

ORGANS OF HEMOLYMPHOID SYSTEM

*Department of Histology, Cytology and Embryology
of the General Medicine Faculty*

Pirogov Russian National Research Medical University

BLOOD SYSTEM

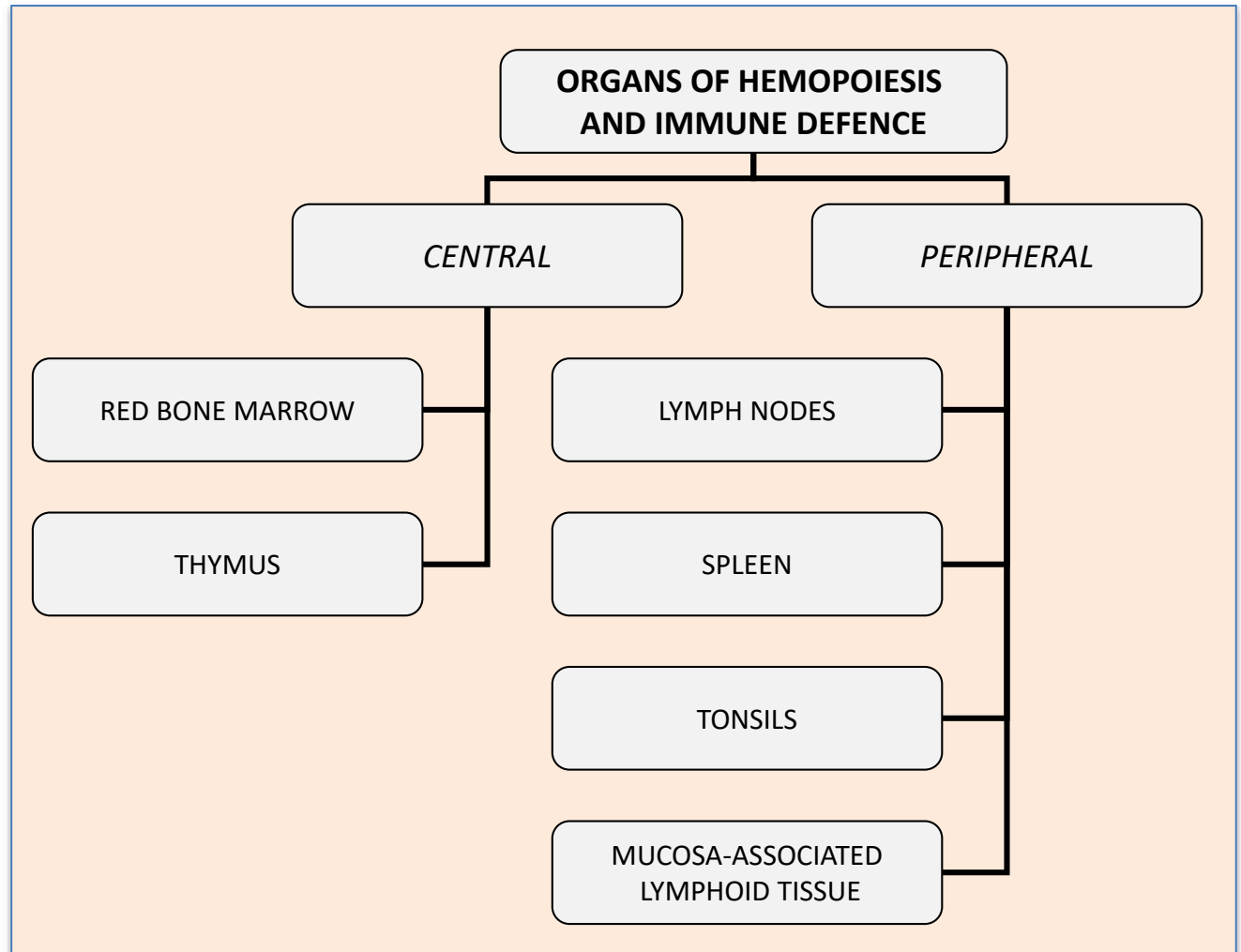
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graph TD; A[BLOOD SYSTEM] --> B[BLOOD]; A --> C[ORGANS OF HEMOPOIESIS]
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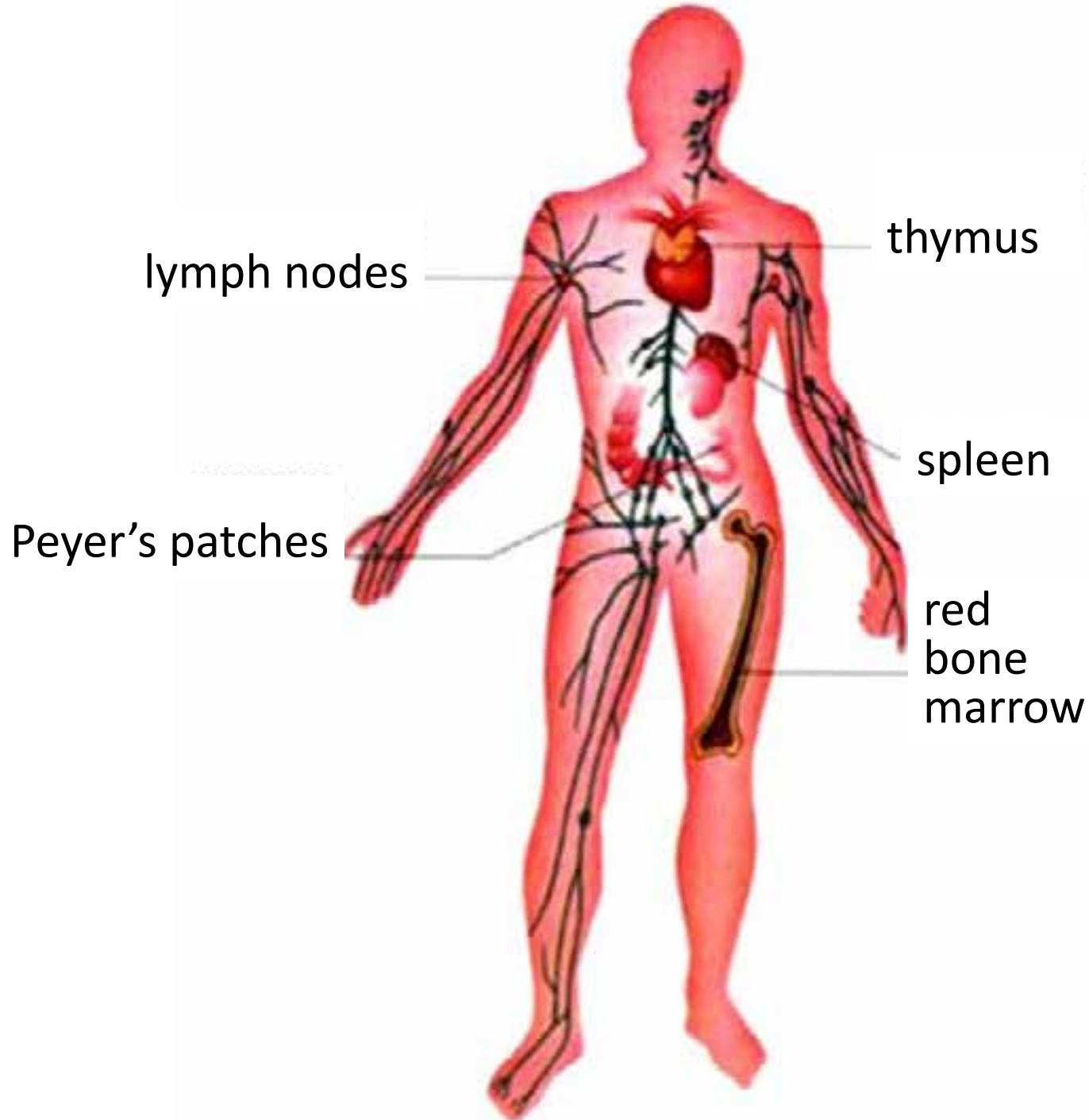
BLOOD

**ORGANS OF
HEMOPOIESIS**

FUNCTIONS of organs of hemopoiesis and immune defence

- Formation of blood cells
- Immunological surveillance of host cells
- Defence against microorganisms and foreign substances





HEMOPOIESIS

PRENATAL

- **Histogenesis of blood as tissue**
- **Blood regeneration**
 - Renewal of blood cells
 - Replacement of blood cells

POSTNATAL

- **Blood regeneration**
 - Renewal of blood cells
 - Replacement of blood cells

EMBRYONIC HEMOPOIESIS

Stages:

I — mesoblastic

II — hepatolienal

III — thymicomedullar

Yolk sac wall, chorion,

amniotic stalk

from 2-3 ---- 9 weeks

Liver

from 5 - 40 weeks

Thymus

from 9 weeks

Lymph nodes

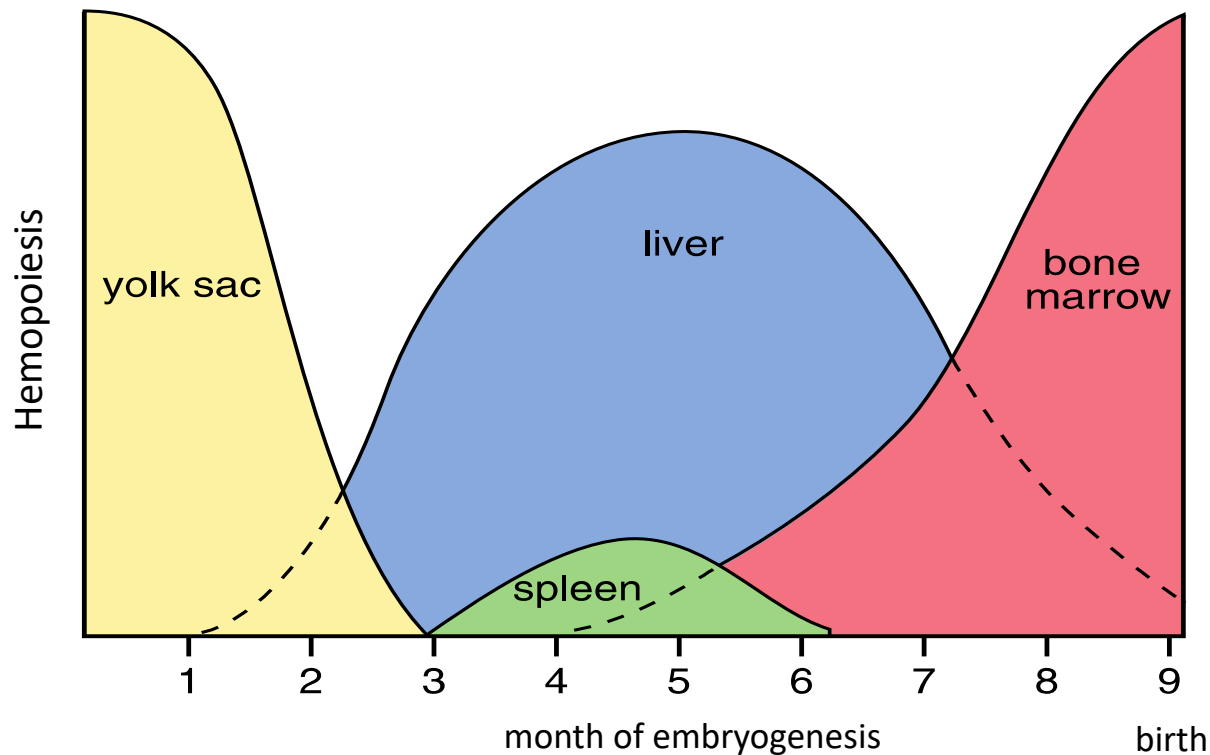
from 10 weeks

Spleen

from 12 weeks

Red bone marrow

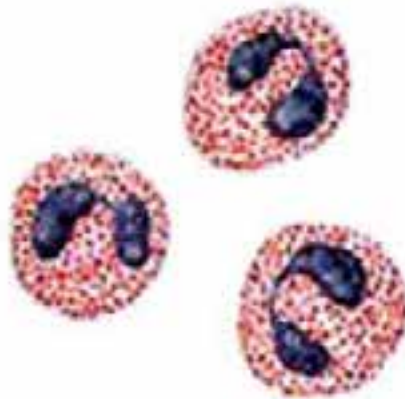
from 10 weeks



FORMED ELEMENTS OF THE BLOOD



Neutrophils



Eosinophils



Basophils



Lymphocytes



Monocytes

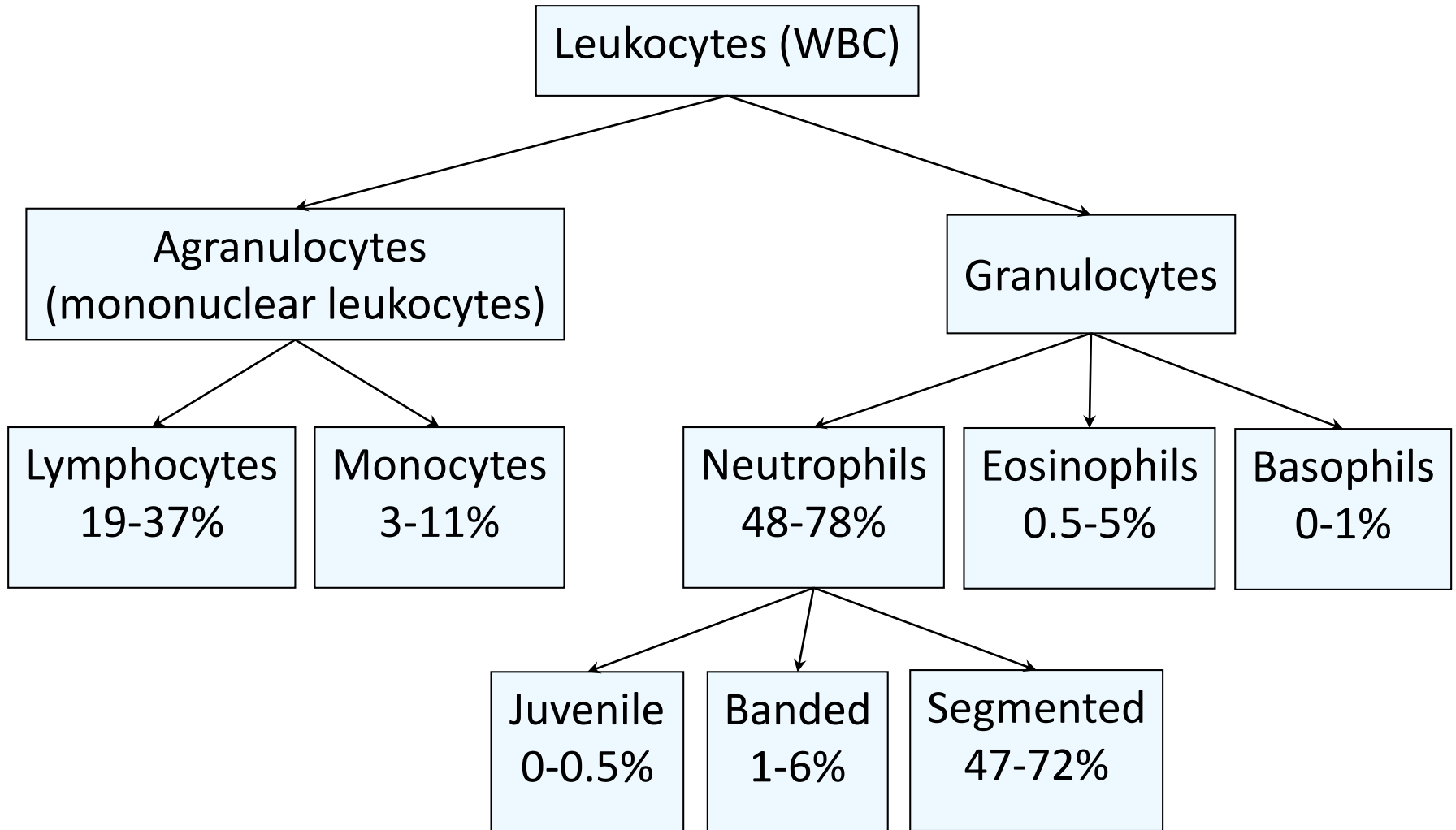


Platelets

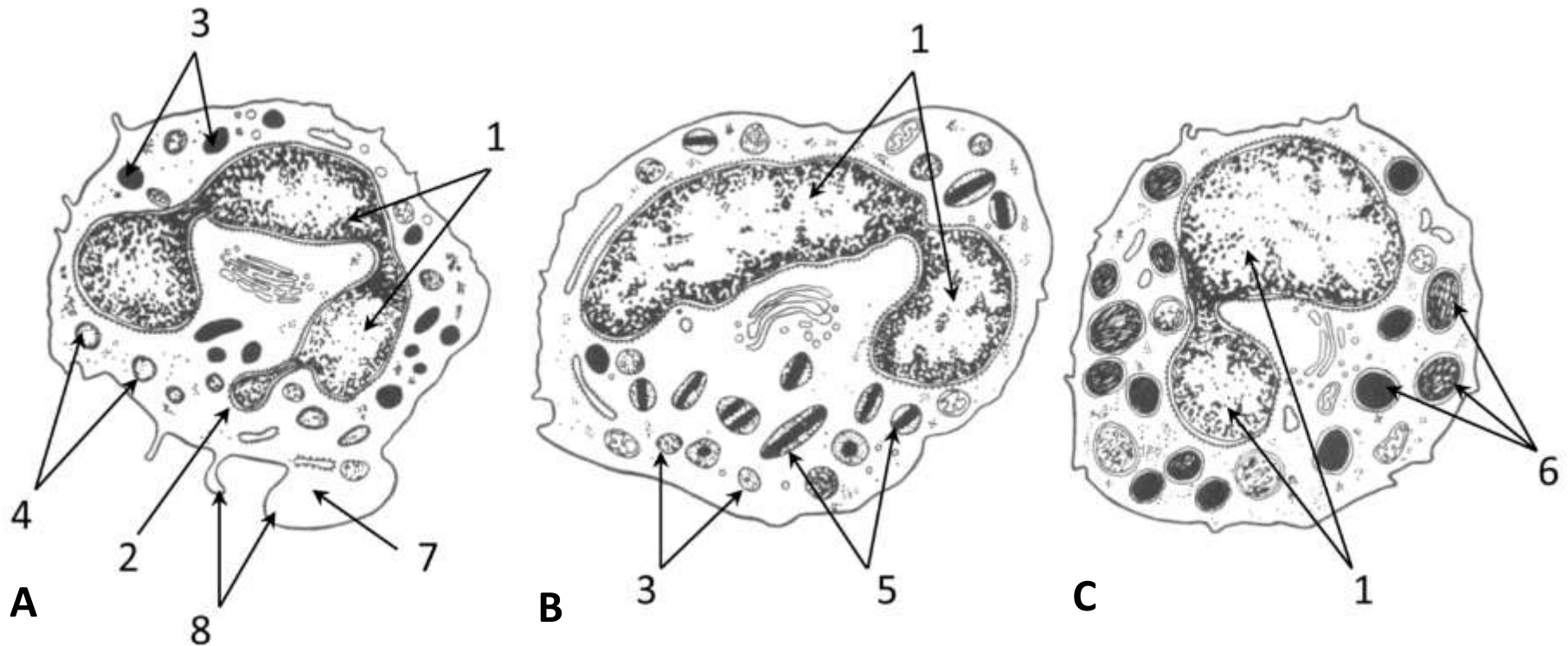


Erythrocytes (RBC)

WHITE BLOOD CELL COUNT DIFFERENTIAL



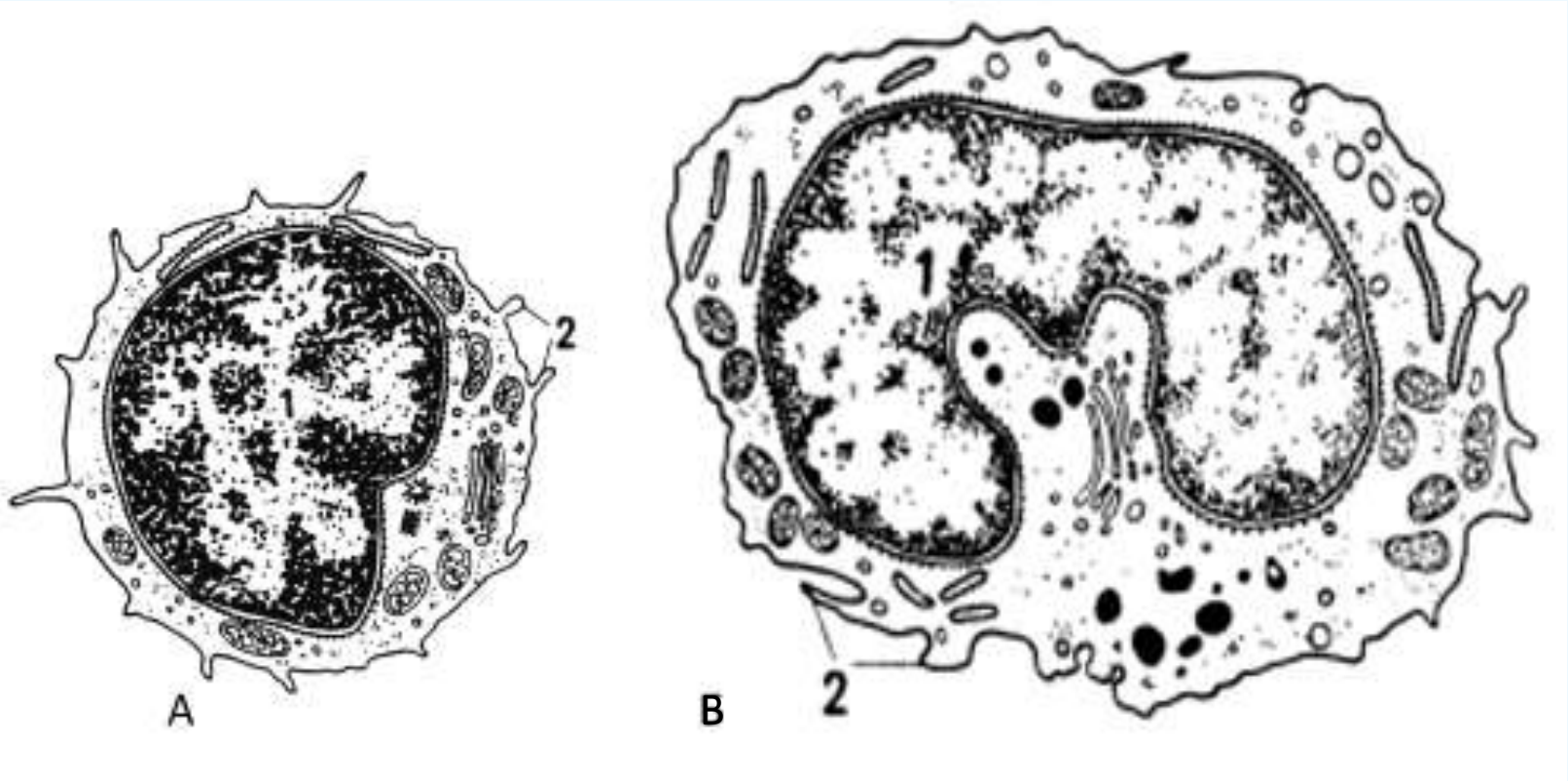
STRUCTURE OF GRANULOCYTES



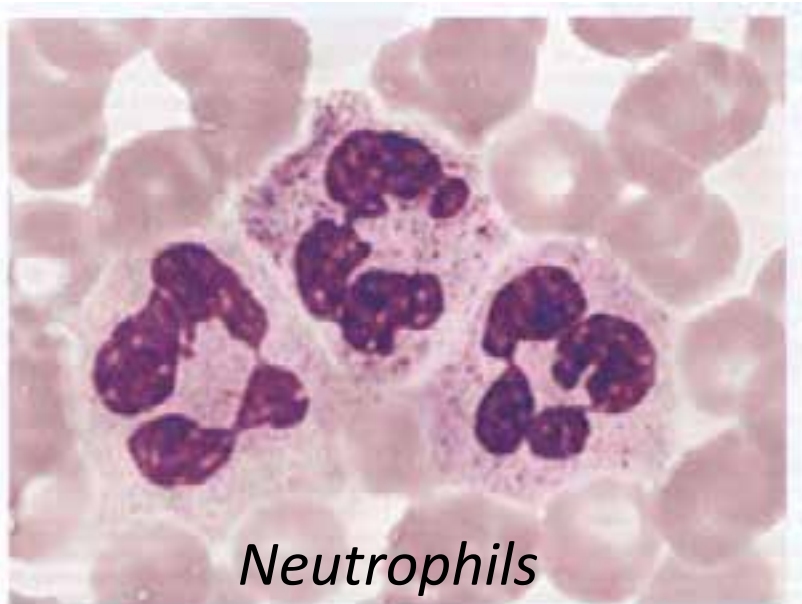
A — *segmented neutrophil* (“seg”); B — *eosinophil*; C — *basophil*:

1 — segments of the nucleus; 2 — Barr body of the inactivated X chromosome (in females only); 3 — primary (asurophilic) granules; 4 — secondary (specific) granules; 5 — mature specific granules of the eosinophil, contain crystalloid; 6 — granules of the basophil, vary by size and density; 7 — peripheral zone that is free from organelles; 8 — microvilli and pseudopodia

STRUCTURE OF AGRANULOCYTES



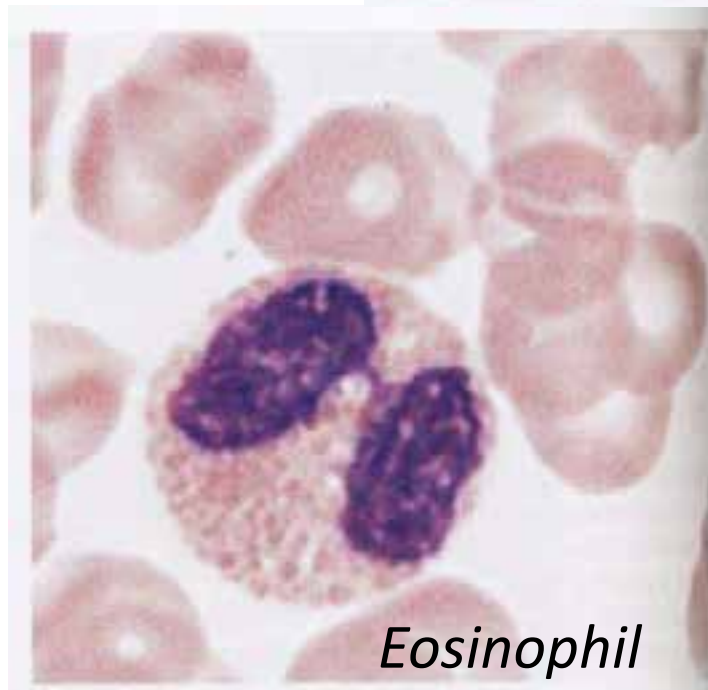
A — lymphocyte; B — monocyte: 1 — nucleus; 2 — microvilli and filopodia



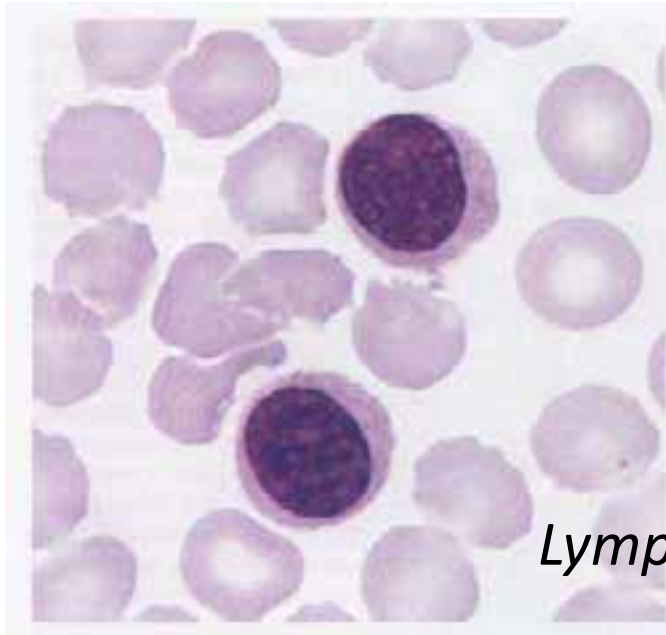
Neutrophils



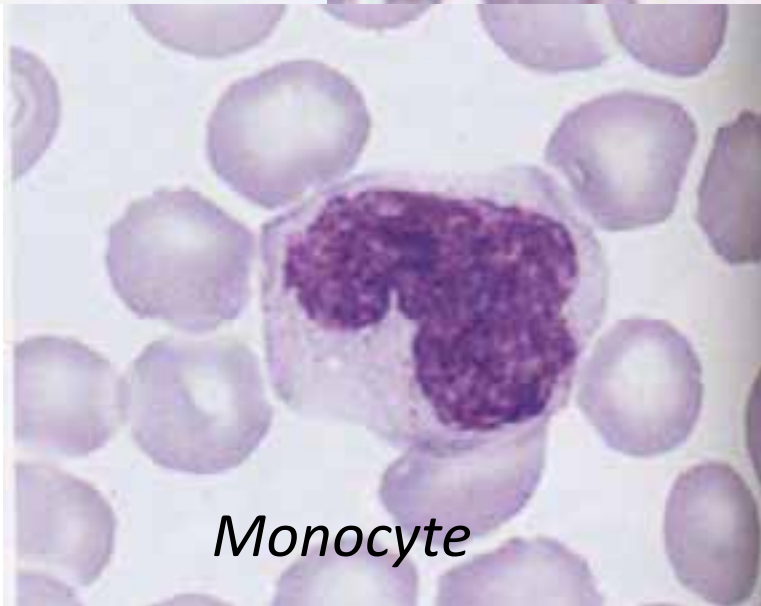
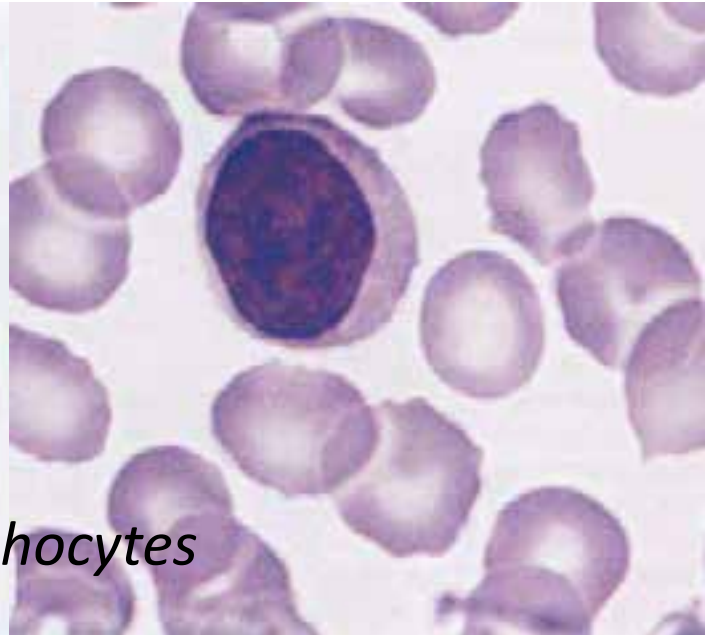
Basophil



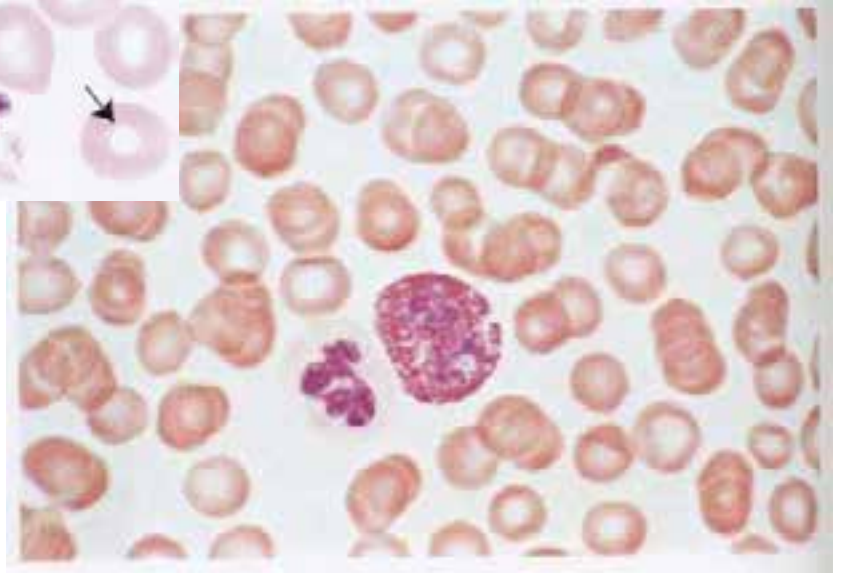
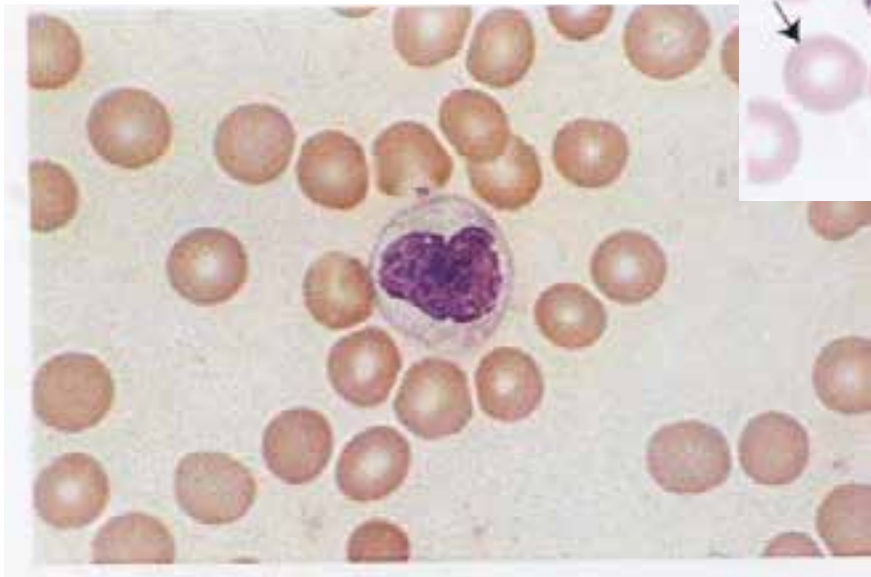
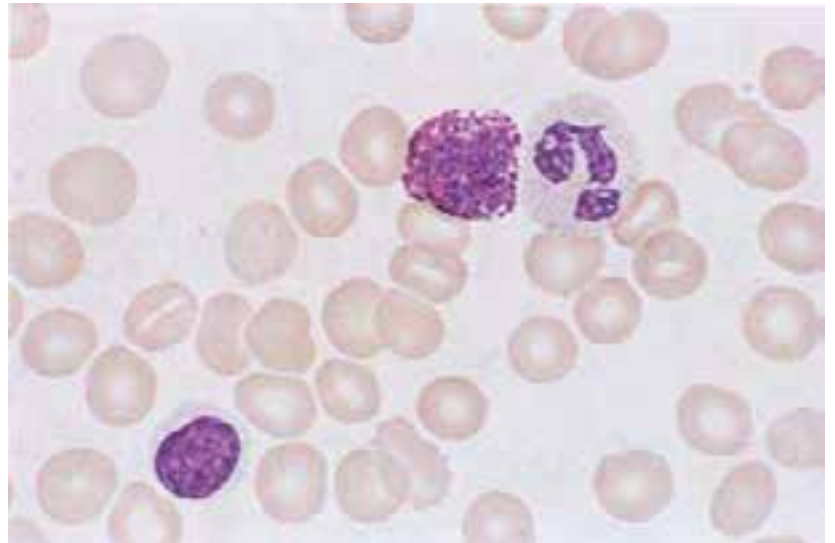
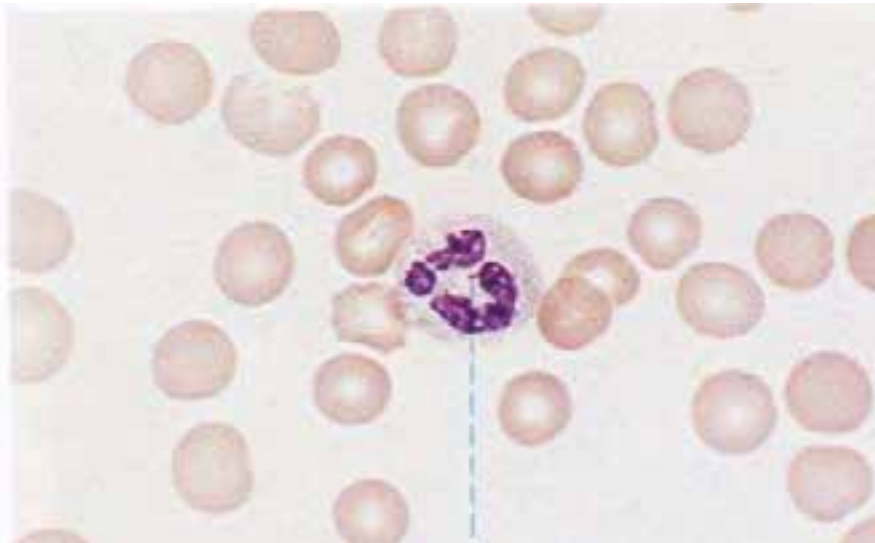
Eosinophil

