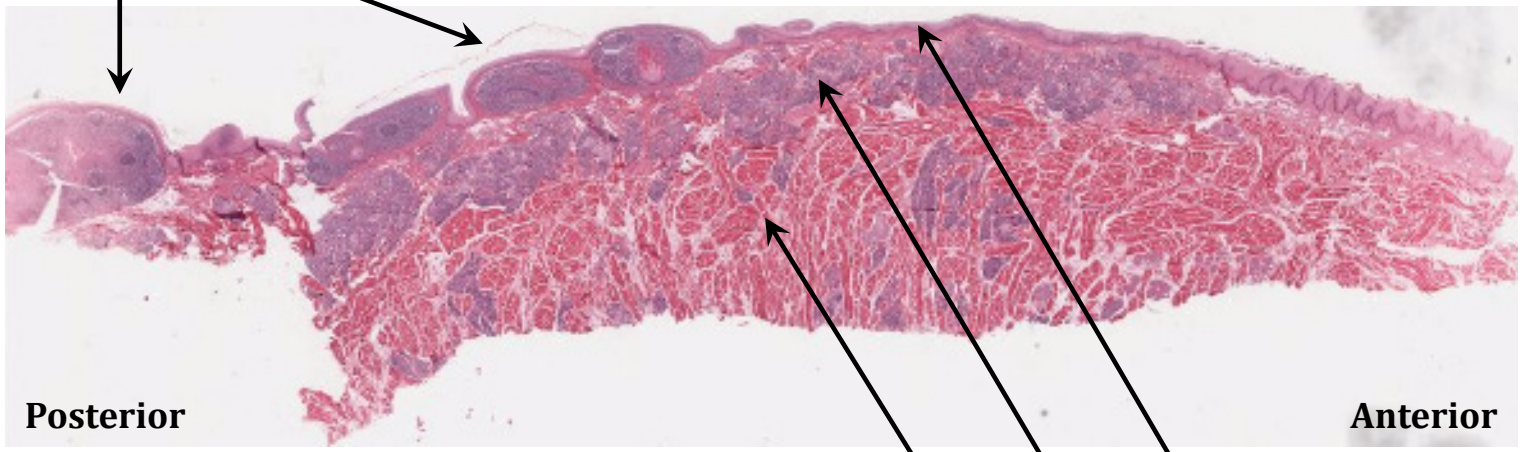
Slide 103 (NW): Lingual Tonsil, H&E

look along the posterior aspect of the dorsum of the tongue to find **lingual tonsils**

the posterior 1/3 of the tongue (pharyngeal aspect of the tongue) is separated from the anterior 2/3 of the tongue by the sulcus terminalis; the two parts of the tongue differ in embryologic origin and innervation; the lingual tonsils are found within the pharyngeal aspect



