

LYMPHATIC SYSTEM

What is the lymphatic system composed of?

Primary structures – development of cells of the immune system

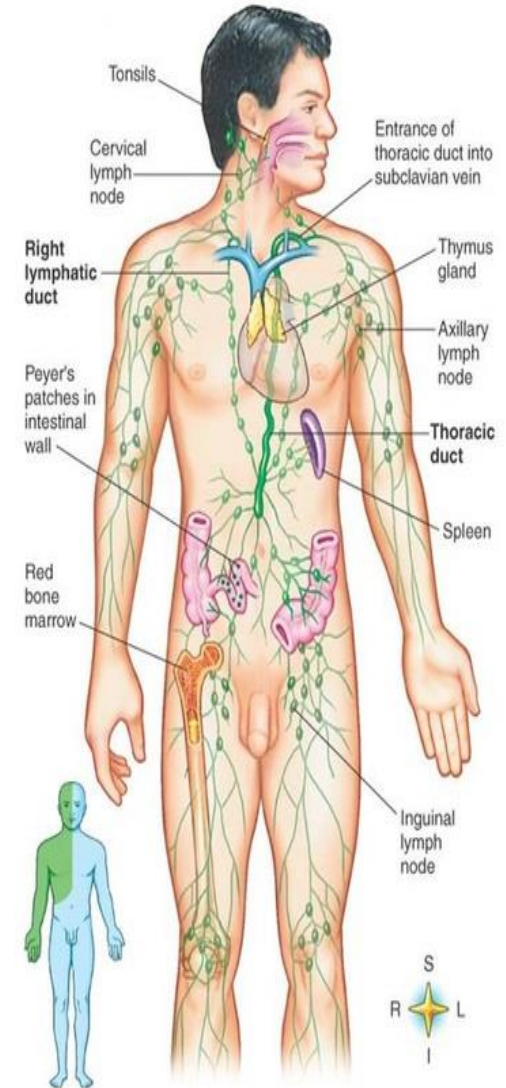
- Bone marrow
- Thymus

Secondary structures – effector functions of the lymphatic functions

- Diffuse lymphatic tissue (MALT, mucosa-associated lymphatic tissue)
- Lymphatic nodules
- Lymph nodes (ca. 400 - 500 in adults)
- Tonsils
- Spleen
- Lymphatic vessels and lymph

Cells – involved in immune response

- Lymphocytes (NK cells, helper T cells, cytotoxic T cells, regulatory T cells, B cells)
- Antigen-presenting cells (incl. dendritic cells, macrophages)
- Neutrophils, basophils, eosinophils



What is the role of the lymphatic system?

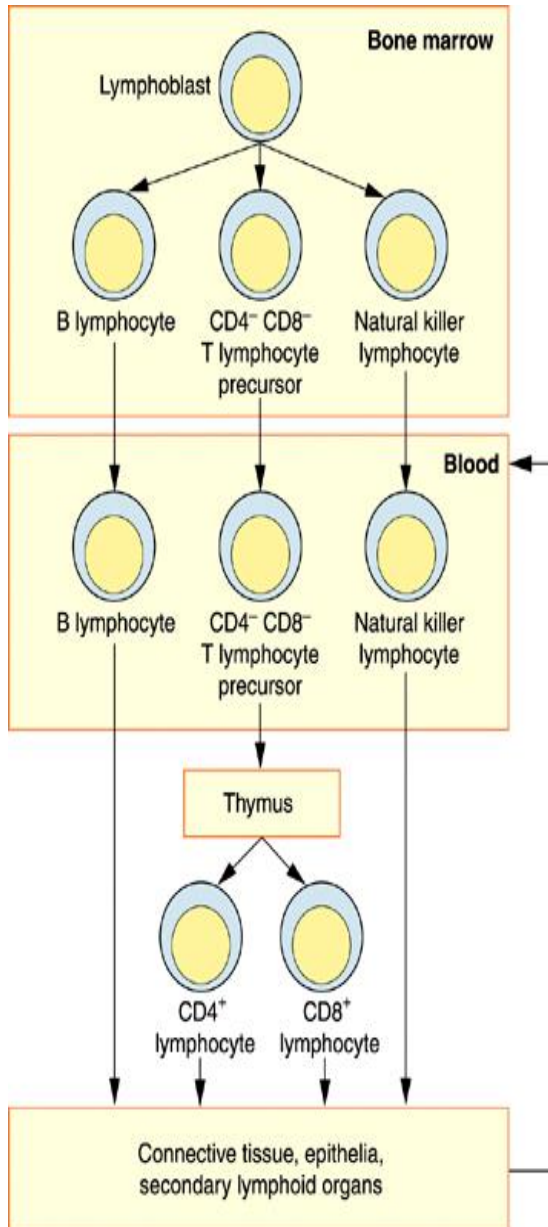
1. Removal of excessive amounts of fluid from body tissues.
2. Absorption of fatty acids and subsequent transport of fat (chyle) to blood vessels.
3. Development of white blood cells.
4. Involvement in immune responses.

Receptors of **innate immunity** recognize **pathogen-associated molecular patterns** (PAMPs) via **pattern-recognition receptors** (PRRs) such as Toll-like receptors (TLRs), mannose receptors and other.

Receptors of **adaptive immunity** (**TCRs** – T cell receptors; **BCRs** – B cell receptors; **MHC class I / II** molecules; **immunoglobulins**) recognize specific **antigens** (i.e. molecules with the ability to induce immune response).

Innate immune response	Adaptive immune response
Nonspecific, directed against any foreign cells.	Specific, directed against cells expressing particular antigens (e.g. specific tumour cells or cells infected with certain strains of viruses).
Faster but less efficient.	Slower but more efficient and precise. Allows for formation of memory cells.
Based on physical barriers (e.g. skin, mucous membranes), chemical barriers (e.g. low pH), antimicrobial substances (e.g. lysozyme).	Humoral response (mediated by antibodies) and cellular response (mediated by cytotoxic T cells)
NK cells, granulocytes, macrophages.	T cells, B cells, antigen-presenting cells (dendritic cells, macrophages and others).

Origin of lymphocytes



Lymphocytes differentiate from lymphoblast precursor cells (lymphoid stem cells) present in the bone marrow. Lymphoblasts are derived from pluripotent hematopoietic stem cells.

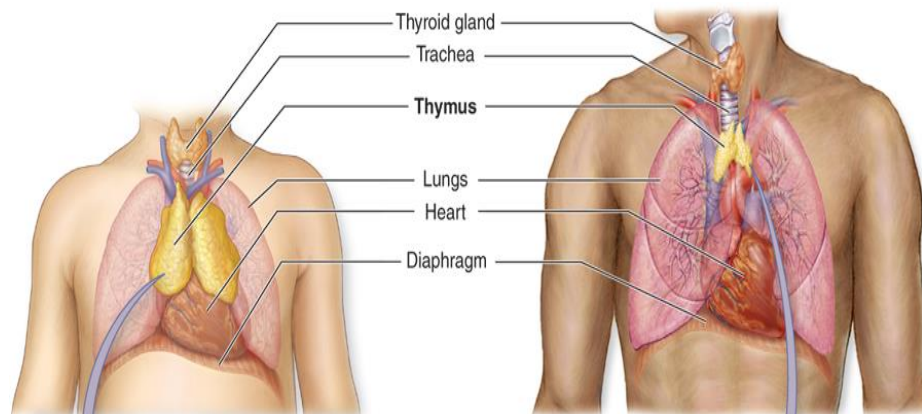
B cells differentiate in bone marrow microenvironment into mature B cells. Their name is derived from „bursa of Fabricius” (lymphatic tissue in birds, responsible for development of lymphocytes).

T cells develop in the bone marrow but later they travel with blood to the thymus where they undergo selection and differentiation.

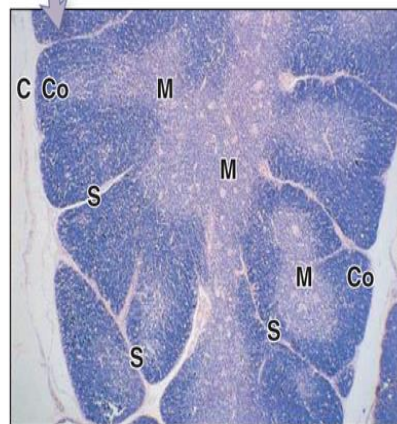
Hence, „T” in their name refers to „thymus”.

Thymus

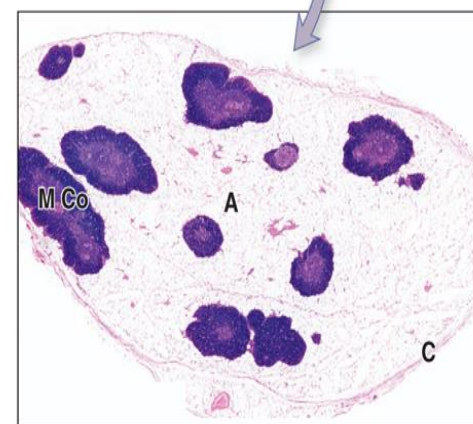
- A **bilobed organ** located in **the mediastenum**.
- Surrounded with a connective tissue capsule that forms trabaculae extending into the parenchyma dividing the thymus into **thymic lobules**.
- Crucial role in **development and differentiation of T cells**.
- Most active between late stages of gestation and early puberty.
- **With the onset of puberty, the organ undergoes atrophy (involution)**, shrinking in size and being replaced by connective tissue. The atrophy is induced by increasing level of sex hormones.



(a) Child (left) and adult (right) thorax, anterior view



(b) Micrograph of child's thymus

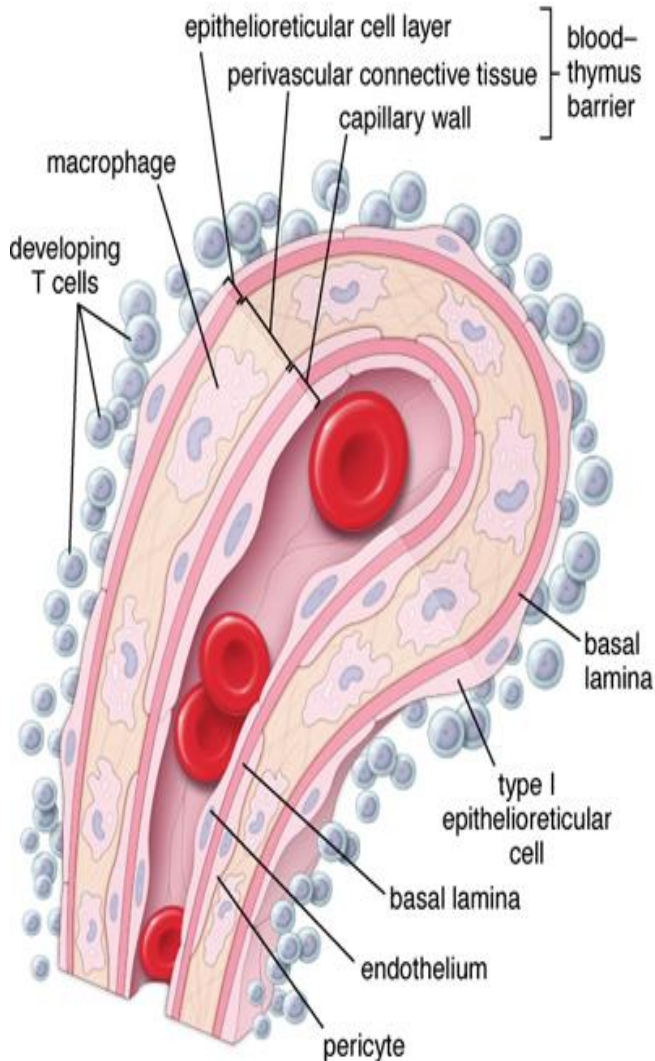


(c) Micrograph of adult's thymus

Source: Anthony L. Mescher: Junqueira's Basic Histology: Text and Atlas, 15th Edition. Copyright © McGraw-Hill Education. All rights reserved.