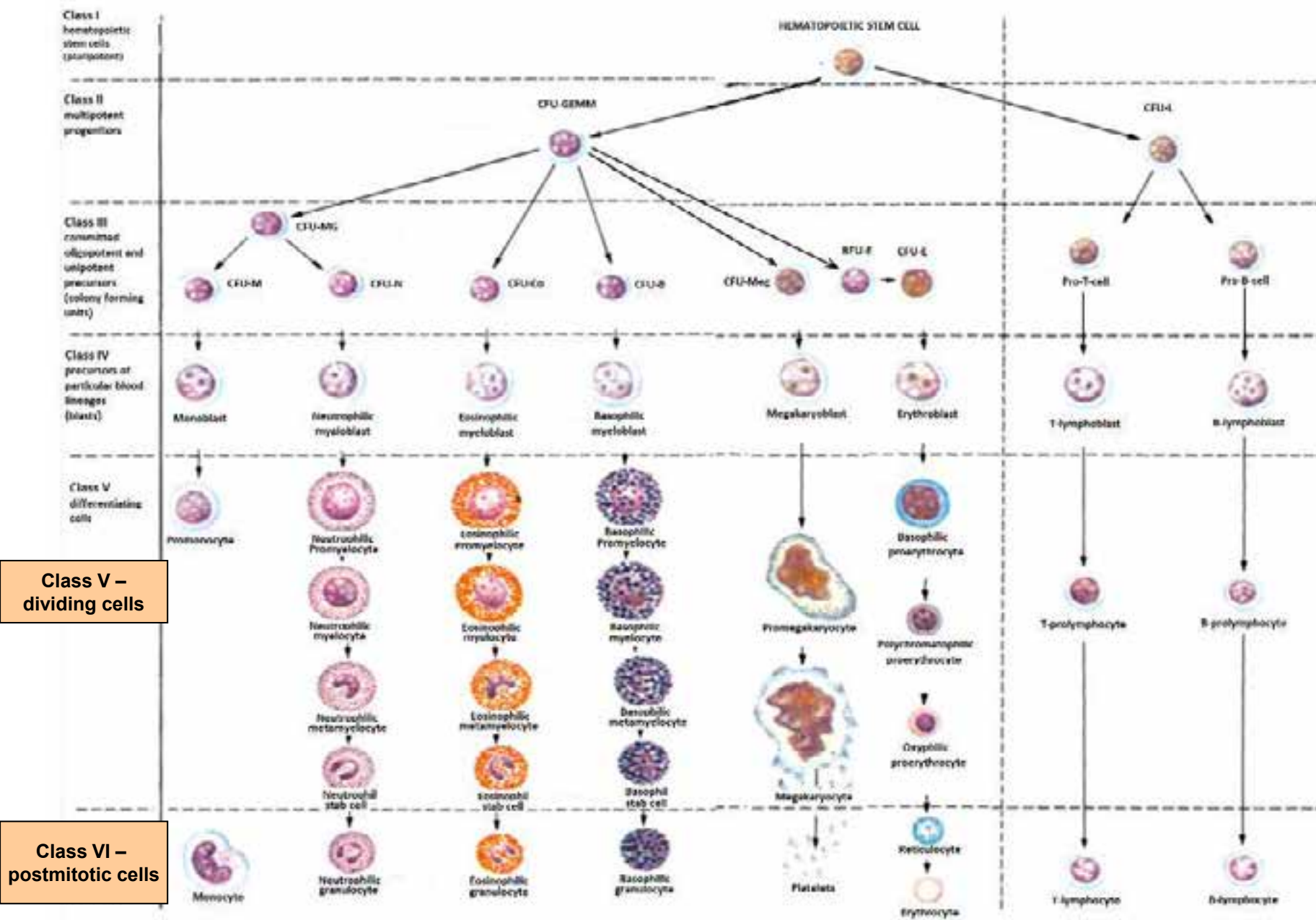


Lymphocytes



Monocyte





Complete differentiation inside tissues

Complete differentiation in peripheral organs of hemopoiesis and immune defence



Monocyte



Macrophages



spleen



red bone marrow



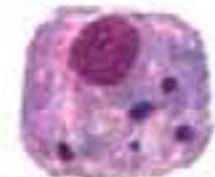
lymph nodes



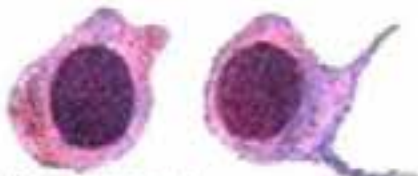
alveolar



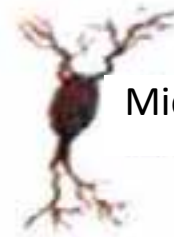
pleural



peritoneal



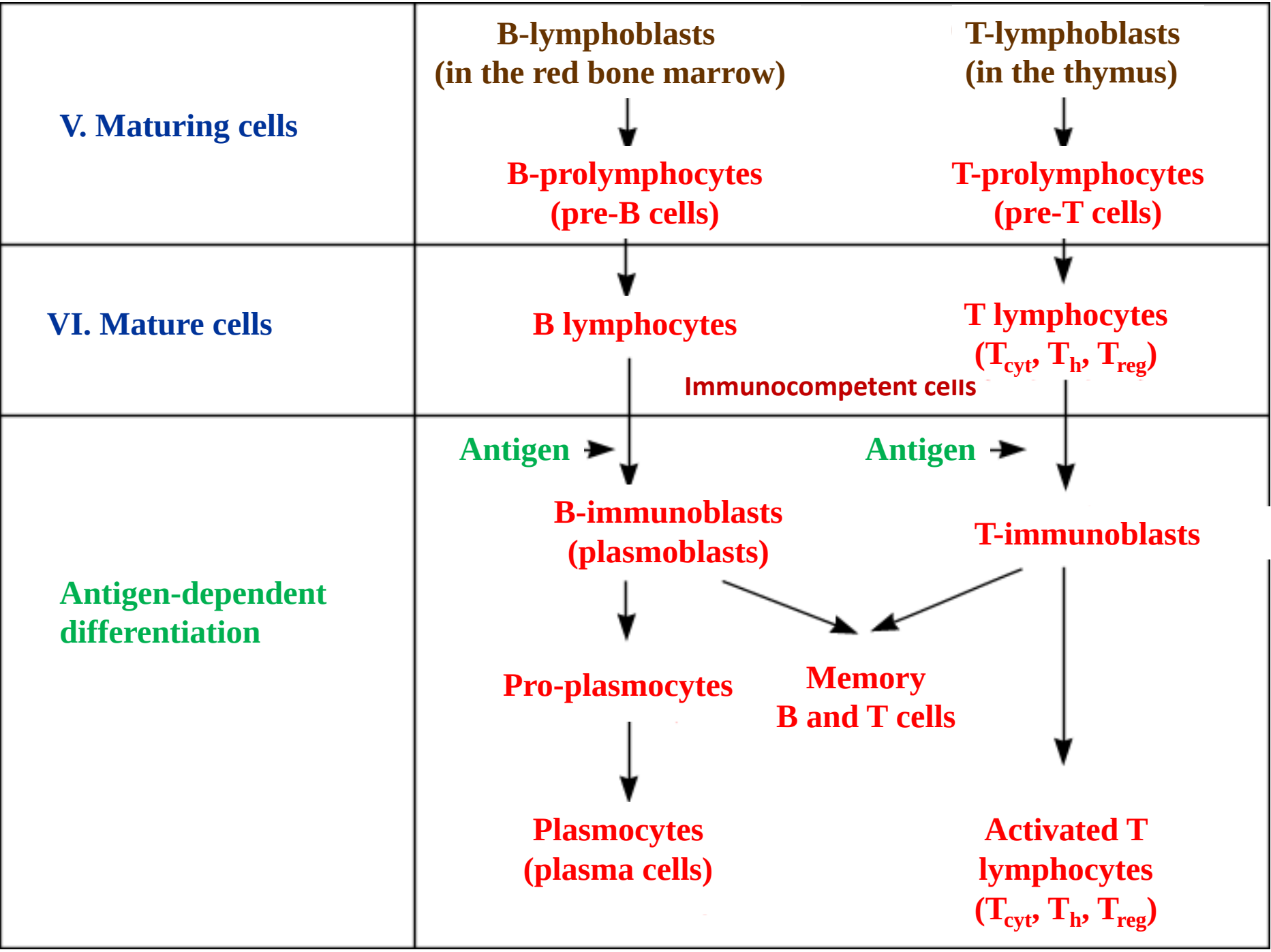
Histiocytes and the Kupffer's cells



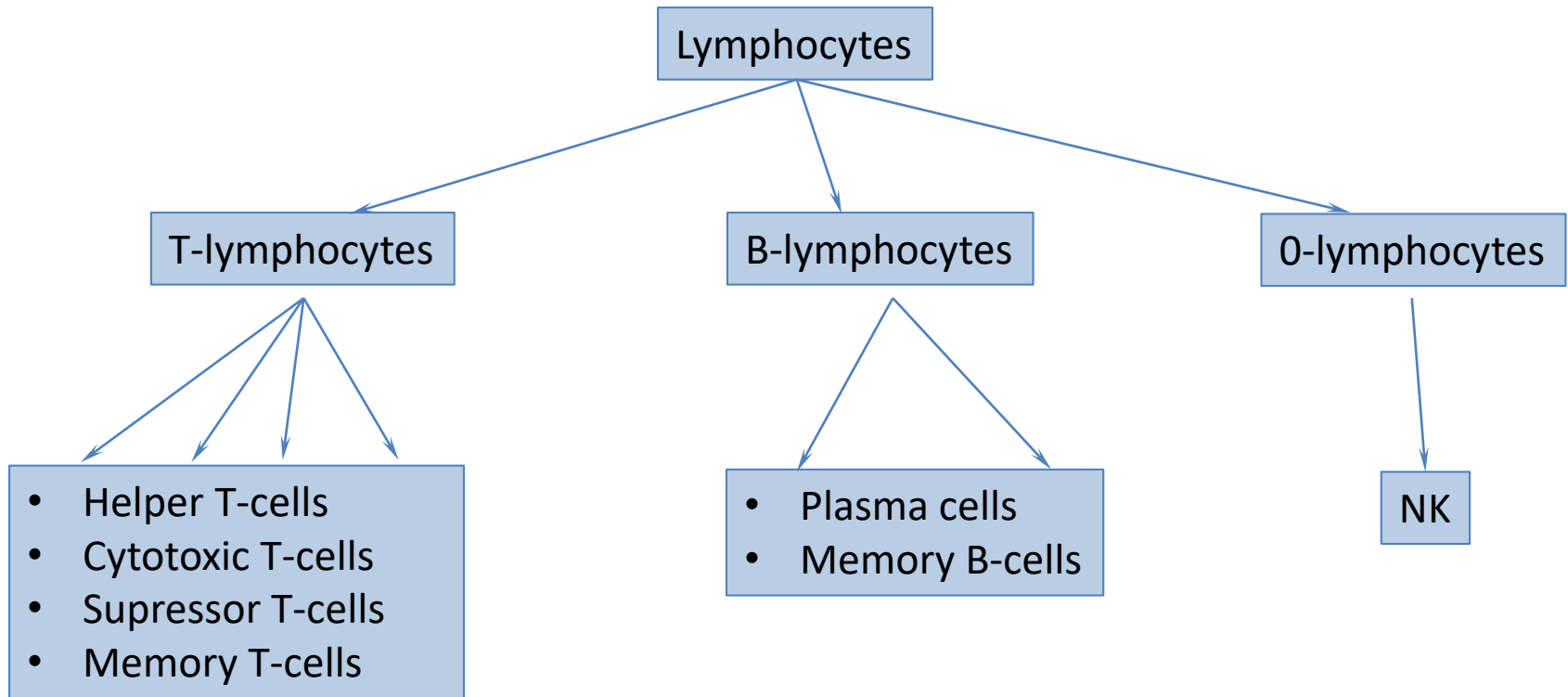
Microglia



Dendritic cells



LYMPHOCYTE POPULATIONS



Percentage of lymphocyte types to the total number of lymphocytes in blood:

T-cells — 65—80 %,

B-cells — 8—20 %,

NK-cells — 5—20 %

LYMPHOCYTOPOIESIS IMMUNITY

Lymphocytes are the main cells of the immune system. They provide:

- **humoral immunity** (*antibodies releasing*)
- **cell-mediated immunity** (*contact interaction with target cells*)
- **Regulation of the activity of other types of cells that are involved in immune response**

Humoral immunity –
neutralization and destruction of foreign agents/substances
Reaction : Antigen-Antibody

Cell-mediated immunity –
destruction of damaged host cells and foreign cells
Reaction: damaged host cell/foreign cell-cytotoxic T-cell

FUNCTIONS OF LYMPHOCYTES

T-lymphocytes

- Helper T-cells
- Cytotoxic T-cells
- Suppressor T-cells
- Memory T-cells

B-lymphocytes

- Plasma cells
- Memory B-cells

0-lymphocytes

NK

Cytotoxic (CD8+) T-cells — destroy virus-infected cells, tumor cells etc. — ***cell-mediated immunity reactions***

Helper (CD4+) T-cells — when activated, synthesize and secrete cytokines (IL-1, IL-2, IL-4, IL-5, IL-6), regulate (stimulate) the intensity of the immune response

Suppressor T-cells (regulatory T-cells) — regulate the intensity of the immune response by suppressing the activity of helper T-cells; prevent the development of autoimmune reactions; protect the body from the undesirable consequences of the immune response, from excessive inflammation and auto-aggression

Plasma cells — synthesize antibodies that interact with soluble antigens, participate in the opsonization of foreign microorganisms, etc. — ***humoral immunity reactions***

Memory T- and B-cells — provide a rapid immune response upon repeated invading of the antigen

NK cells — destruction of self cells that are inaccessible to the action of cytotoxic T-cells

Stages of T-cell and B-cell lymphopoiesis:

LYMPHOCYTOPOIESIS

1. Medullary stage — first three classes

2. Antigen-independent differentiation stage

- ✓ in the central organs immunogenesis (classes 4, 5 and 6)
 - Red bone marrow — for B-lymphopoiesis
 - Thymus — for T-lymphopoiesis
 - *without encountering a foreign antigen*
 - *gene rearrangement occurs*
 - *T- and B-cell receptors and other receptors are formed*

IMMUNOCYTOPOIESIS

3. Antigen-dependent differentiation stage

- ✓ in peripheral lymphoid organs
 - *encounter with a foreign antigen occurs*
 - *activation, blast transformation, proliferation*
 - *completion of differentiation*

HEMATOPOIETIC COMPONENT

Developing blood cells

MYELOID TISSUE:

- erythrocytes,
- platelets,
- granulocytes,
- monocytes

LYMPHOID TISSUE

- lymphocytes

ORGANS OF HEMOPOIESIS STRUCTURE

STROMAL COMPONENT

- *Loose connective tissue*
- *macrophages*
- *antigen presenting cells*
- *adipocytes*

- *reticular tissue*
(epithelioreticular tissue - thymus)

VASCULAR COMPONENT

- blood vessels (arteries and veins)*
- somatic type hemocapillaries*

- sinusoidal type hemocapillaries*
- venous sinuses (postcapillary venules)*

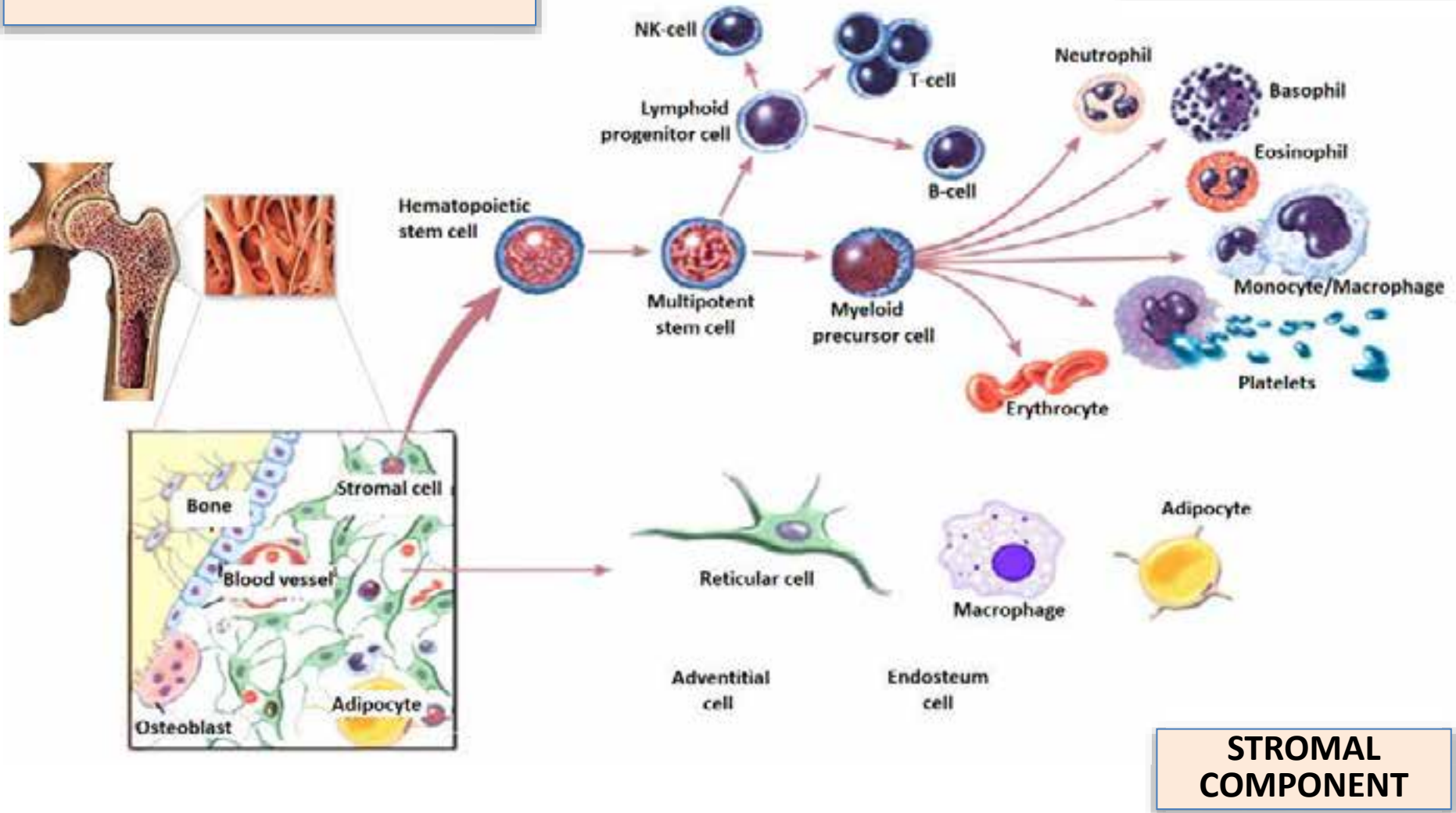
- postcapillary venules with high endothelium*

RED BONE MARROW

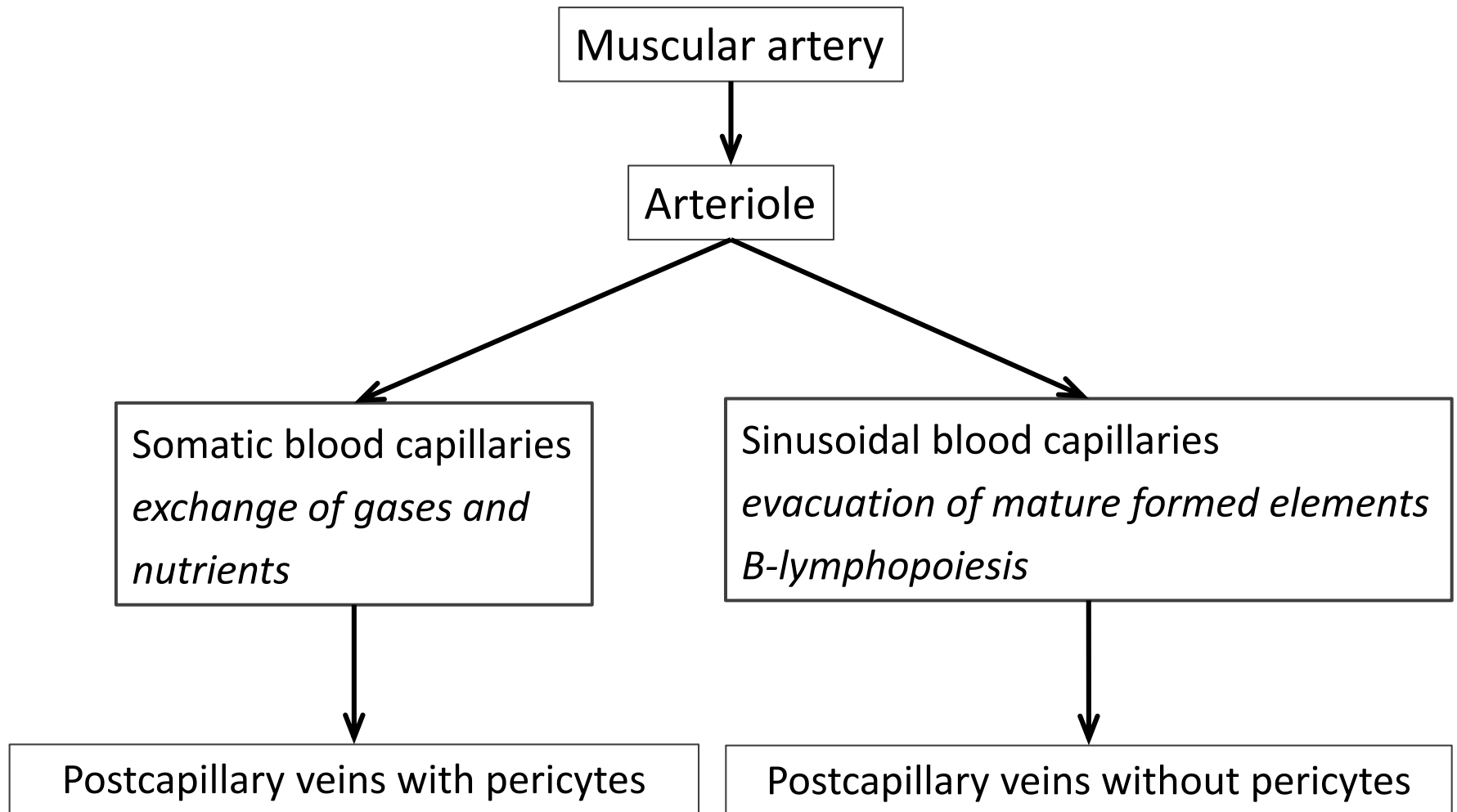
- formation of blood cells
- antigen-independent differentiation of B-lymphocytes

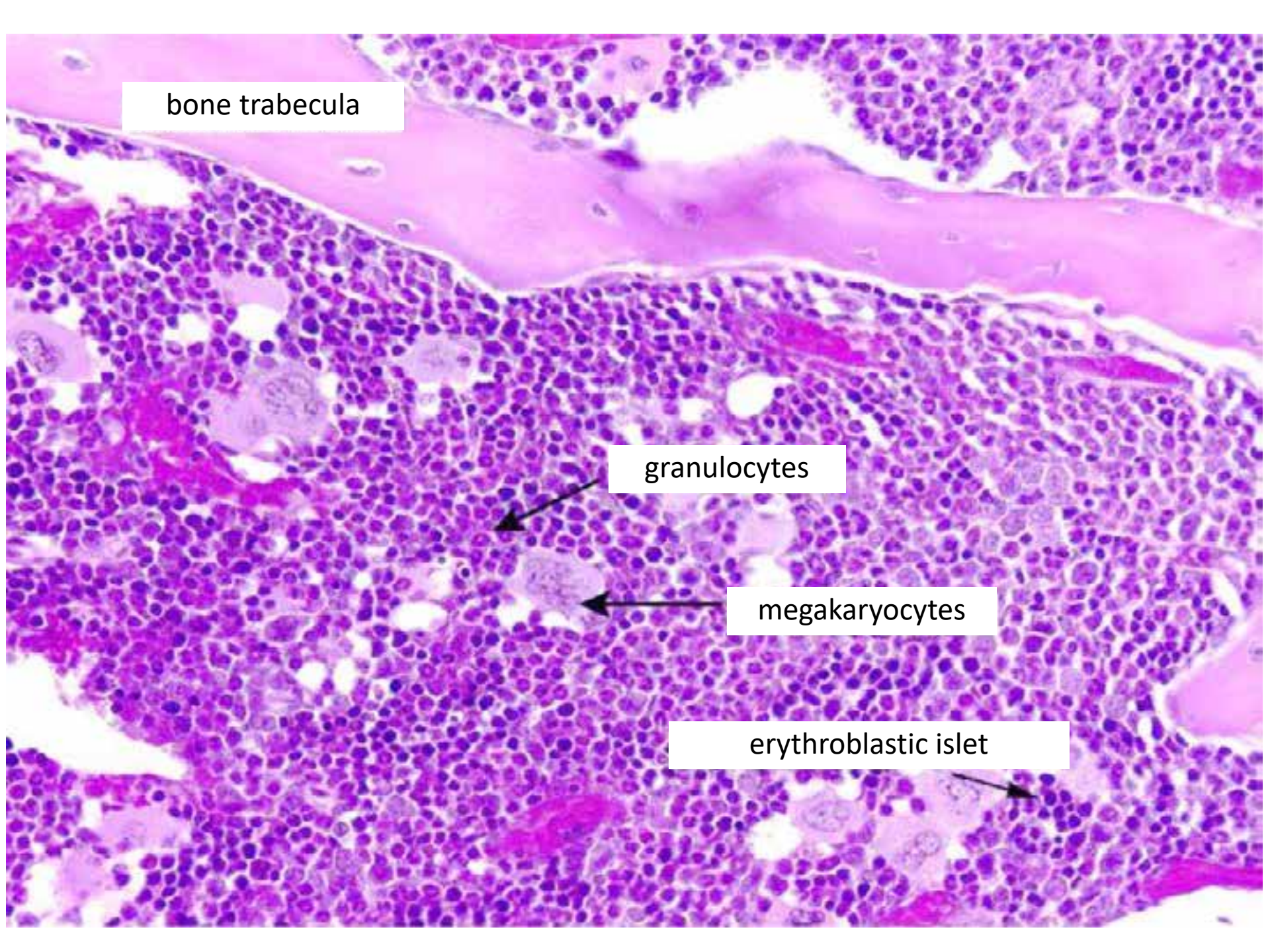
VASCULAR COMPONENT

HEMATOPOIETIC COMPONENT



VASCULAR SYSTEM OF THE RED BONE MARROW





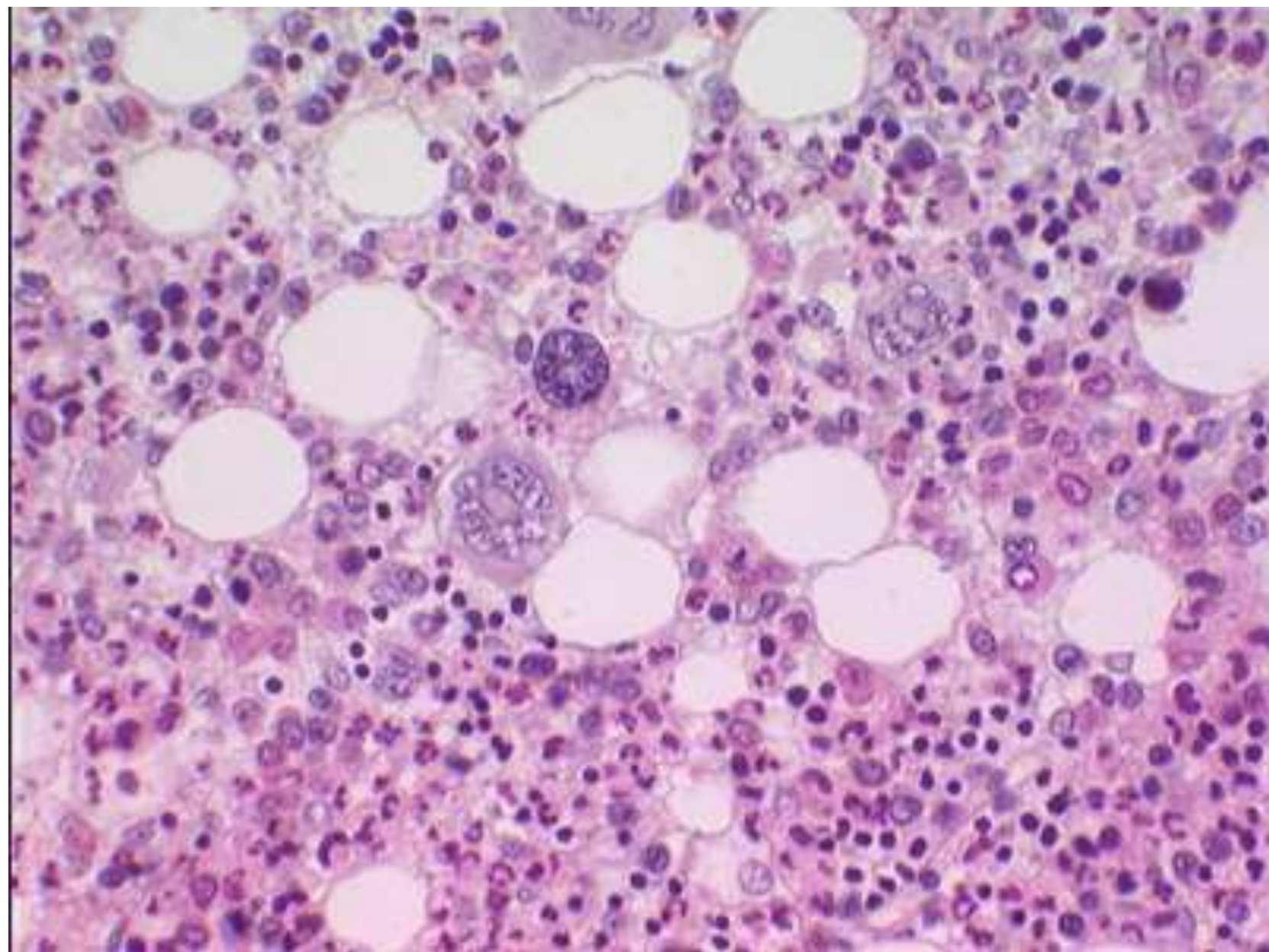
bone trabecula

This histological image shows a section of bone marrow. The bone trabeculae are visible as pink, irregular structures. The marrow is densely populated with various cells, including granulocytes, megakaryocytes, and an erythroblastic islet. Arrows point from the labels to the corresponding structures in the image.

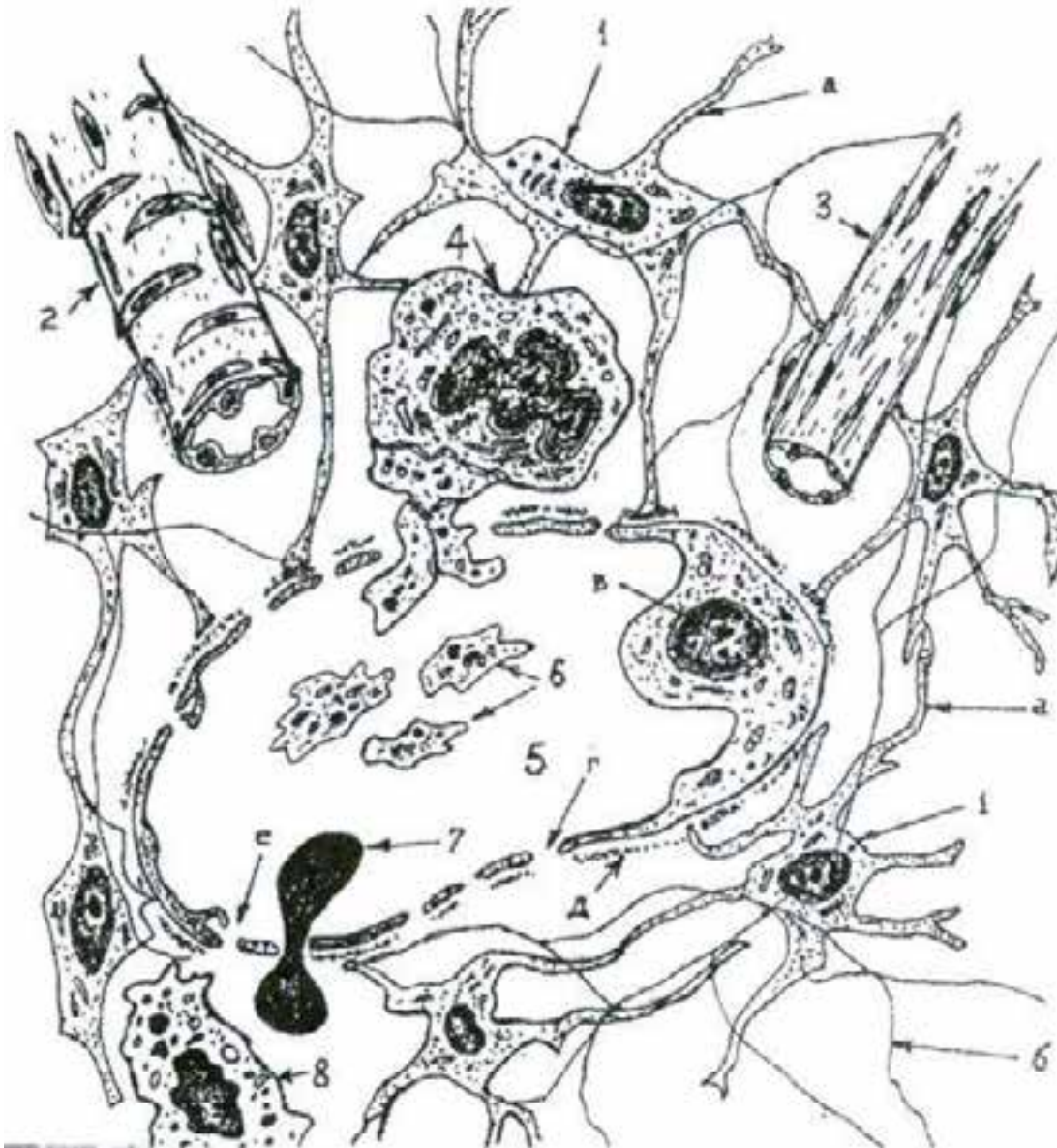
granulocytes

megakaryocytes

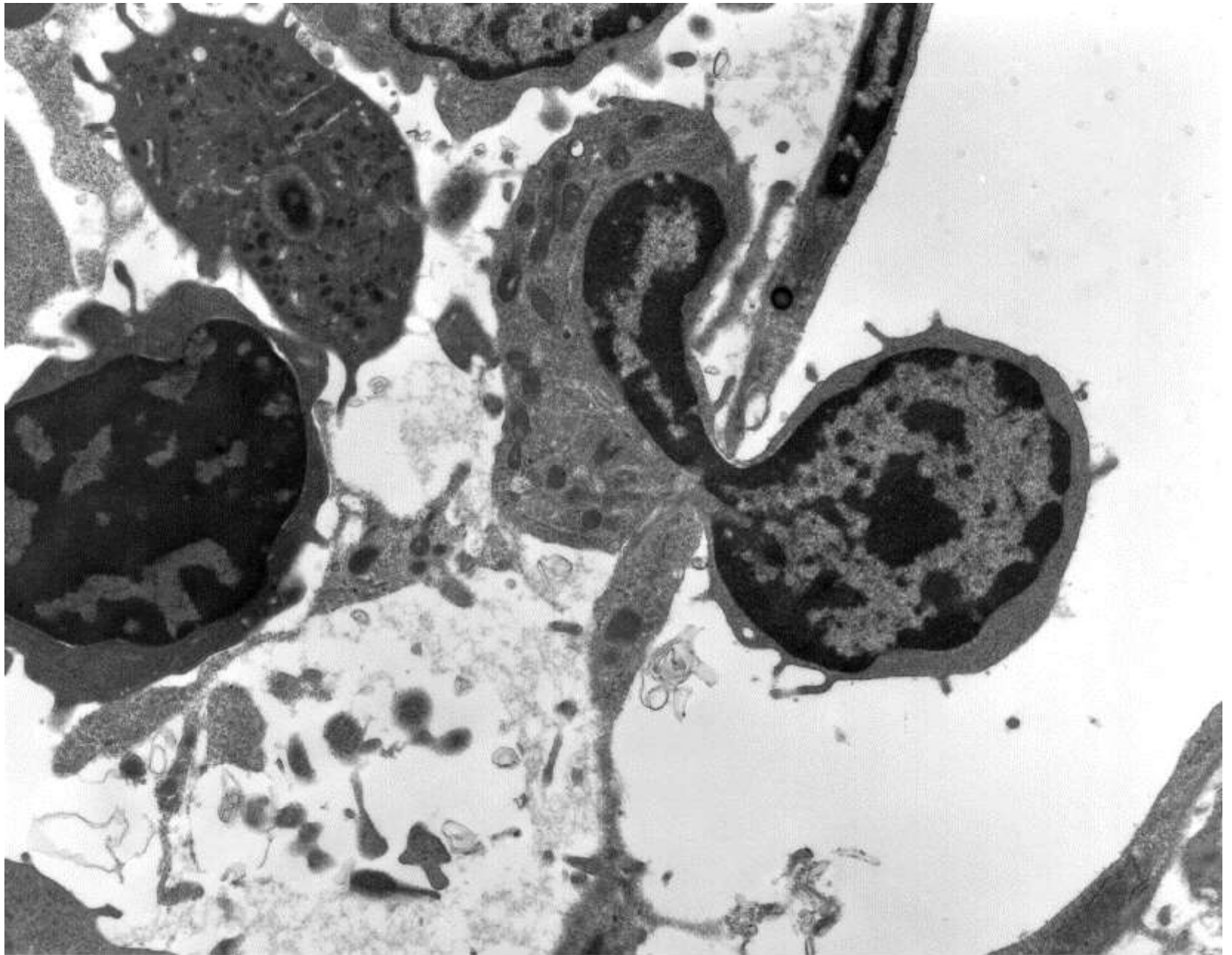
erythroblastic islet



BLOOD-TISSUE BARRIER OF THE RED BONE MARROW



- 1- reticular cells
(a- processes,
6- reticular fibers)
- 2- precapillary arteriole,
- 3- postcapillary venule,
- 4- megakaryocyte
- 5- sinusoidal capillary
(b- endothelial cell nucleus,
r- migration pores,
d- discontinuous
basement membrane)
- 6- blood platelets
- 7- erythrocyte
- 8- macrophage