stratified squamous epithelium

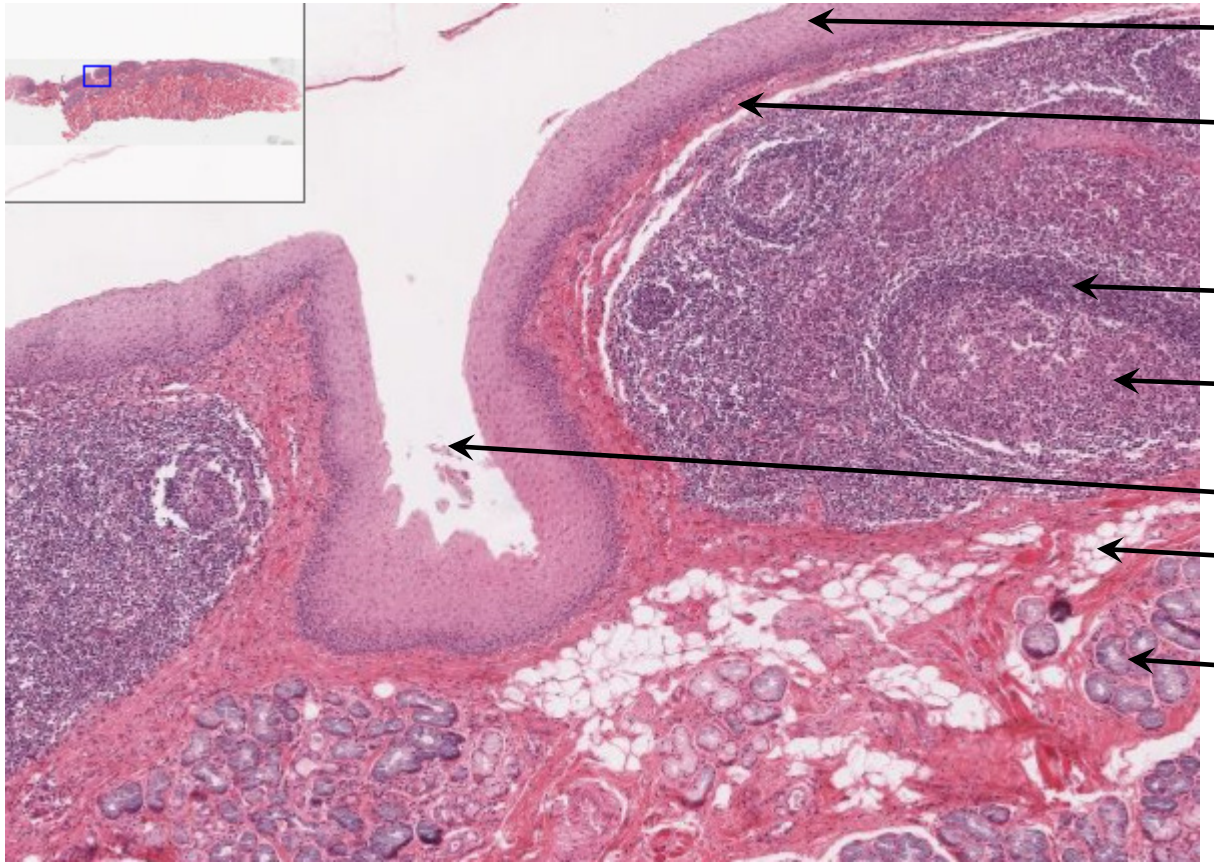
posterior lingual glands

skeletal muscle

Lab 14 – Lymphoid System

IUSM – 2016

Slide 103 (NW): Lingual Tonsil, H&E

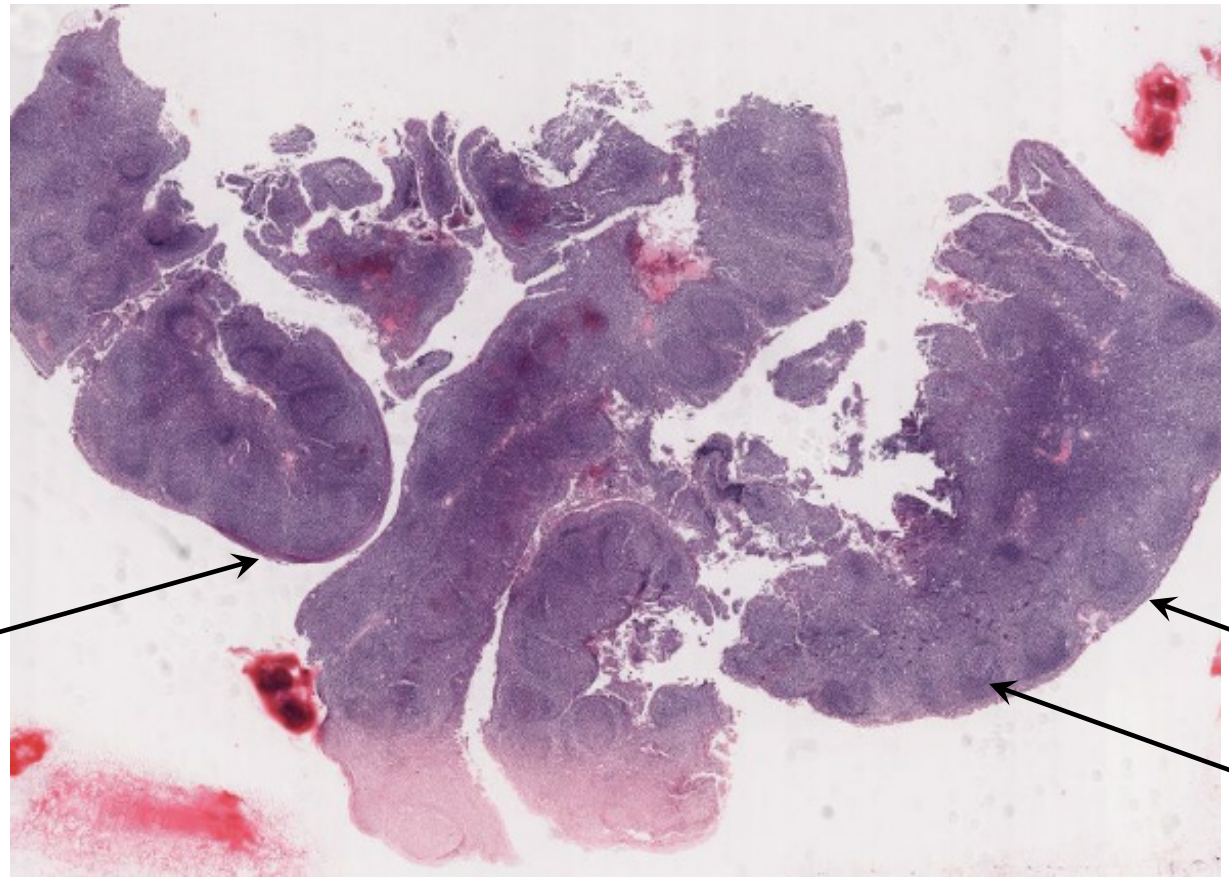


as in the lymph node, **lymphoid nodules** can be classified as either primary or secondary based upon exposure to antigen and lymphocyte activation; most nodules are secondary with an eosinophilic **germinal center** full of enlarged, proliferating B cells and plasma cells; surrounding the germinal center is the **mantle zone** of small, heterochromatic lymphocytes

Lab 14 – Lymphoid System

IUSM – 2016

Slide 102 (NW): Pharyngeal Tonsil, H&E



the **pharyngeal tonsil** (**adenoids** – Gr. "gland-like") is a single mass of lymphoid tissue in the posterior wall of the nasopharynx; unlike the palatine and lingual tonsils which are lined with stratified squamous epithelium, the pharyngeal tonsil is generally covered by respiratory epithelium (pseudostratified ciliated columnar epithelium); however, it is not uncommon to see regions of the tonsil covered with stratified squamous epithelium

Lab 14 – Lymphoid System

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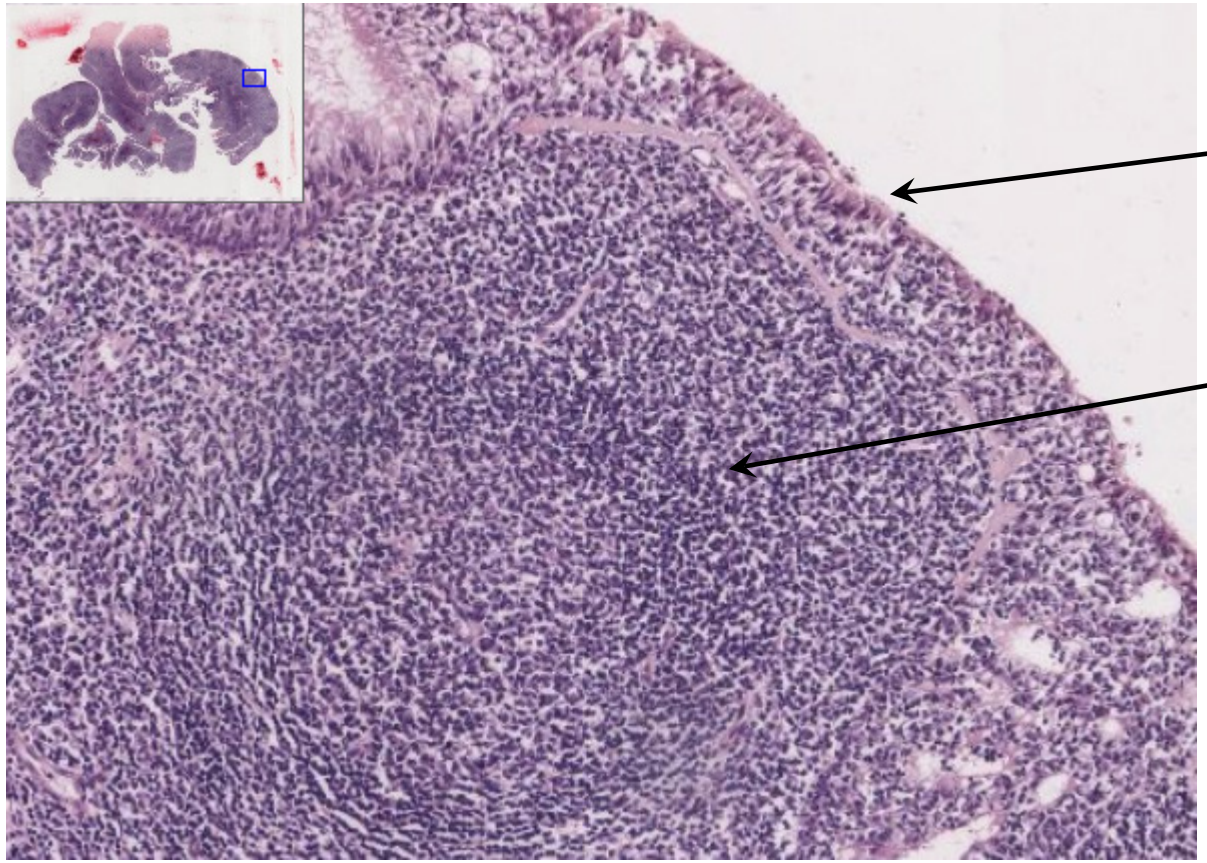
Slide 102 (NW): Pharyngeal Tonsil, H&E



respiratory epithelium (PCCE) distinguishes this as the pharyngeal tonsil

lymphoid nodule consisting of an outer **mantle zone** (basophilic) surrounding the inner **germinal center** (eosinophilic)