Thymus-dependent areas – areas of different organs occupied by T cells, e.g. paracortex in lymph nodes or PALS in the spleen.

Blood-thymus barrier

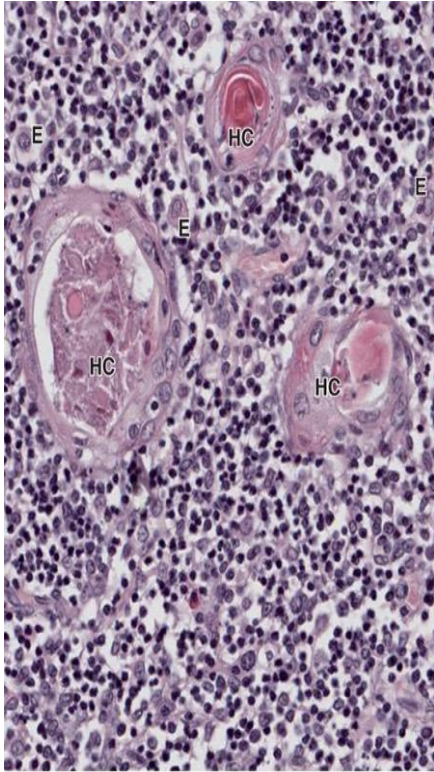


Blood-thymus barrier protects developing thymocytes from exposure to antigens and immunocompetent T cells.

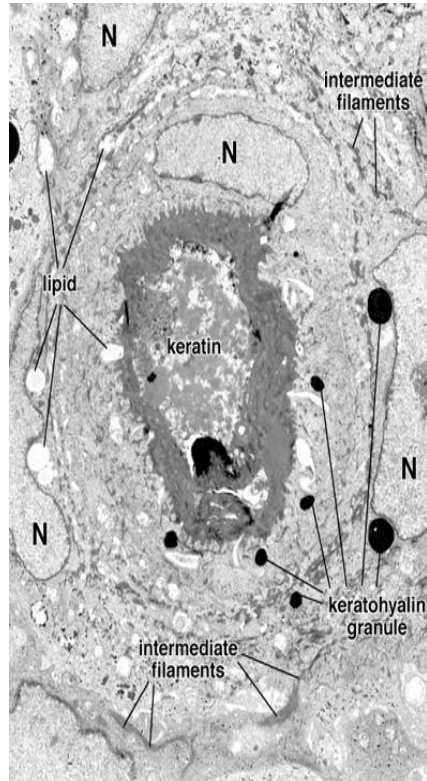
It is composed of 3 main elements:

- 1) Capillary endothelium with cells connected by tight junctions, and its basal lamina.
- 2) Perivascular connective tissue with macrophages that phagocytose antigens escaping from blood vessels.
- 3) Thymic epithelial cells and their basal lamina.

Hassall's corpuscles



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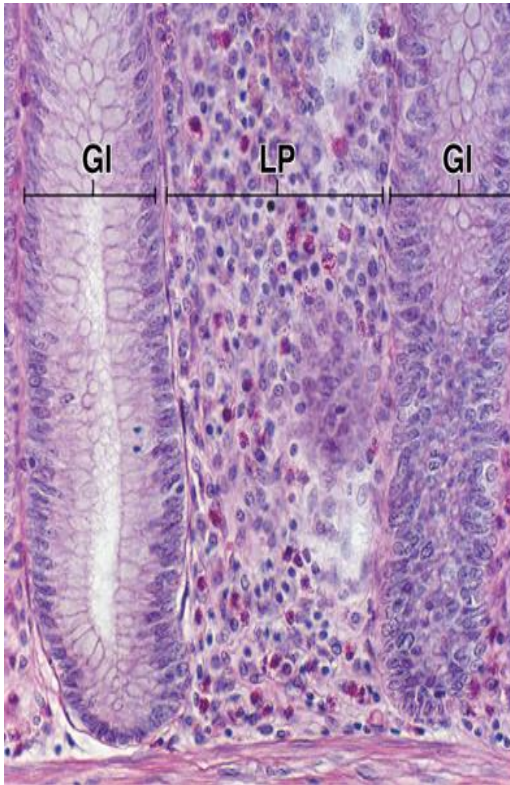
Hassall's corpuscles (up to 100 μm in diameter) are derived from thymic epithelial cells (TECs) and their number **increases with age**.

They **produce interleukins (including IL-4 and IL-7) and cytokines (including TSLP) that are involved in regulation of the development and differentiation of thymocytes**.

Hassall's corpuscles contain keratohyalin granules, lipid droplets and bundles of intermediate filaments. Their centres may be keratinized.

Cells that form Hassall's corpuscles are bound by desmosomes.

Diffuse lymphatic tissue



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Accumulations of lymphatic tissue (mostly B cells but also T cells, eosinophils and antigen-presenting cells) not enclosed by connective tissue and present in the mucosa of the alimentary canal, respiratory tract and genitourinary tract.

MALT (Mucosa-Associated Lymphatic Tissue):

GALT (Gut-Associated Lymphatic Tissue) +

BALT (Bronchi-Associated Lymphatic Tissue)

Cells present in MALT respond to antigens and initiate immune response.

Excessive amounts of diffuse lymphatic tissue (lymphocyte infiltration) in mucosa indicates an inflammatory process.

Lymphatic nodules (lymphatic follicles)

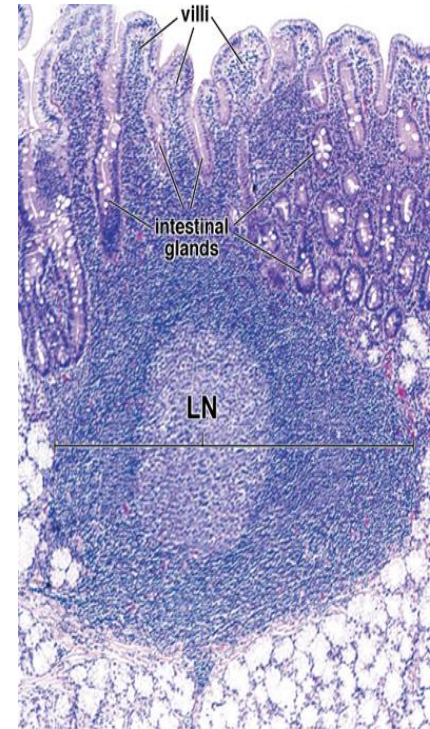
Primary nodules (not stimulated by antigens).

Secondary nodules (activated; after contact with antigens):

- **Germinal centre** – contains proliferating lymphoblasts and plasmablasts (B cells undergoing activation) and follicular dendritic cells (FDCs). The presence of a germinal centre is a morphologic indication of a response to an antigen.
- **Corona (mantle zone)** – outer ring of smaller B cells and plasma cells.

No connective tissue capsule.

Lymphatic nodules are present in the mucosa of many organs and in tonsils, lymph nodes, and the spleen.



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Lymph node

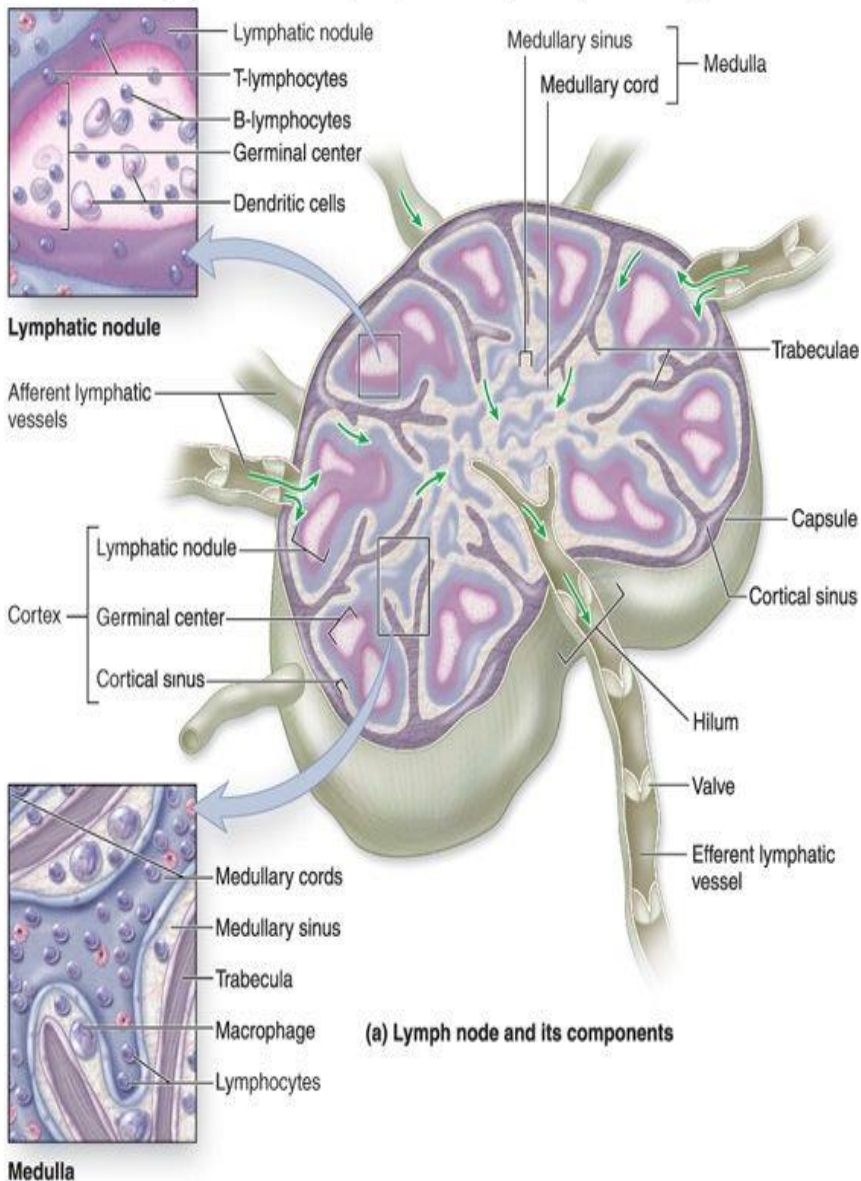
Each lymph node drains lymph from a particular region of the body. T and B cells present in lymph nodes respond to antigens delivered with lymph. Lymph nodes also house memory cells.