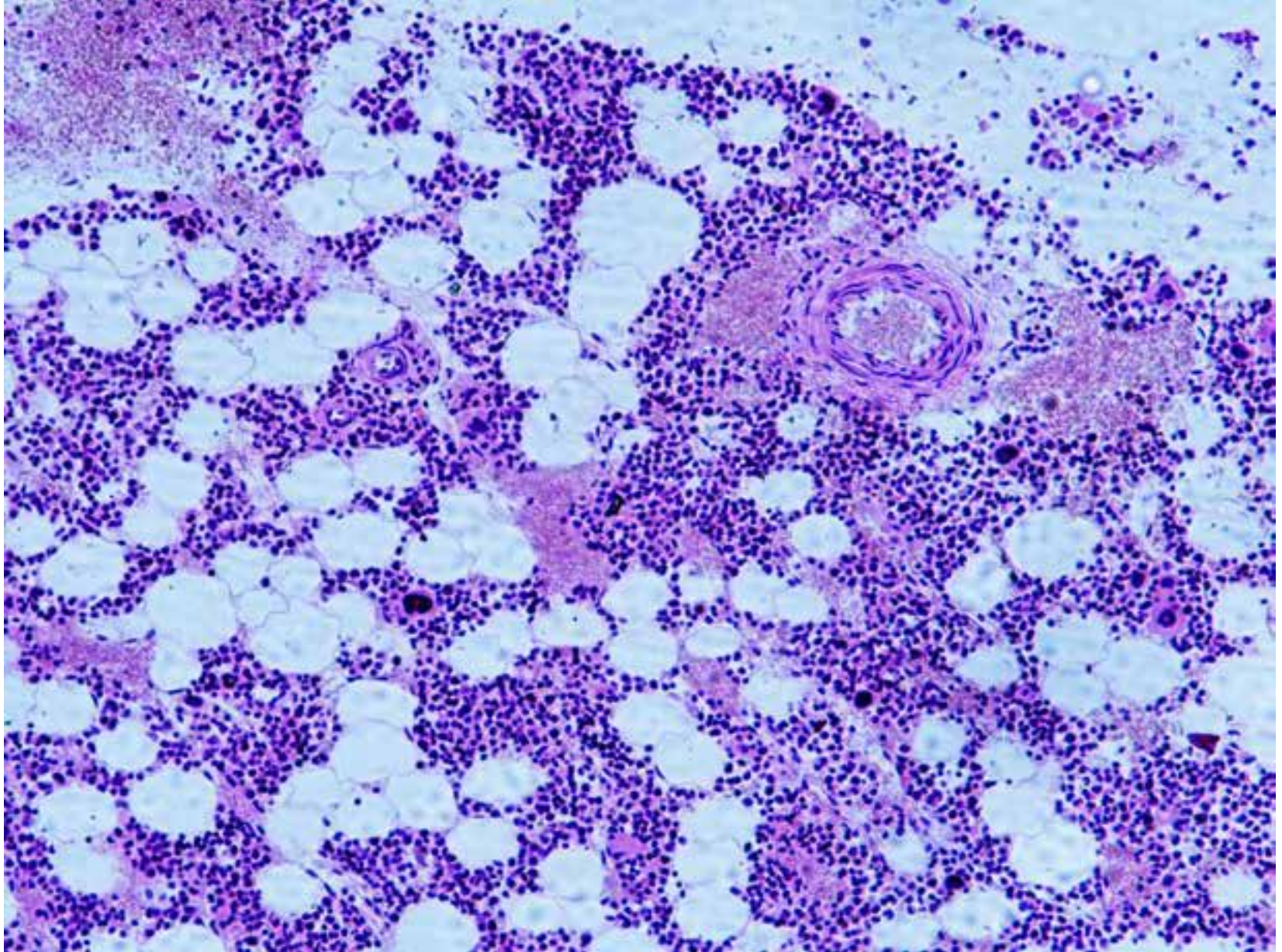


3 µm

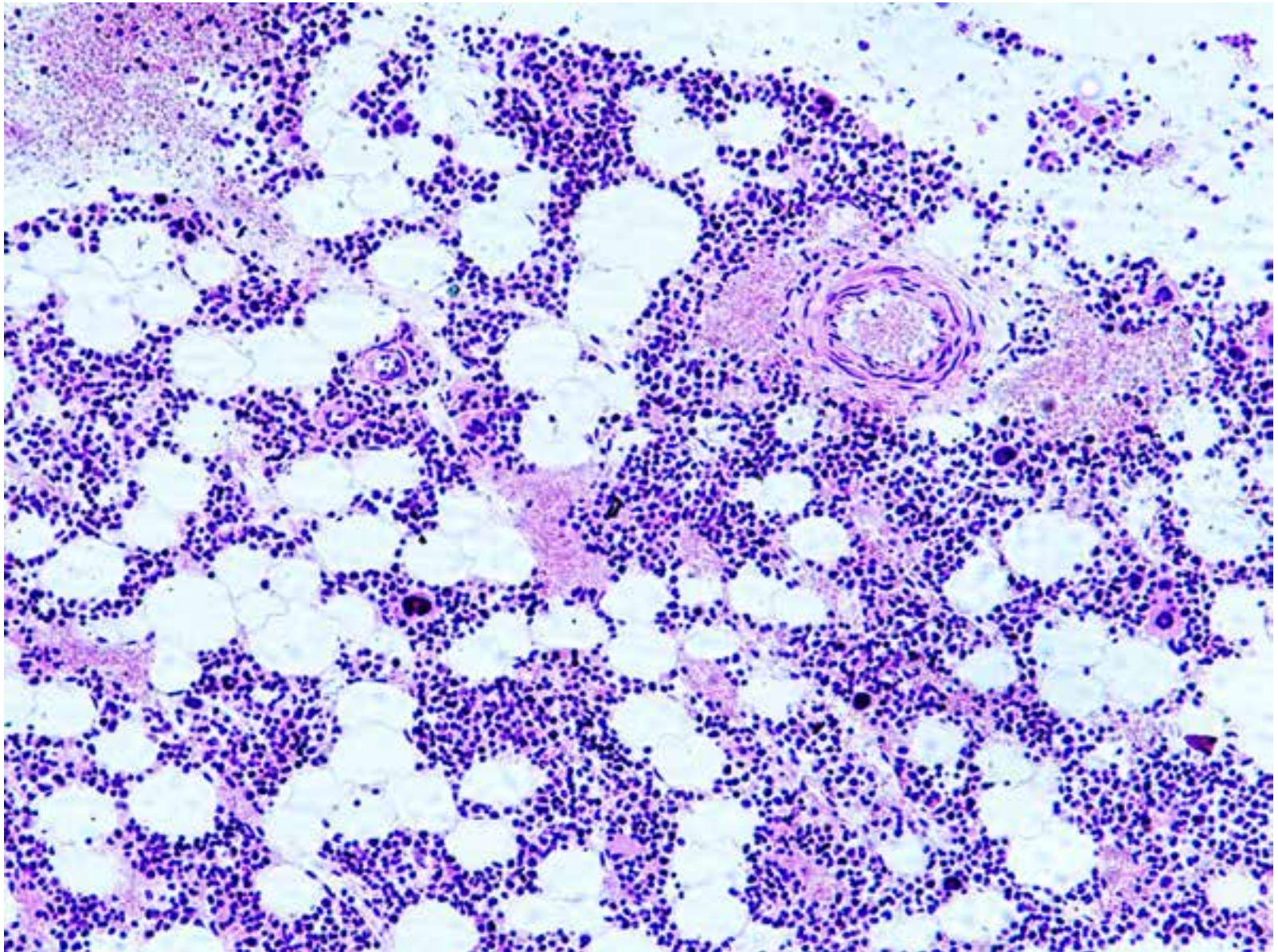
Knoesp/marrow#0000-5

1/7/0 KEM

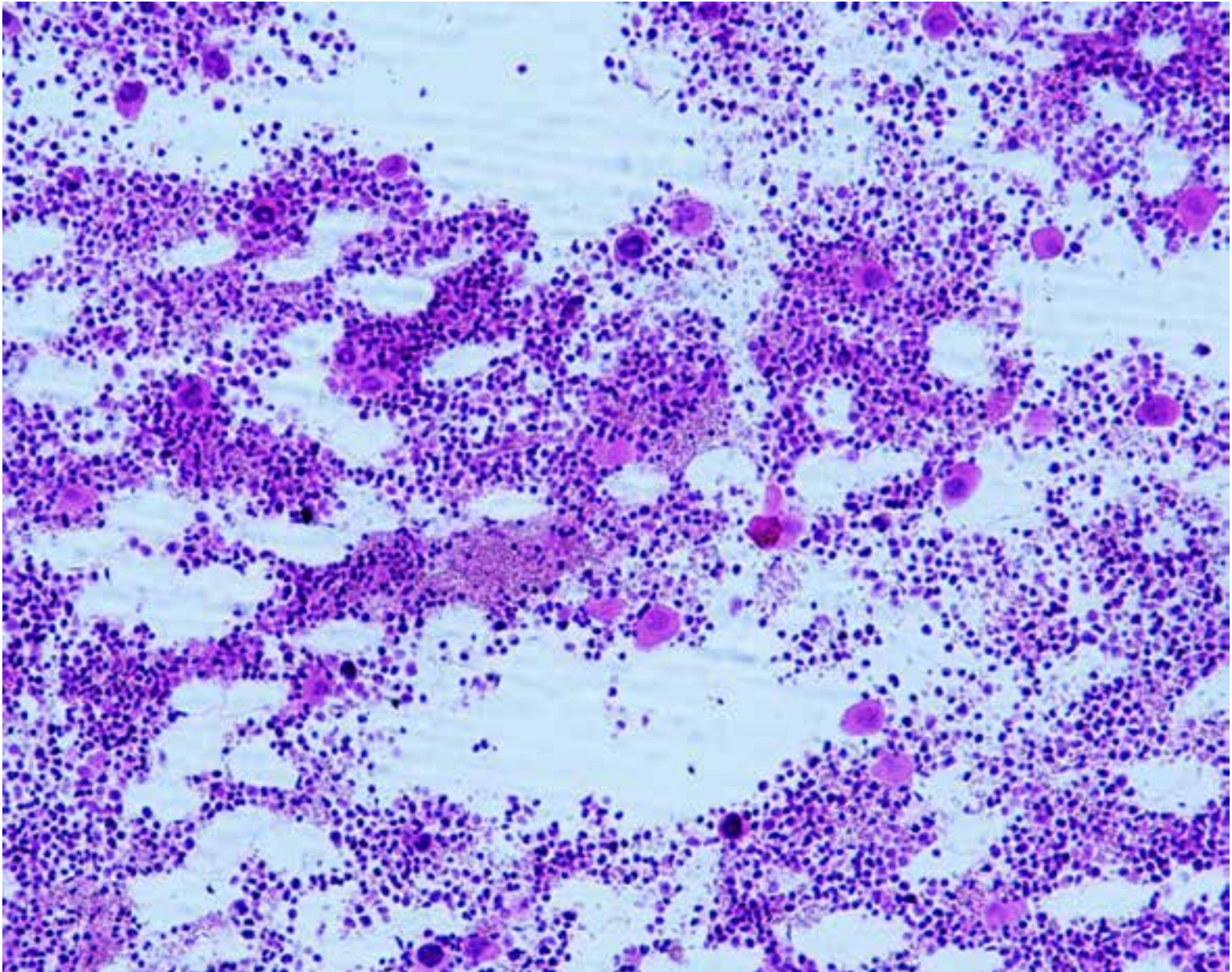
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



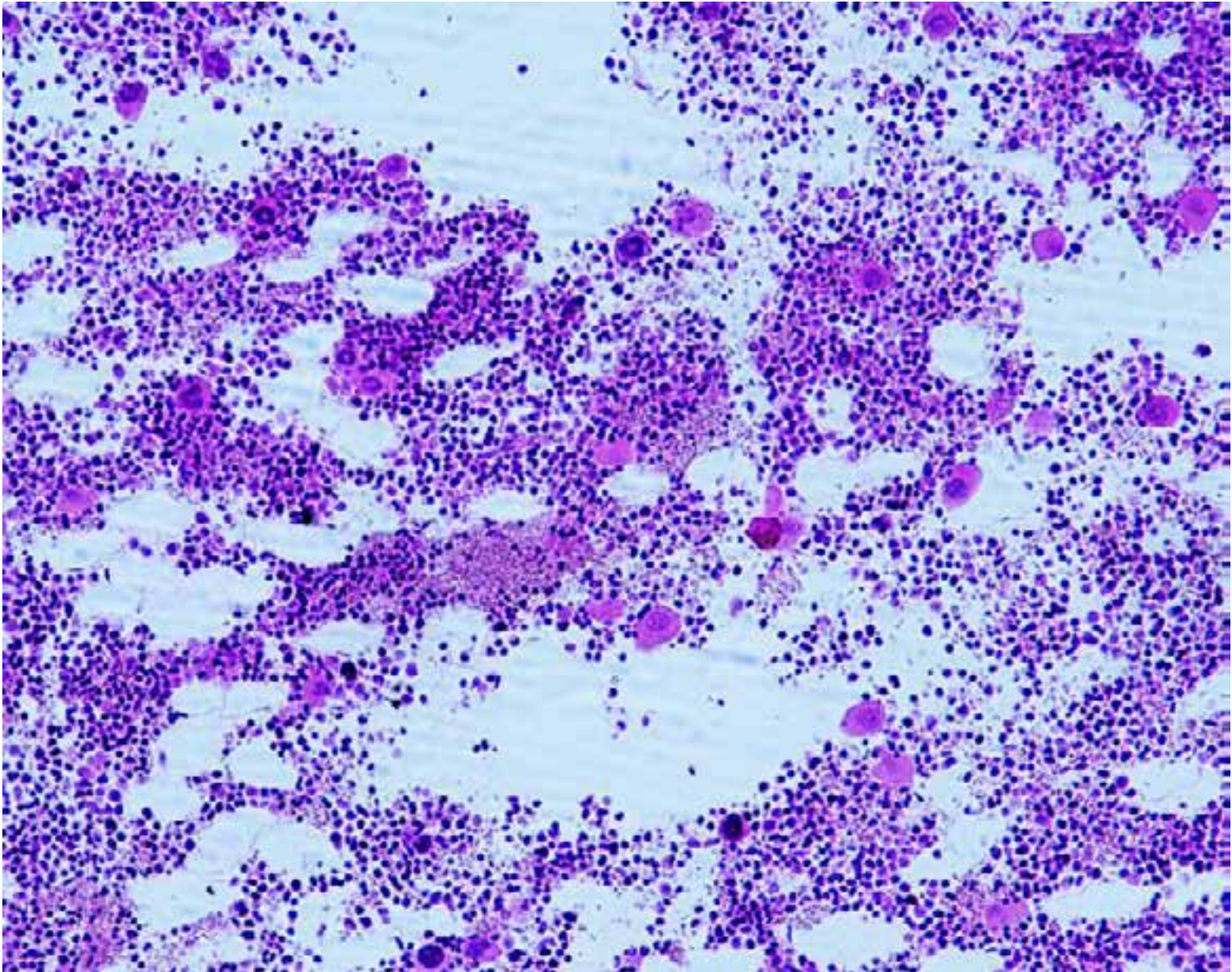
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



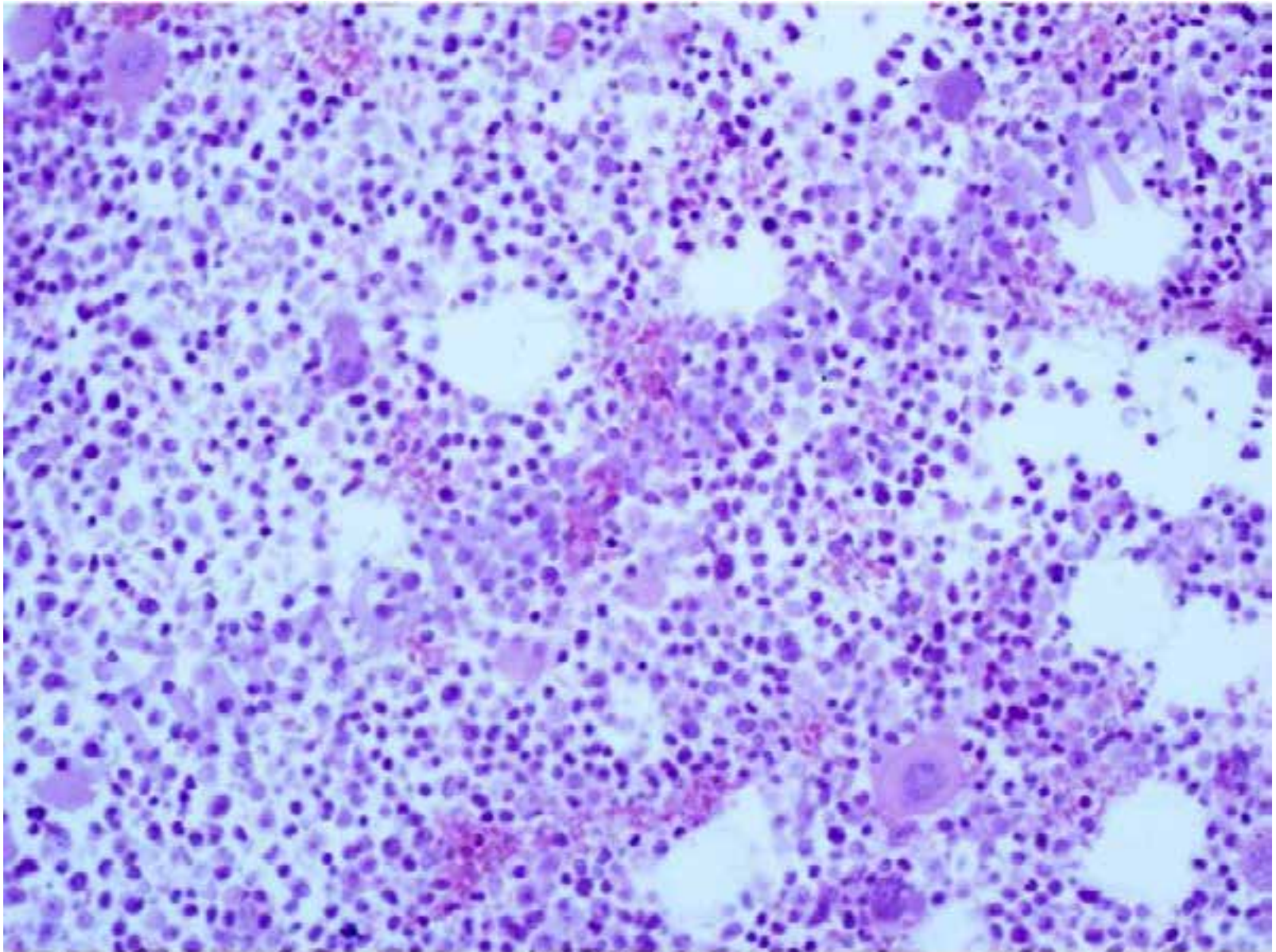
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



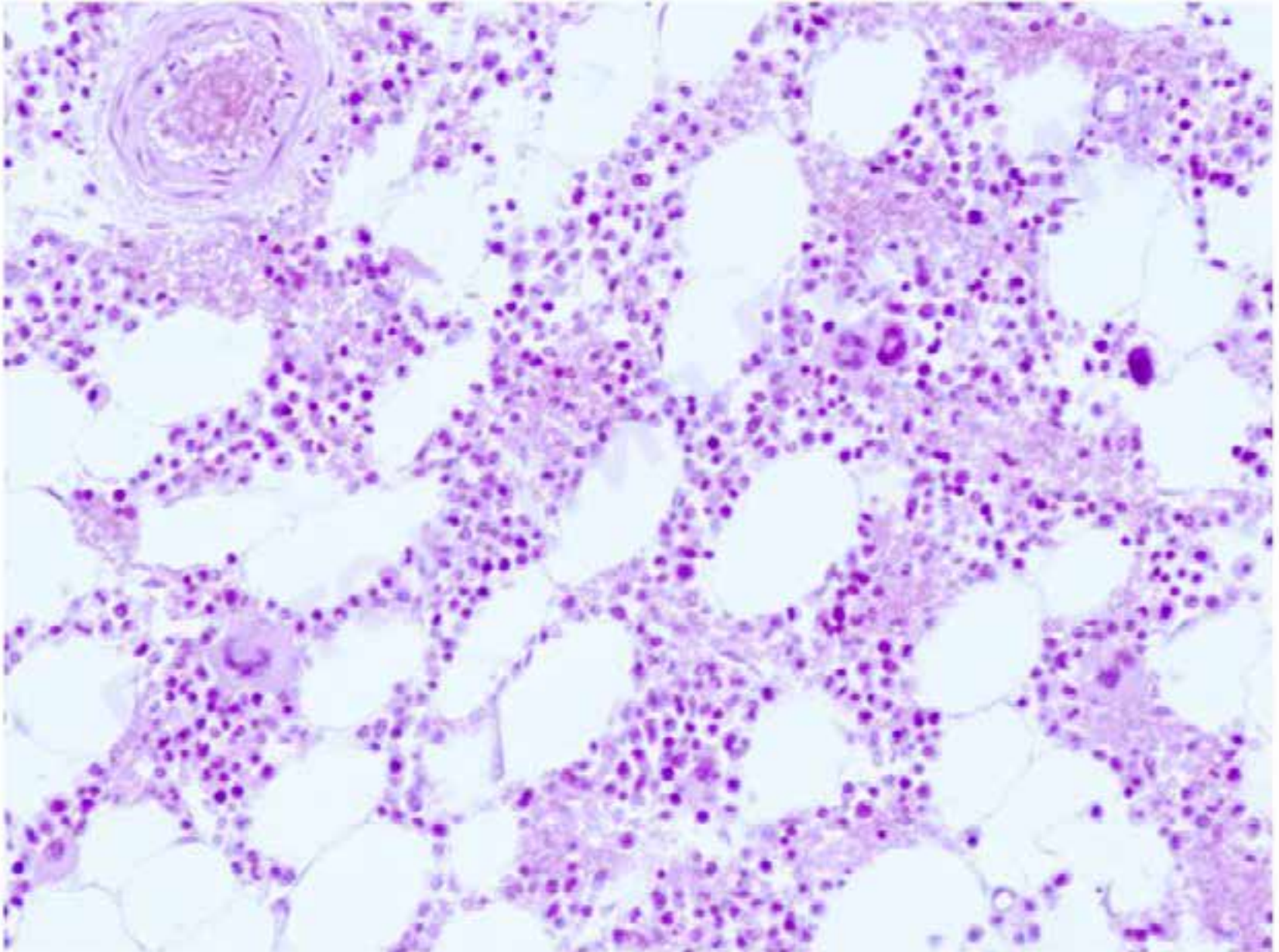
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



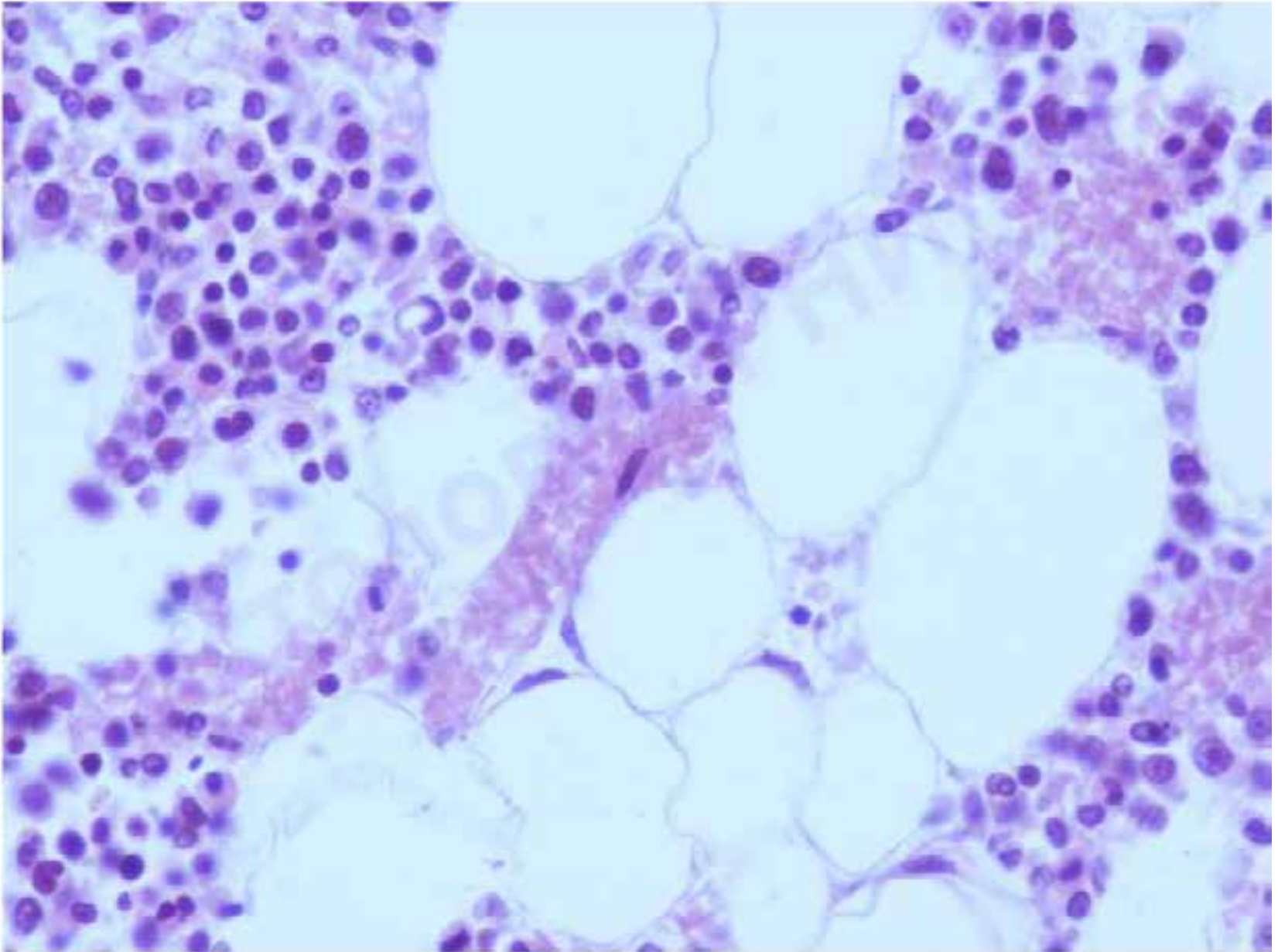
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



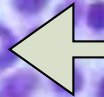
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



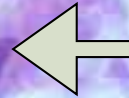
Sinusoidal capillary



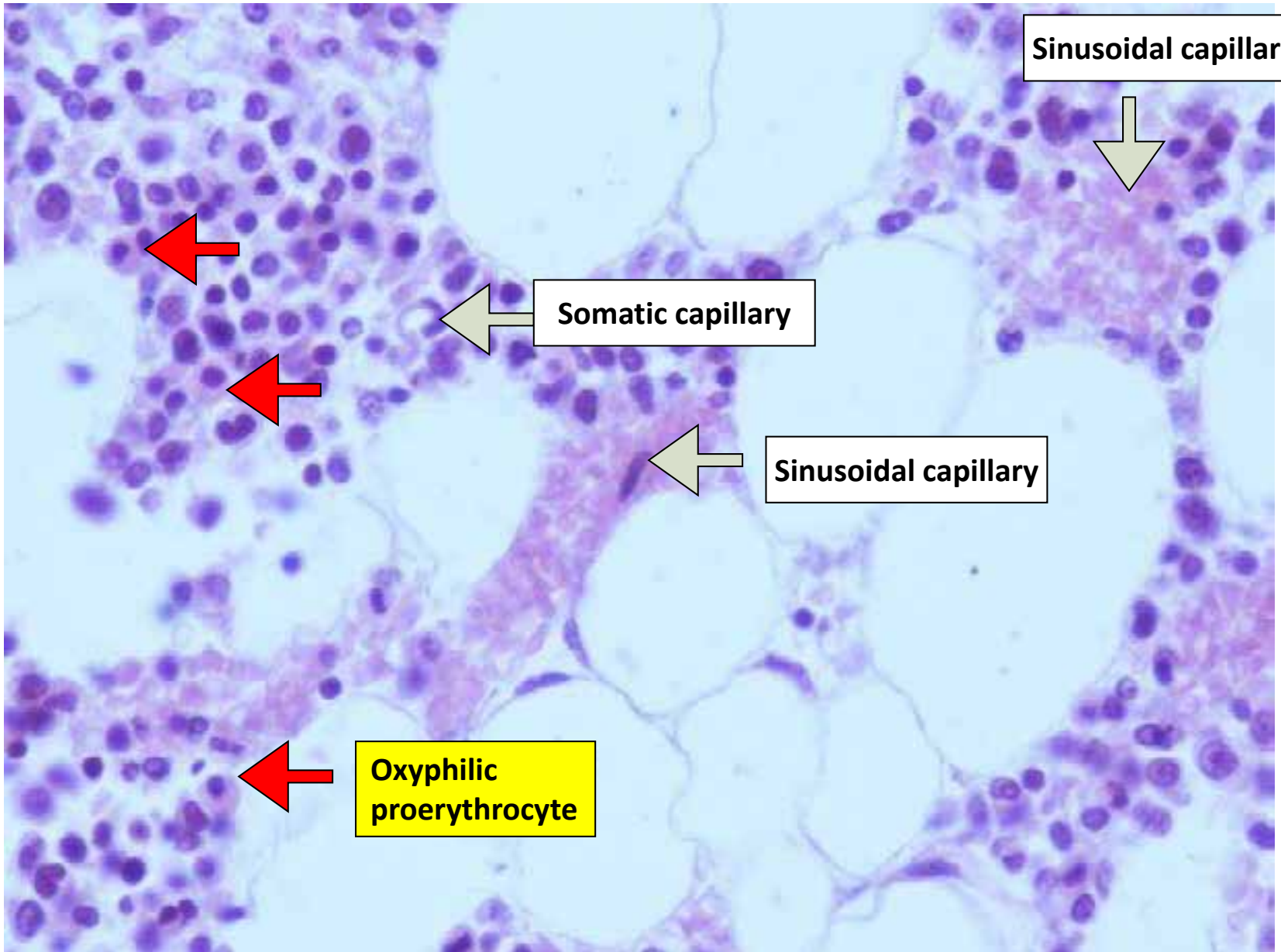
Somatic capillary



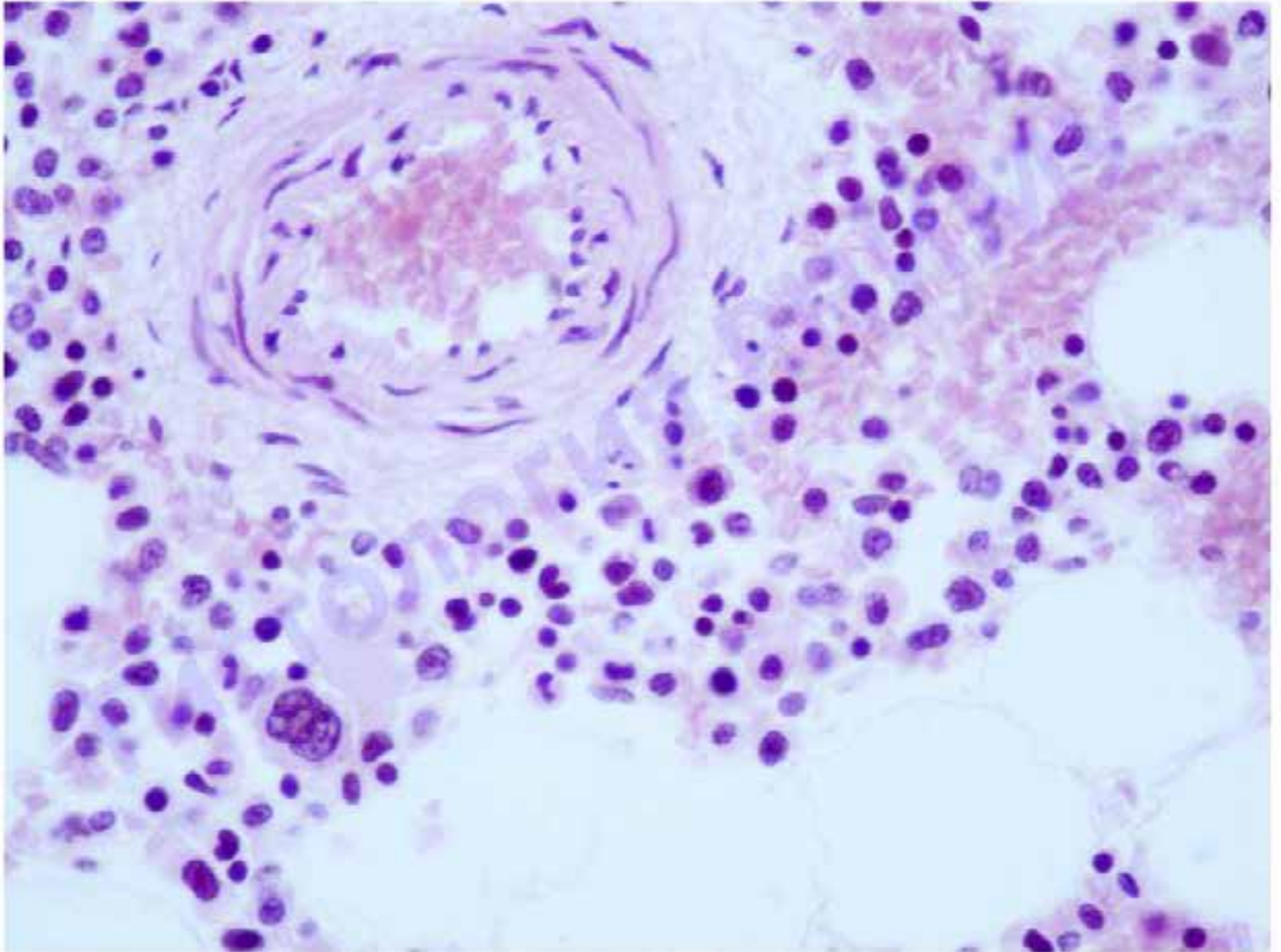
Sinusoidal capillary



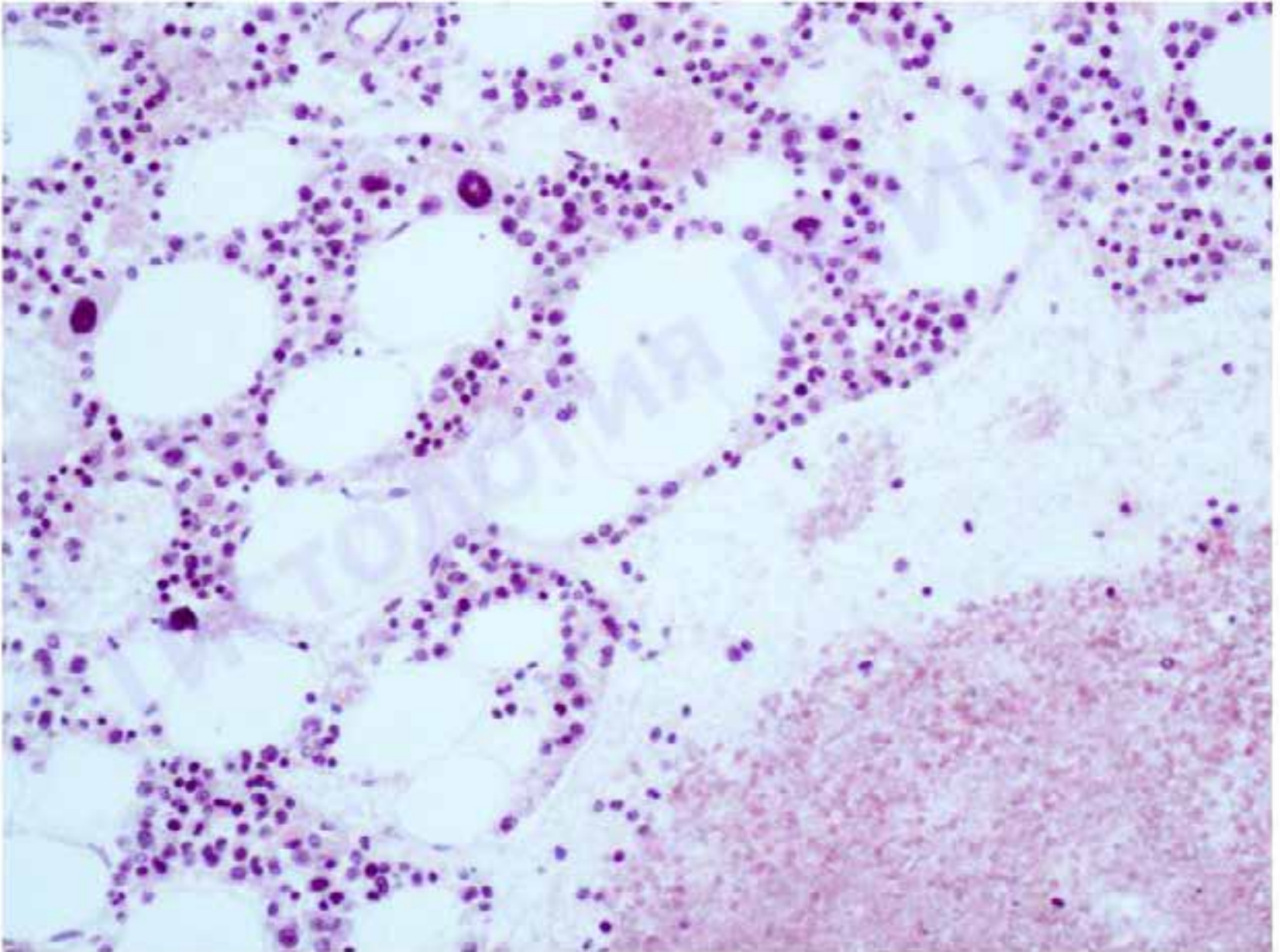
**Oxyphilic
proerythrocyte**



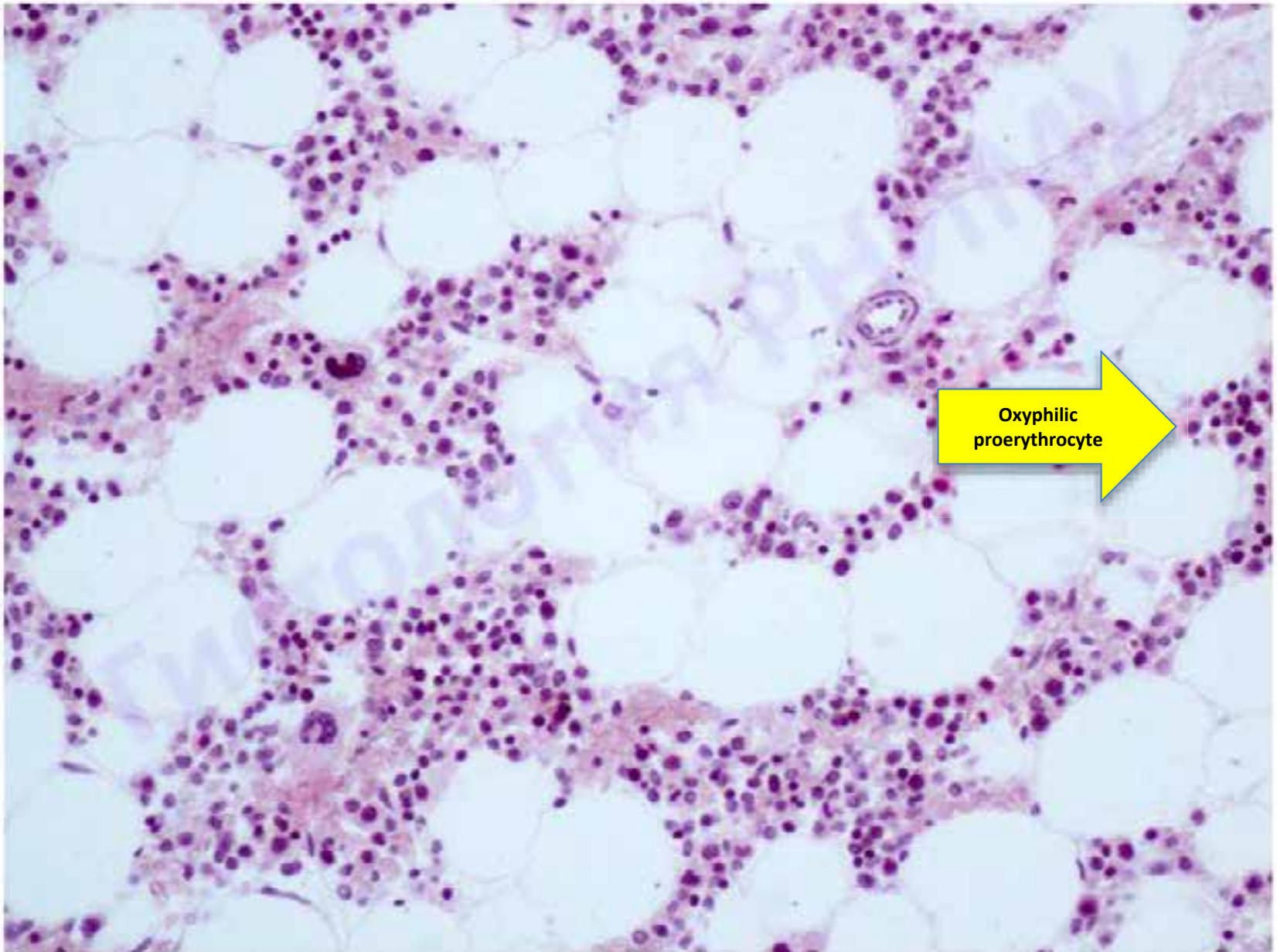
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



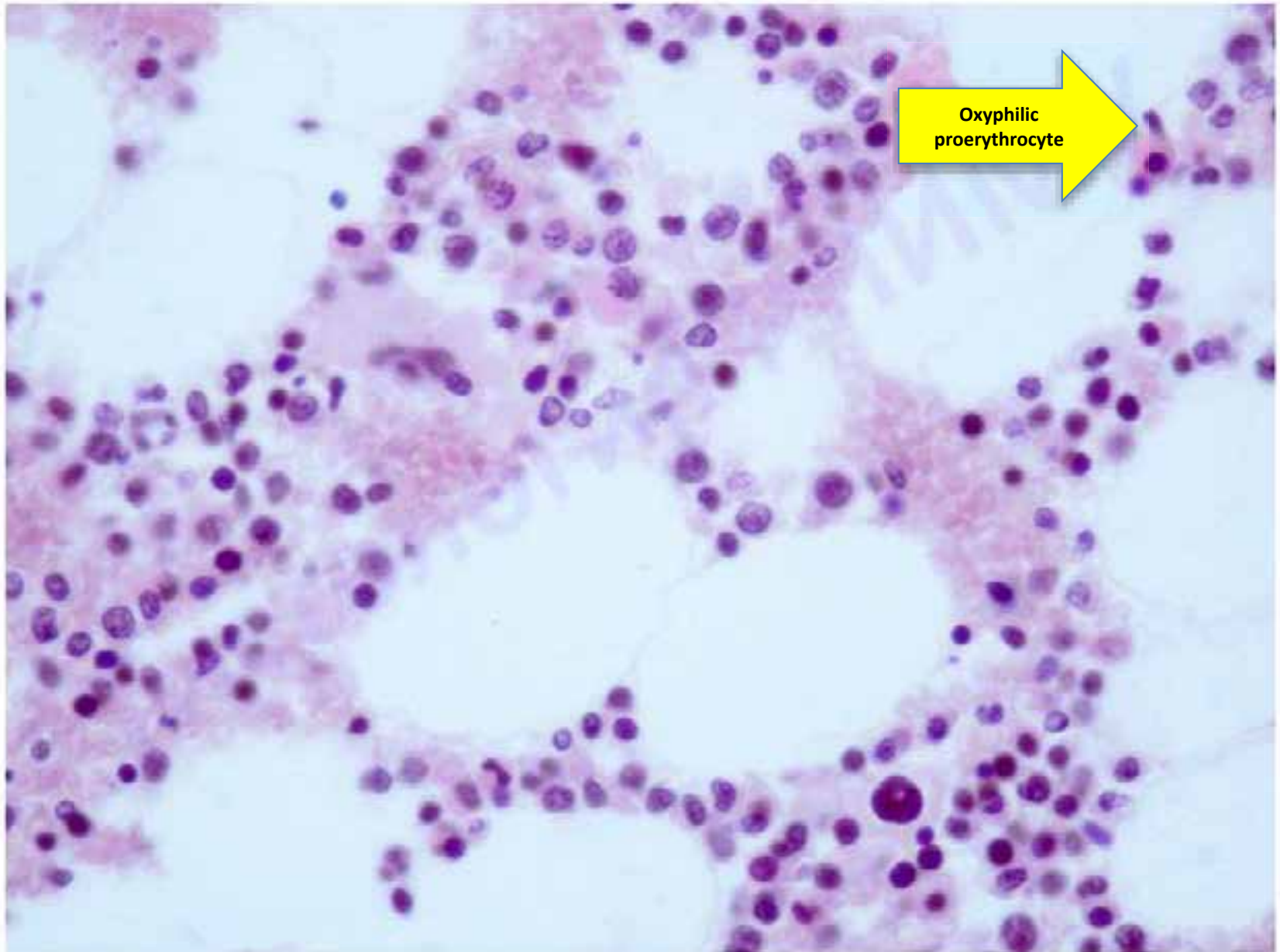
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