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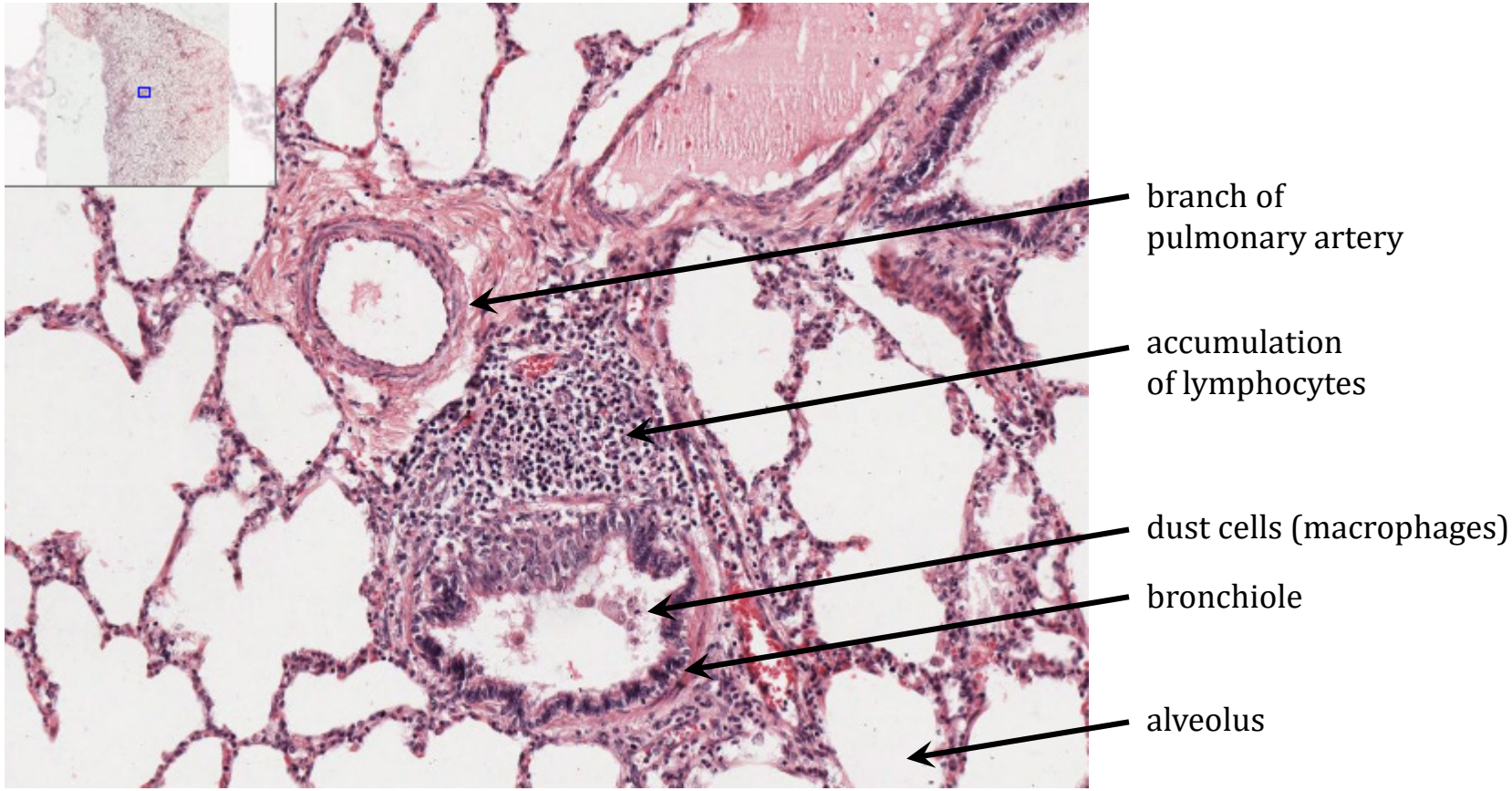
Slide 97: Lung, H&E



BALT (**bronchus-associated lymphoid tissue**) consists of the lymphoid tissue associated with the mucosa of the bronchi and bronchioles within the lungs

Lab 14 – Lymphoid System

IUSM – 2016

Slide 27: Ileum, H&E

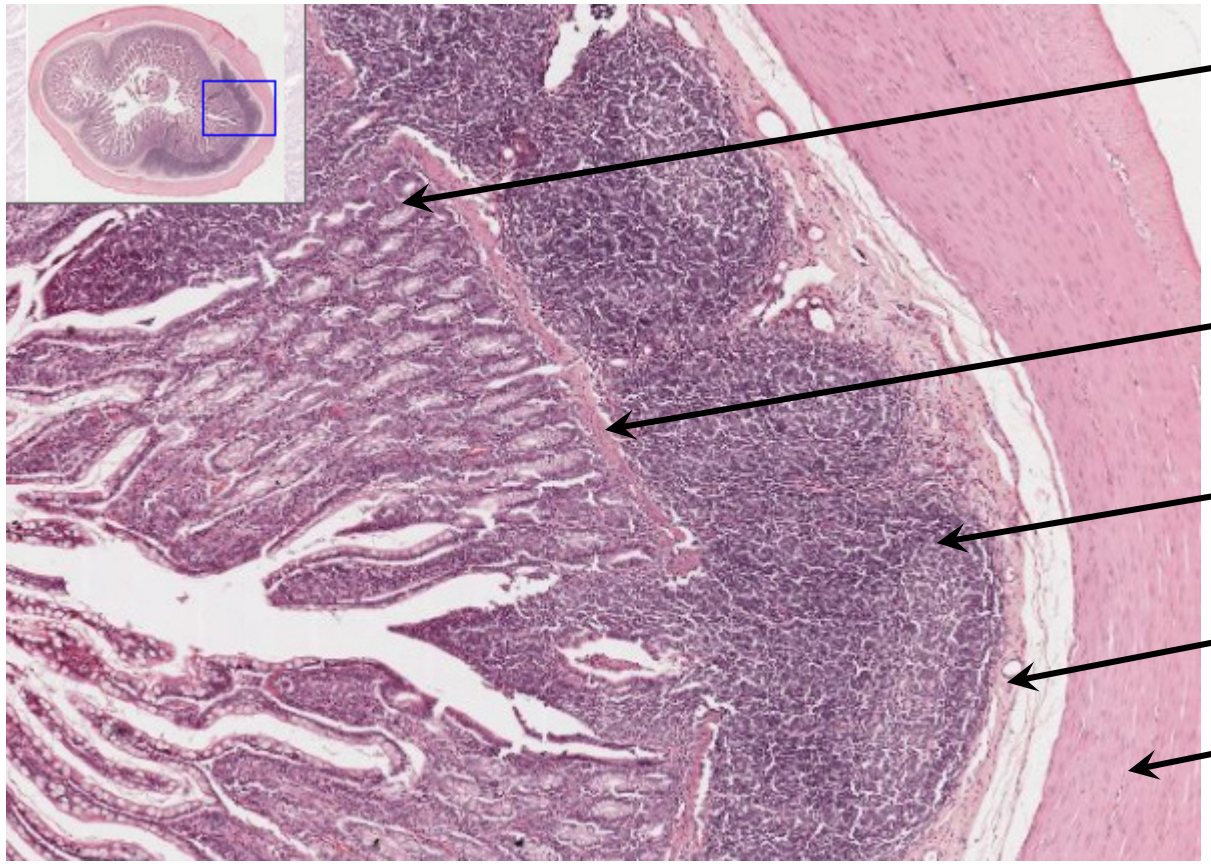
look within the wall of the ileum to see the collection of **lymphoid nodules** known as **Peyer's patches** (Pie-er)