Cortex:

- Superficial (nodular) cortex – contains lymphatic nodules.
- Paracortex – contains most of T cells present in the lymph node.

Medulla – (medullary) cords of lymphatic tissue (mostly B cells, plasma cells, macrophages and dendritic cells) separated by medullary sinuses.

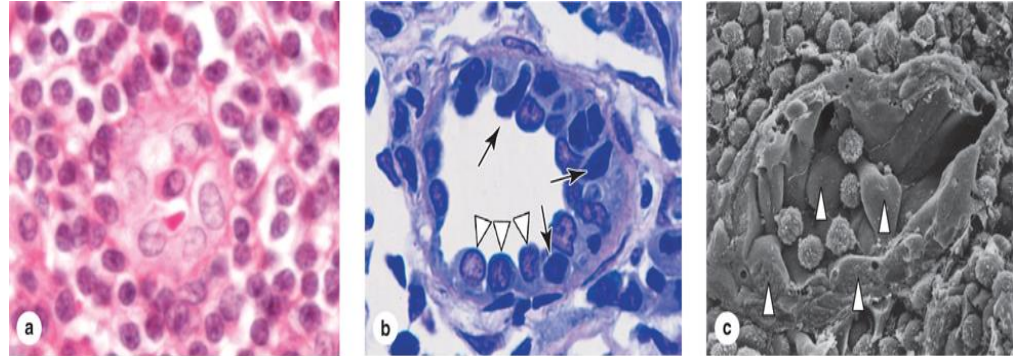
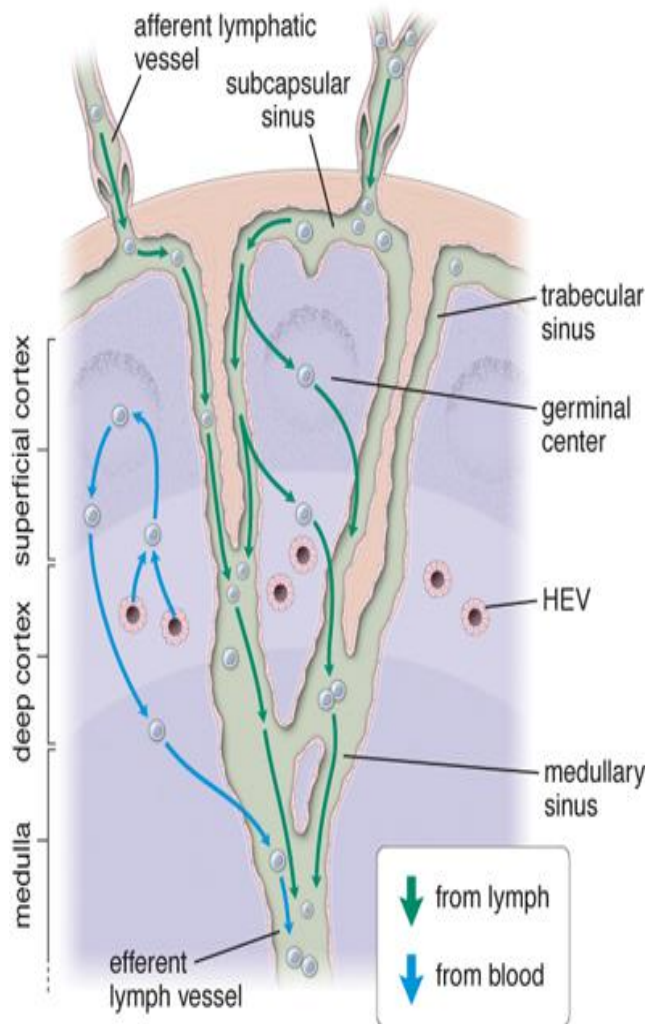
Stroma of lymph nodes is composed of reticular cells (fibroblast-like cells) and reticular fibres (type III collagen).



Flow of the lymph direction:

afferent vessels → subcapsular sinuses → trabecular sinuses → medullary sinuses → efferent vessels

Lymphocyte circulation within a lymph node

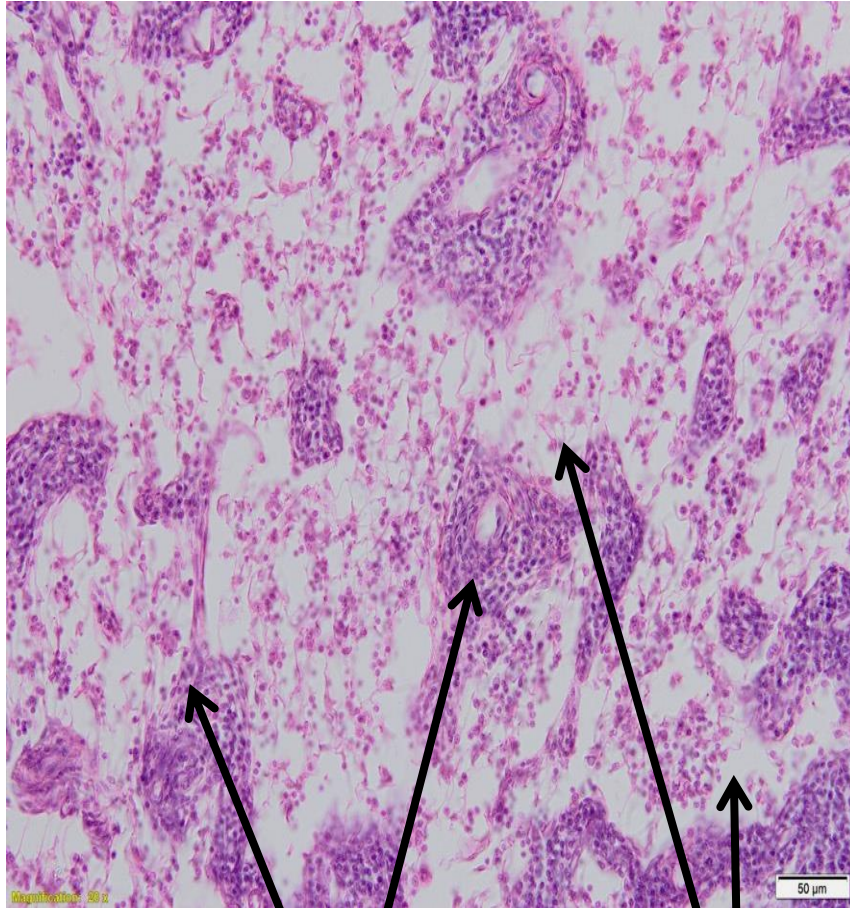


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High endothelial venules (HEVs) – present in the paracortex (deep cortex); allow for migration of lymphocytes from blood into lymph nodes. However, ca. 10% of lymphocytes enter lymph nodes via afferent lymphatic vessels.

Cells of HEVs contain large amounts of **aquaporin-1** molecules. Rapid resorption of the interstitial fluid via water channels into bloodstream causes lymph entering via afferent vessels to be drawn into the paracortex by solvent drag.

Lymph node medulla



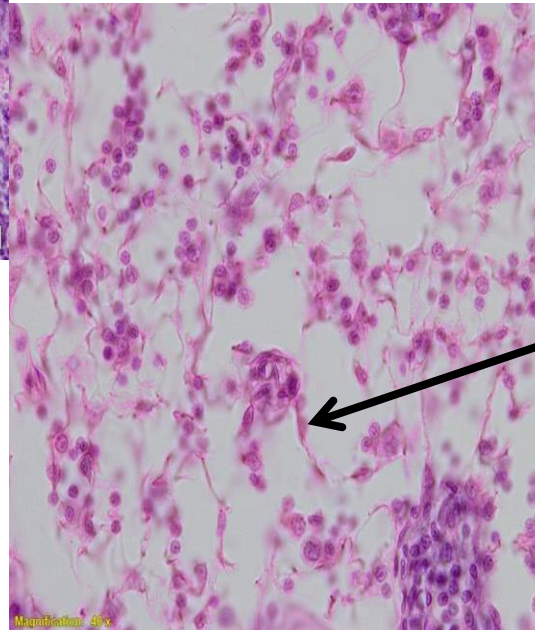
Stevens & Lowe's Human Histology
2002

MEDULLARY
CORDS

MEDULLARY
SINUS

Lymphatic sinuses are NOT open spaces WITHOUT BORDERS. Particularly in the medulla, macrophages' processes, along with the reticular fibers surrounded by reticular cell processes, span the lumen of the sinus and form a crisscrossing meshwork that retards the free flow of lymph and enhances its filtration.

Antigenic material and transformed cells of metastatic cancer are **trapped by this mechanical filter** and then phagocytosed by macrophages.