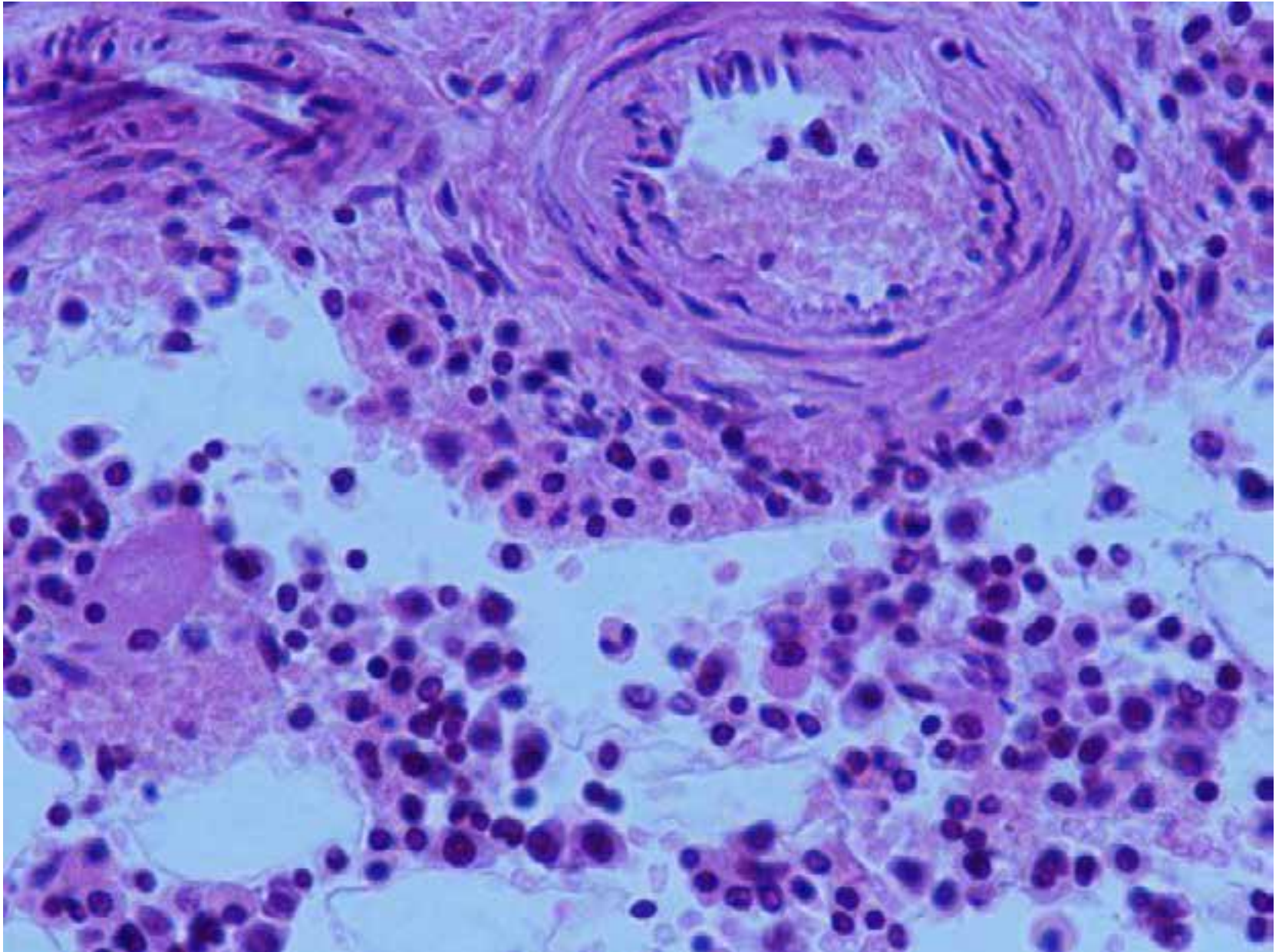
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



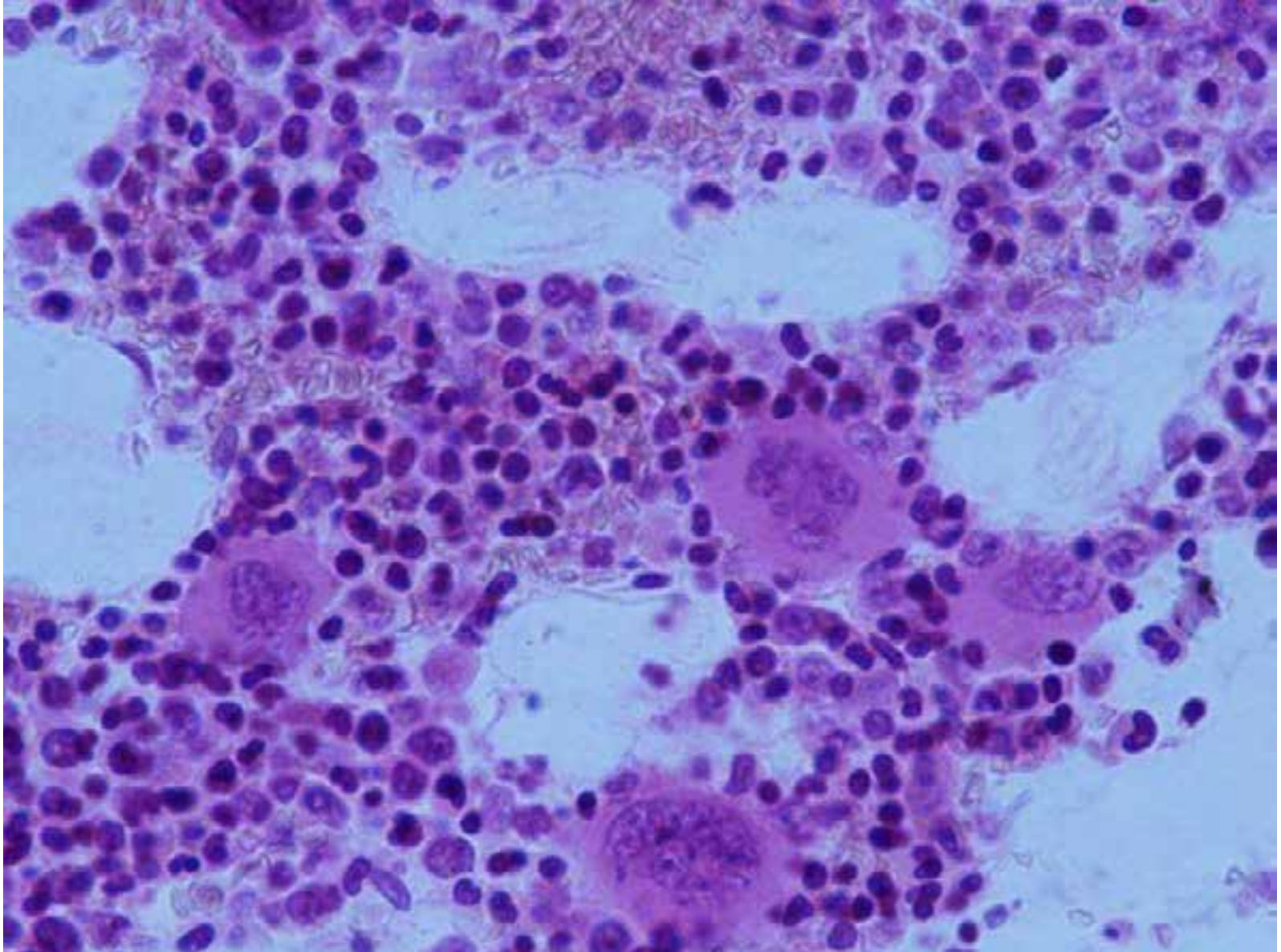
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



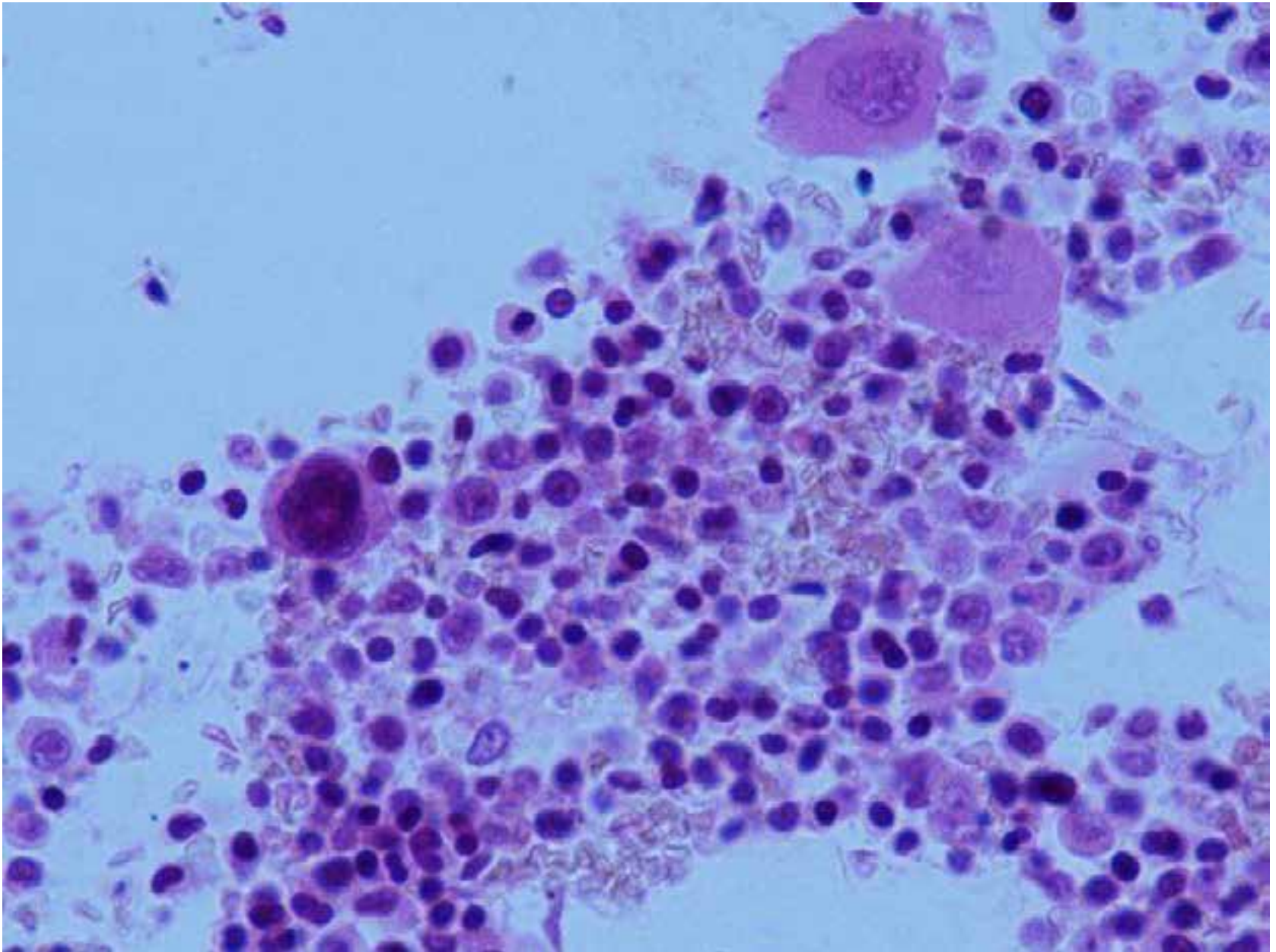
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



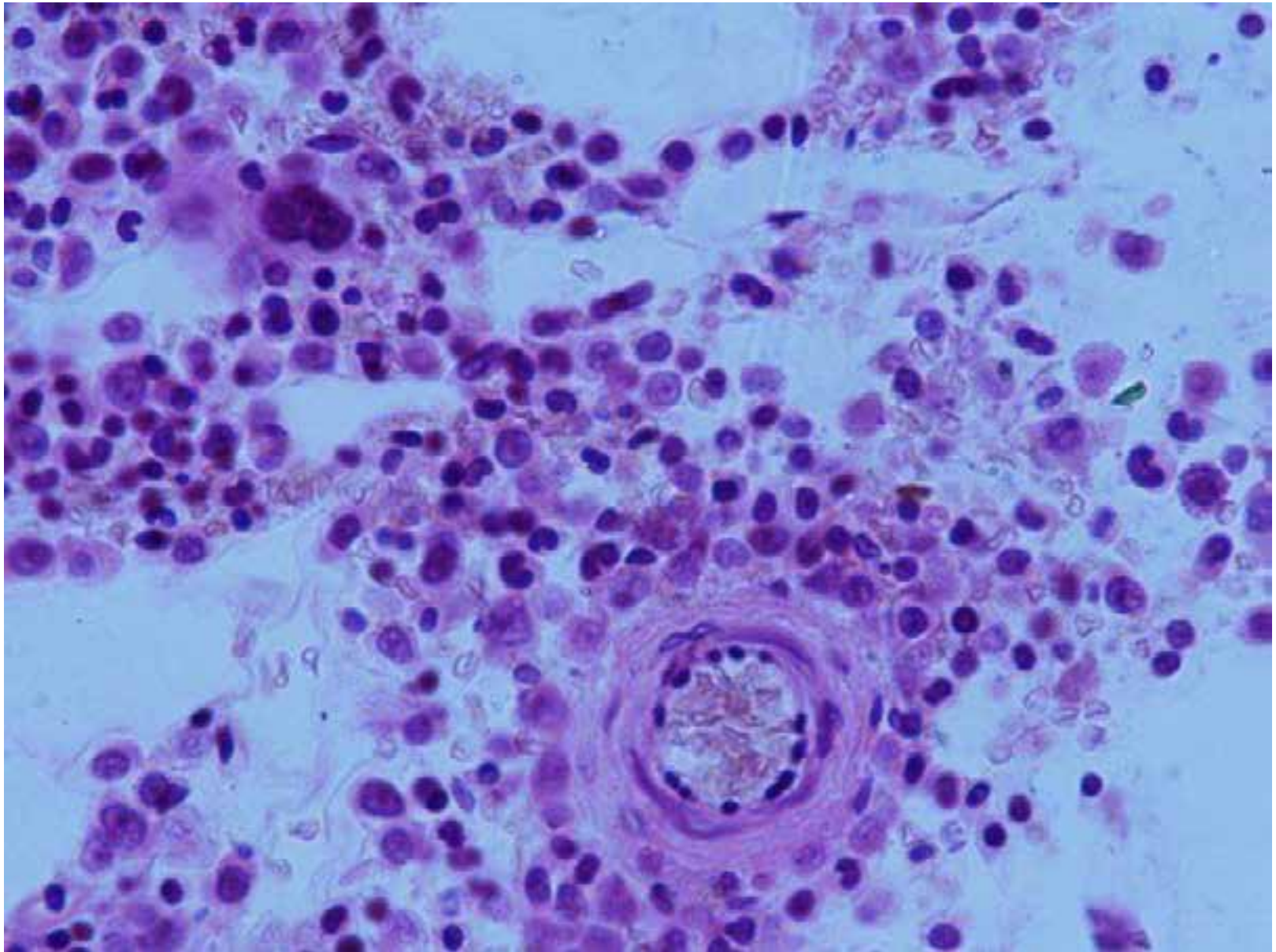
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



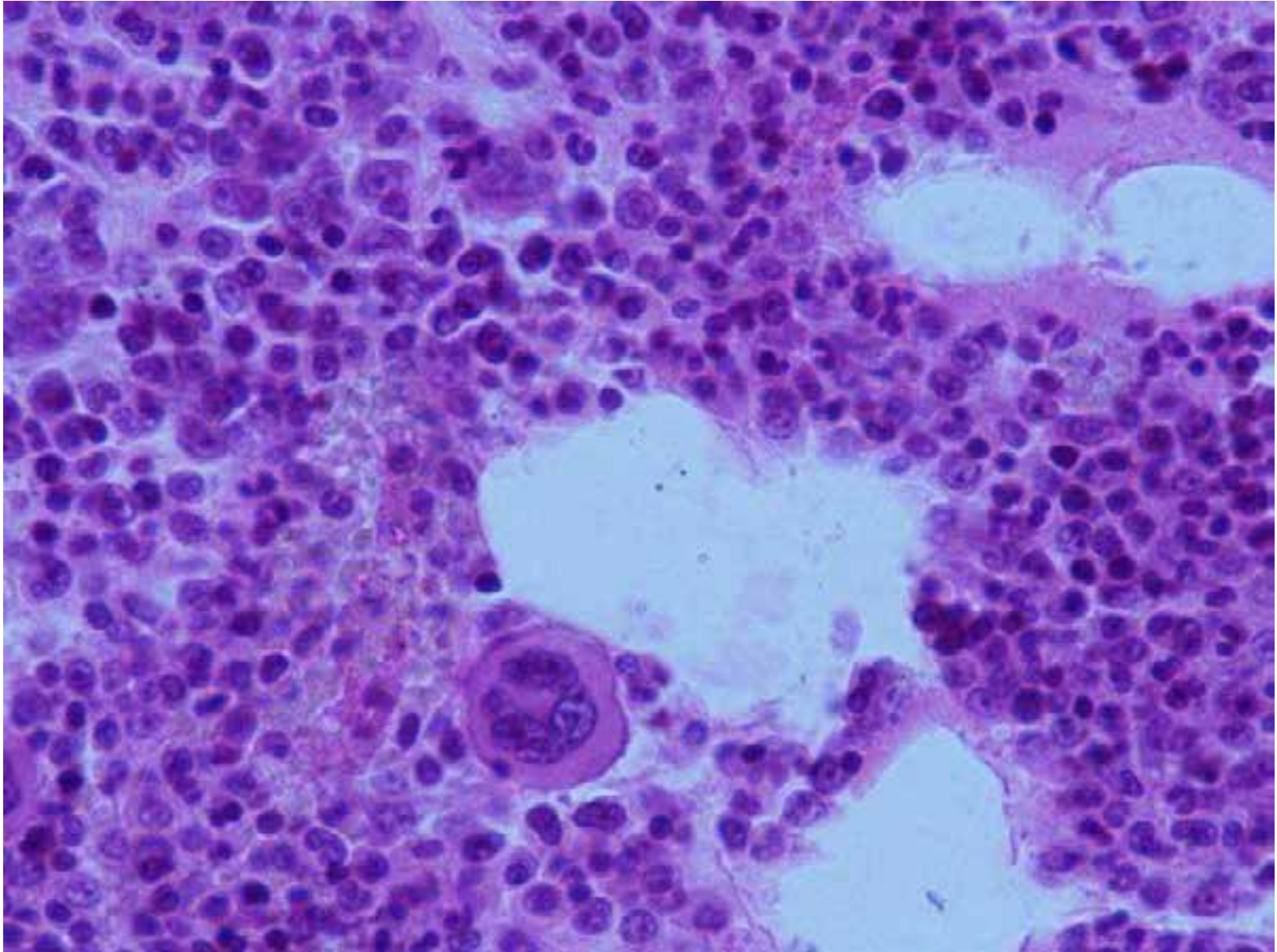
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



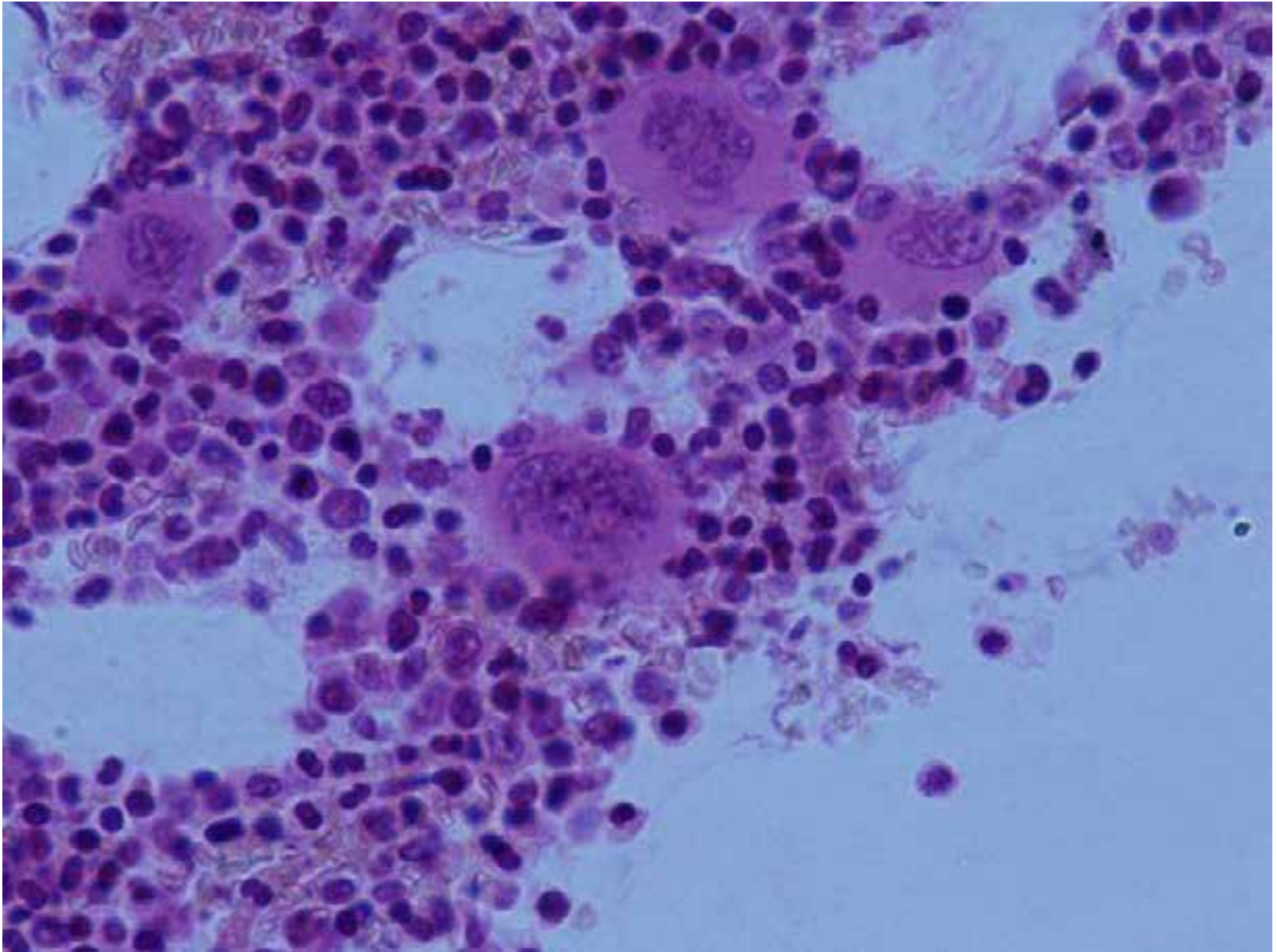
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



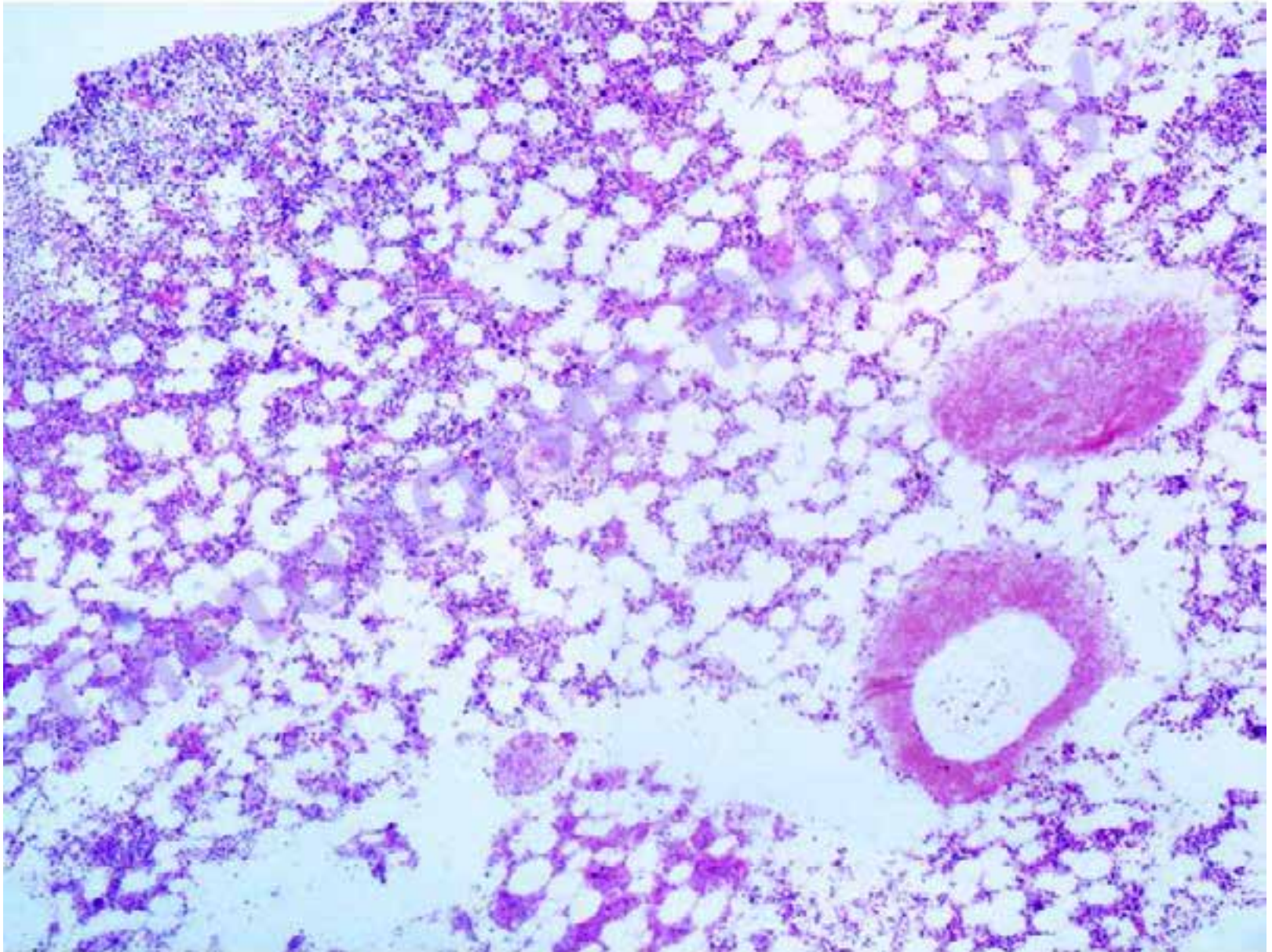
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



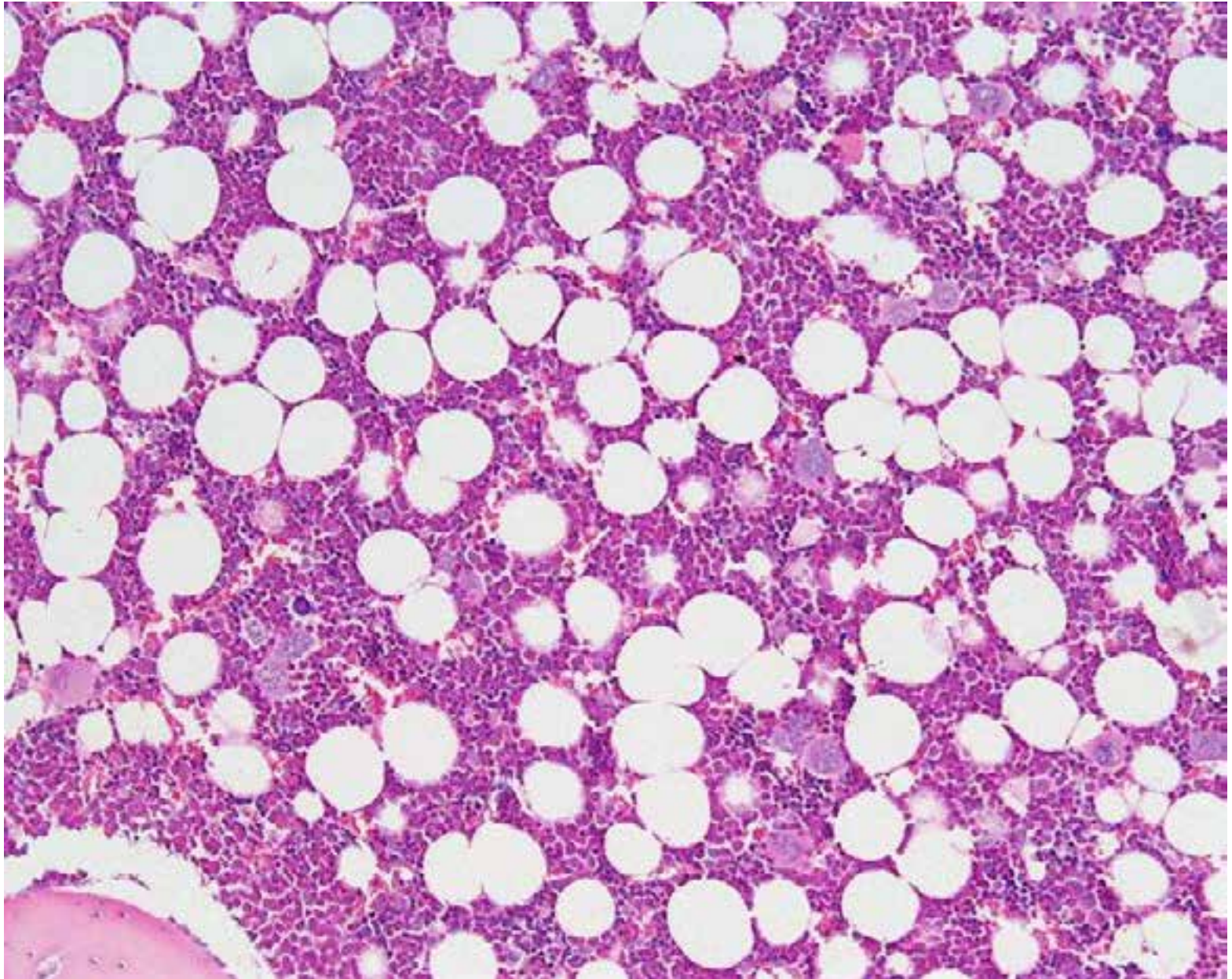
*Slide №115. Section of the red bone marrow
Hematoxylin-eosin staining*



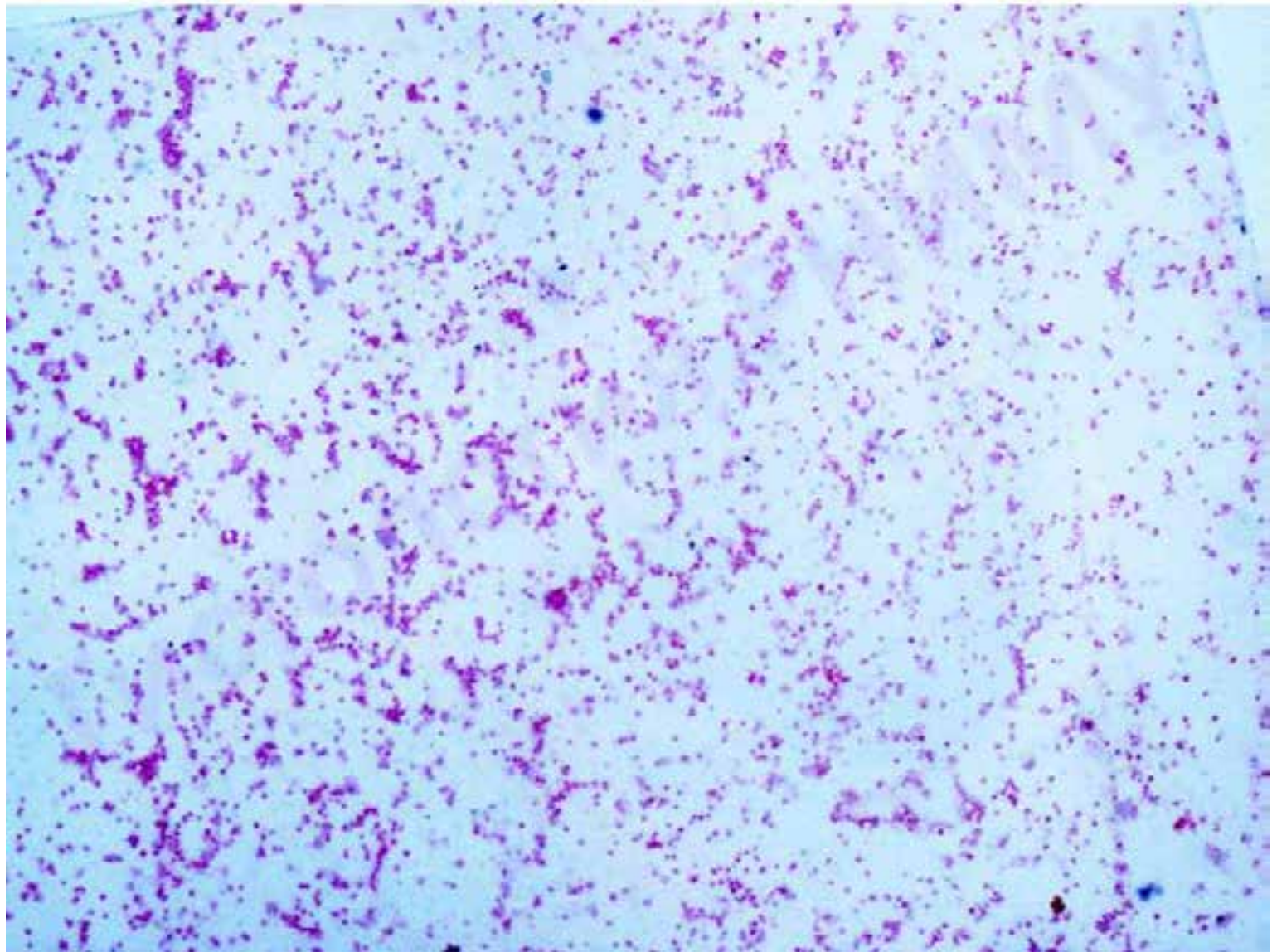
CONVERSION OF RED BONE MARROW INTO YELLOW



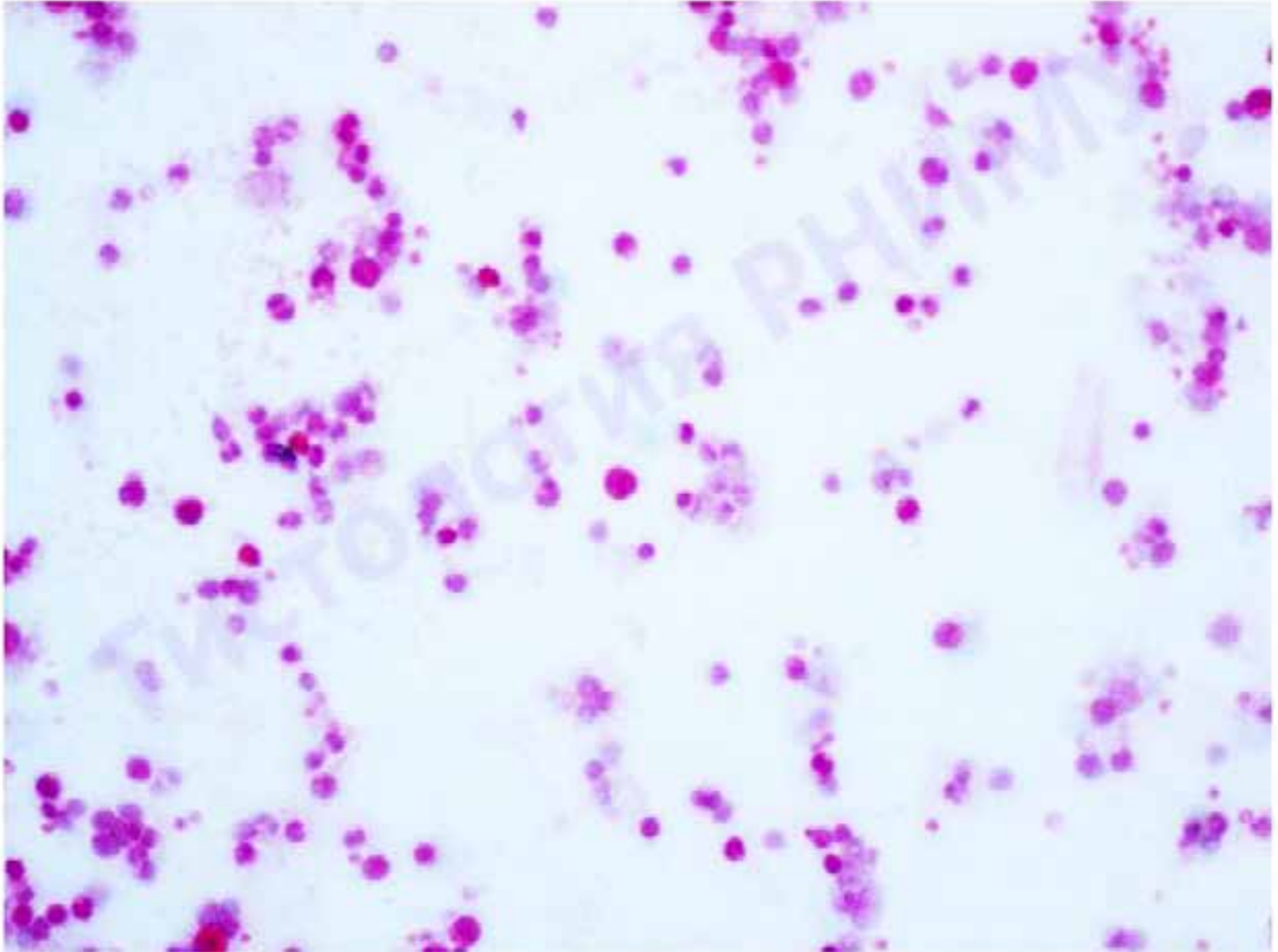
CONVERSION OF RED BONE MARROW INTO YELLOW



*Slide №116. Smear of the red bone marrow
staining Azur II – eosin*



*Slide №116. Smear of the red bone marrow
staining Azur II – eosin*



CENTRAL ORGANS OF HEMOPOIESIS

Antigen-independent differentiation and proliferation of T and B cells
(exposure to antigens is excluded)