GALT (**gut-associated lymphoid tissue**) is lymphoid tissue found within the mucosa of the wall of the alimentary canal (digestive tract); **lymphoid nodules** are most abundant as aggregates known as **Peyer's patches** in the ileum (most distal segment of the small intestine); in discussing the digestive tract, Peyer's patches will serve as a distinguishing characteristic in identifying the ileum

Lab 14 – Lymphoid System

IUSM – 2016

Slide 27: Ileum, H&E



as with all MALT, **Peyer's patches** lack afferent lymphatic vessel; instead, antigen gets to the nodules from the lumen of the intestine by being transferred across the apical surfaces of M-cells, which are unique cells in the epithelium lining the lumen directly above the Peyer's patches (M-cells are not generally seen in light microscopy)

Lab 14 – Lymphoid System

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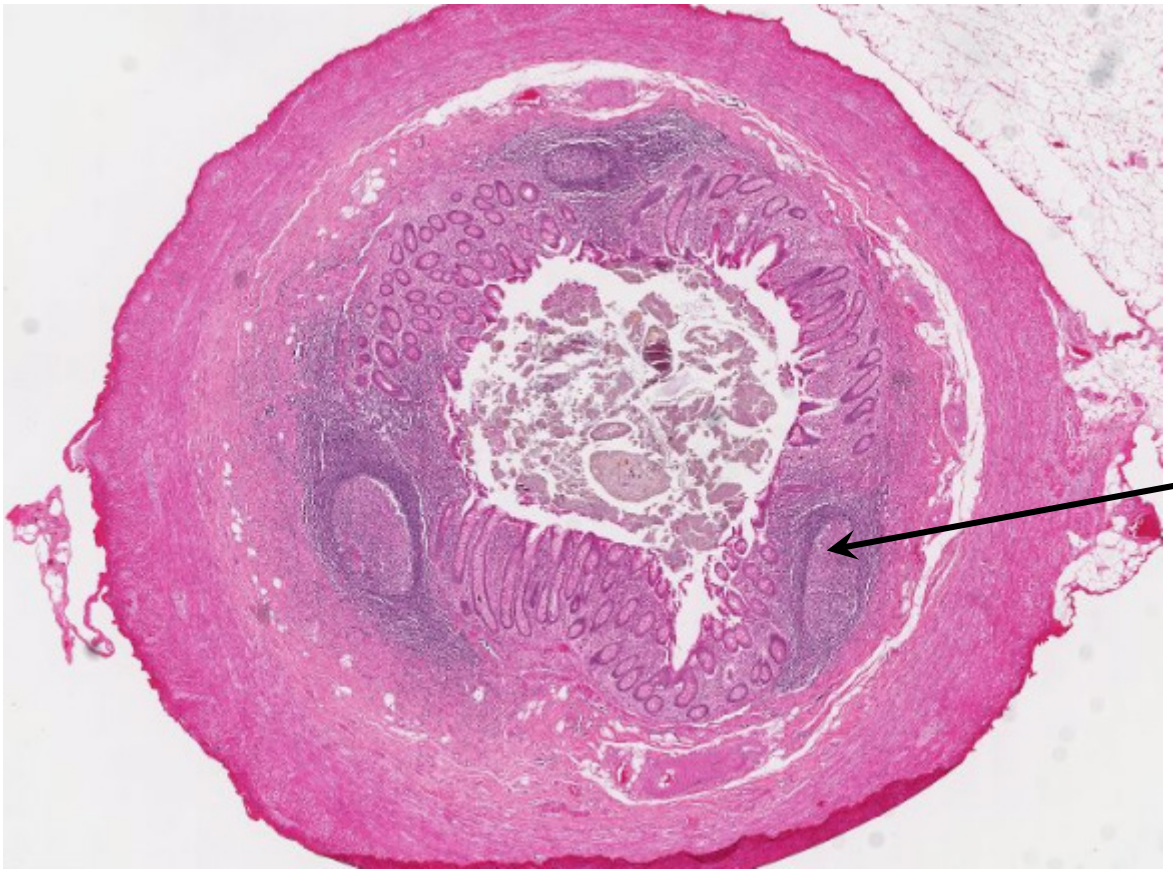
Slide 41: Appendix, H&E