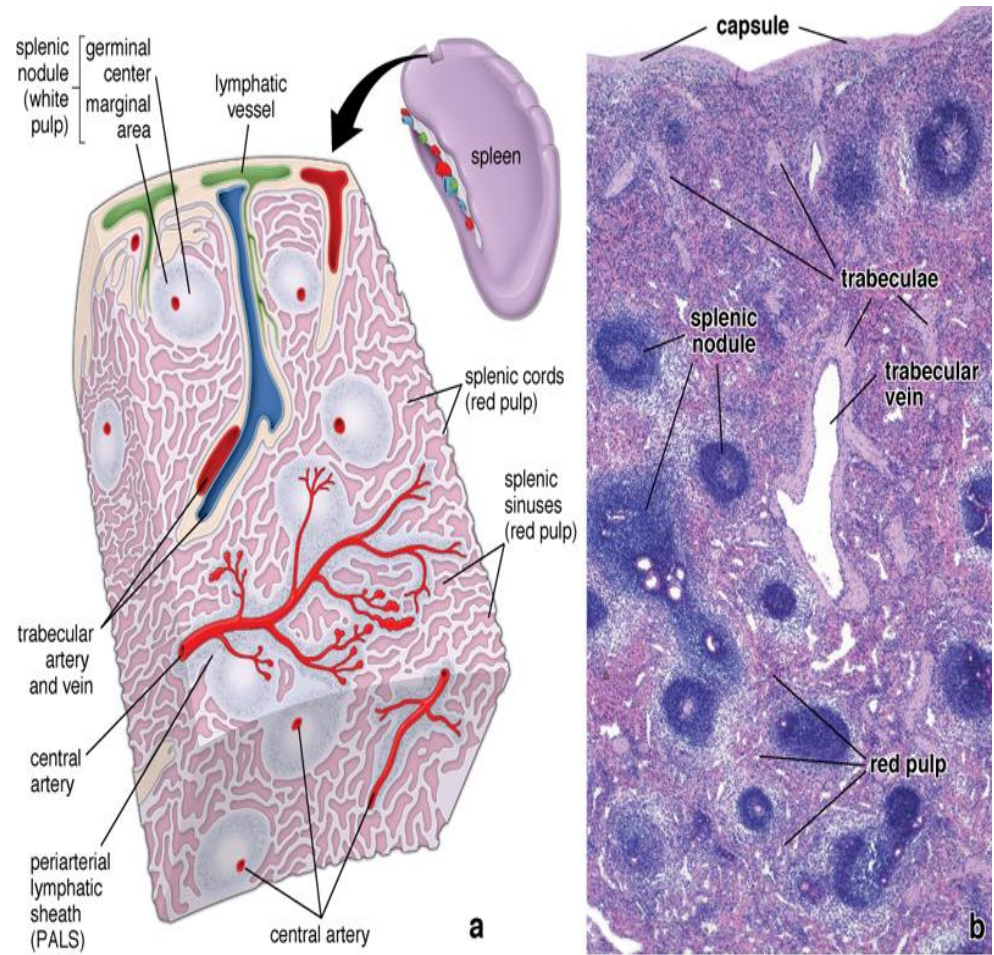
RETICULAR
CELLS

Stevens & Lowe's Human Histology
2002

Spleen

The spleen is enclosed by a dense connective tissue **capsule** from which **trabeculae** extend into the parenchyma of the organ.

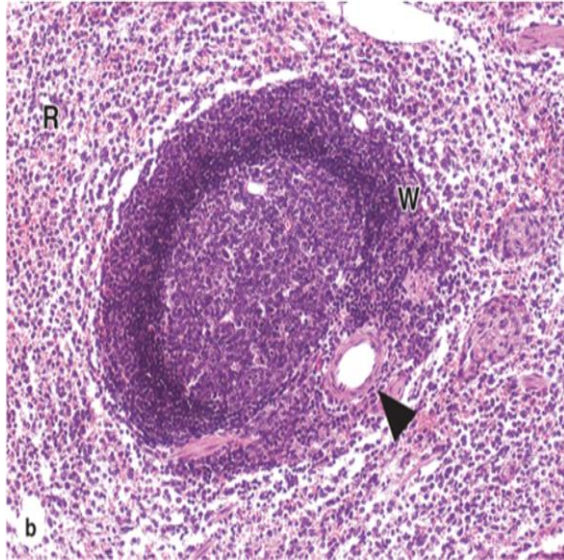
The connective tissue of the capsule and trabeculae contains **myofibroblasts**. In many mammals, NOT in HUMANS, the spleen holds large volumes of red blood cells in reserve.



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The human spleen normally retains relatively little blood, but it has the **capacity for contraction** by means of the **contractile cells** in the capsule and trabeculae.

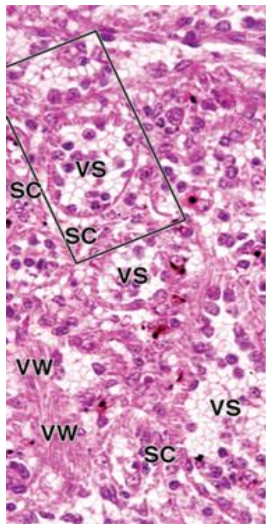
Red and white pulp of the spleen



Mescher AL. Junqueira's Basic Histology: Text and Atlas, 15th ed. McGraw-Hill Education

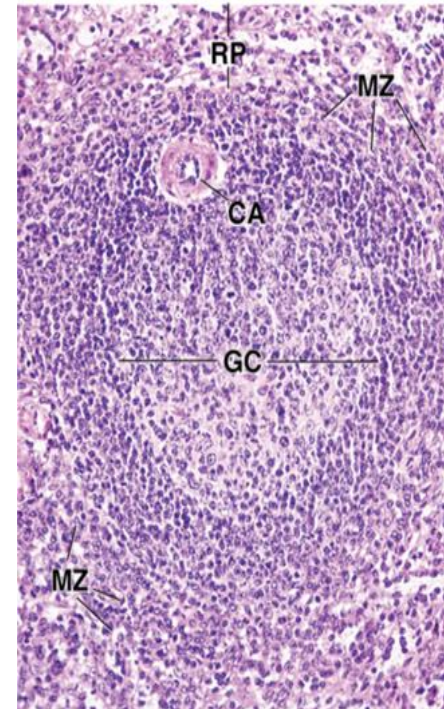
The **white pulp (W)** consists of lymphatic tissue, mostly lymphocytes. In H&E–stained sections, white pulp appears basophilic because of the dense heterochromatin in the nuclei of the numerous lymphocytes.

Red pulp (R) has a red appearance in the fresh state as well as in histologic sections because it contains large numbers of red blood cells.



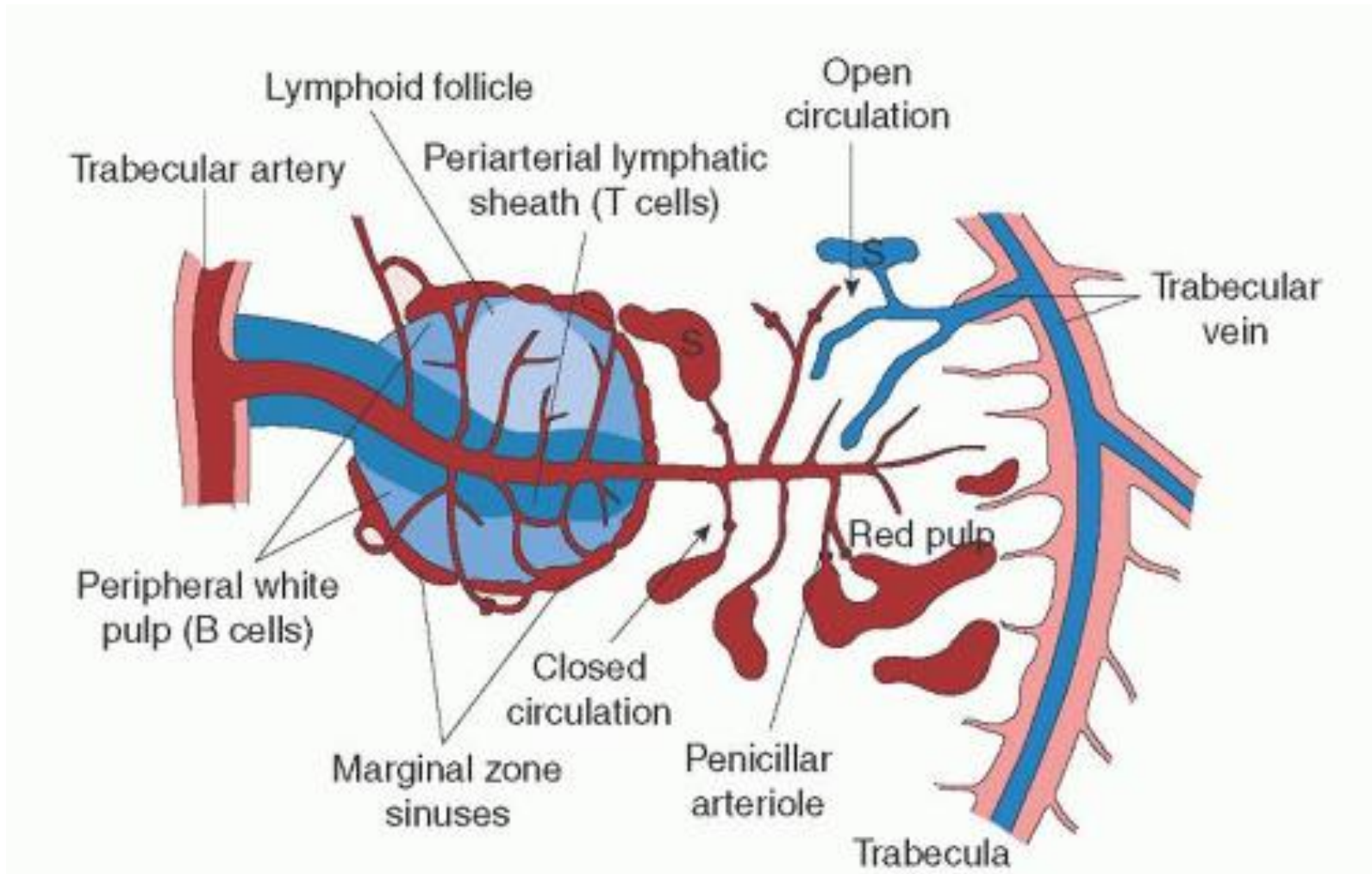
VS – splenic sinuses
 SC – **splenic cords** (loose meshwork of reticular cells and reticular fibers + erythrocytes, granulocytes, macrophages, plasma cells and dendritic cells)

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GC – germinal centre
 CA – central arteriole
 MZ – marginal zone
 RP – red pulp

Spleen blood circulation



Functions of the spleen

Immune system functions of the spleen include:

- antigen presentation by APCs (mostly dendritic cells and macrophages) and initiation of immune response,
- activation and proliferation of B and T lymphocytes,
- production of antibodies against antigen present in circulating blood, and
- removal of macromolecular antigens from the blood.

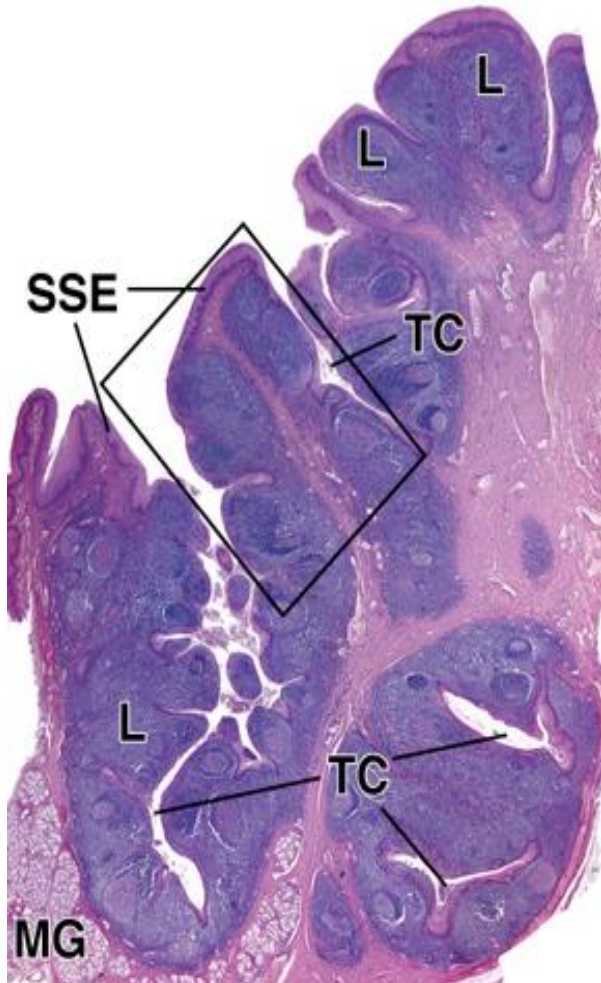
Activation and proliferation of T cells and differentiation of B cells and plasma cells, as well as secretion of antibodies, occur **in the white pulp of the spleen**; in this regard, the white pulp is the equivalent of other lymphatic organs.