- 1 — red bone marrow (*in the cancellous portions of the flat bones and the epiphyses of the long bones; in children and adolescents also in the diaphyses*)
- 2 — thymus

PERIPHERAL ORGANS OF HEMOPOIESIS

Antigen-dependent differentiation and proliferation of T and B cells
(is possible only after stimulation with an antigen)

- 1 — mucosa-associated lymphoid tissue (*including the tonsils, the appendix, Peyer's patches, BALT etc.*)
- 2 — lymph nodes
- 3 — spleen

DEVELOPMENT OF THE THYMUS

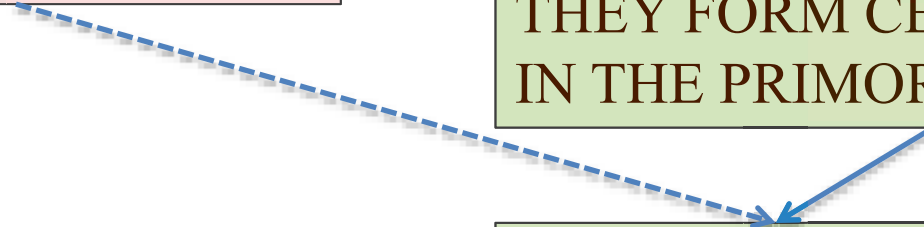
PHARYNGEAL GUT
EPITHELIUM



EPITHELIAL CORDS
ANTERIOR TO THE GUT



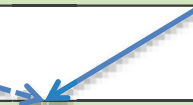
EPITHELIAL STROMA
OF THE THYMUS



T CELL PRECURSORS ARRIVE
FROM THE RED BONE MARROW



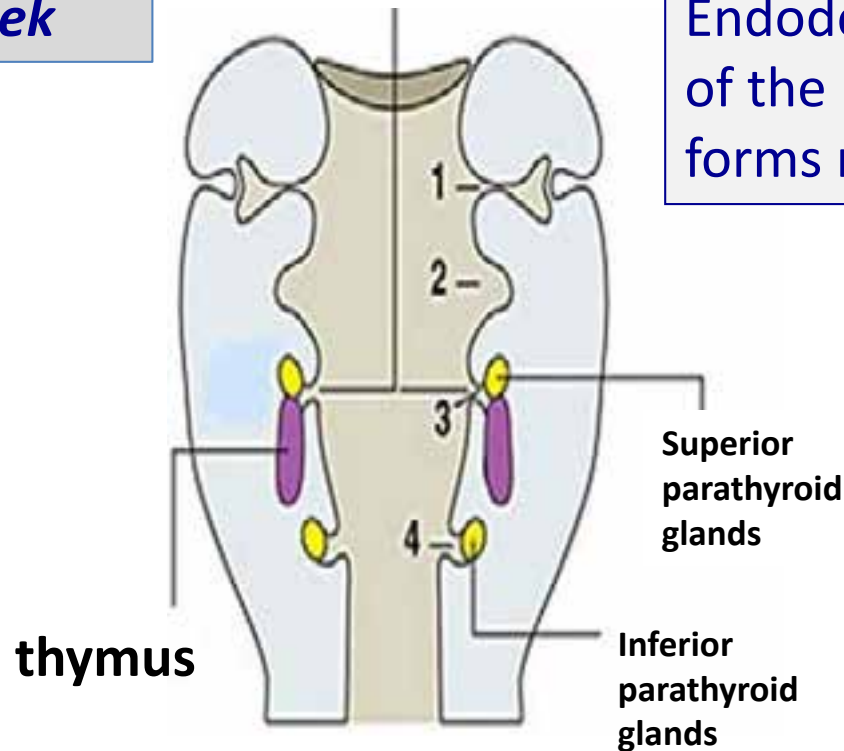
THEY FORM CELL COLONIES
IN THE PRIMORDIAL THYMUS



**LYMPHOID TISSUE
OF THE THYMUS**

DEVELOPMENT OF THE THYMUS

4th week



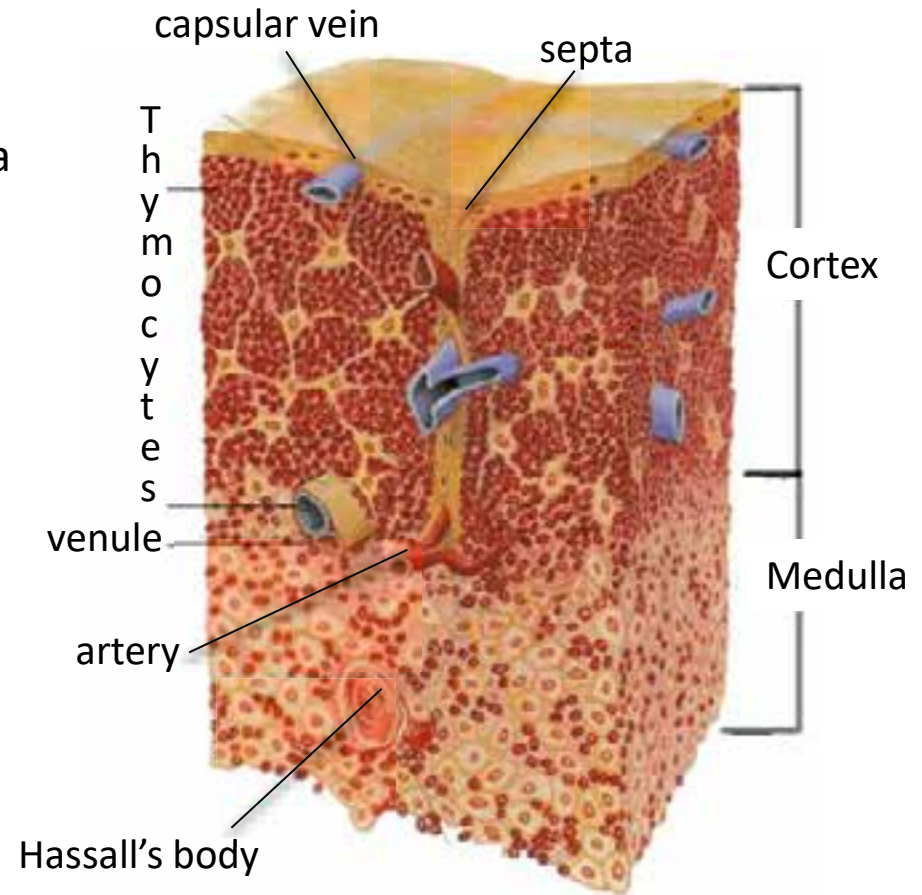
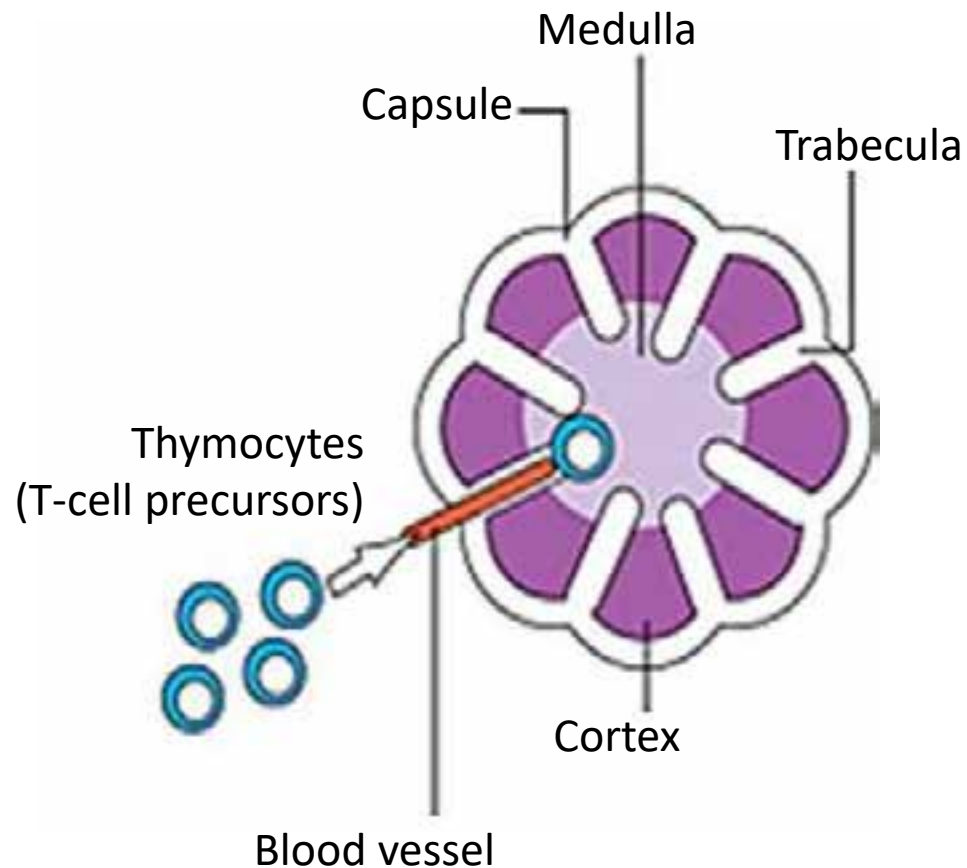
Endodermal epithelium of the III pharyngeal pouch forms multiple tubules

7th week

Epithelial tubular cords become submerged by the underlying mesenchyme

14th week

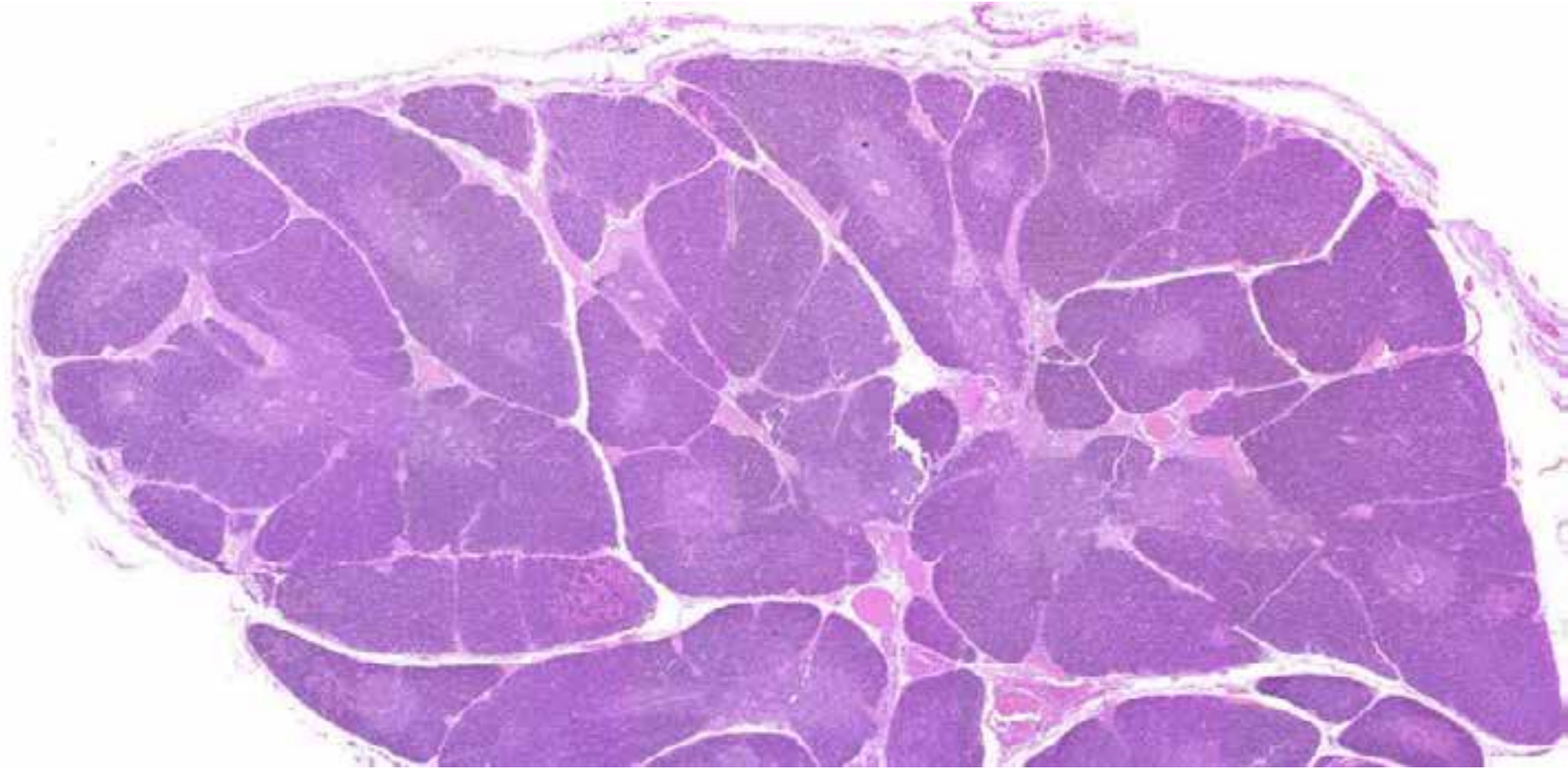
**T cell precursors
colonize the epithelial stroma of the thymus**



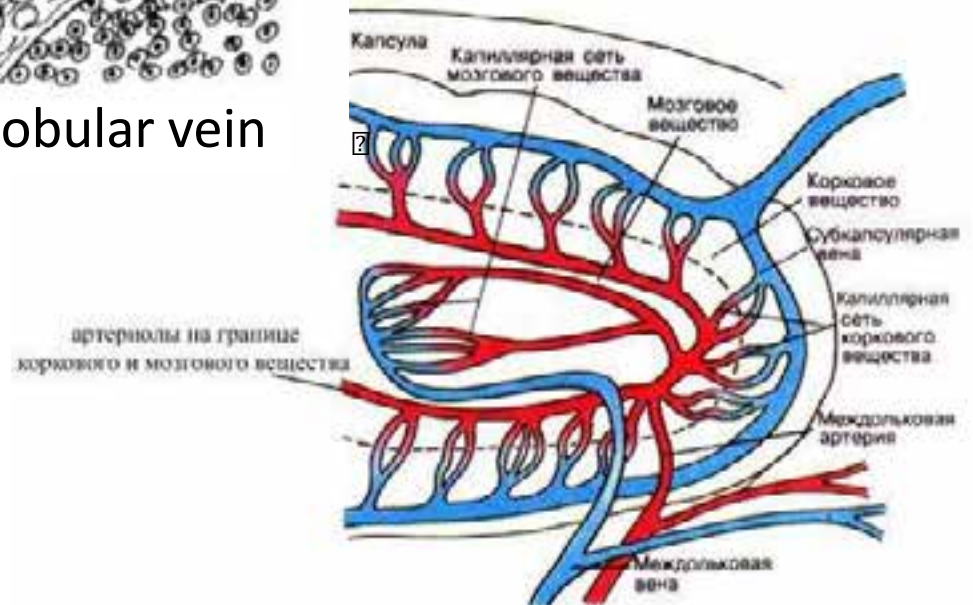
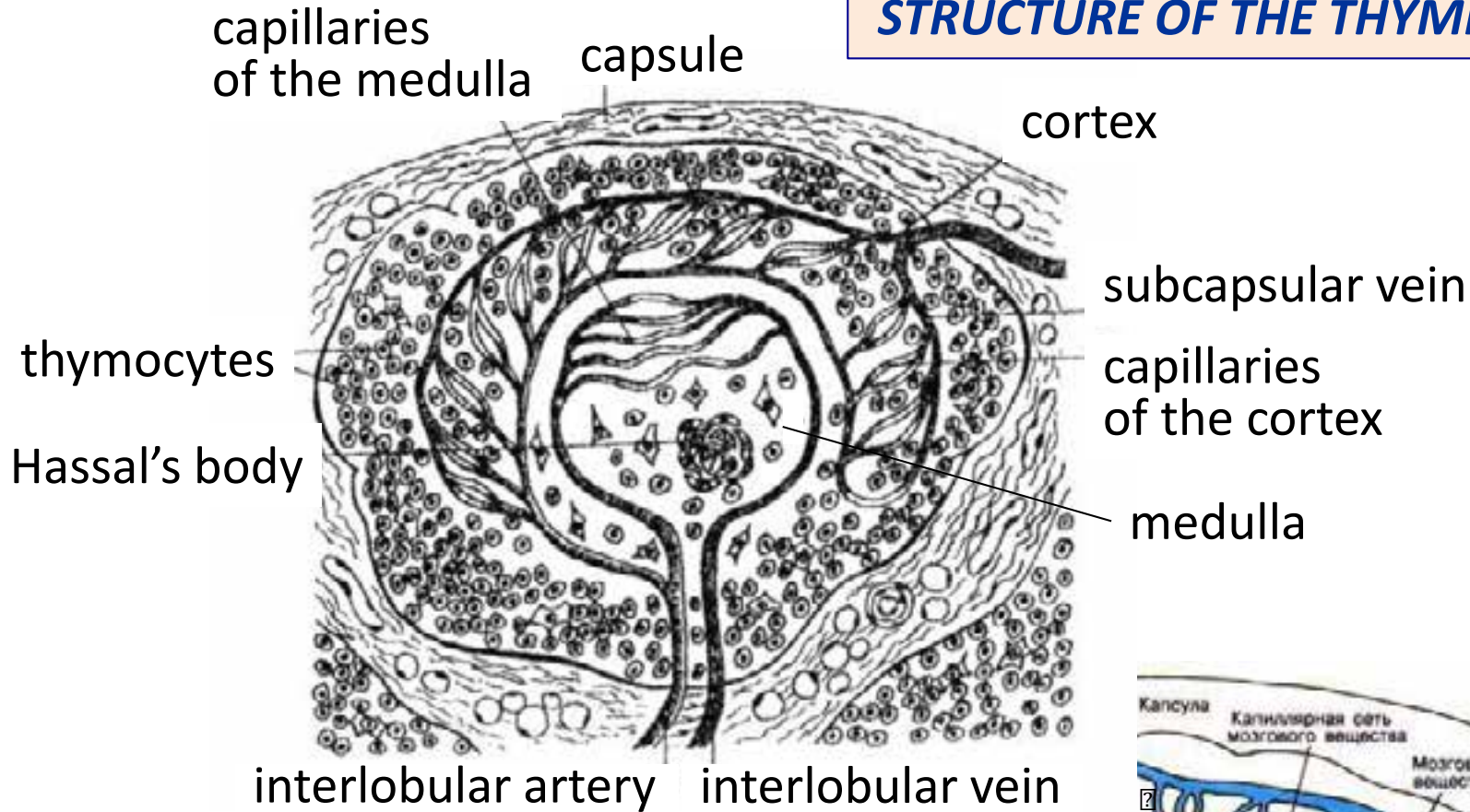
17th week