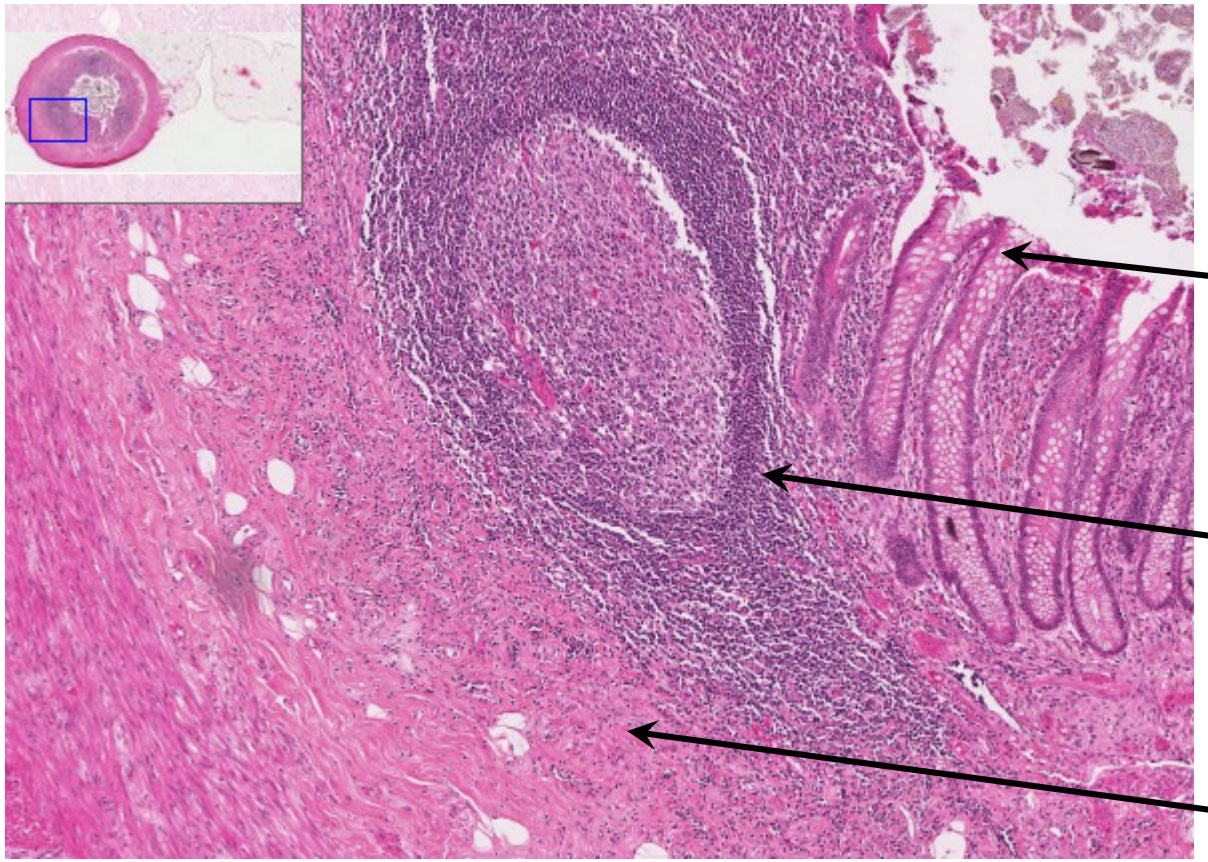


look within the mucosa and submucosa of the wall of the vermiform appendix to see the **lymphoid nodules**

Lab 14 – Lymphoid System

IUSM – 2016

Slide 41: Appendix, H&E



mucosa of simple columnar epithelium, with numerous goblet cells, and an underlying lamina propria of loose CT, with many infiltrated lymphocytes

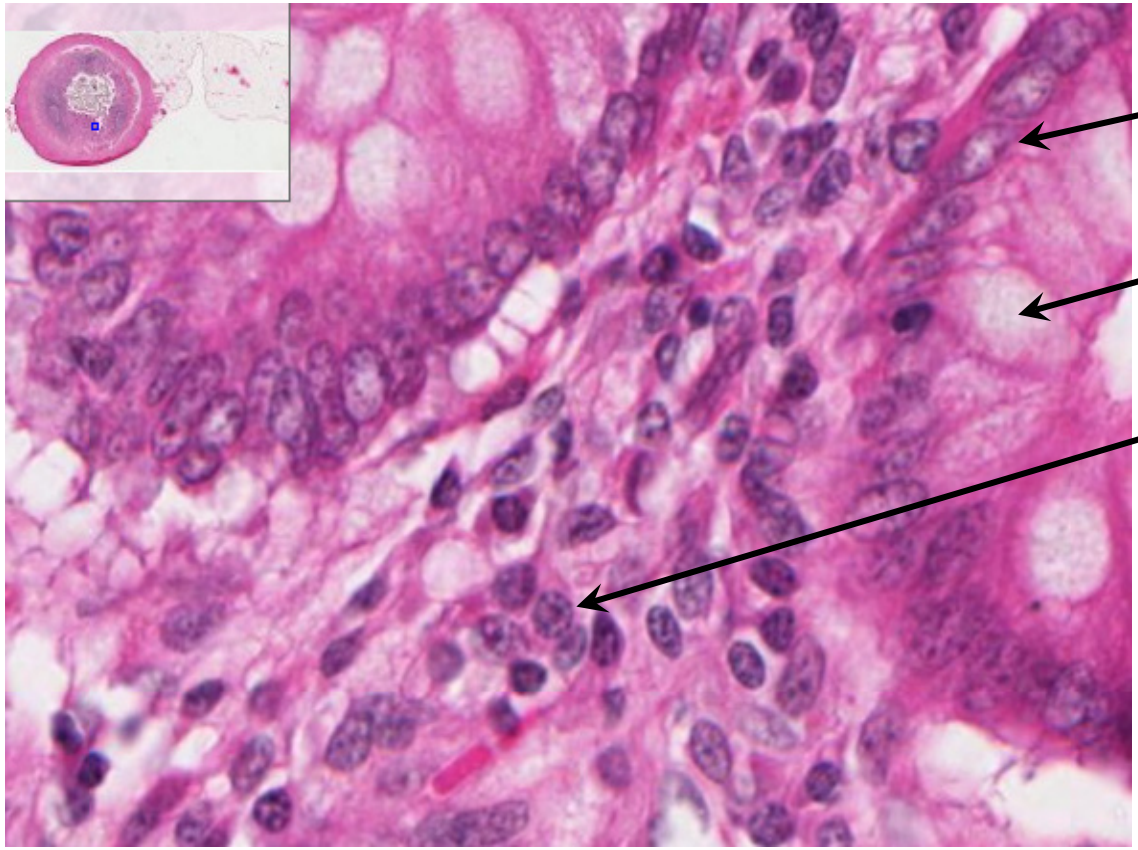
lymphoid nodule with outer **mantle zone** (basophilic) and inner **germinal center** (eosinophilic)