Hemopoietic functions of the spleen include:

- removal (phagocytosis by macrophages) and destruction of senescent, damaged, and abnormal erythrocytes and platelets;
- retrieval of iron from erythrocyte hemoglobin;
- formation of erythrocytes during early fetal life; and
- storage of blood, especially red blood cells, in some species.

Palatine tonsil

L – lymphatic tissue
TC – tonsillar crypts
SSE – stratified squamous epithelium



The **palatine tonsils** are paired structures consisting of masses of lymphatic tissue located on either side of the pharynx. They, along with the pharyngeal tonsils (adenoids) and lingual tonsils, form a ring at the entrance to the oropharynx (**Waldeyer's ring**).

Structurally, the tonsils contain numerous **lymphatic nodules located in the mucosa**. The stratified squamous epithelium that covers the surface of the palatine tonsil (and pharyngeal) dips into the underlying connective tissue forming many crypts, the **tonsillar crypts**. The walls of these crypts contain lymphatic nodules.

The palatine and pharyngeal tonsils can become inflamed due to repeated infection in the oropharynx and nasopharynx and can harbor bacteria that cause **repeated infections** if they are overwhelmed.

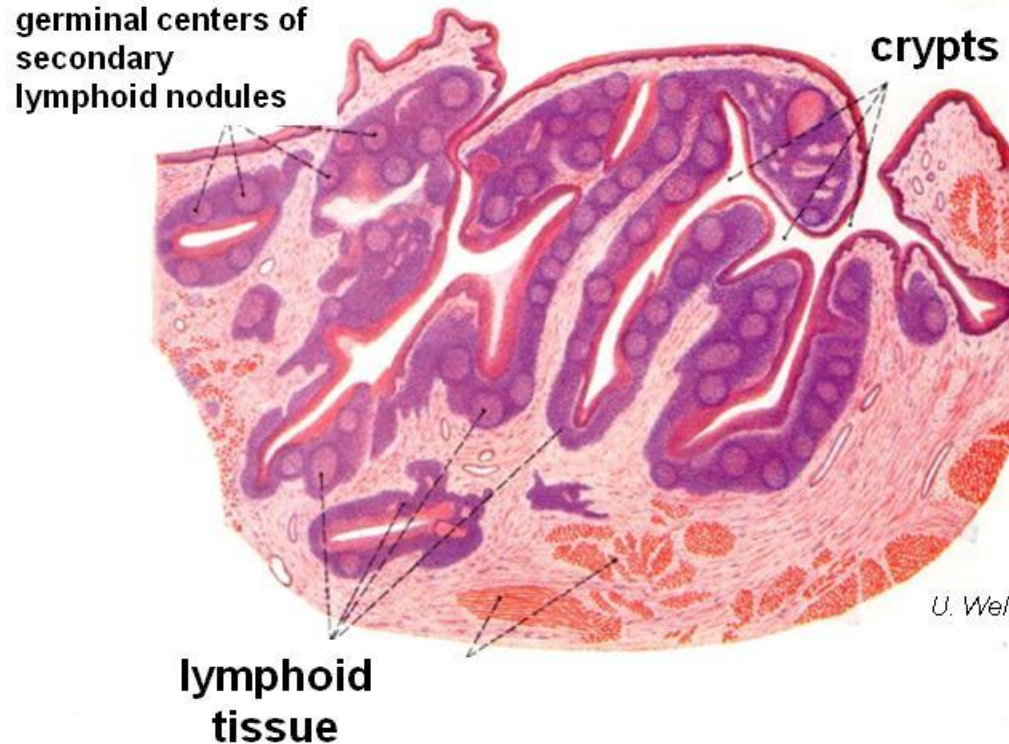
When this occurs, the inflamed tonsils are removed surgically (**tonsillectomy and adenoidectomy**).

Tonsils

Name	Epithelium	Capsule	Crypts
adenoids = pharyngeal tonsils	ciliated pseudostratified (respiratory epithelium)	Yes Incomplete	No
palatine tonsils	non-keratinized stratified squamous	Yes	Many branched
lingual tonsils	non-keratinized stratified squamous	No/Yes	Many

Palatine tonsils - bilateral

- are located in the lateral walls of the oral part of the pharynx



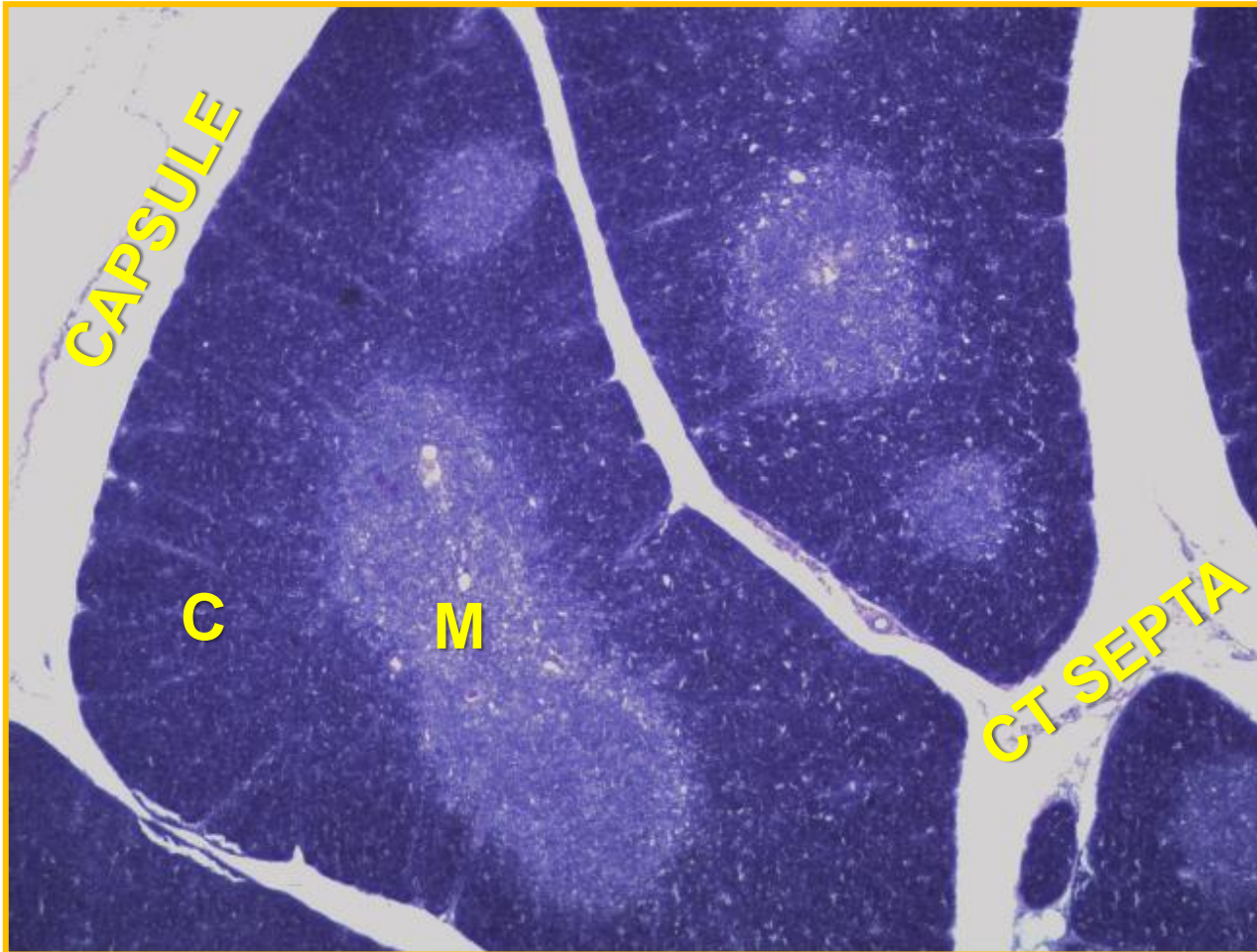
U. Welsch, „Atlas histologii Sobotty“, 2002

- possess **crypts** (10-20), deep invaginations of the non-keratinized **stratified squamous epithelium**, frequently containing debris
- an epithelium often becomes so densely infiltrated by lymphocytes that may be difficult to recognize

Practical part

THYMUS (young)

Slide no. 23



The **capsule** of the **thymus**, composed of dense, irregular collagenous **connective tissue**, sends **septa** into the lobes, subdividing them into **incomplete lobules**.

Each lobule is composed of a **cortex** and a **medulla**, although the medulla of adjacent lobules are confluent with each other.