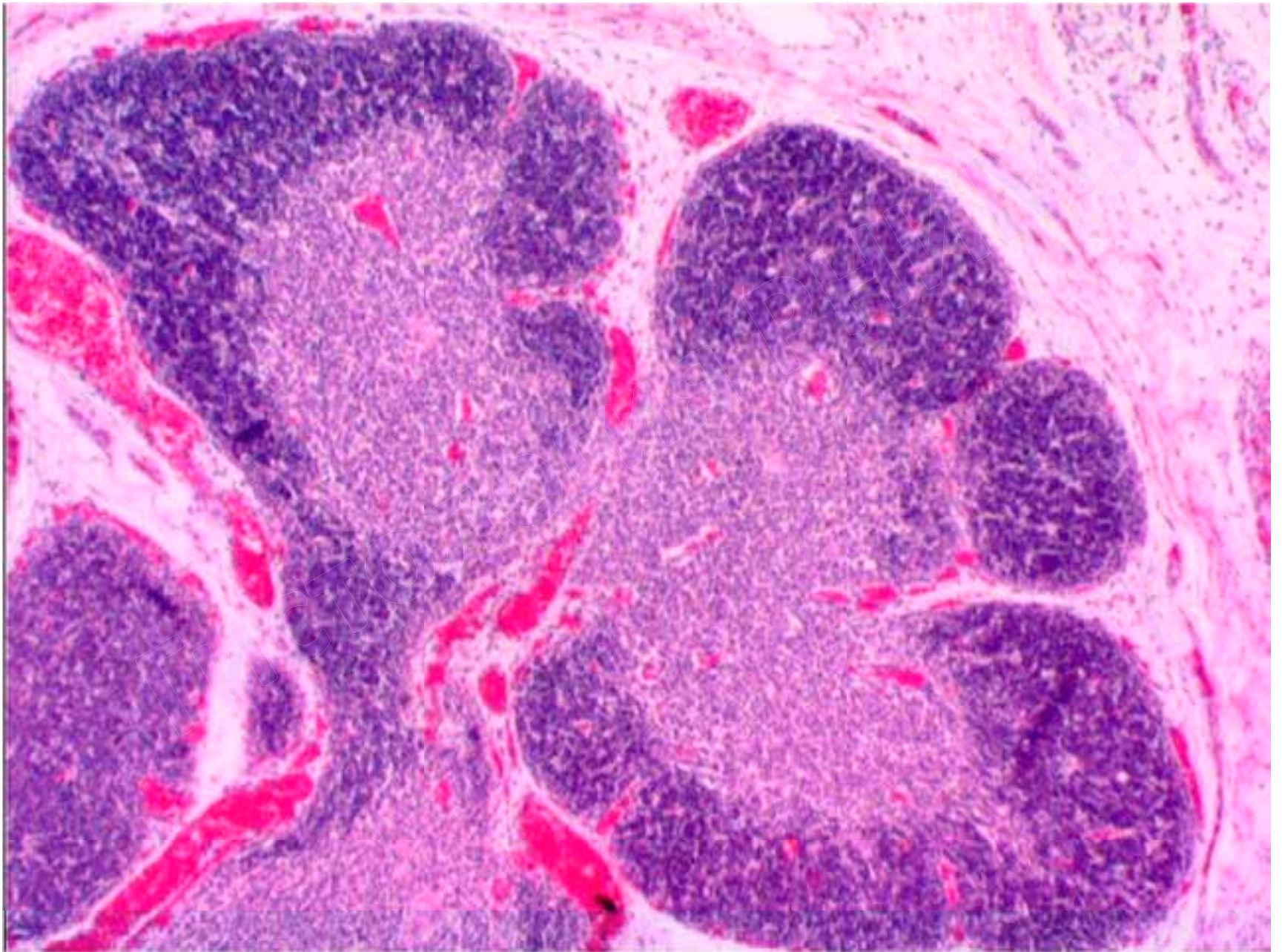
Beginning of T cell production

*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



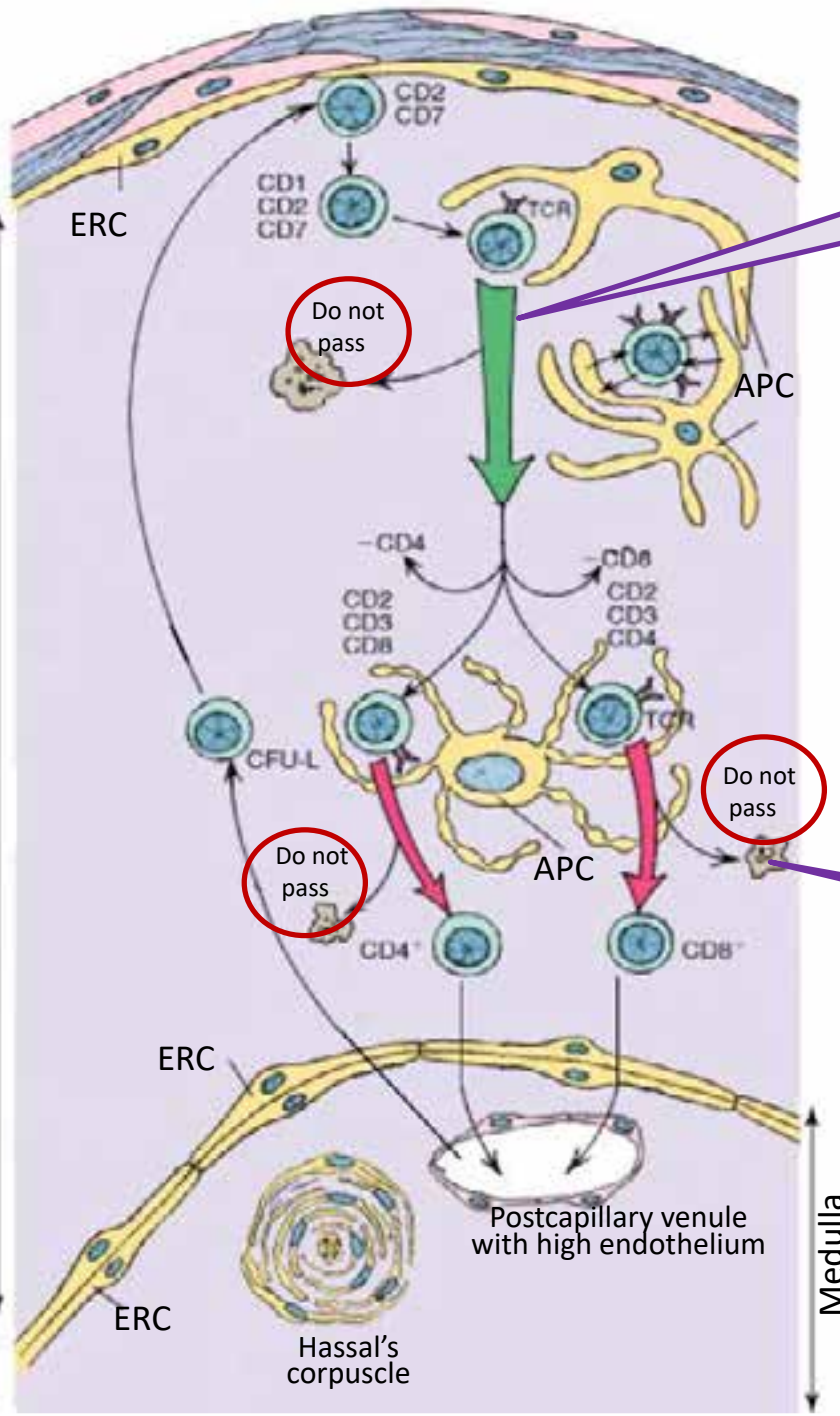
STRUCTURE OF THE THYMIC LOBULE





Thymic lobule

Cortex



POSITIVE SELECTION

NEGATIVE SELECTION

T
H
Y
M
I
C

L
O
B
U
L
E

C
O
R
T
E
X

Subcapsular
cortex

Deep
cortex

M
E
D
U
L
L
A

CD4-CD8-TKP-

CD4+CD8+TKP+

CD4+CD8+TKP+

CD4+CD8+TKP+

CD4-CD8+TKP+

CD4+CD8-TKP+

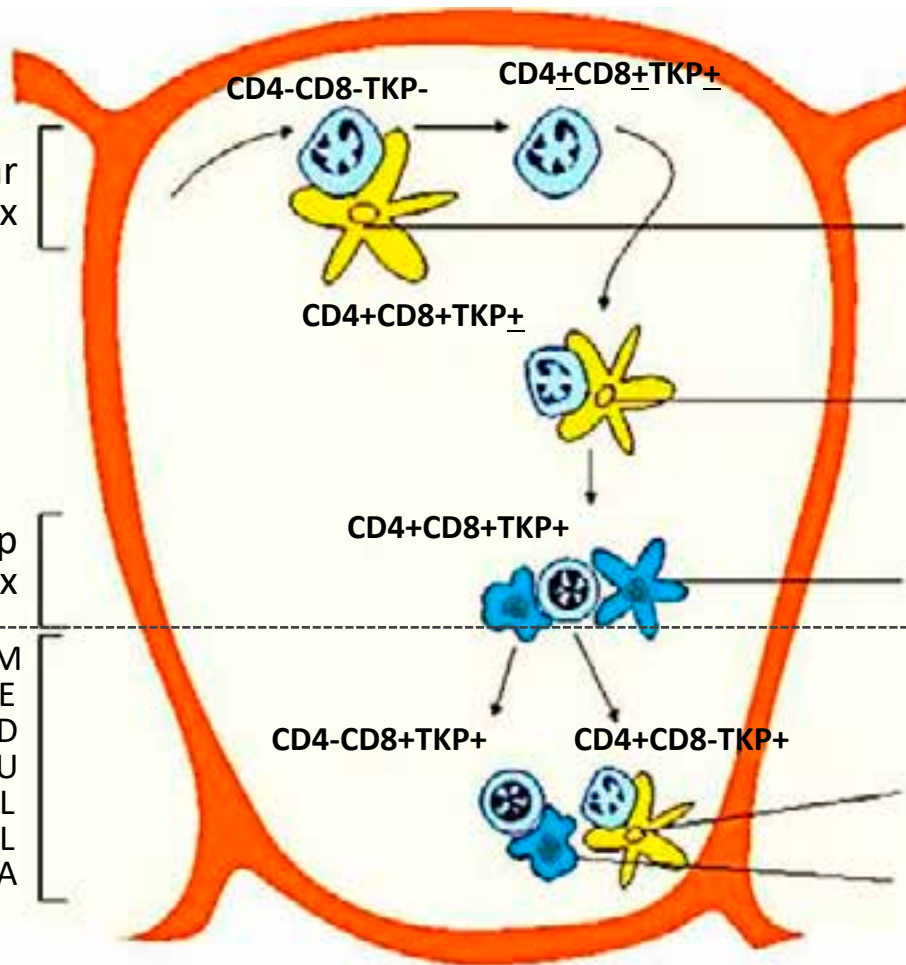
Epithelioreticular
nurse cell

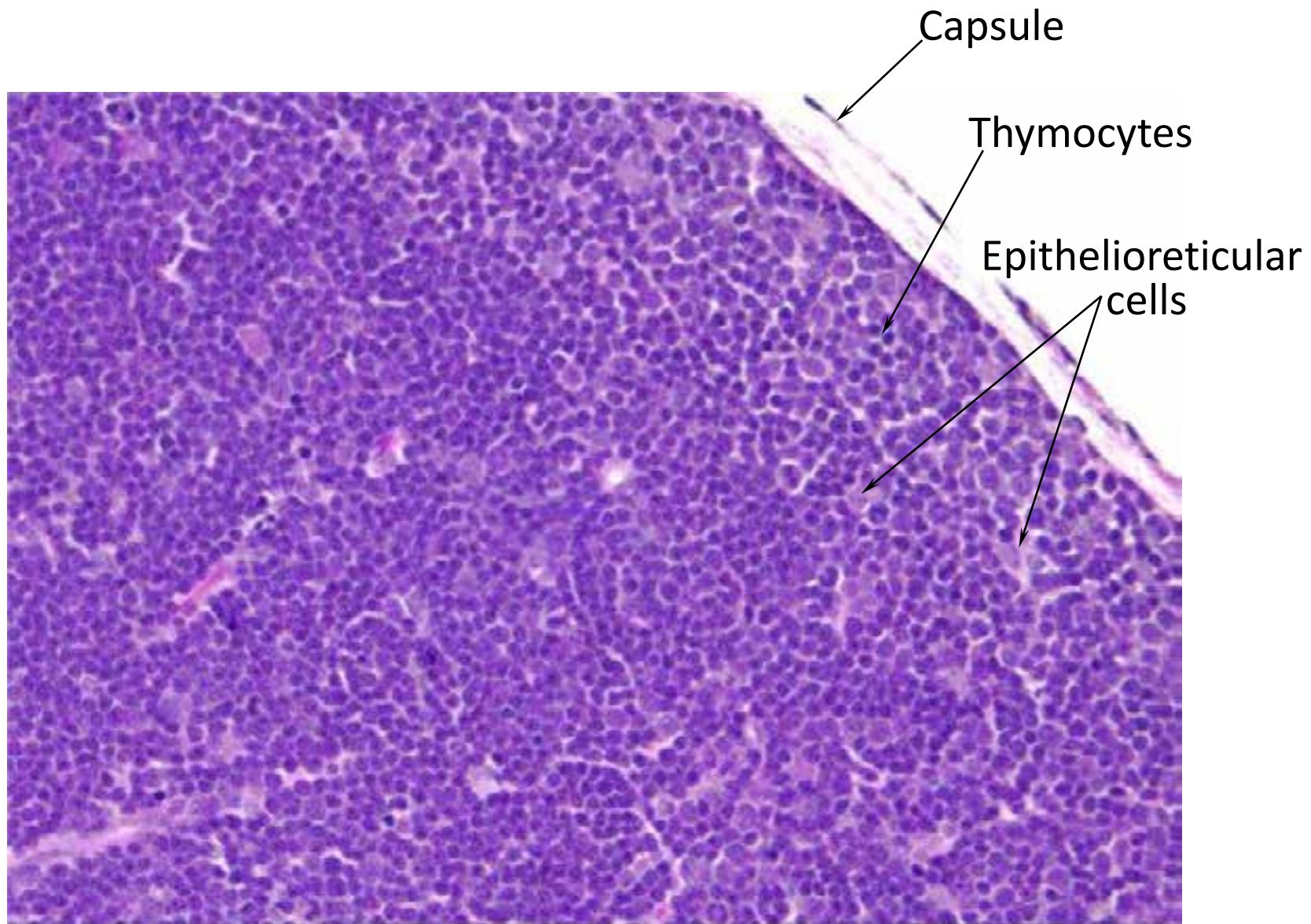
Epithelioreticular
cell of the cortex

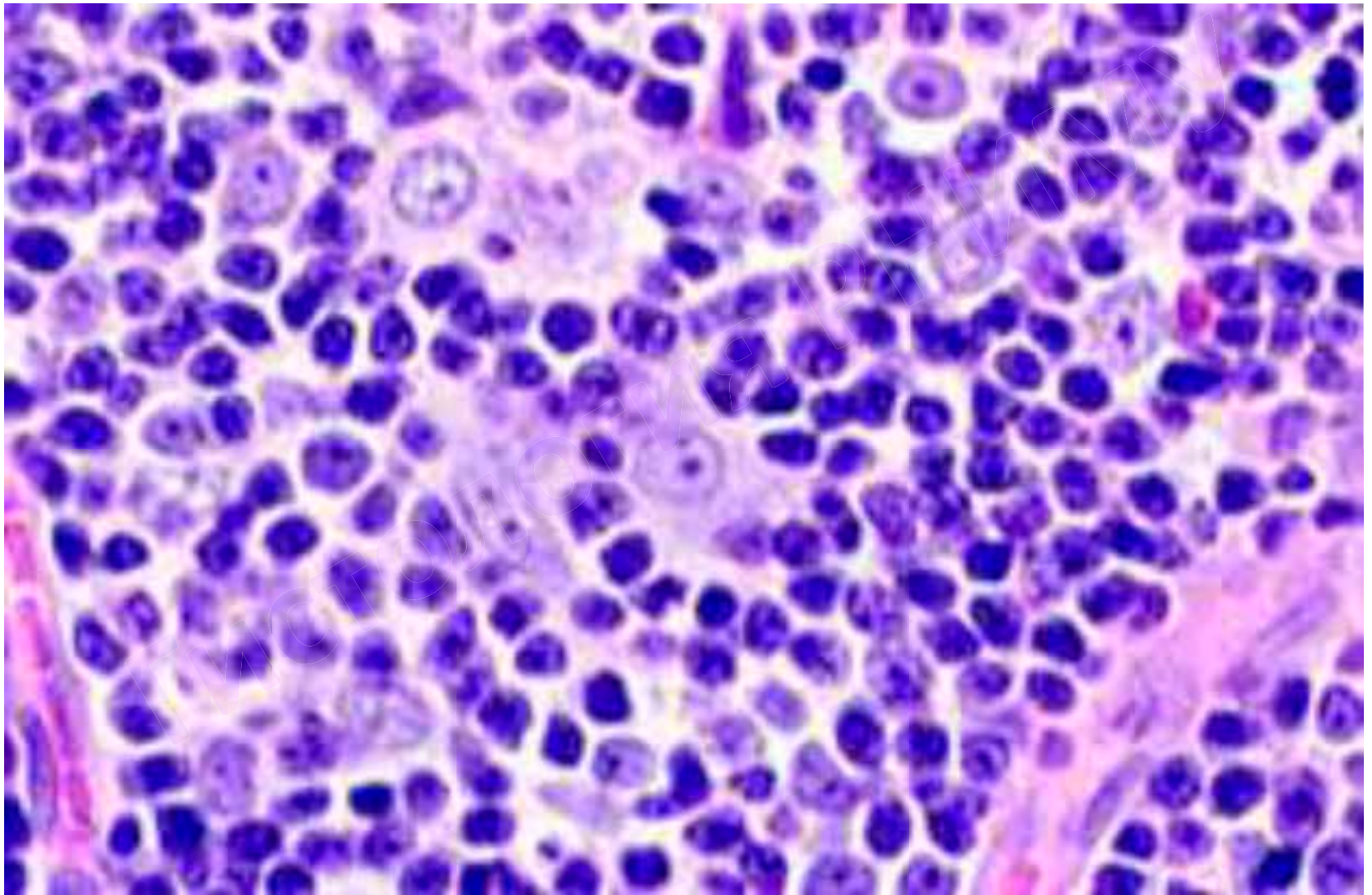
Dendritic cell

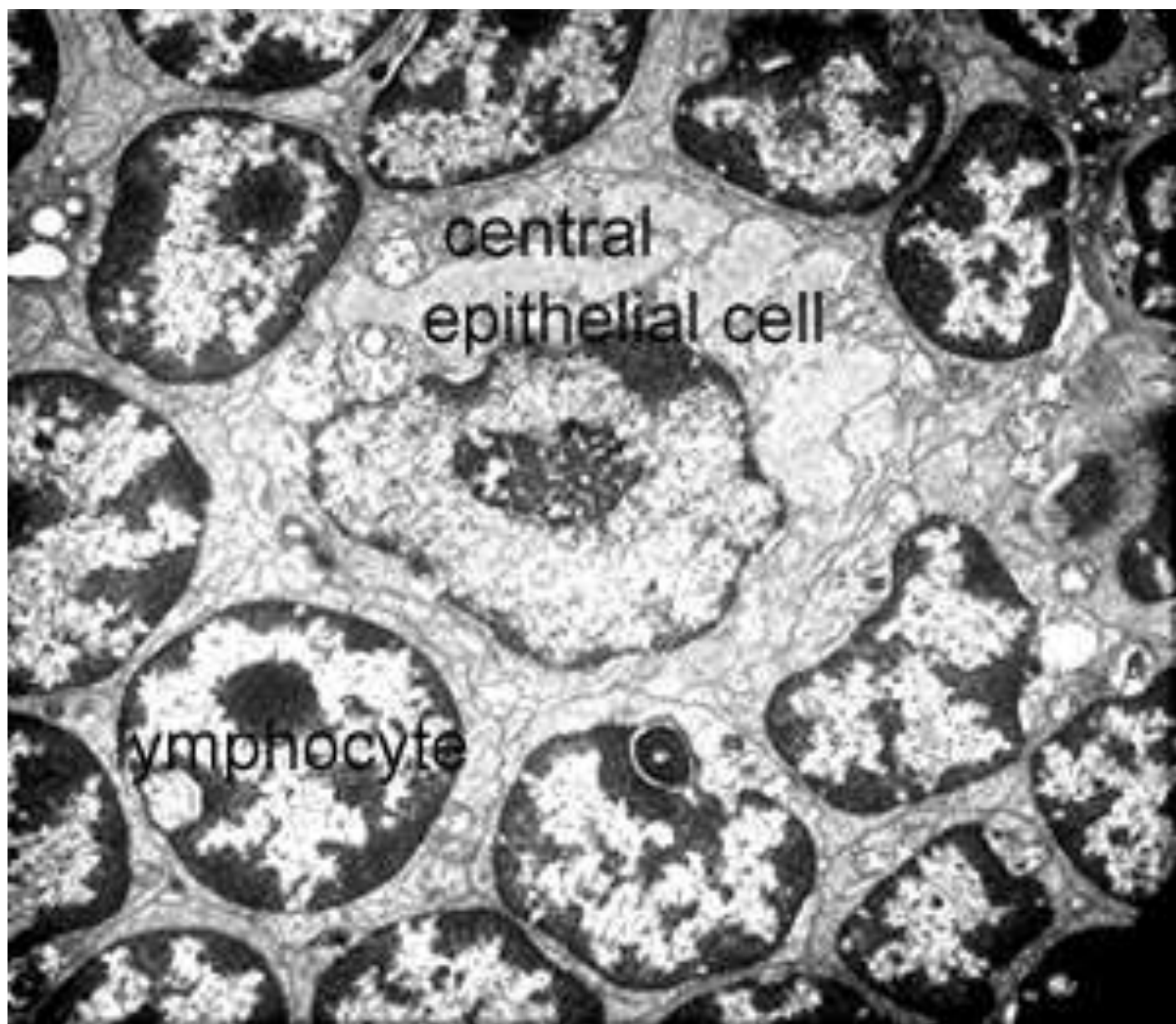
Epithelioreticular
cell of the medulla

Macrophage

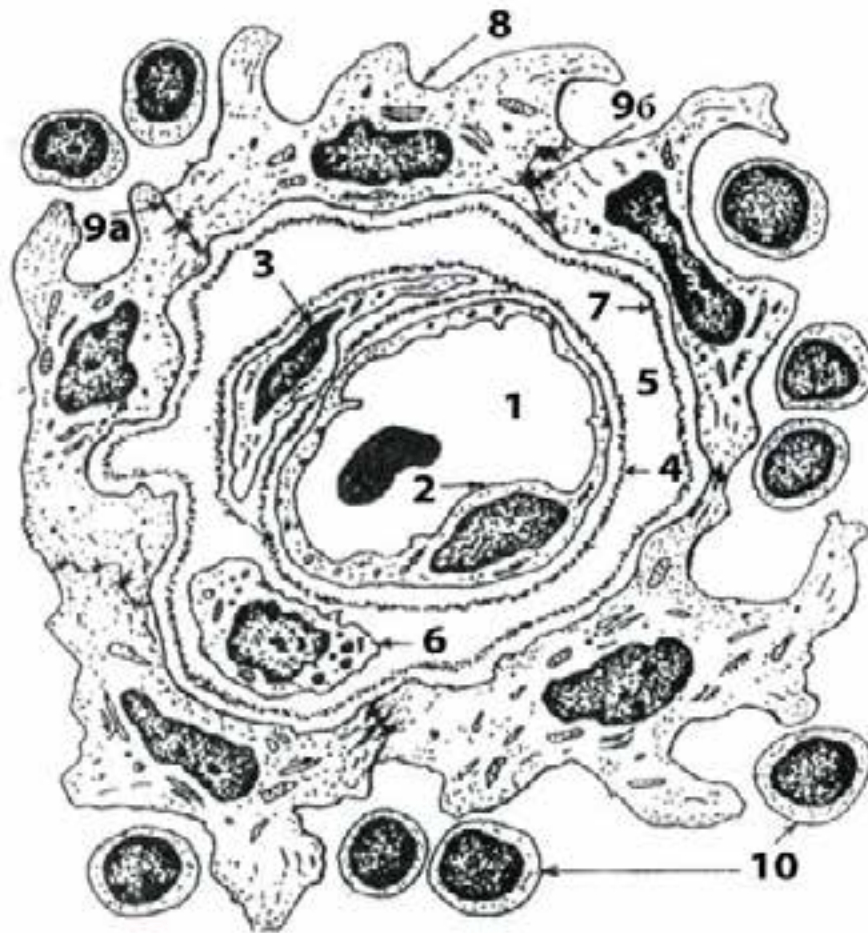




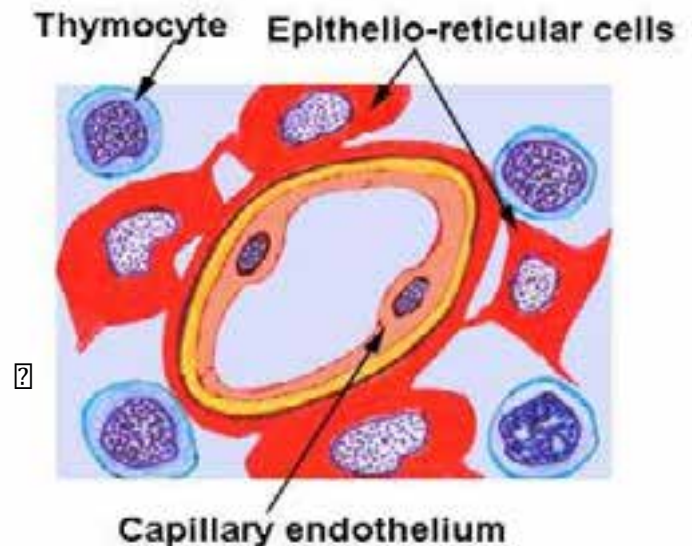




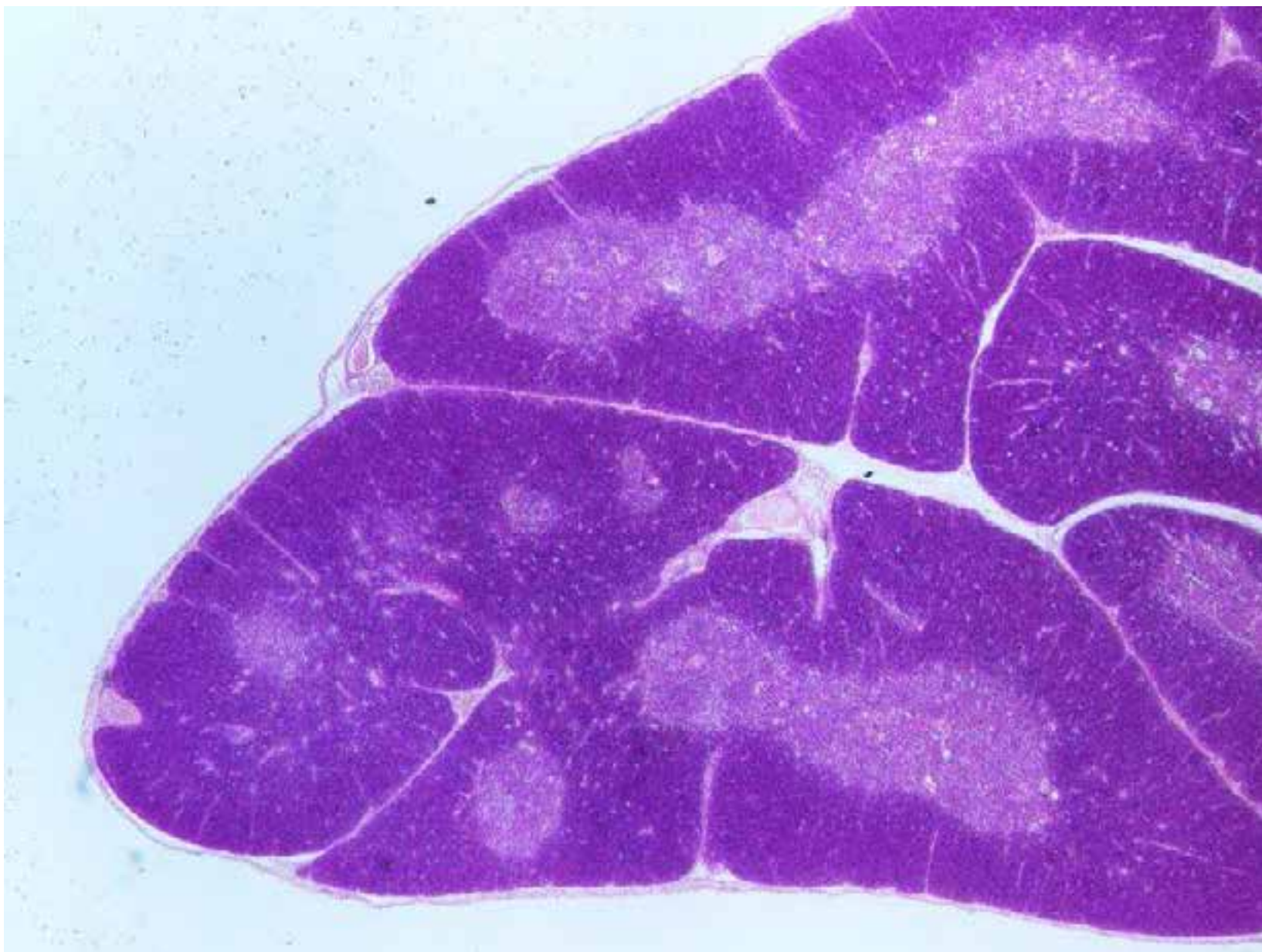
BLOOD-THYMUS BARRIER



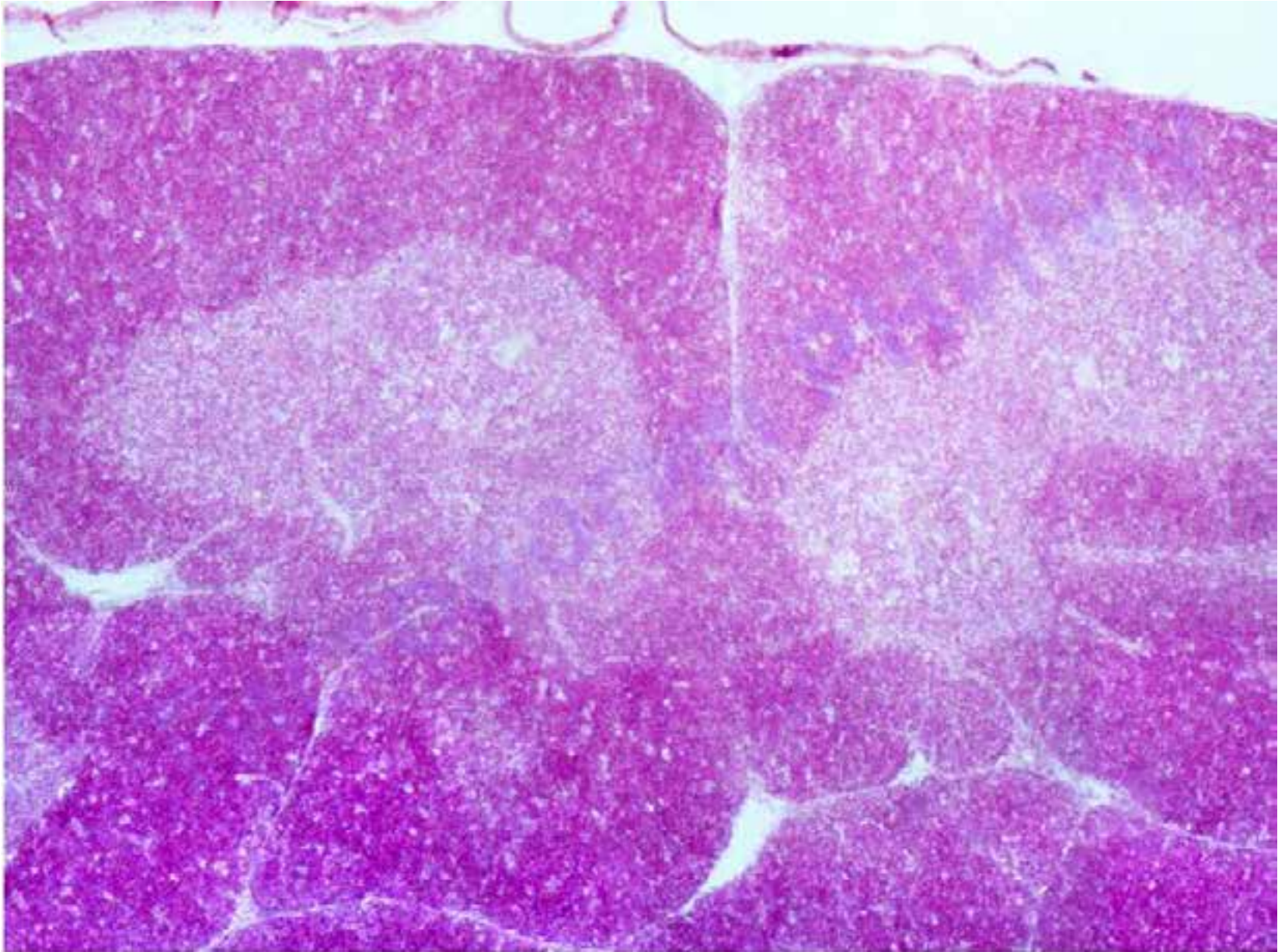
- 1- capillary of somatic type,
- 2- endothelial cell,
- 3- pericyte,
- 4- basement membrane of the capillary,
- 5- perivascular space,
- 6- macrophage,
- 7- basement membrane of the epithelioreticular cells,
- 8- epithelioreticular cells,
- 9- cell junctions (a: tight junctions; b: desmosomes),
- 10- thymocytes



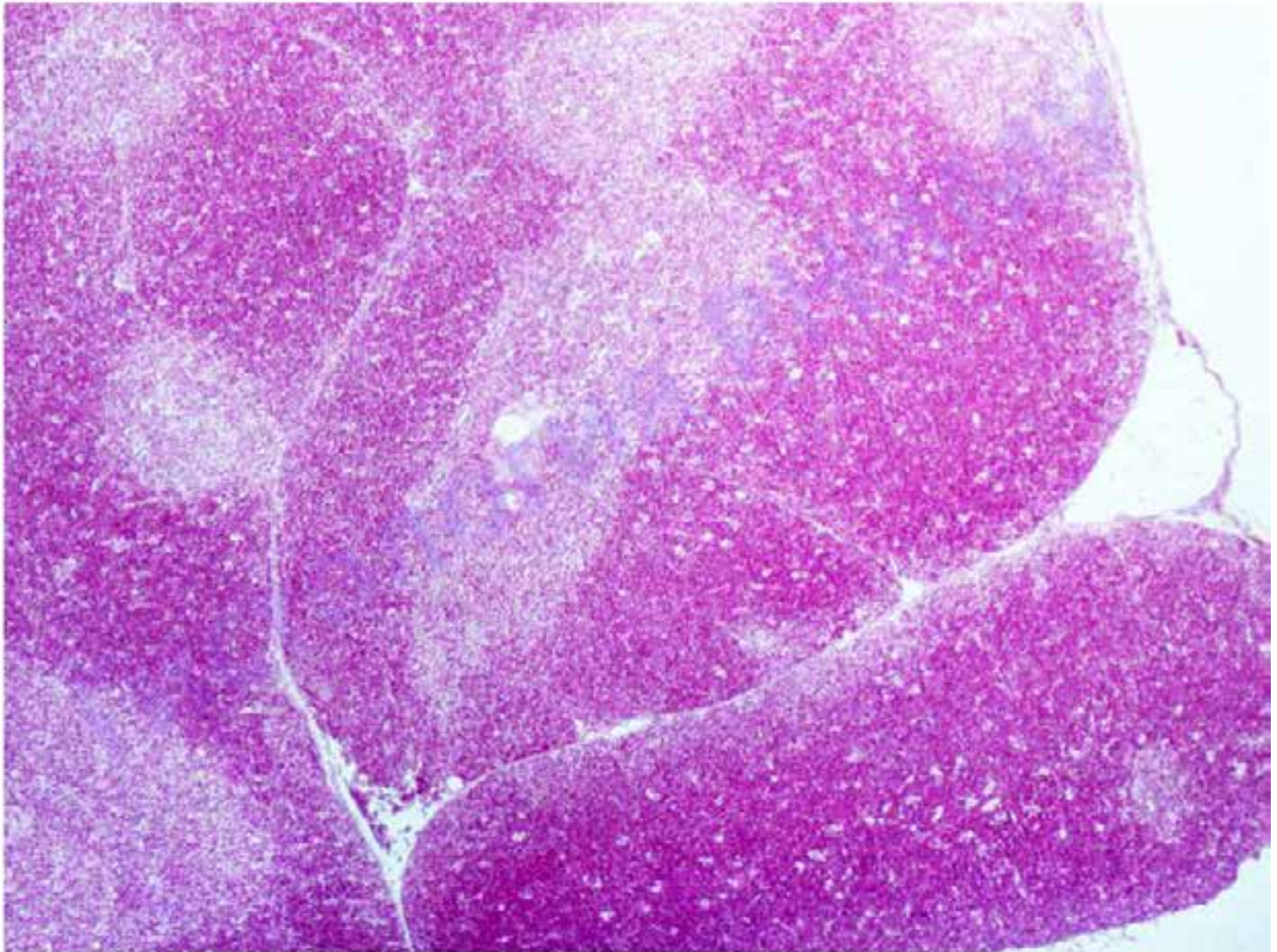
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



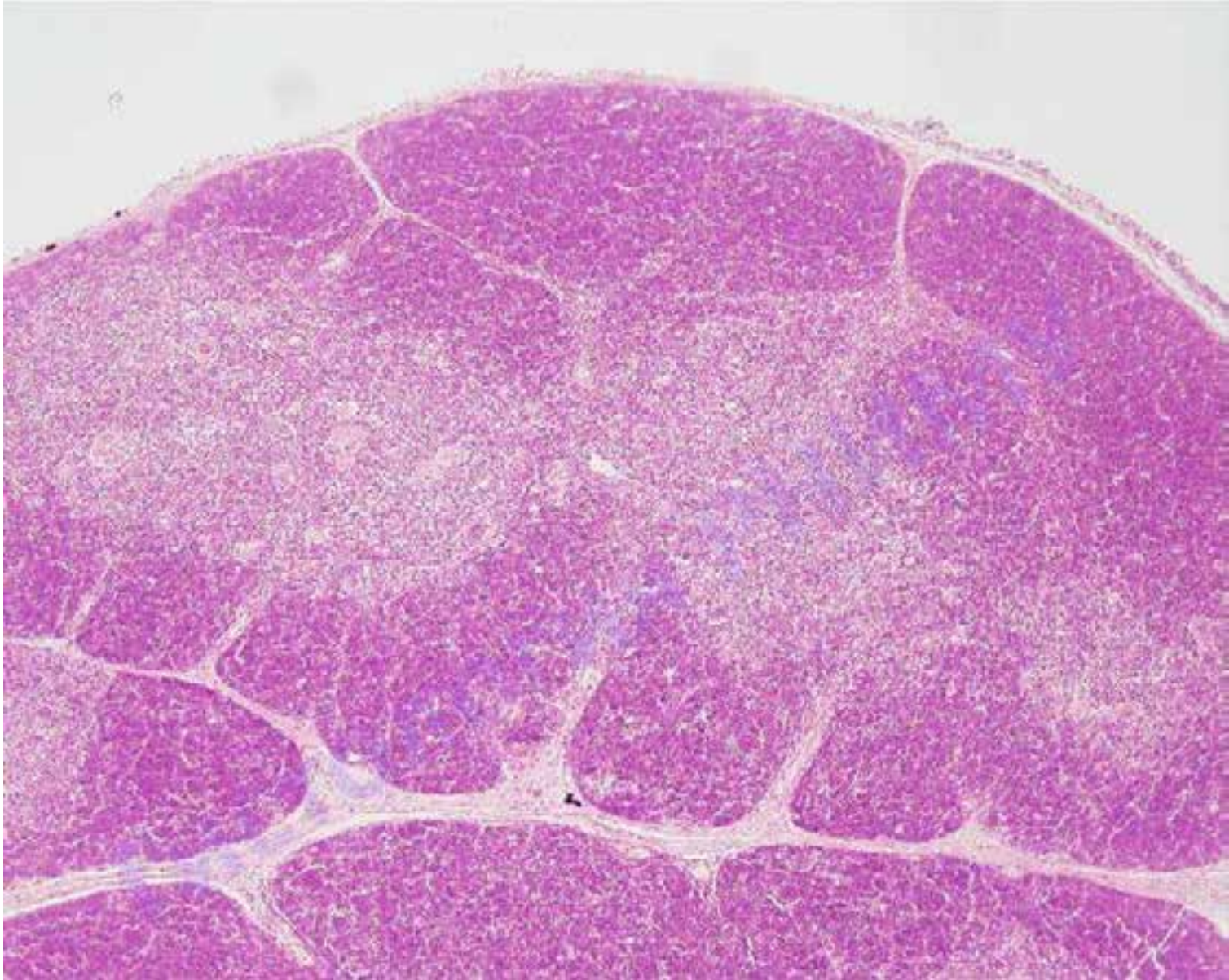
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



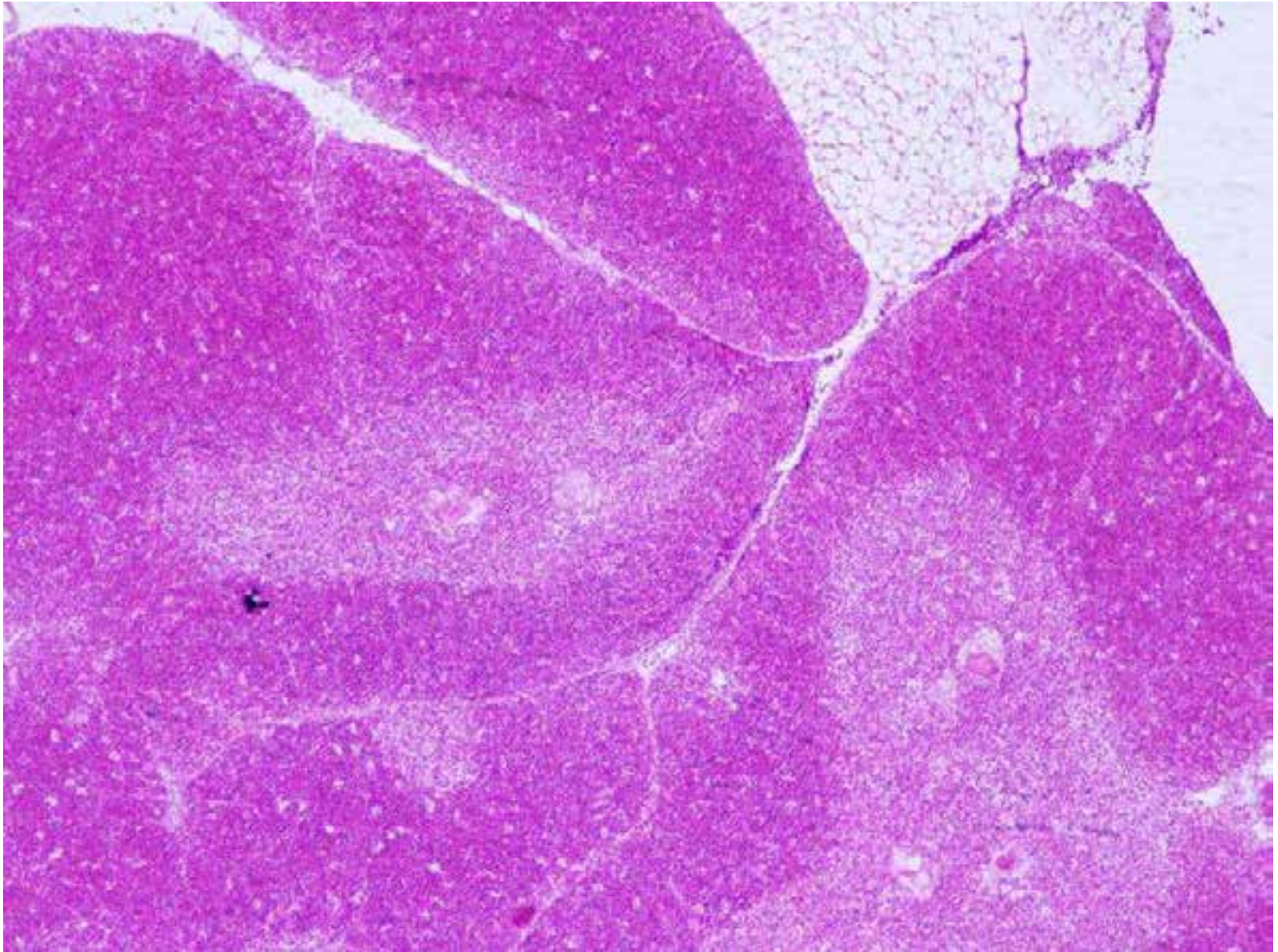
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



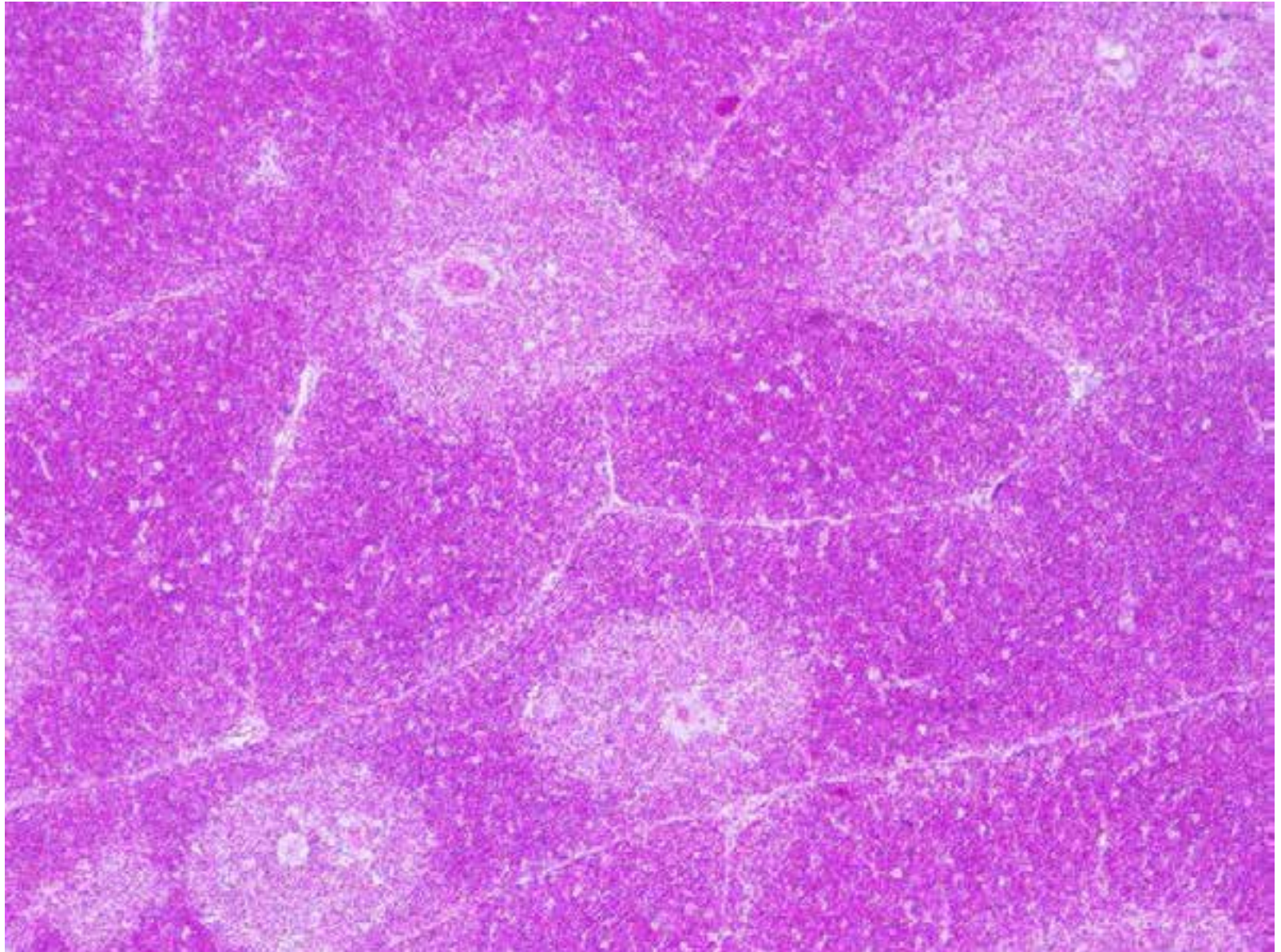
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



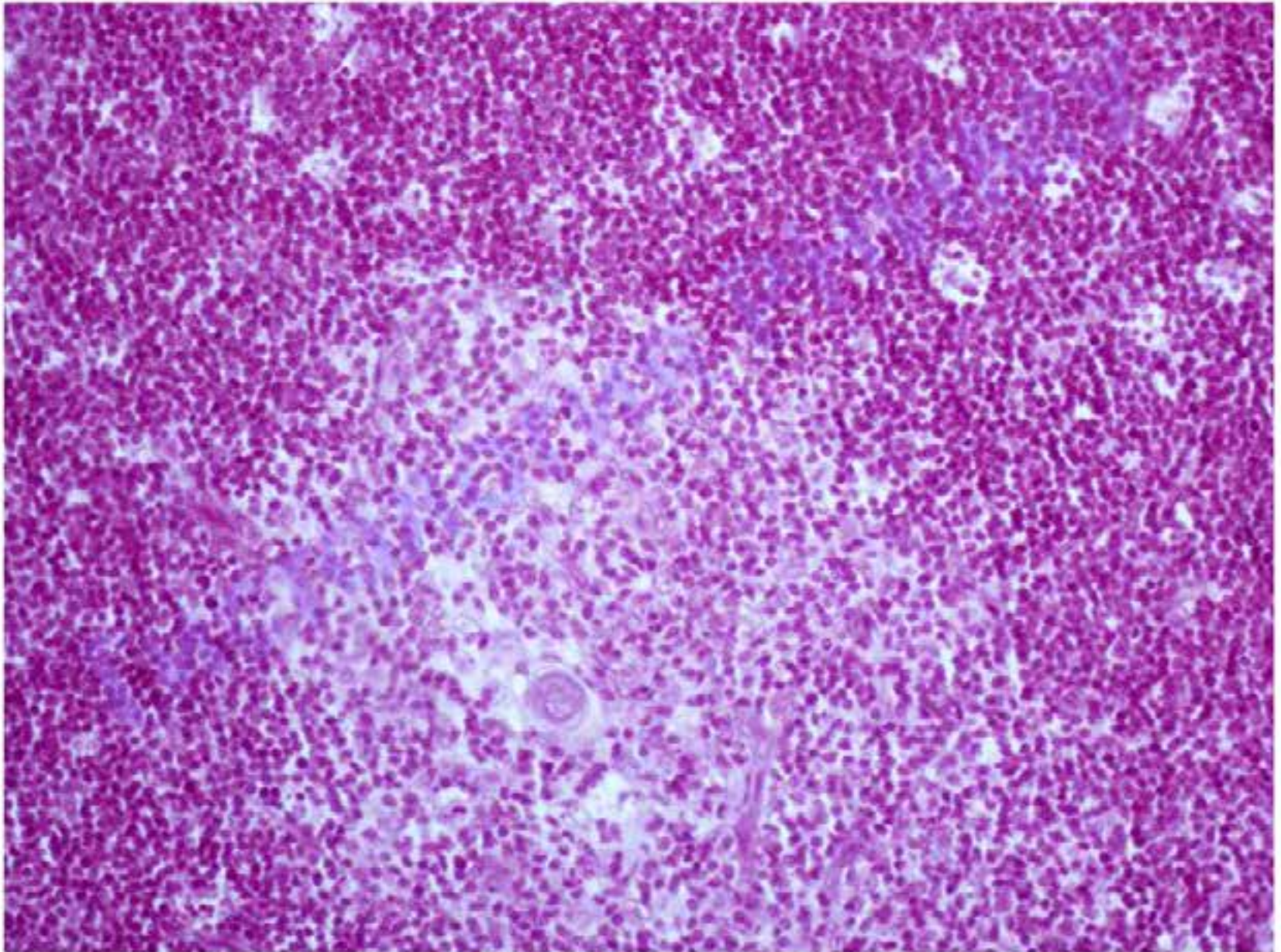
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



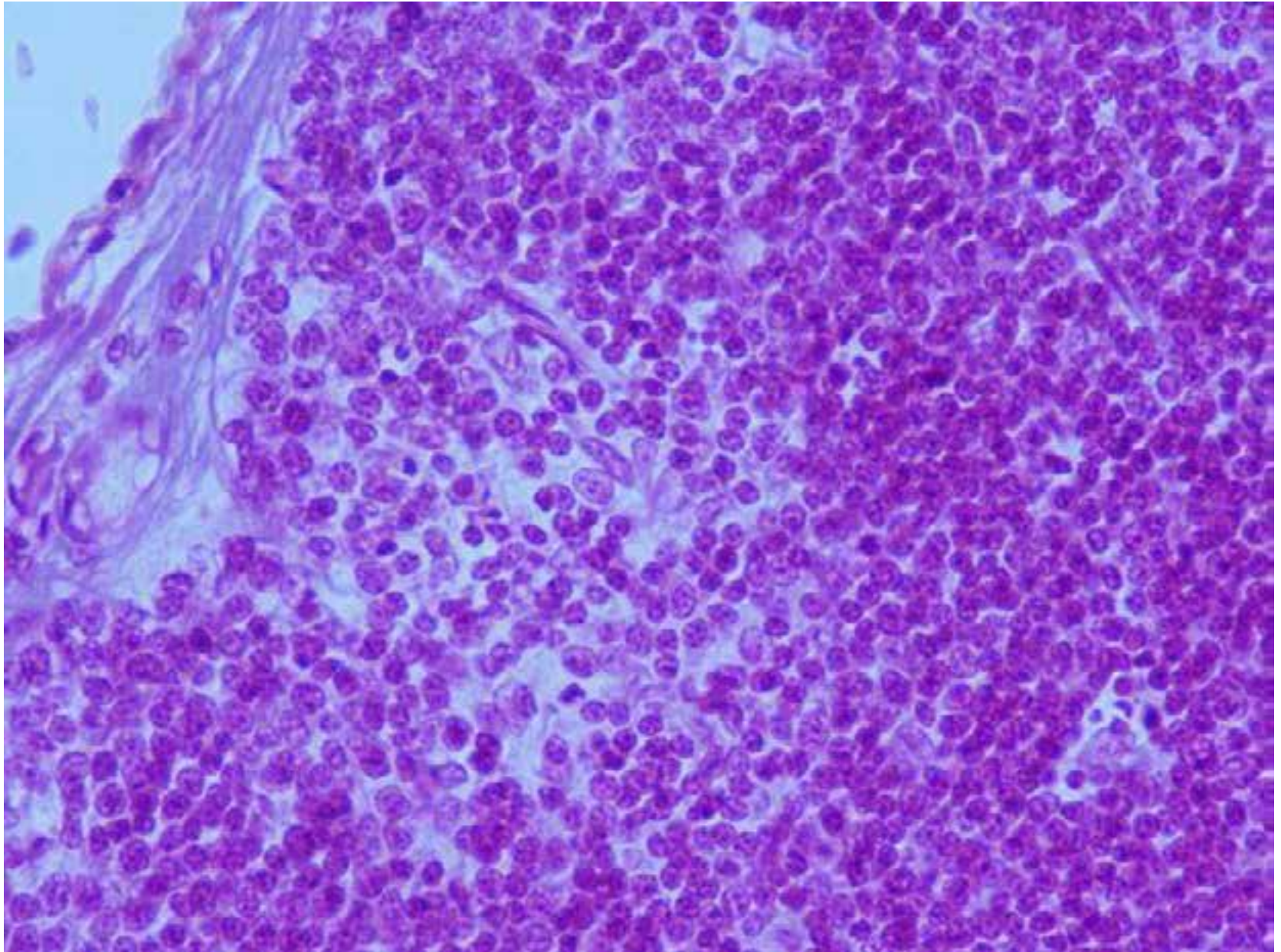
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



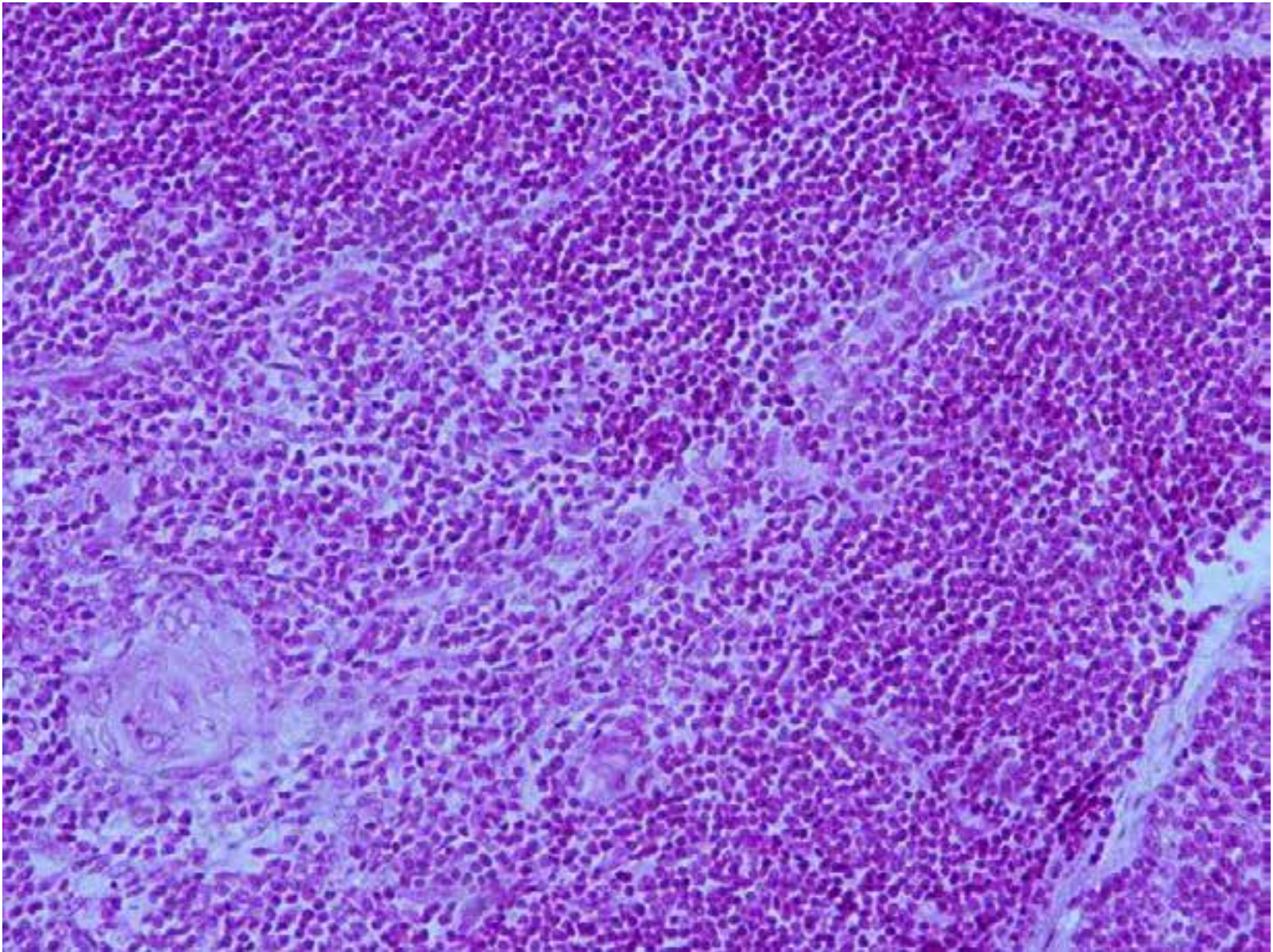
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