submucosa connective tissue

Lab 14 – Lymphoid System

IUSM – 2016

Slide 41: Appendix, H&E



nuclei of epithelial cells

goblet cell

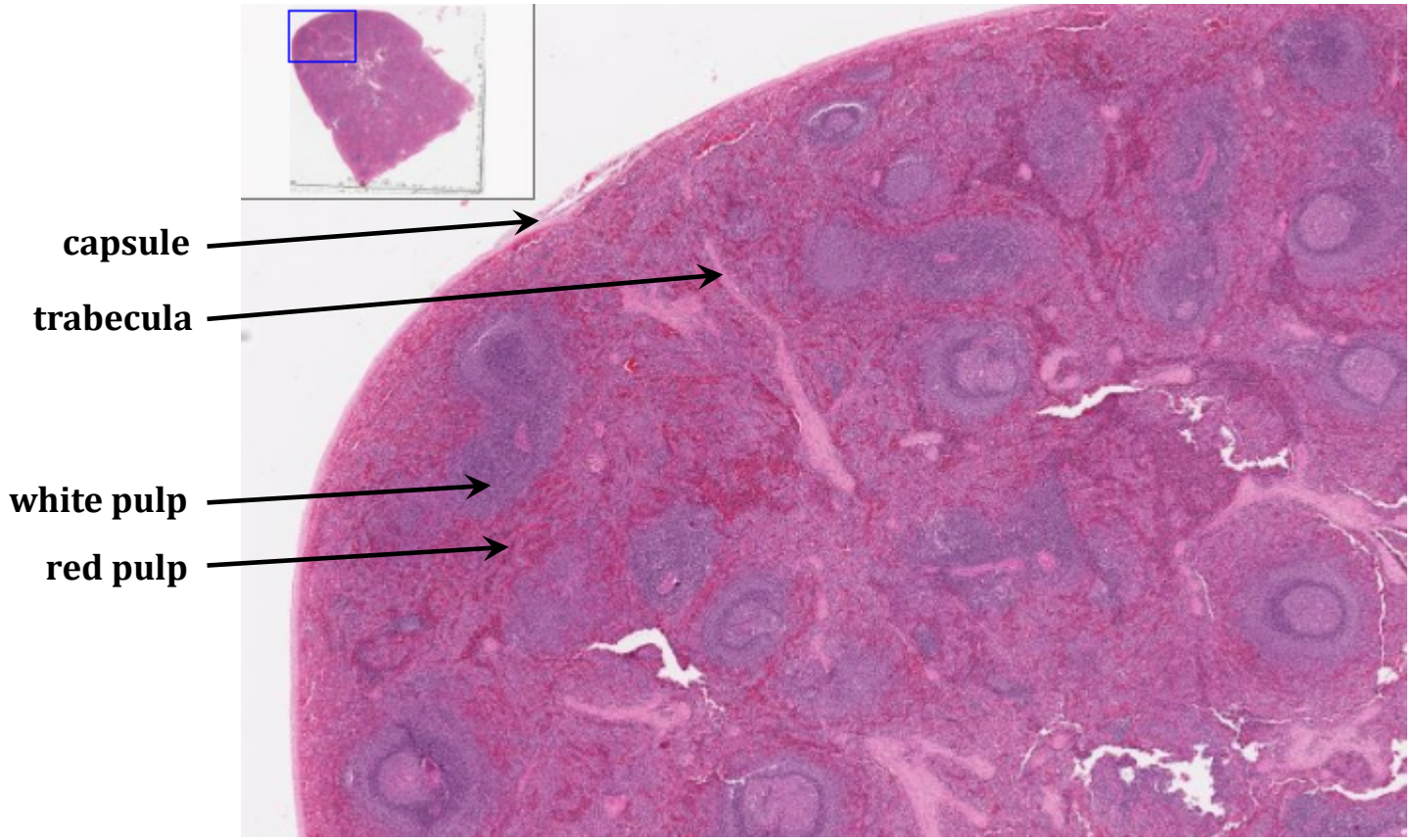
extensive populations of **plasma cells** may be found within the loose CT of the lamina propria; they have a round, eccentrically-located nucleus and amphophilic cytoplasm

the arrangement of heterochromatin along the periphery of the nucleus can produce the distinctive "clock face" appearance

Lab 14 – Lymphoid System

IUSM – 2016

Slide 68: Spleen, H&E

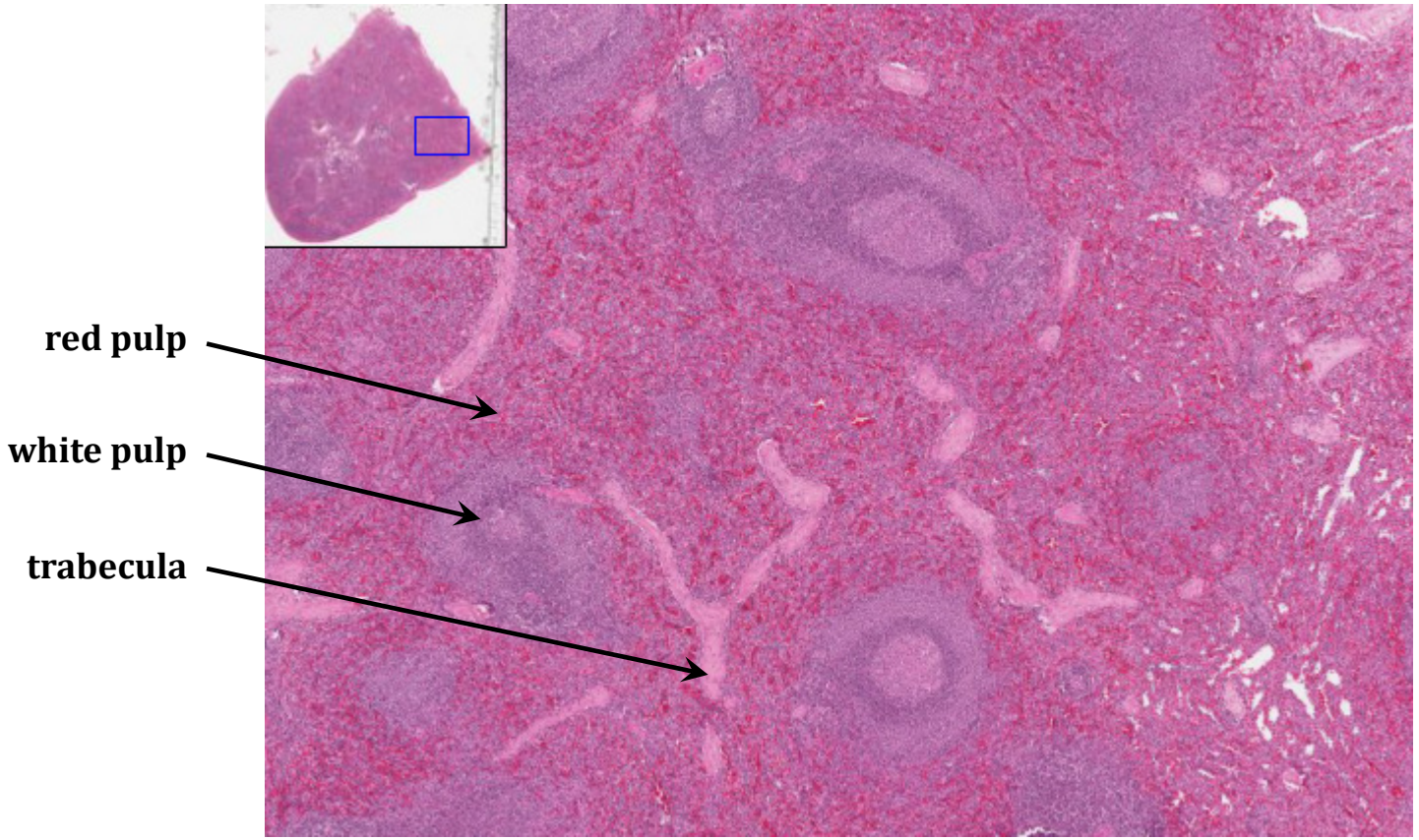


the **spleen** is the largest single accumulation of lymphoid tissue in the body and the main site of removal of old RBCs from the blood; it is surrounded by a **capsule** of dense CT with **trabeculae** penetrating into the parenchyma (trabeculae from the hilum contain neurovascular bundles); the parenchyma (**splenic pulp**) is divided into the **white pulp** (20% of the spleen), consisting of lymphoid tissue, and the **red pulp** (majority) where old RBCs are removed and destroyed