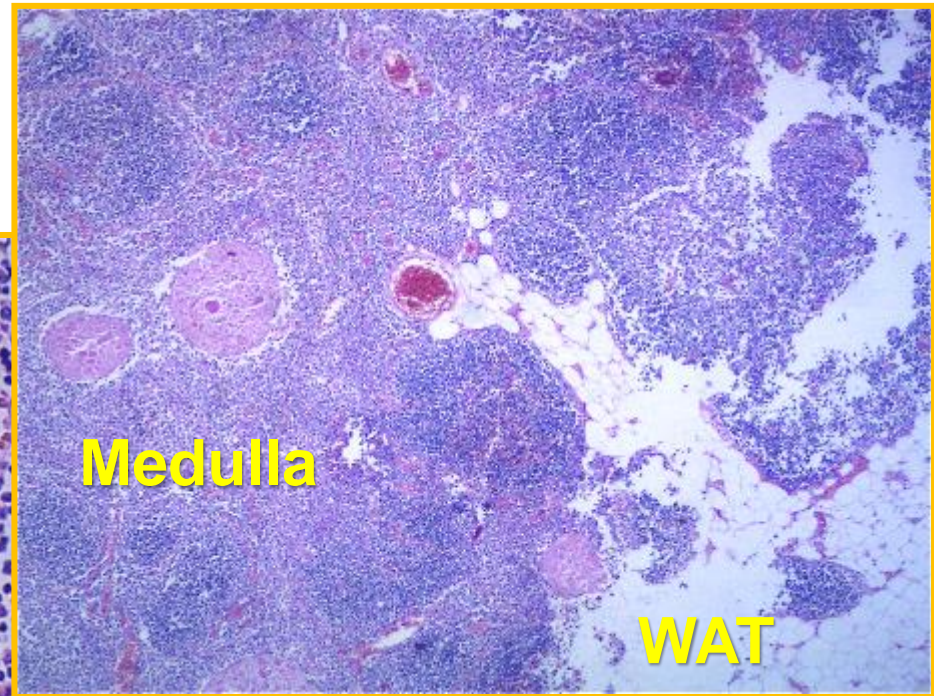
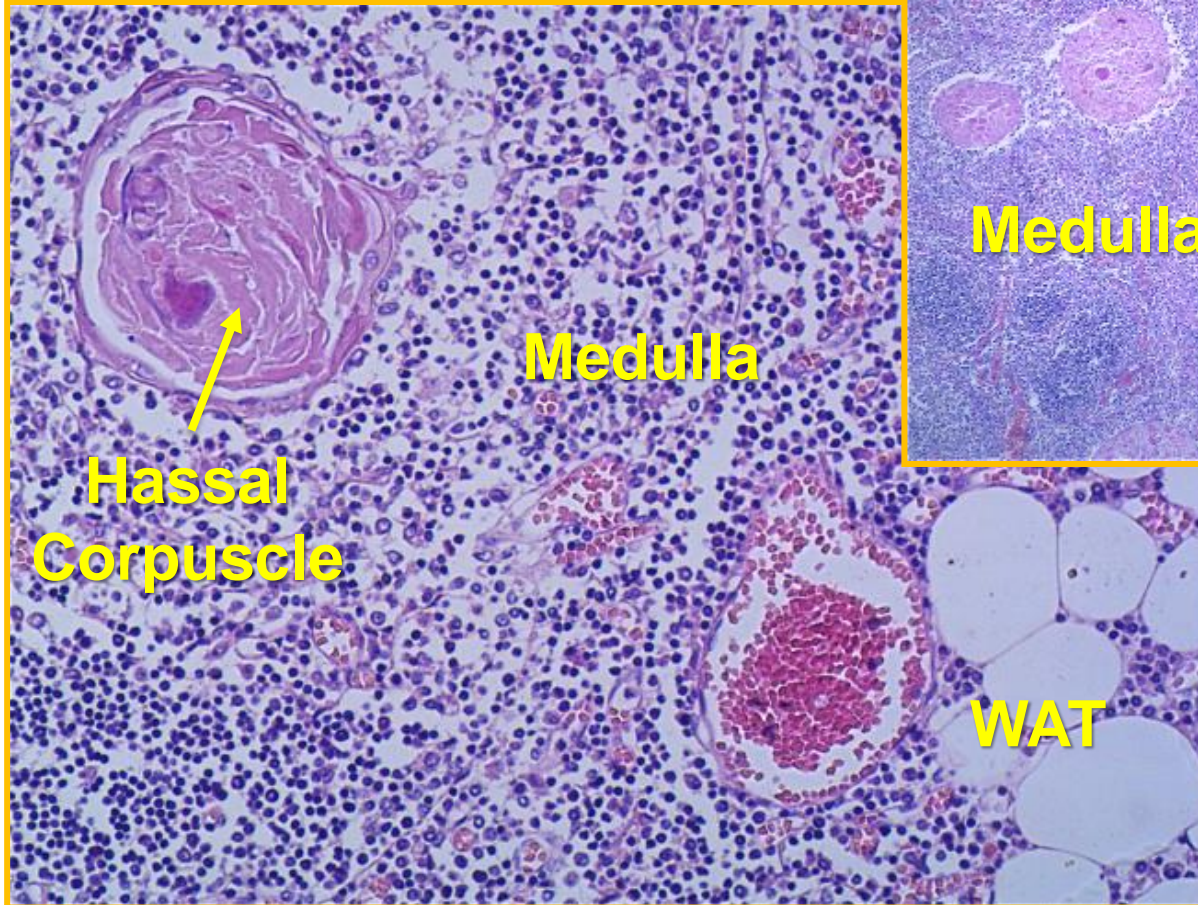
KHIEC Olsztyn

The **cortex (C)** consists of developing T cells (**thymocytes**), macrophages, dendritic cells and reticular epithelial cells.

The **medulla (M)** contains large numbers of reticular epithelial cells (with their large and light-stained nuclei) and **mature T cells**, which are loosely packed, causing the medulla to stain lighter than the cortex.

THYMUS (involuted)

Slide no. 24



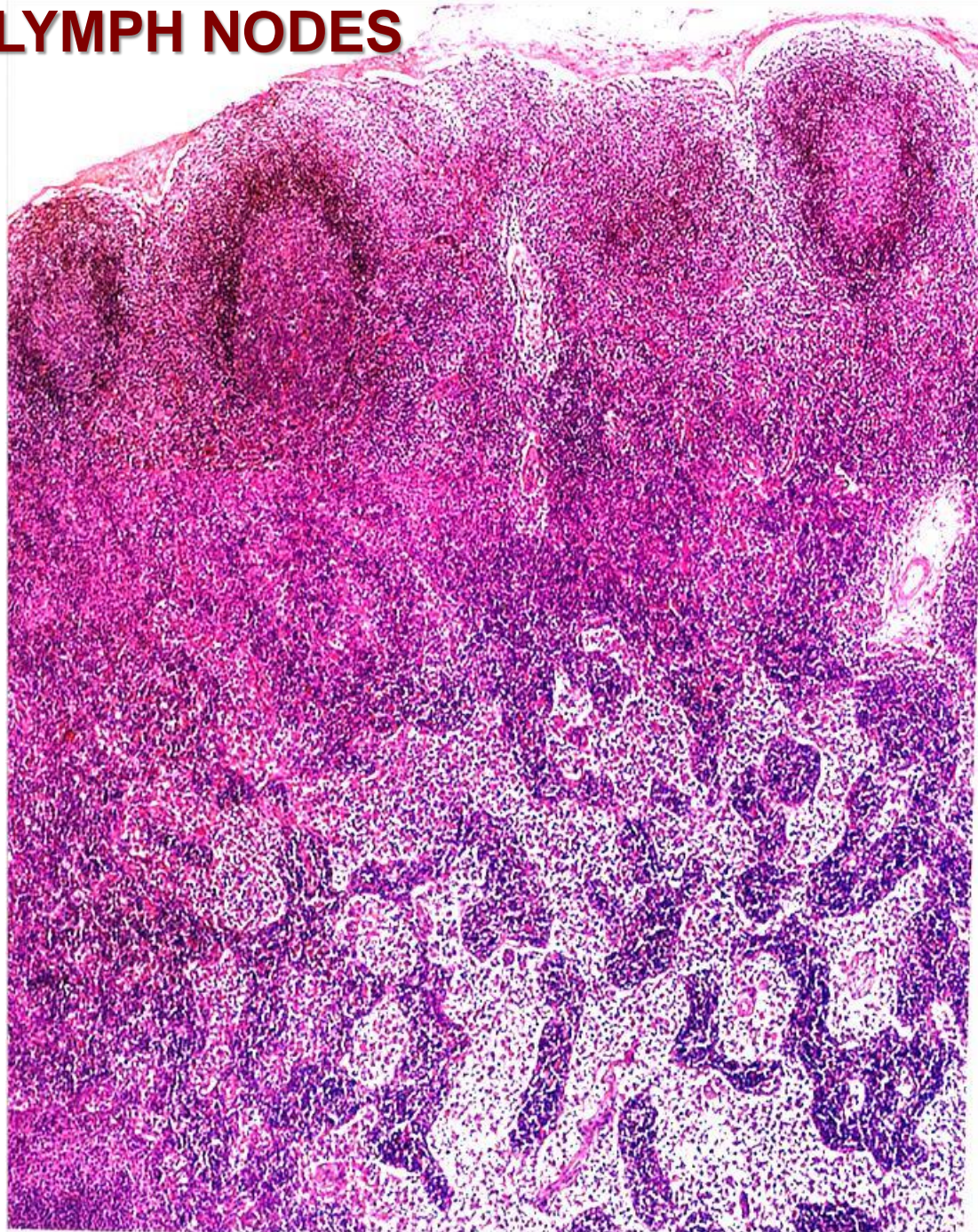
KHIEC Olsztyn

In humans thymus is fully developed before birth and **begins to involute** near the time of **puberty** becoming infiltrated by **adipose cells** and gradually shrinking in size and function. This atrophy is due to the increased blood level of sex hormones.

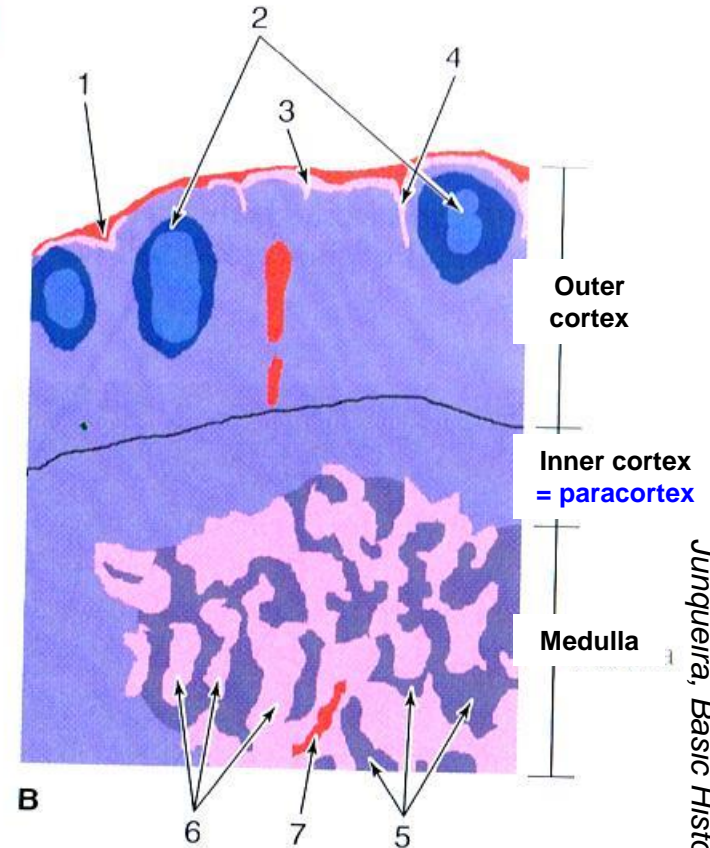
KHIEC Olsztyn

Hassall's corpuscles are present only in the medulla of the thymus and are composed of closely packed whorls of epithelial cells representing **highly keratinized** medullary epithelial cells.