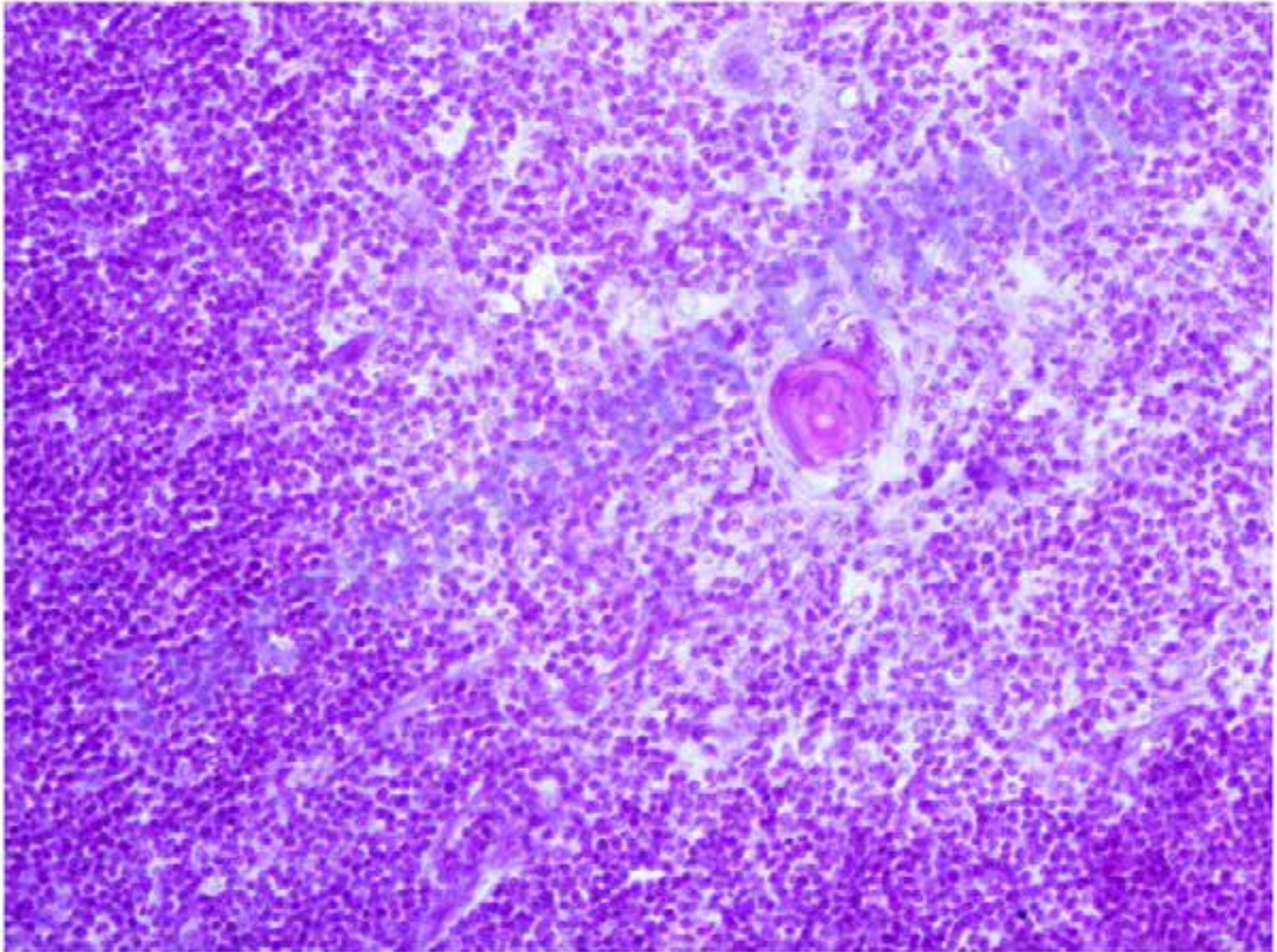
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



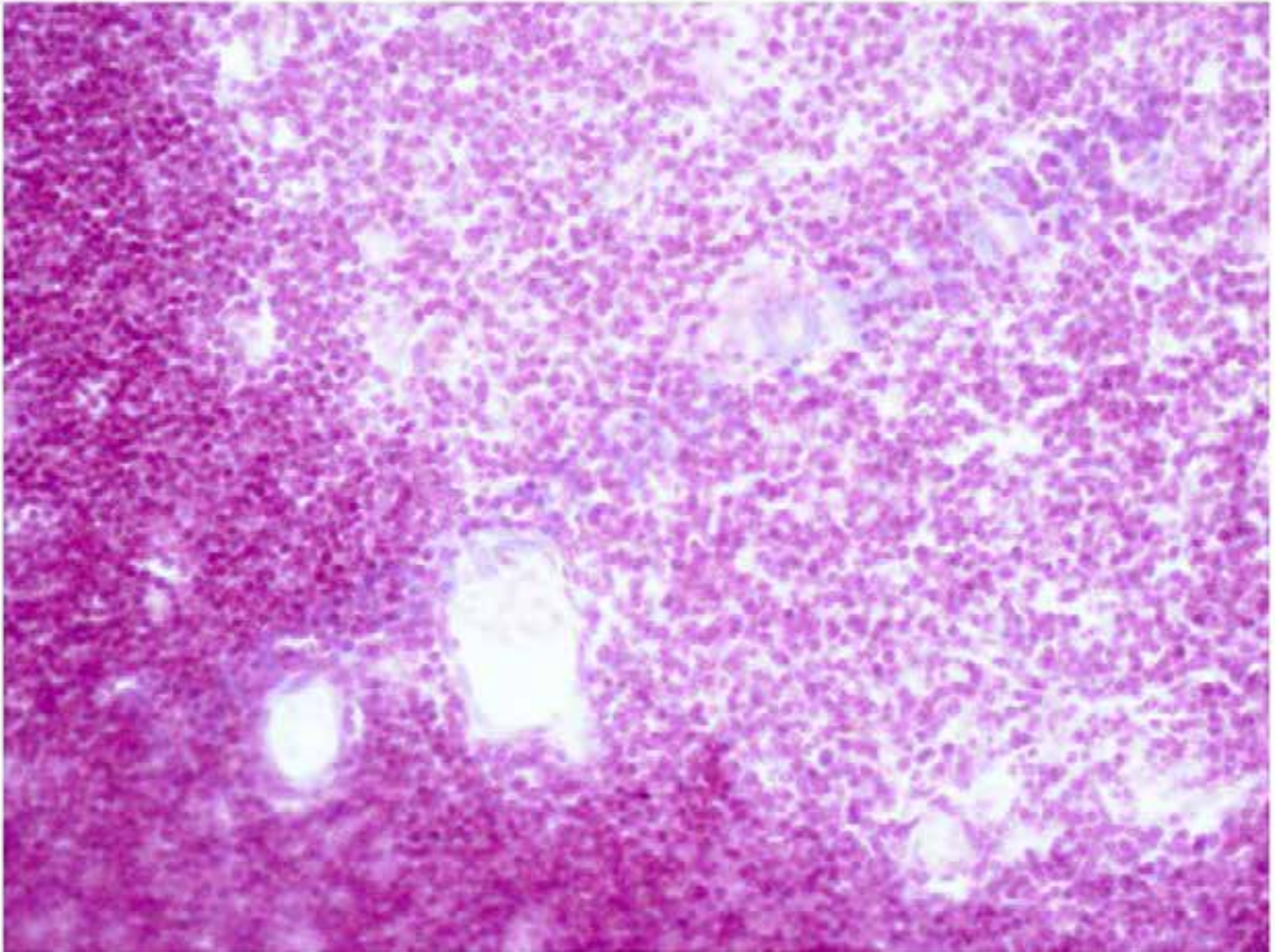
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



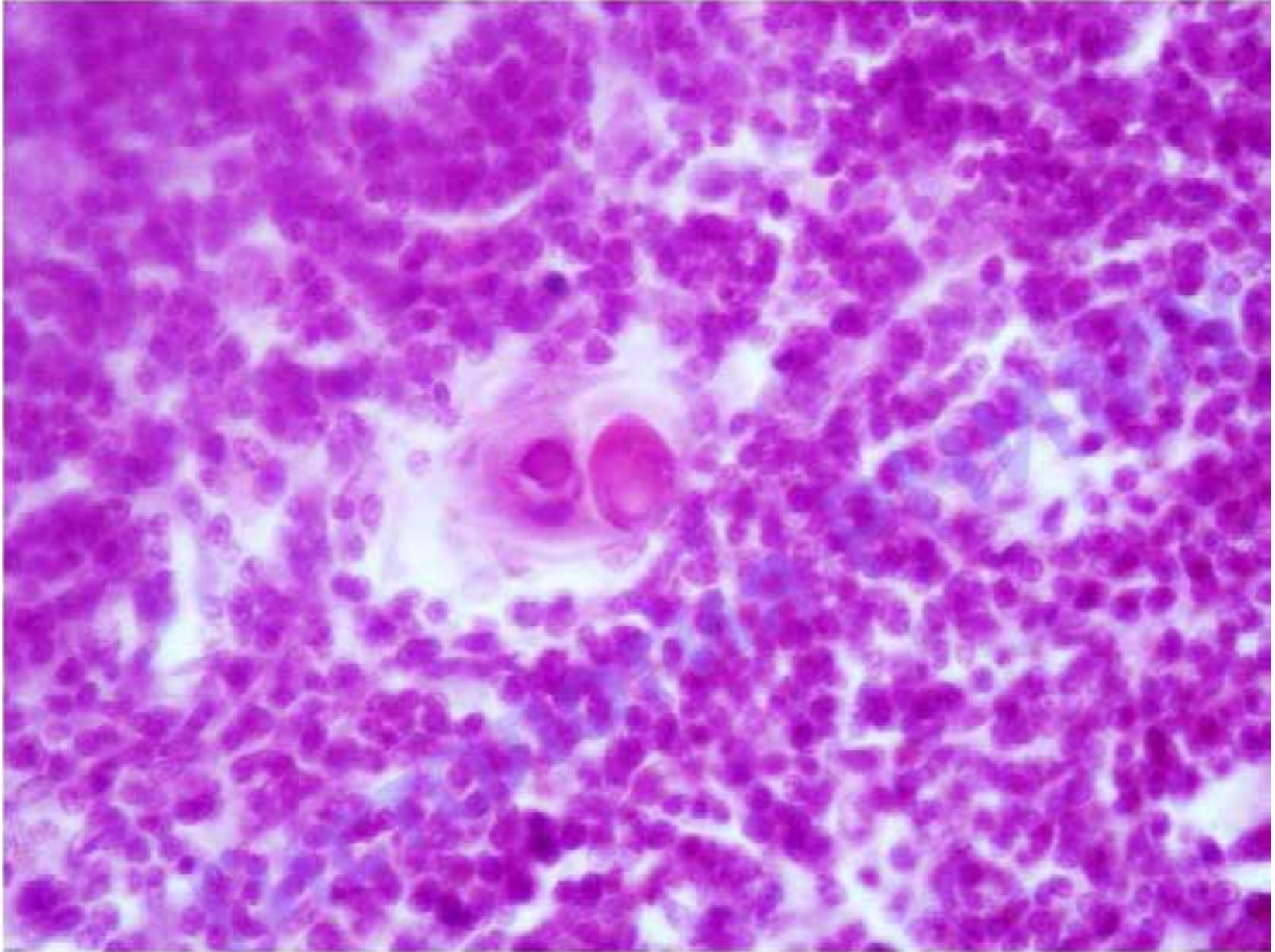
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



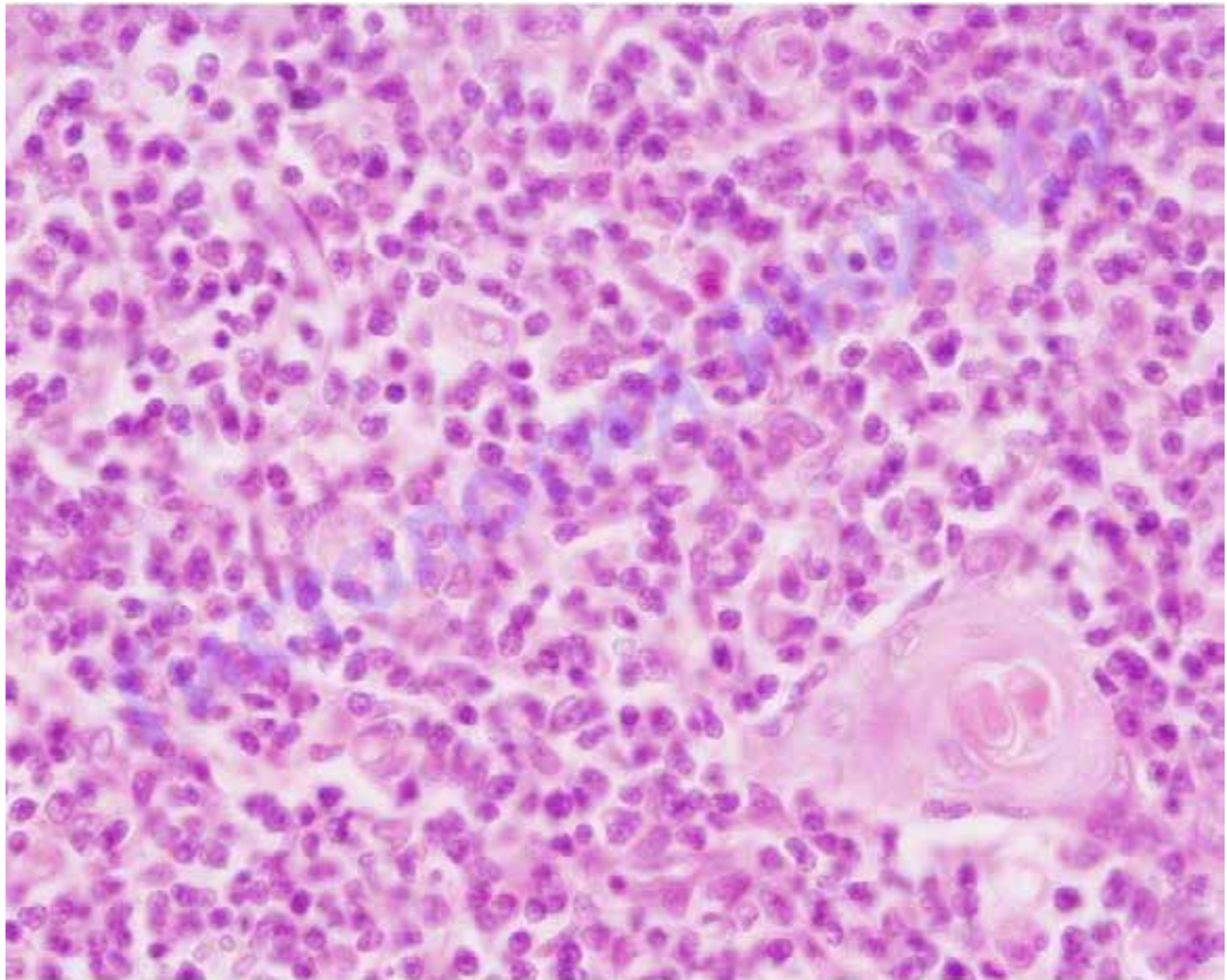
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



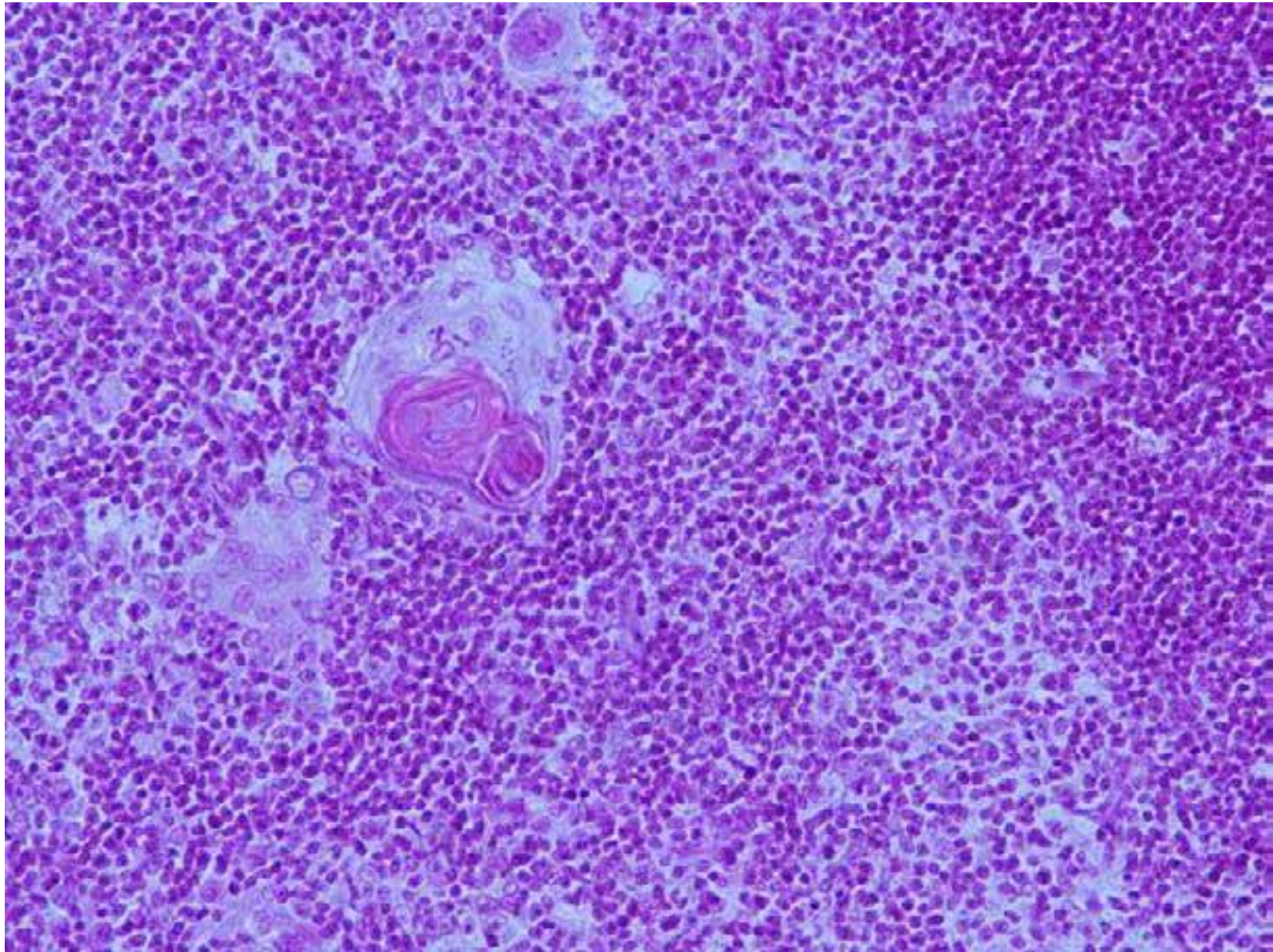
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



*Slide №117. Section of the thymus
Hematoxylin-eosin staining*

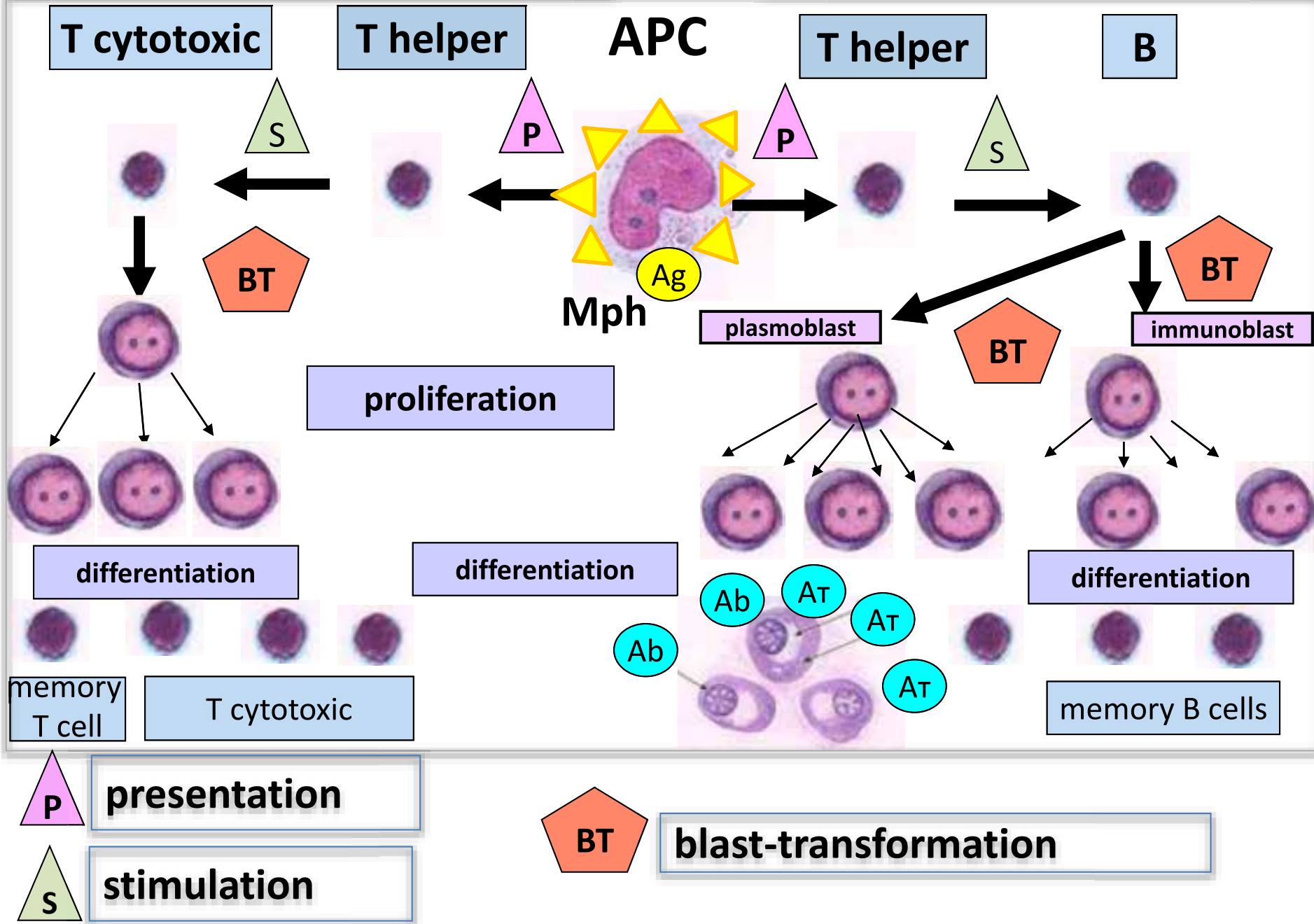


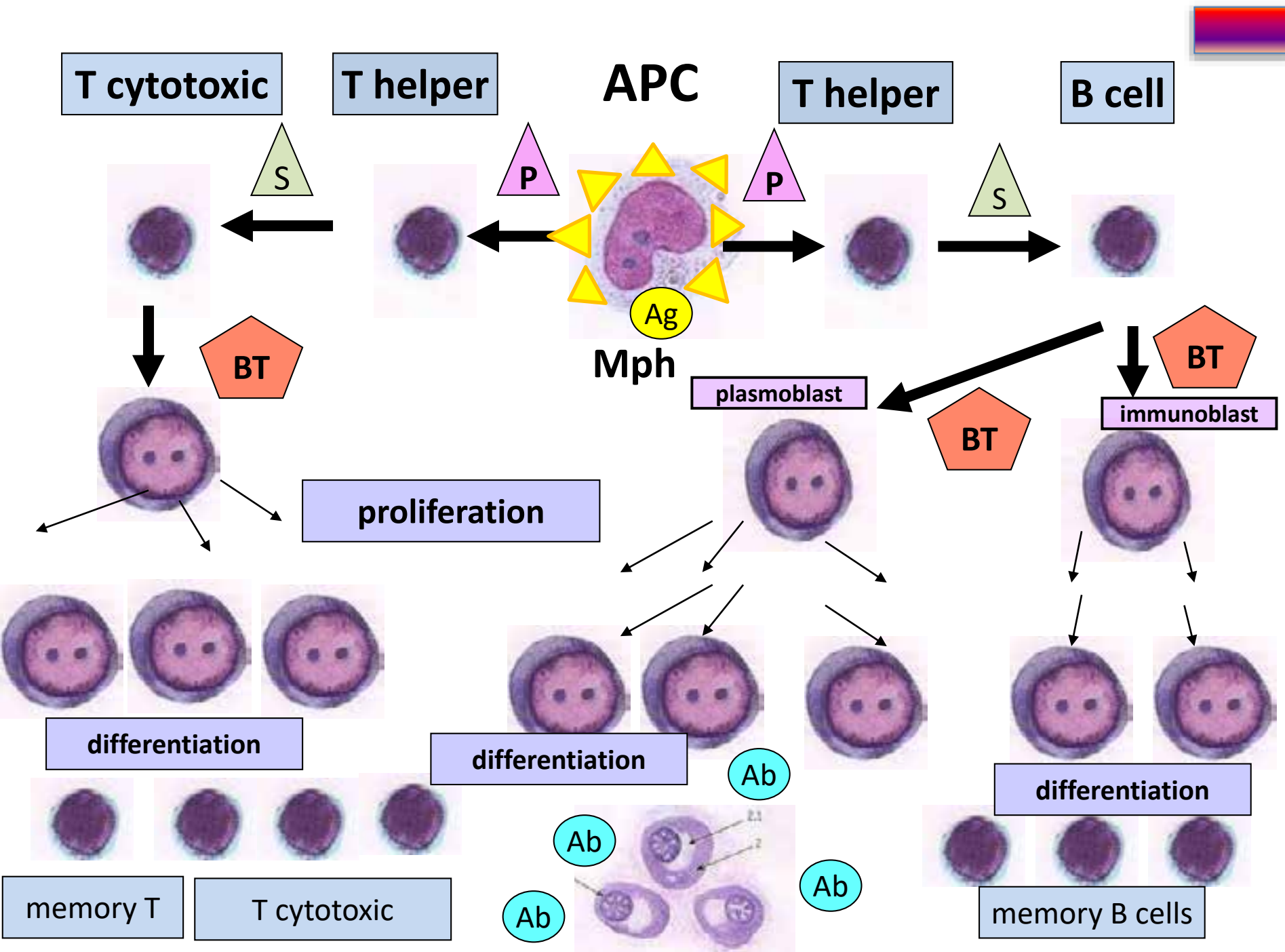
*Slide №117. Section of the thymus
Hematoxylin-eosin staining*



Cell-mediated immunity

Humoral immunity





DEVELOPMENT OF THE LYMPH NODES

2-3 months of the intrauterine life

Lymph sacs are formed as expansions of the blood and lymph vessels
Surrounding mesenchyme gives rise to the reticular tissue, the capsule, and the trabeculae of the lymph nodes
Marginal and medullary sinuses form

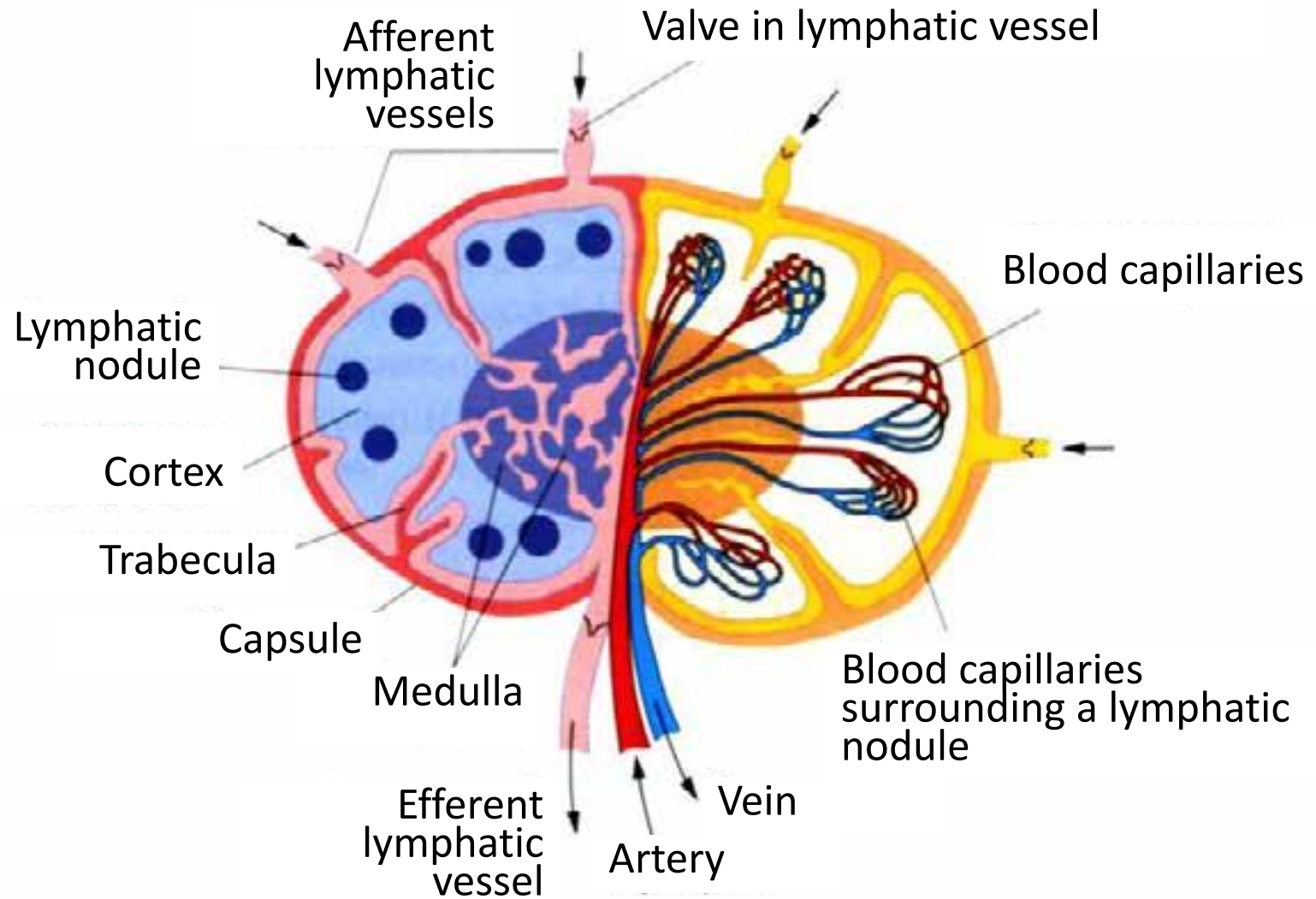
4th month

Cortical and medullary portions of the lymph nodes are formed (respectively, primary lymphatic nodules and medullary cords). B cells colonize the cortex, T cells colonize the paracortical zone

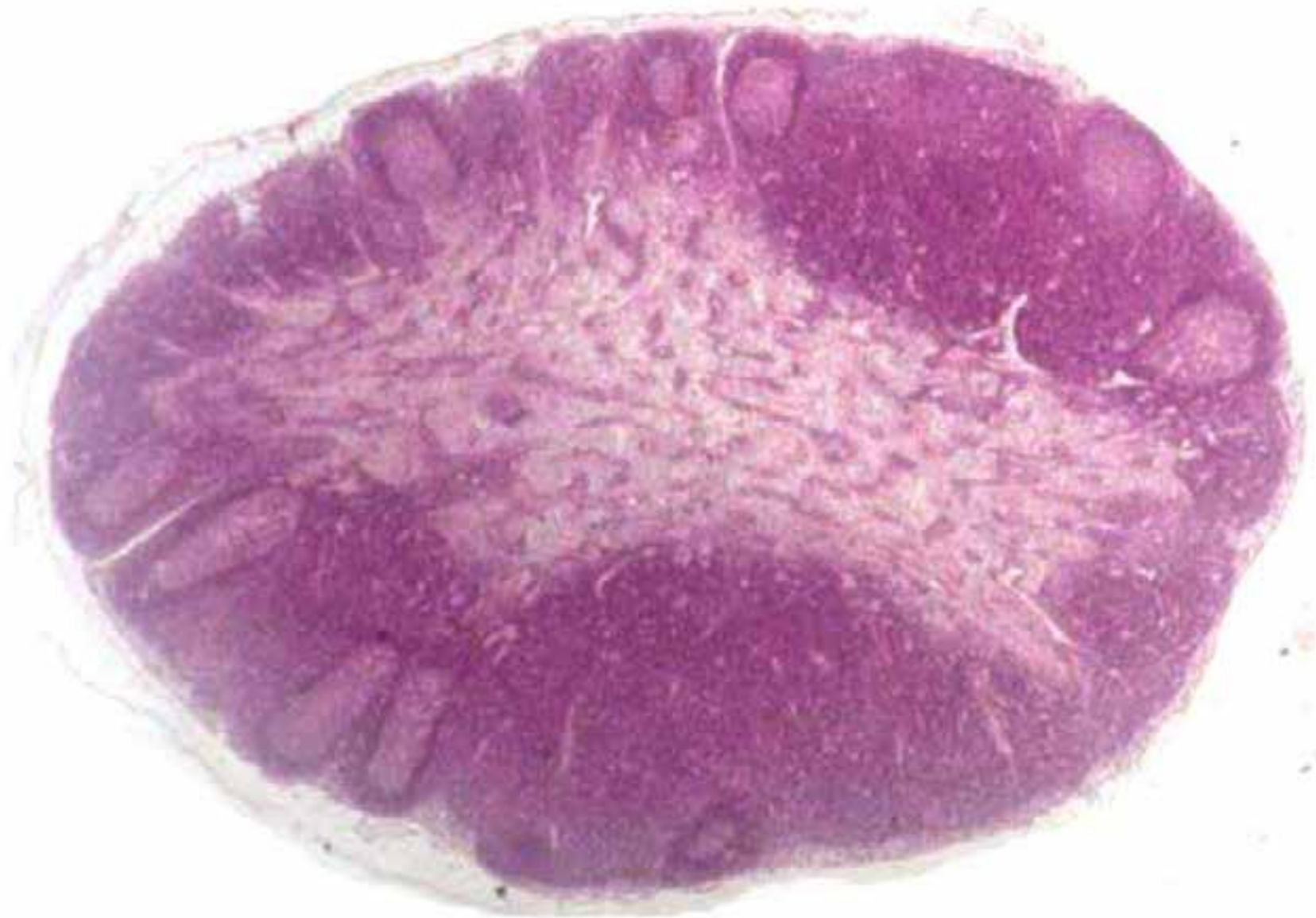
from the 6th month

Lymph nodes acquire their definitive structure

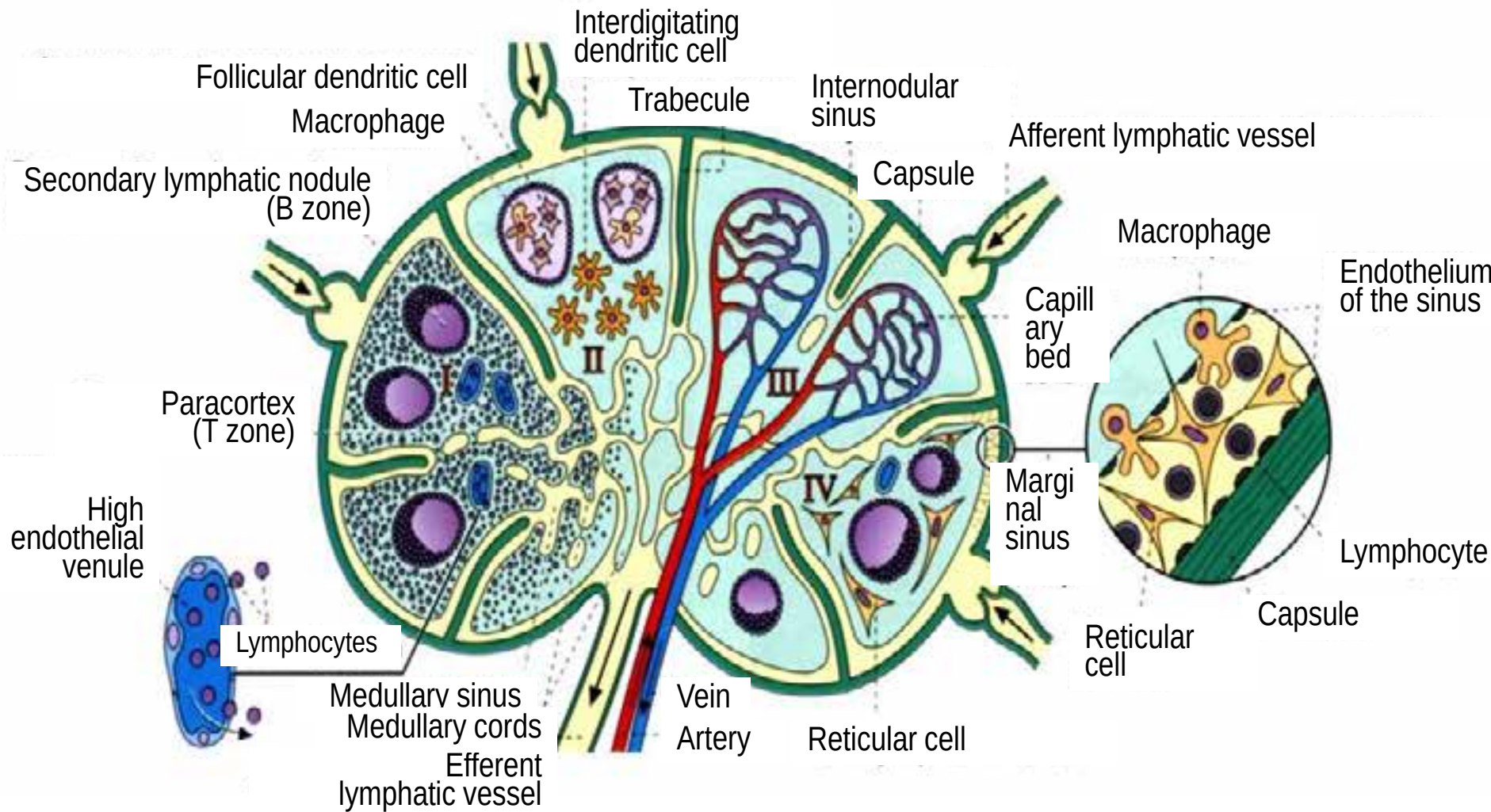
STRUCTURE OF THE LYMPH NODE



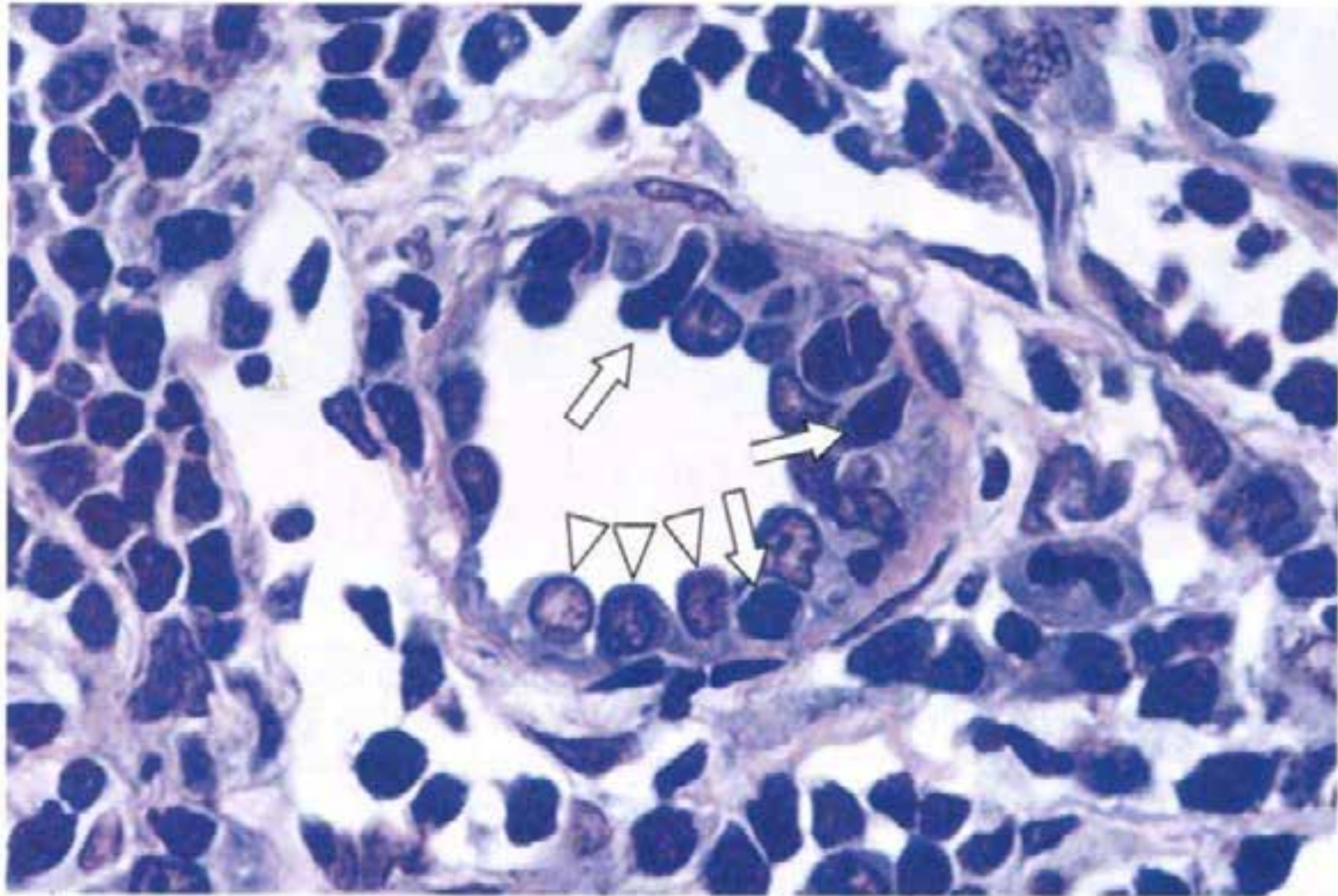
Slide №118. Section of a lymph node
Hematoxylin-eosin staining