Lab 14 – Lymphoid System

IUSM – 2016

Slide 68: Spleen, H&E

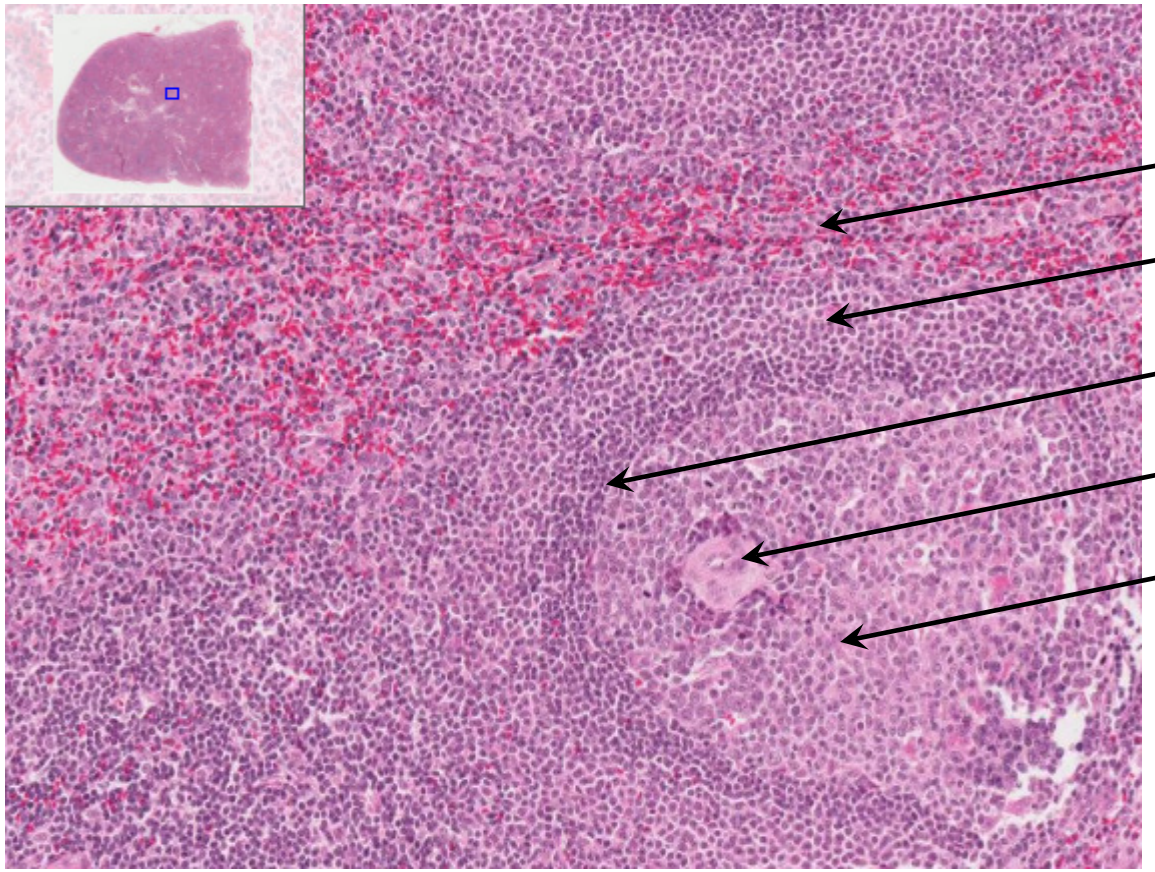


unlike the other immune organs, the spleen monitors the blood – not the lymph – for antigens; *central arterioles* branch from the *trabecular arteries* and carry blood into the splenic pulp: first the blood passes through the **white pulp** where the vessels are encased by lymphoid cells (PALS) which can respond to antigens in the blood; from the white pulp, blood continues into the **red pulp** where old RBCs are filtered out before the blood exits the spleen

Lab 14 – Lymphoid System

IUSM – 2016

Slide 68: Spleen, H&E



the **white pulp** consists primarily of heterochromatic lymphocytes, so appears basophilic; **central arteriole** blood vessels, from the trabecular arteries, are encased in concentric aggregates of lymphocytes collectively referred to as the **periarterial lymphatic sheath** (**PALS**) (the central arteriole distinguishes the PALS from a regular lymphoid nodule); however, upon antigen presentations, the lymphocytes can expand into lymphoid nodules, eccentrically displacing the central arteriole