LYMPH NODES



- 1 – capsule
- 2 – lymphoid nodule with germinal center
- 3 – subcapsular sinus
- 4 – intermediate = trabecular = radial sinus



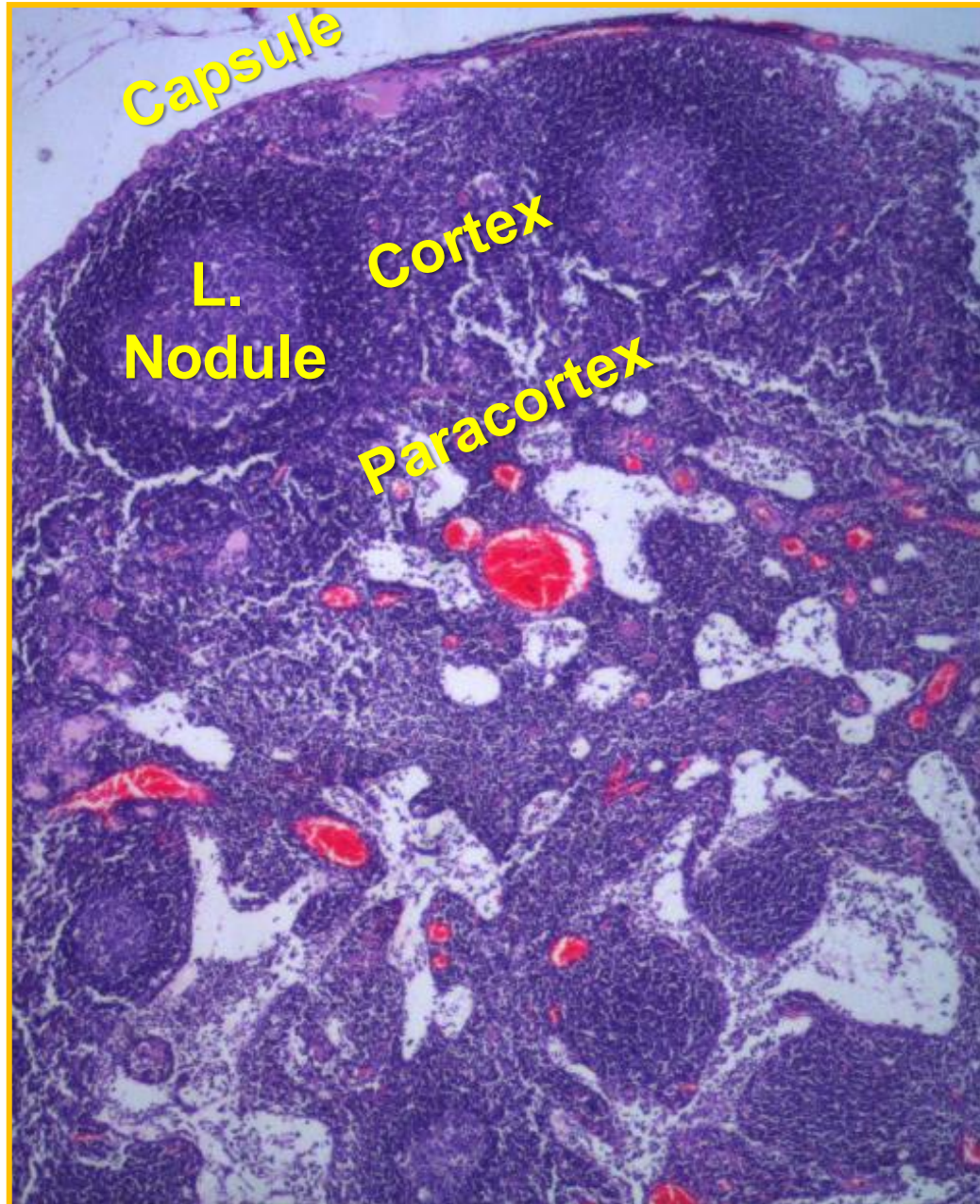
- 5 – medullary cords
- 6 – medullary sinus
- 7 – trabecula

Slide no. 21

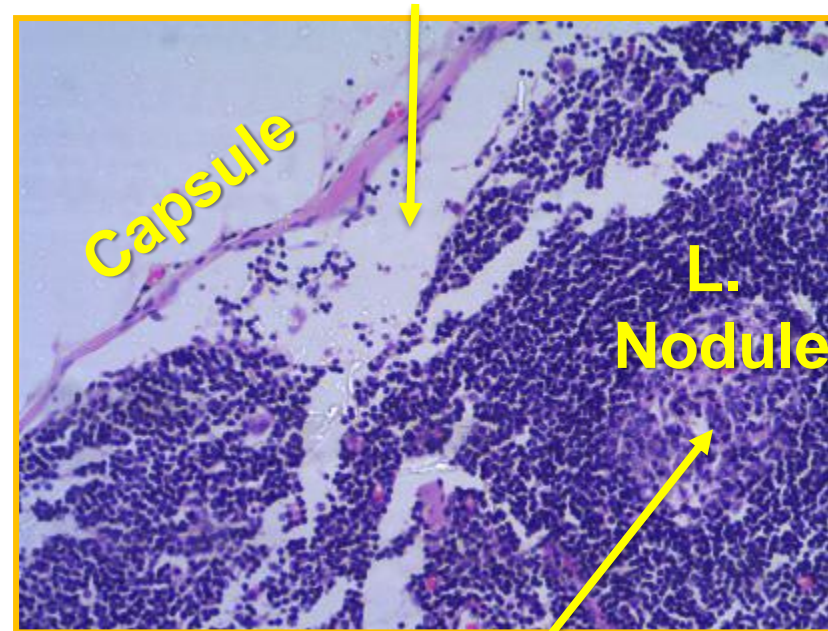
LYMPH NODE

Slide no. 21

Small, encapsulated, oval or kidney-shaped structures that are interposed in the path of lymph vessels to **serve as filters** for the removal of bacteria and other foreign substances



Subcapsular sinus



KHIEC Olsztyn

Germinative center

KHIEC Olsztyn

LYMPH NODE – SINUS and RETICULAR CELLS

Slide no. 21



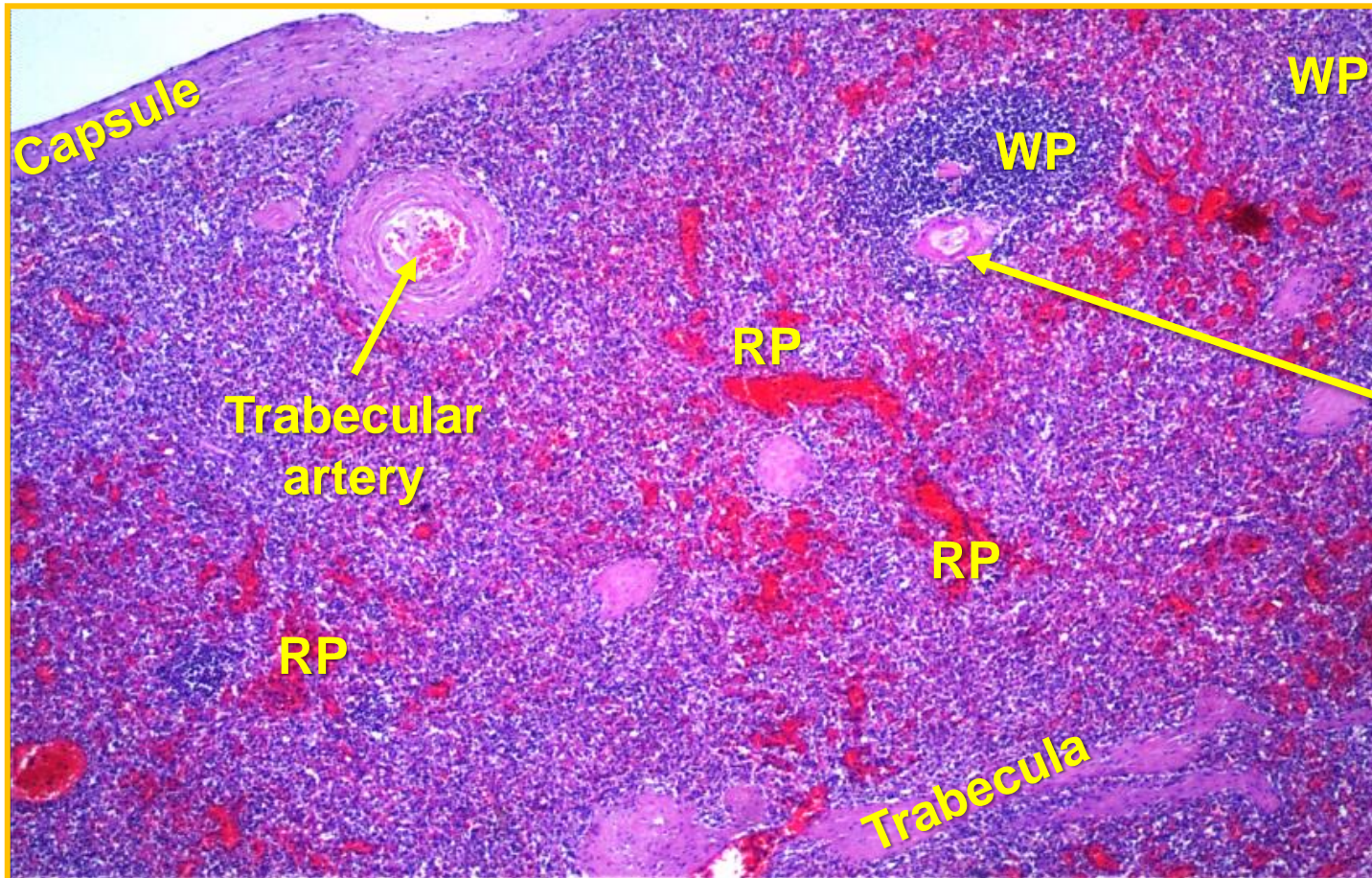
Reticular cells

Eosinophil

Neutrophil

SPLEEN

Slide no. 22

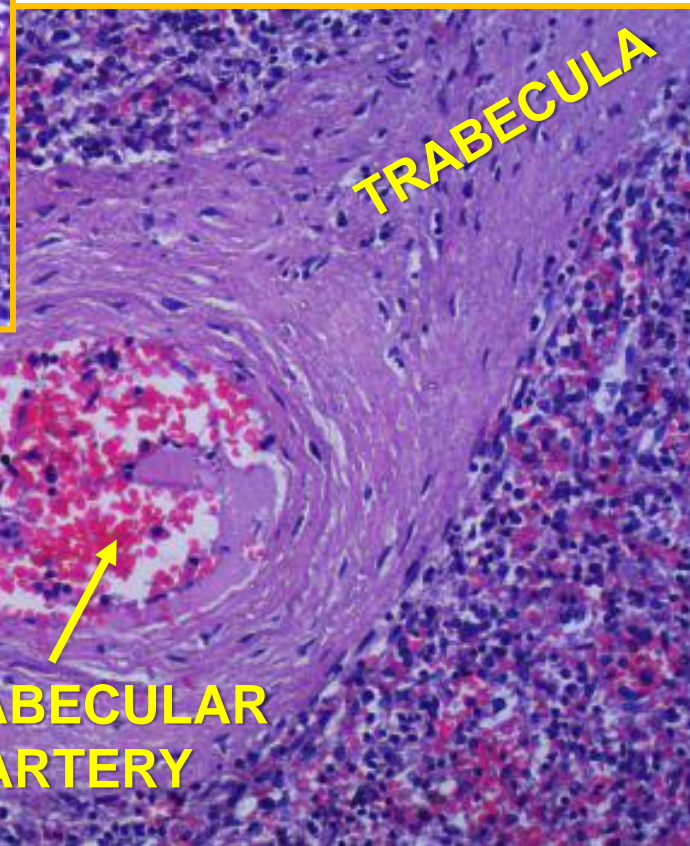
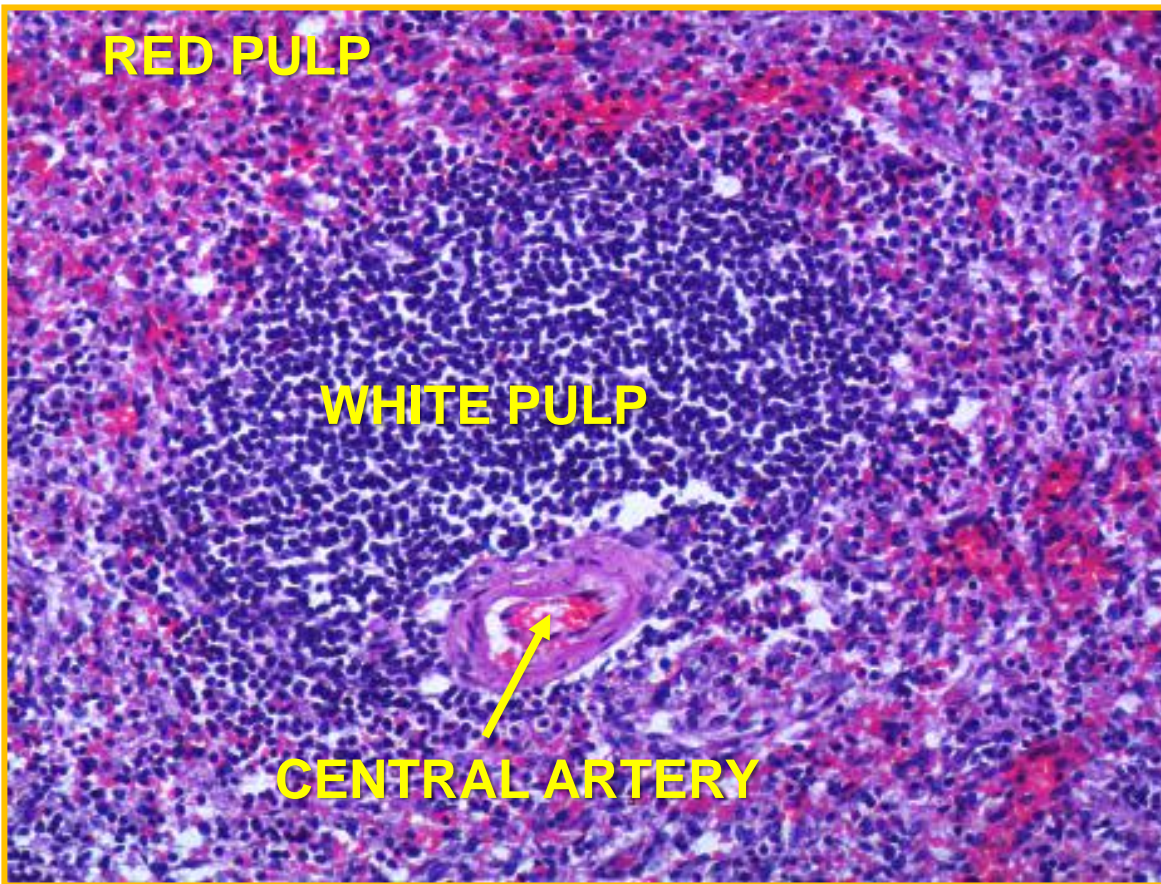


KHIEC Olsztyn

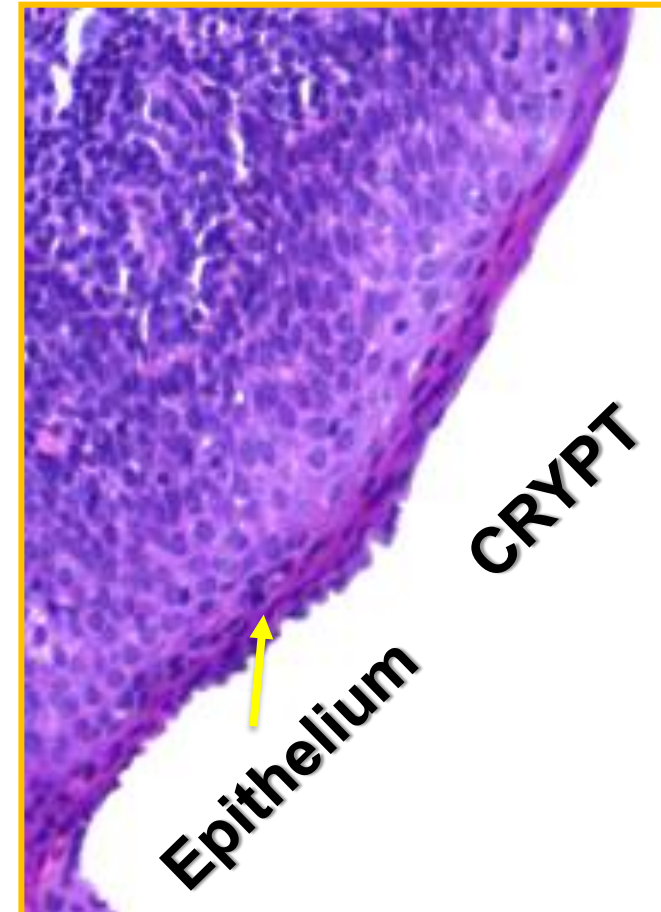
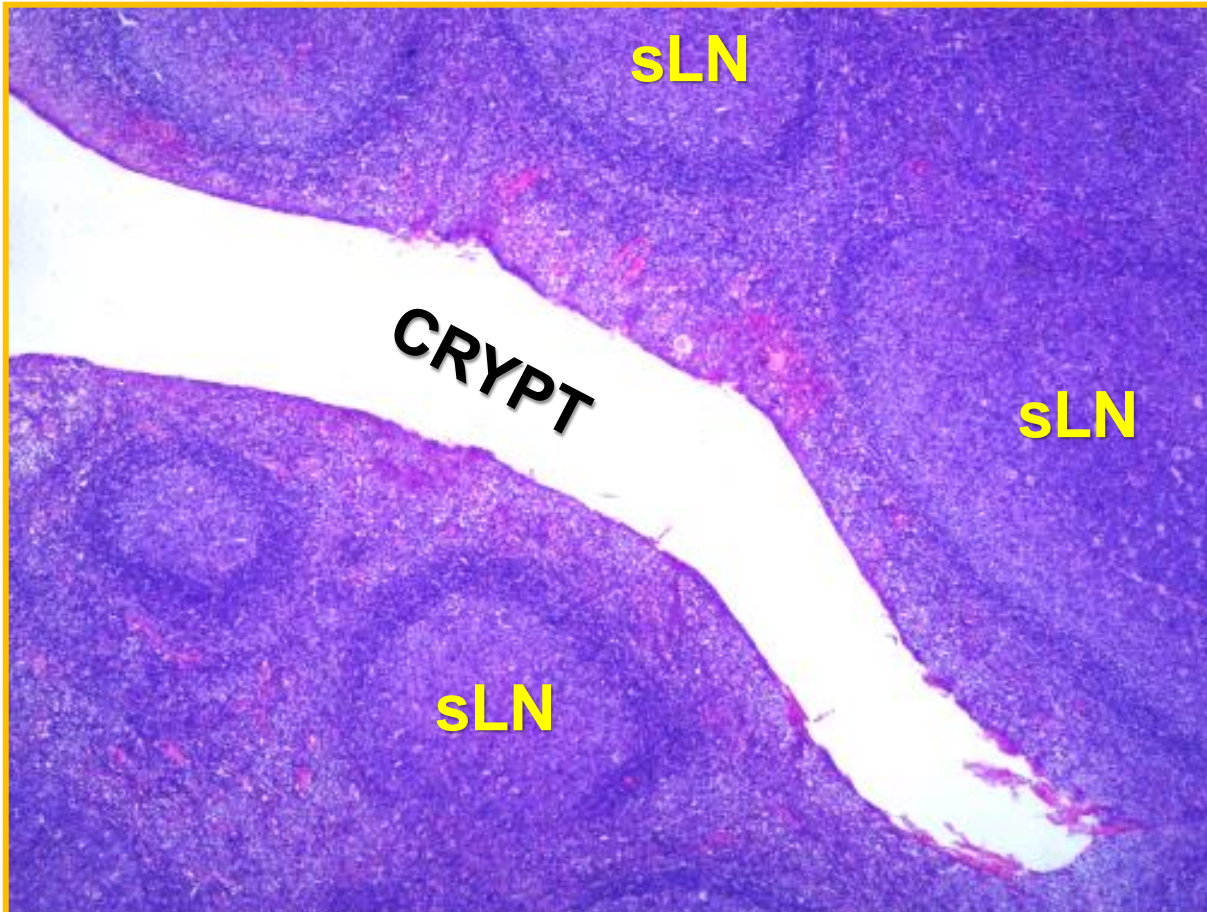
- the largest lymphoid organ in the body
- has **no afferent** lymphatic vessels
- the CT **capsule** is covered by a peritoneum
- branching **trabeculae** derived from the capsule enter the spleen parenchyma (trabecular artery and vein are found in the trabecula)
- the stroma is composed of reticular cells and reticular fibers supporting the two major components: the **white pulp (WP)** and the **red pulp (RP)**

SPLEEN

Slide no. 22



Lymphoid nodule **of the spleen** surrounded by red pulp.
The **central artery** located eccentrically.



- possess **primary and secondary lymphoid nodules (sLN)**
- are separated from subjacent structures by a connective tissue **capsule** - usually acts as a barrier against spreading tonsillar infections.