Lab 14 – Lymphoid System

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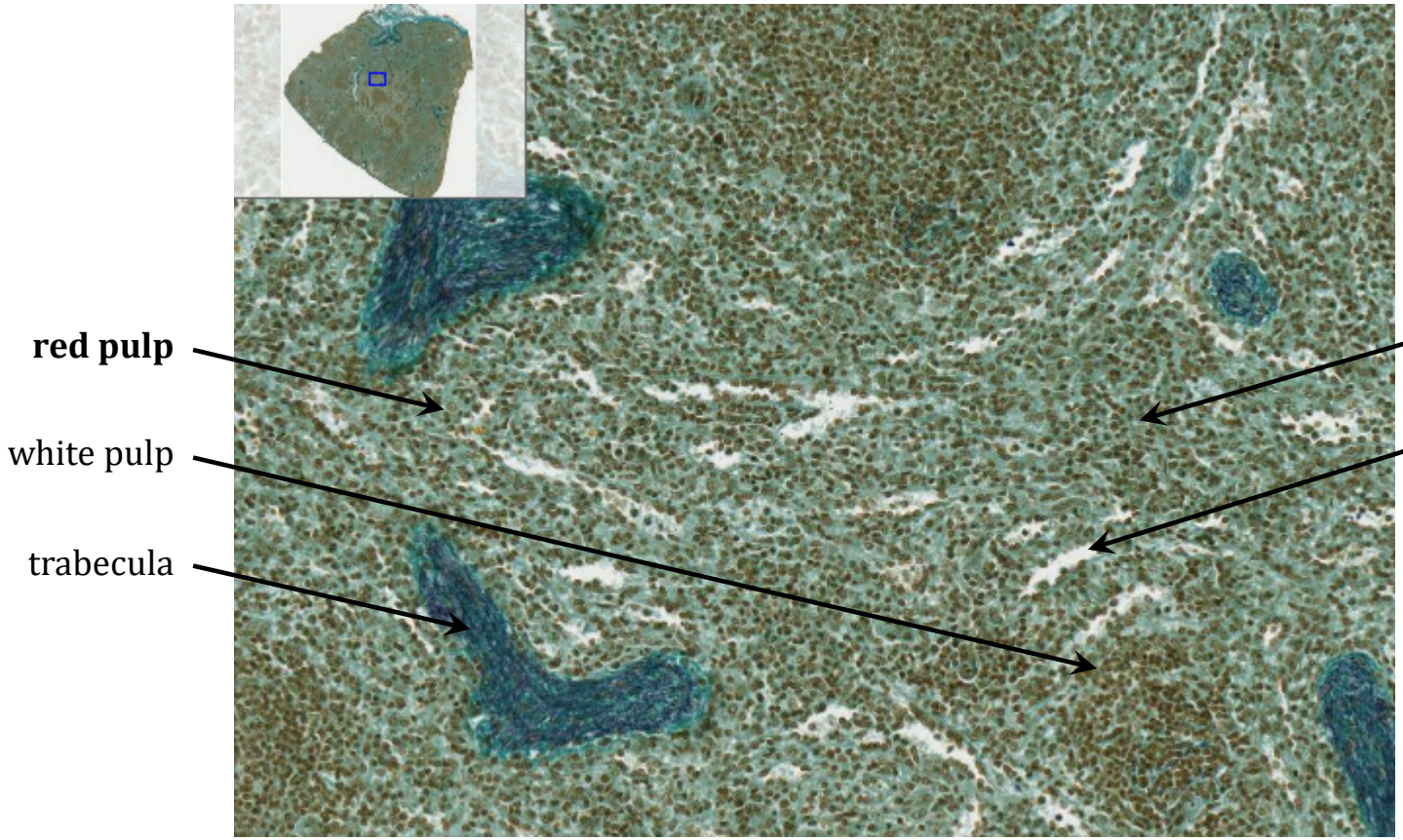
Slide 73: Spleen, Kornhauser's Quad



the **red pulp** composes the majority of the splenic parenchyma; it consists of **splenic cords** with reticular CT and large aggregates of cells and **splenic sinuses** (or sinusoids) lined by specialized epithelial stave cells; in the red pulp, blood exits the endothelium-lined vasculature and travels through the connective tissue cords before re-entering the vasculature

Lab 14 – Lymphoid System

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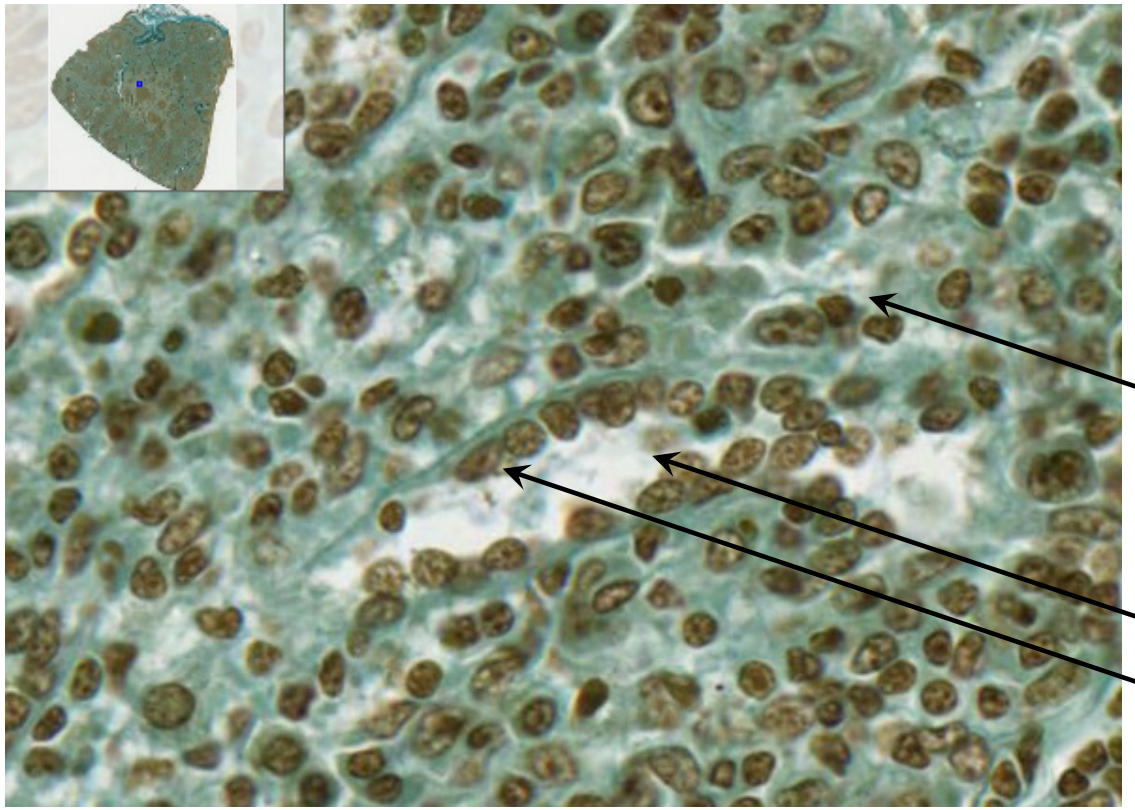

in the **red pulp**, blood can pass through two routes: in **closed circulation**, the blood goes directly into the splenic sinuses and then into veins and exits the spleen; in **open circulation** (maybe the only pathway in humans), the blood leaves the vasculature and enters into the **splenic cords**; from the cords, the plasma and formed elements must pass between the stave cells (elongated epithelial cells) to enter into the splenic sinuses in order to exit the spleen; old or damaged RBCs are incapable of passing between the stave cells and are removed by macrophages; in the absence of the spleen, sinusoids in the liver and bone marrow can serve the role of removing defective RBCs

Lab 14 – Lymphoid System

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  A. Thymus
    1. General Structure
    2. Cortex
    3. Medulla
  B. Lymph Nodes
    1. General Structures
    2. Cortex
    3. Paracortex
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    1. Tonsils
    2. BALT
    3. GALT
      a. Peyer's patches
      b. Vermiform appendix
  D. Spleen
    1. General Structure
    2. White Pulp
    3. Red Pulp
V. **Summary**

Characteristics of Major Lymphoid Structures

	Thymus	**Lymph Node**	**Tonsil**	**GALT**	**Spleen**
Major function:					
Location:					
CT capsule?					
Cortex?					
Medulla?					
Lymphoid follicles?					
Afferent lymphatic vessels?					
Efferent lymphatic vessels?					
HEVs?					
Characteristic features:					