STRUCTURE OF THE LYMPH NODE

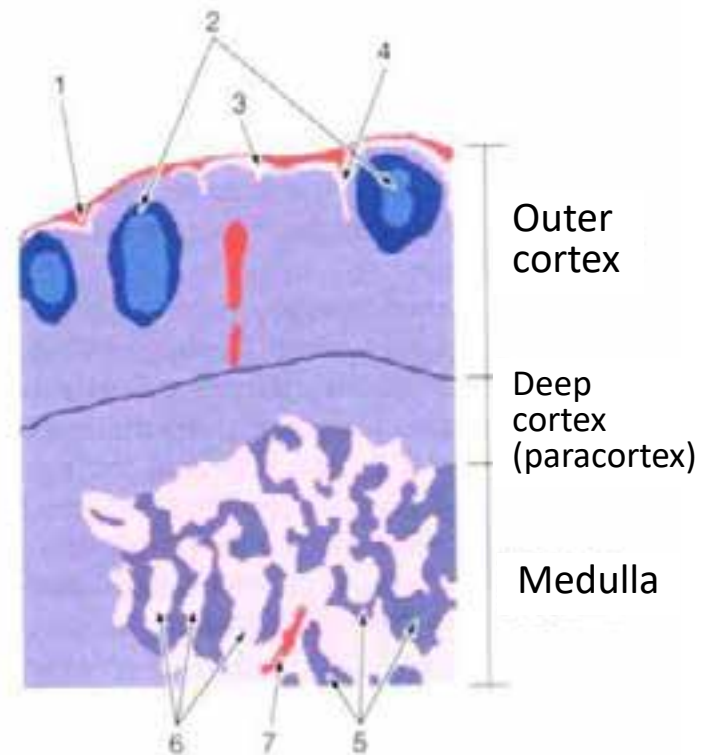
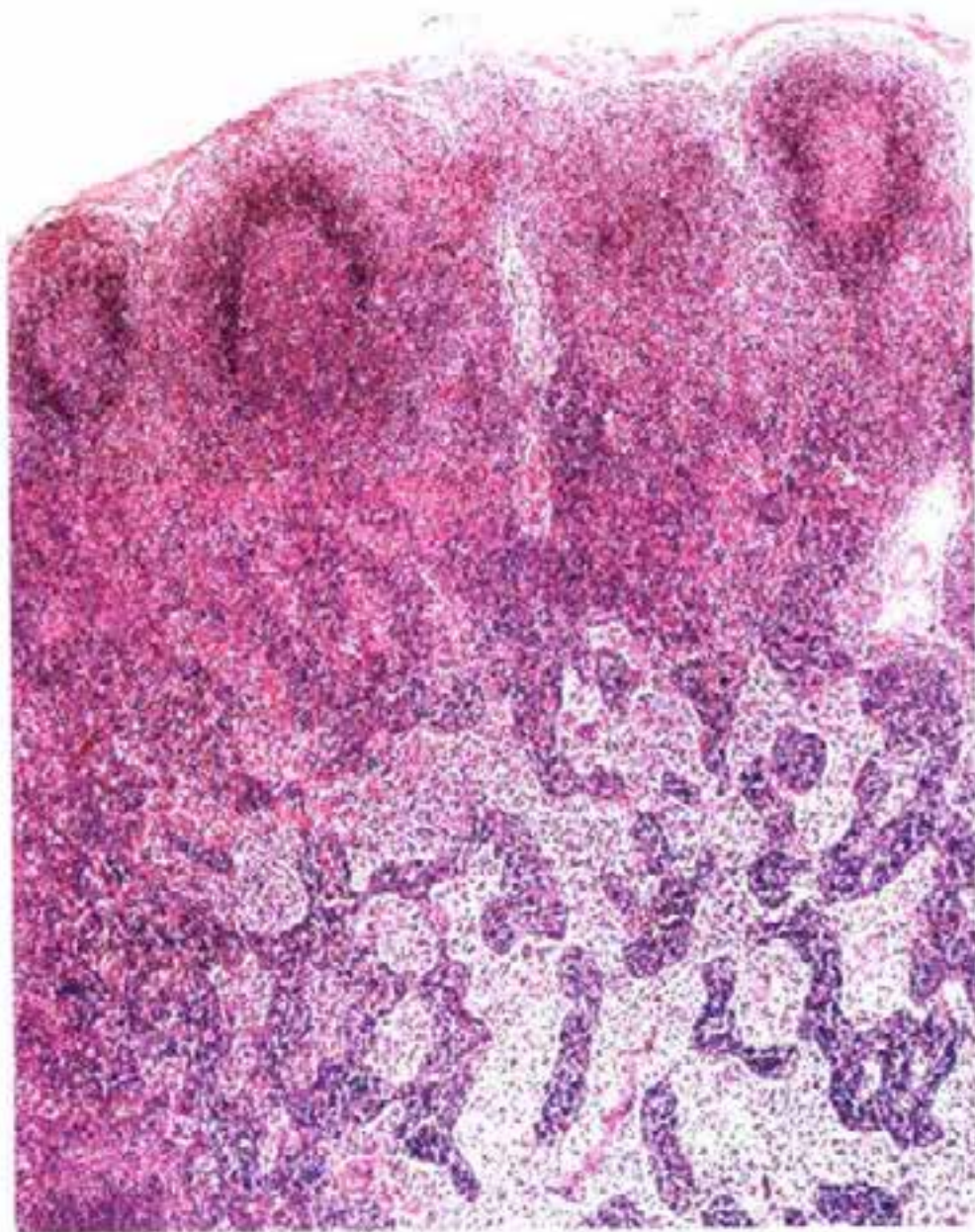


HIGH ENDOTHELIAL VENULE IN A LYMPH NODE



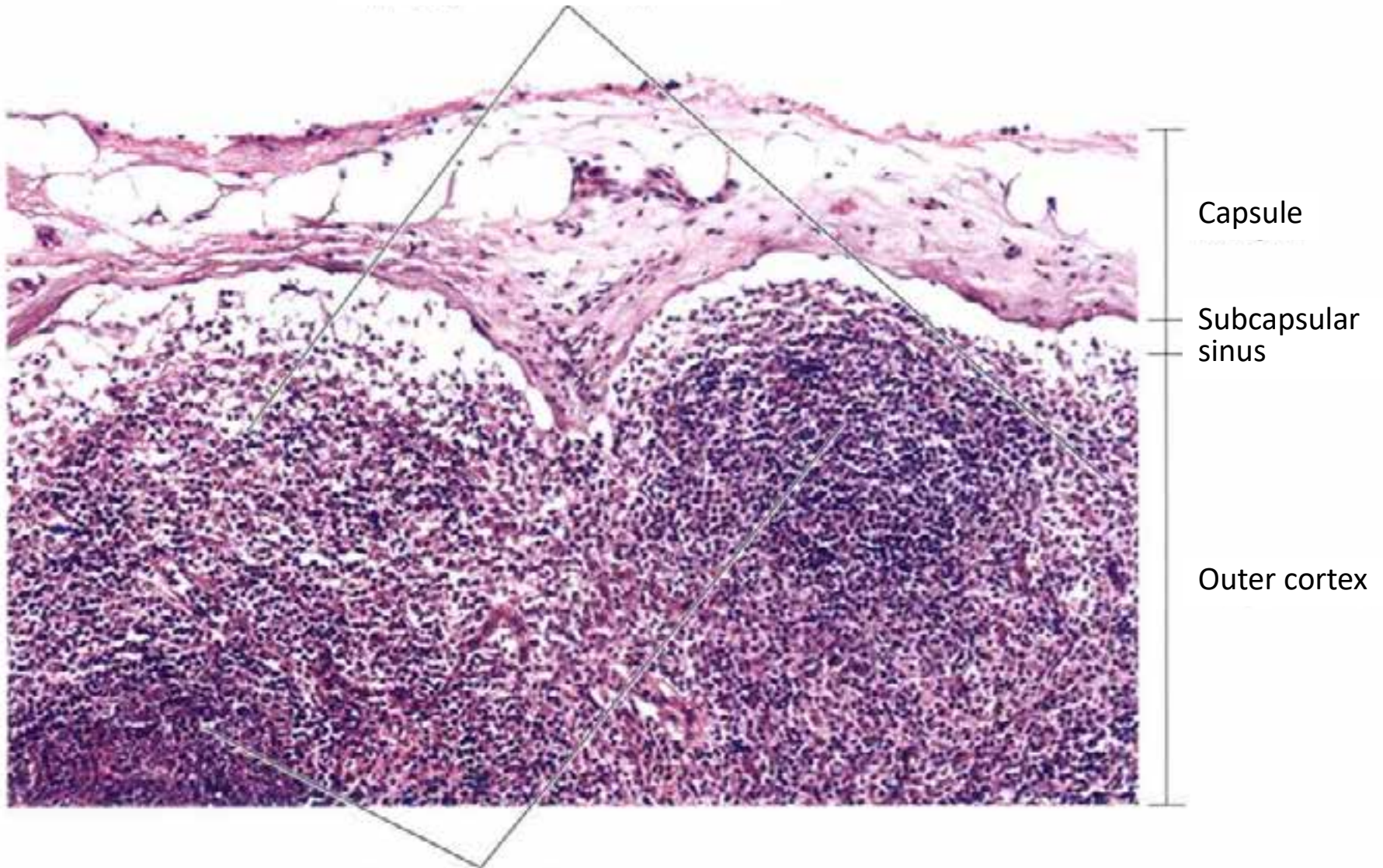
⇒ migrating lymphocytes

▷ endothelial cells



- 1- lymphatic nodule (lymphoid follicle),
- 2- germinal center of the lymphatic nodule,
- 3- subcapsular sinus,
- 4- internodular sinus,
- 5- medullary cords,
- 6- medullary sinus,
- 7- trabecula

Diffuse lymphoid tissue

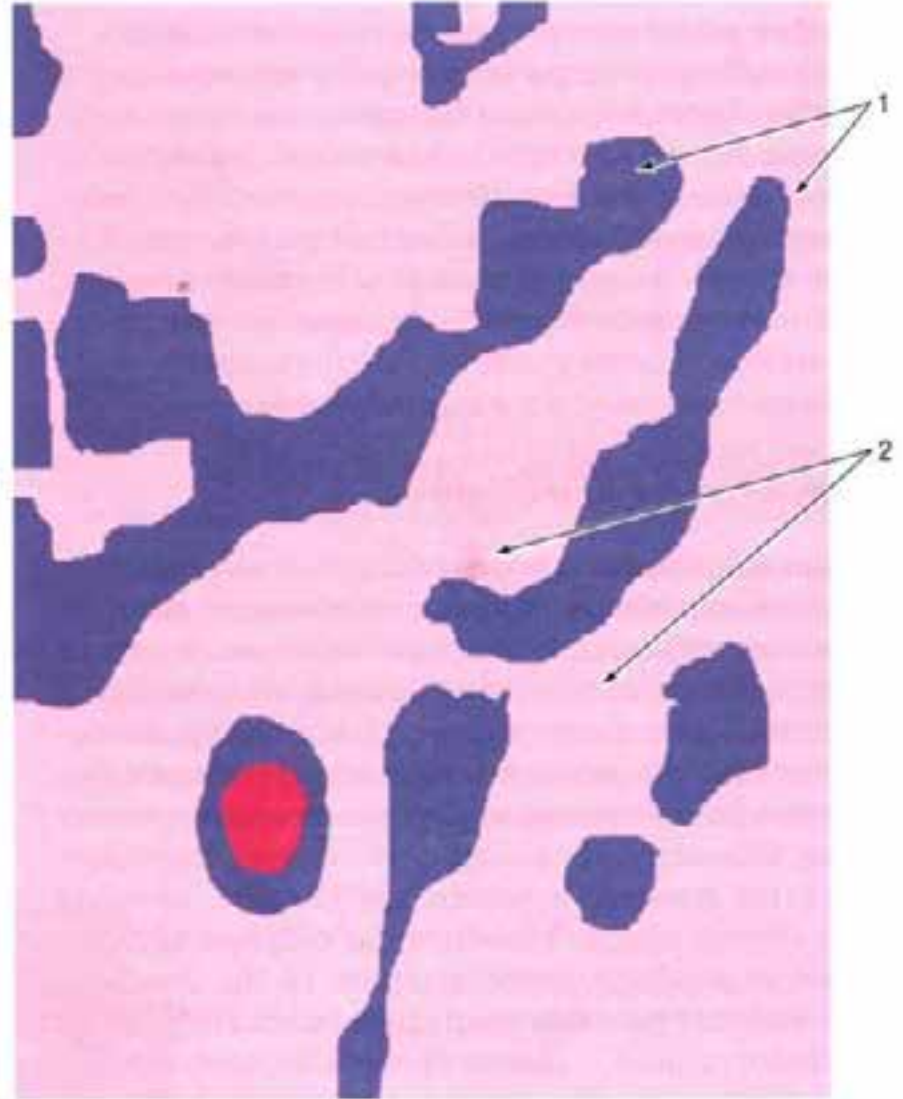
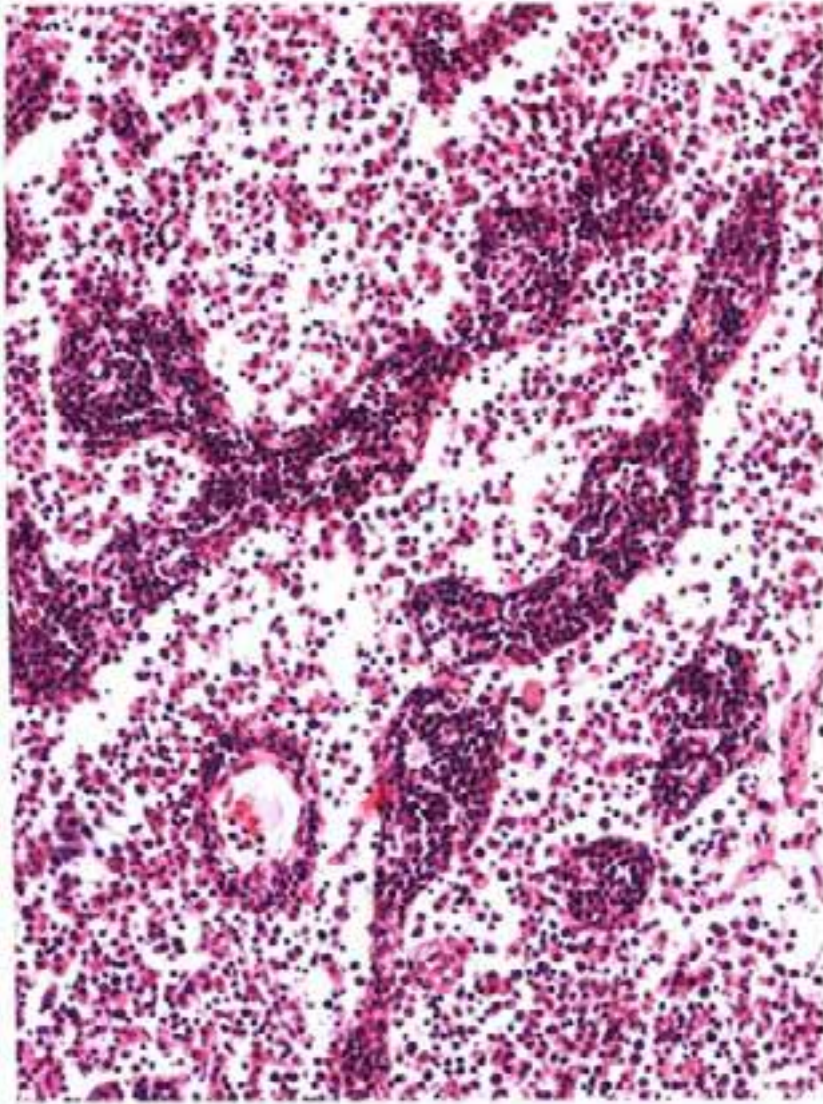


Capsule

Subcapsular
sinus

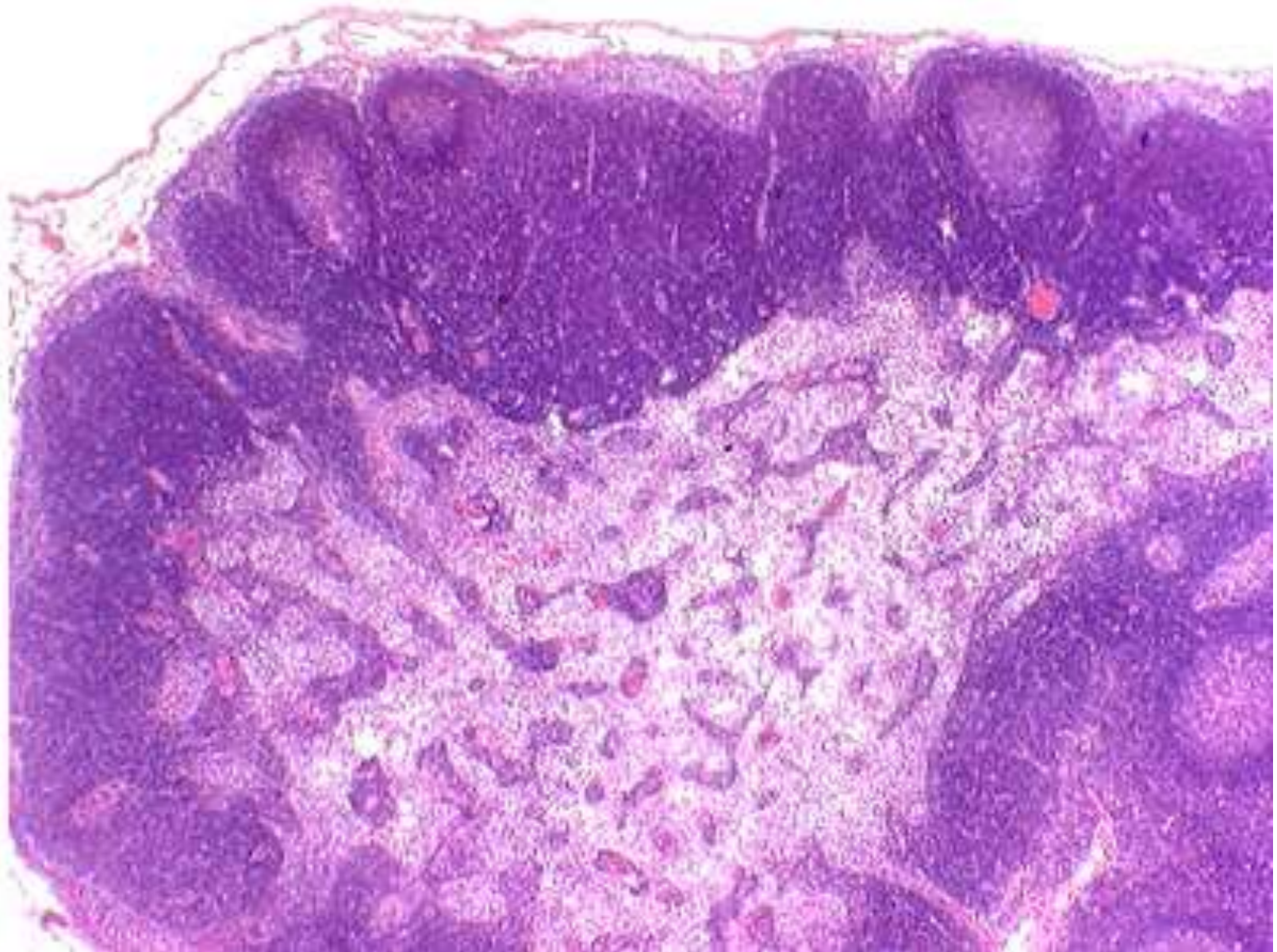
Outer cortex

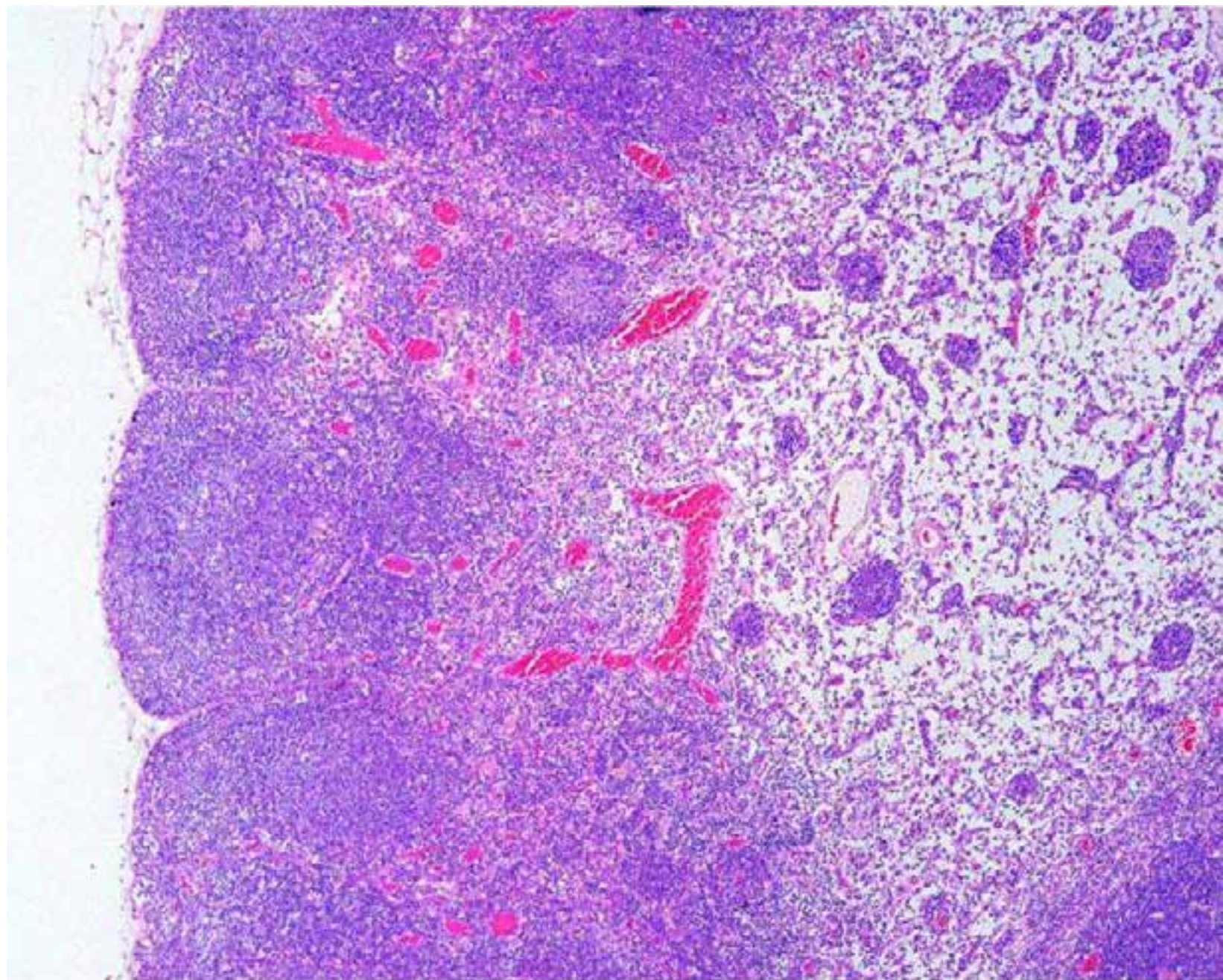
Lymphoid follicles

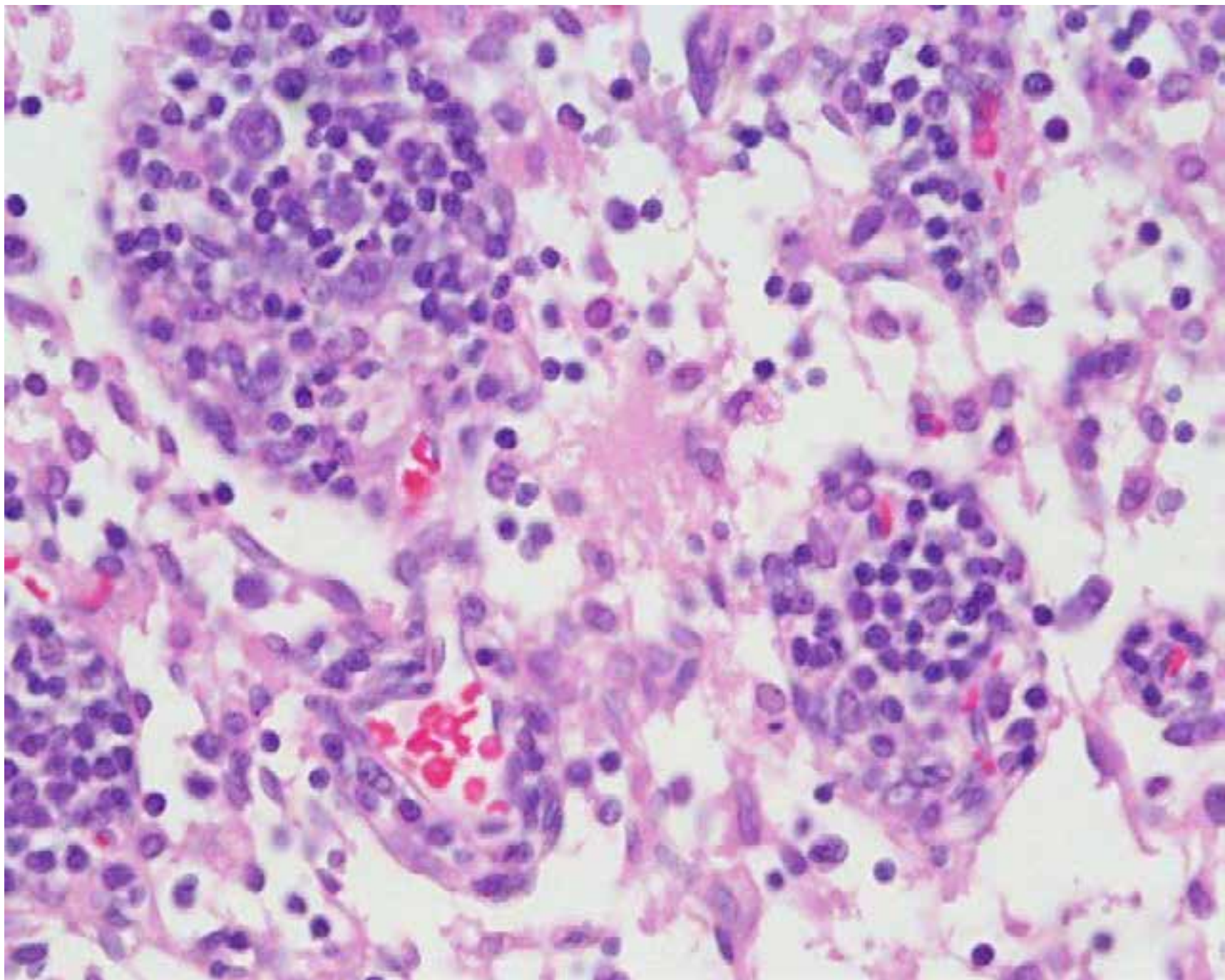


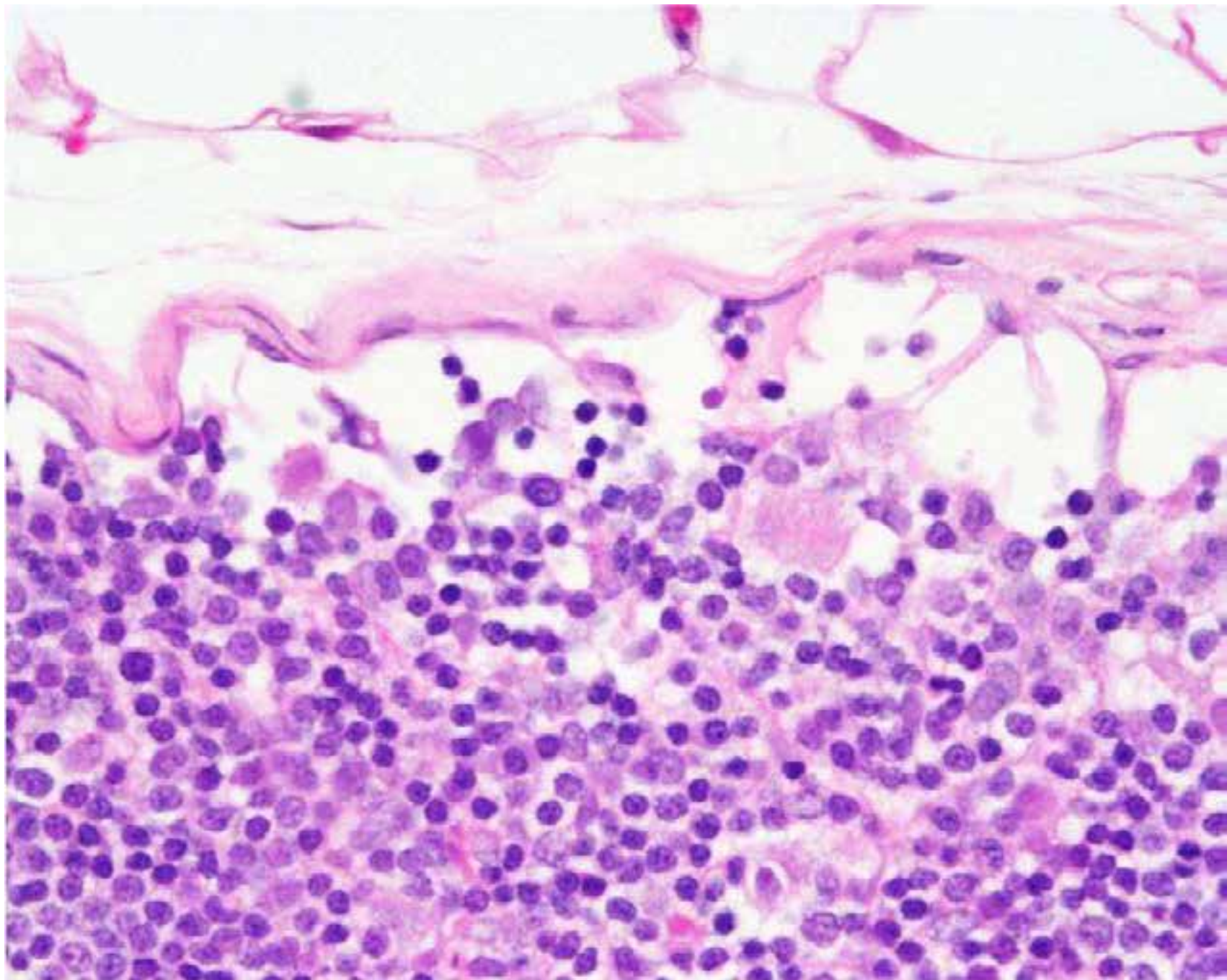
1- medullary cords, 2- medullary sinuses

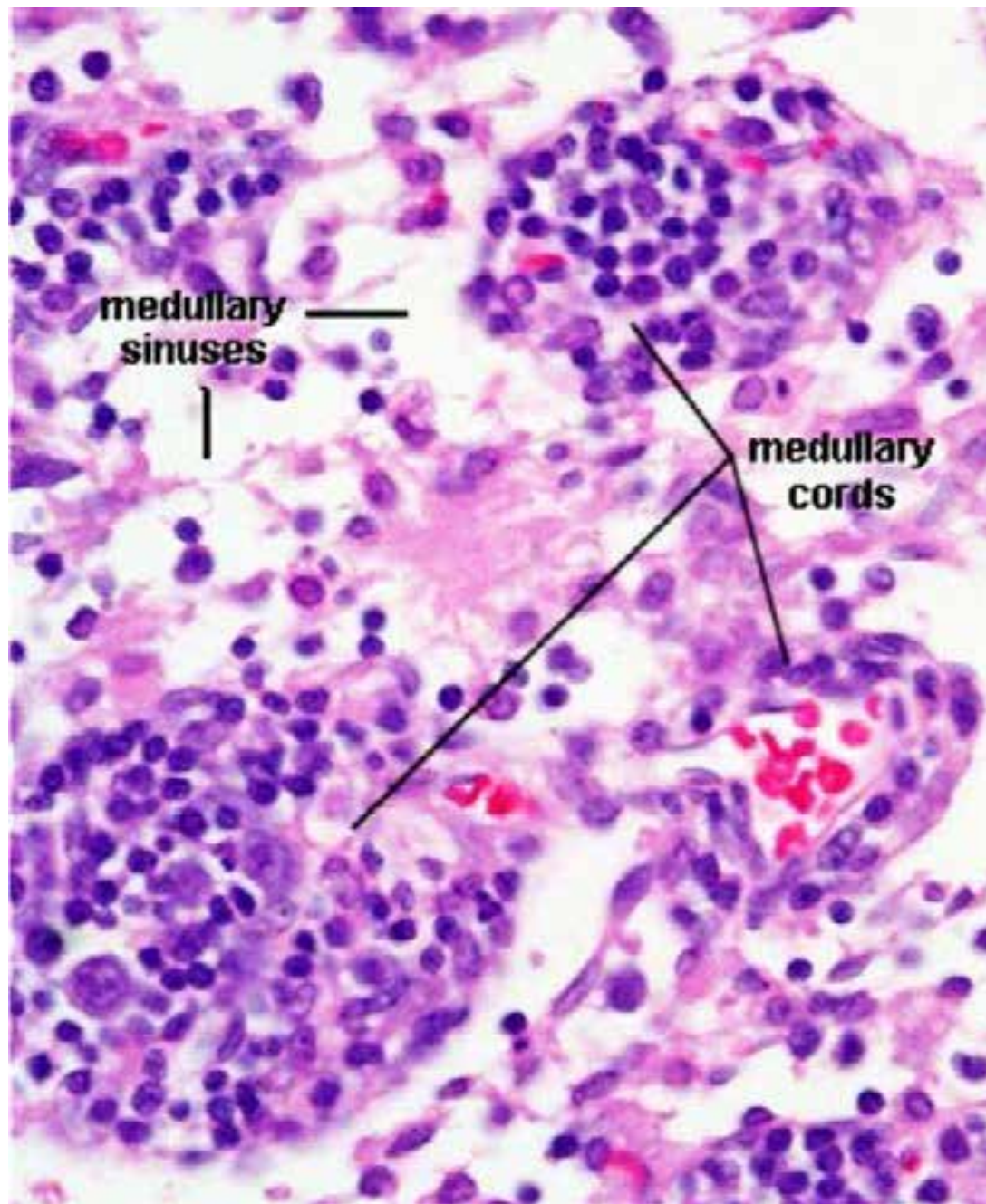
*Slide №118. Section of a lymph node
Hematoxylin-eosin staining*



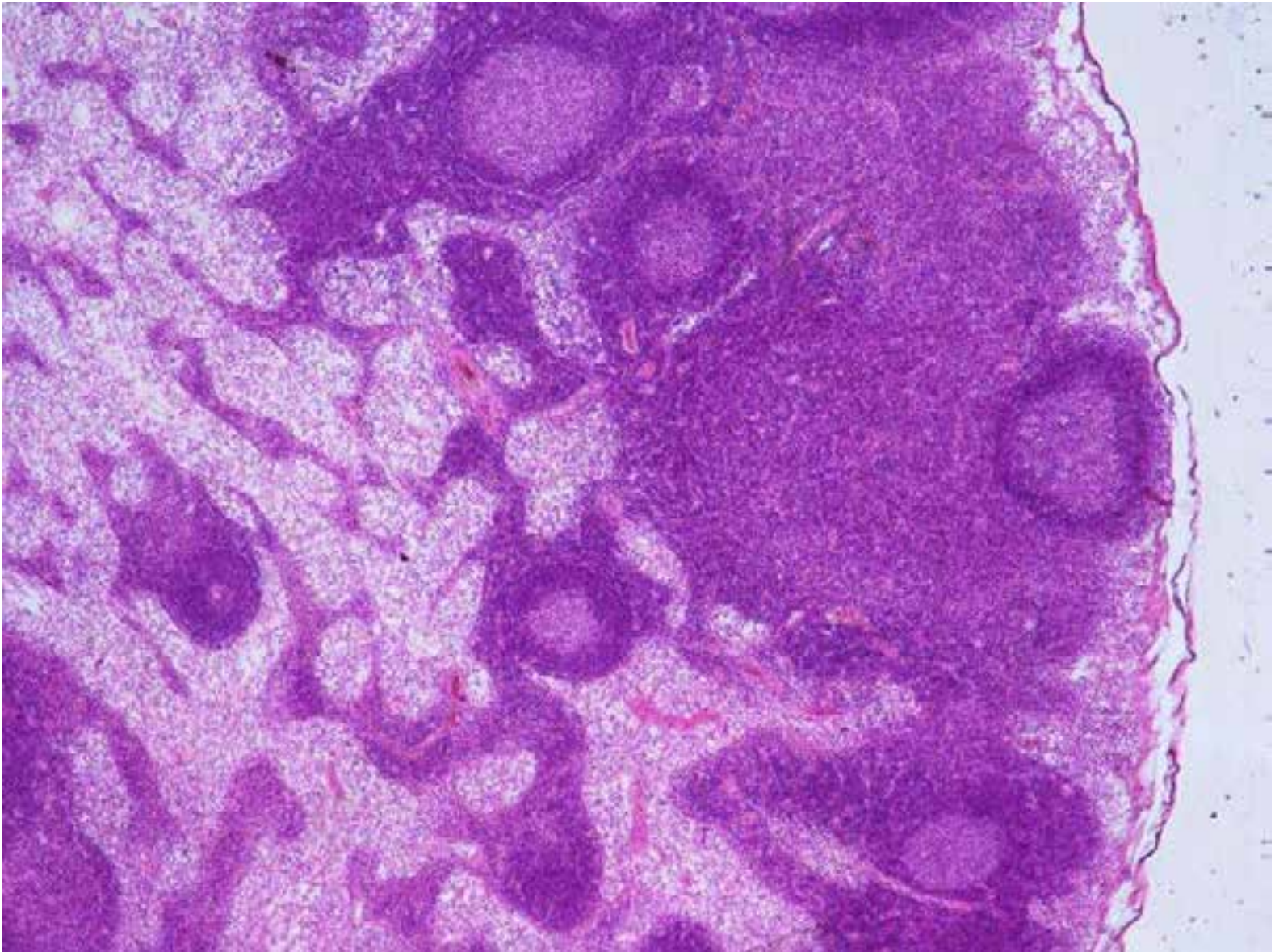






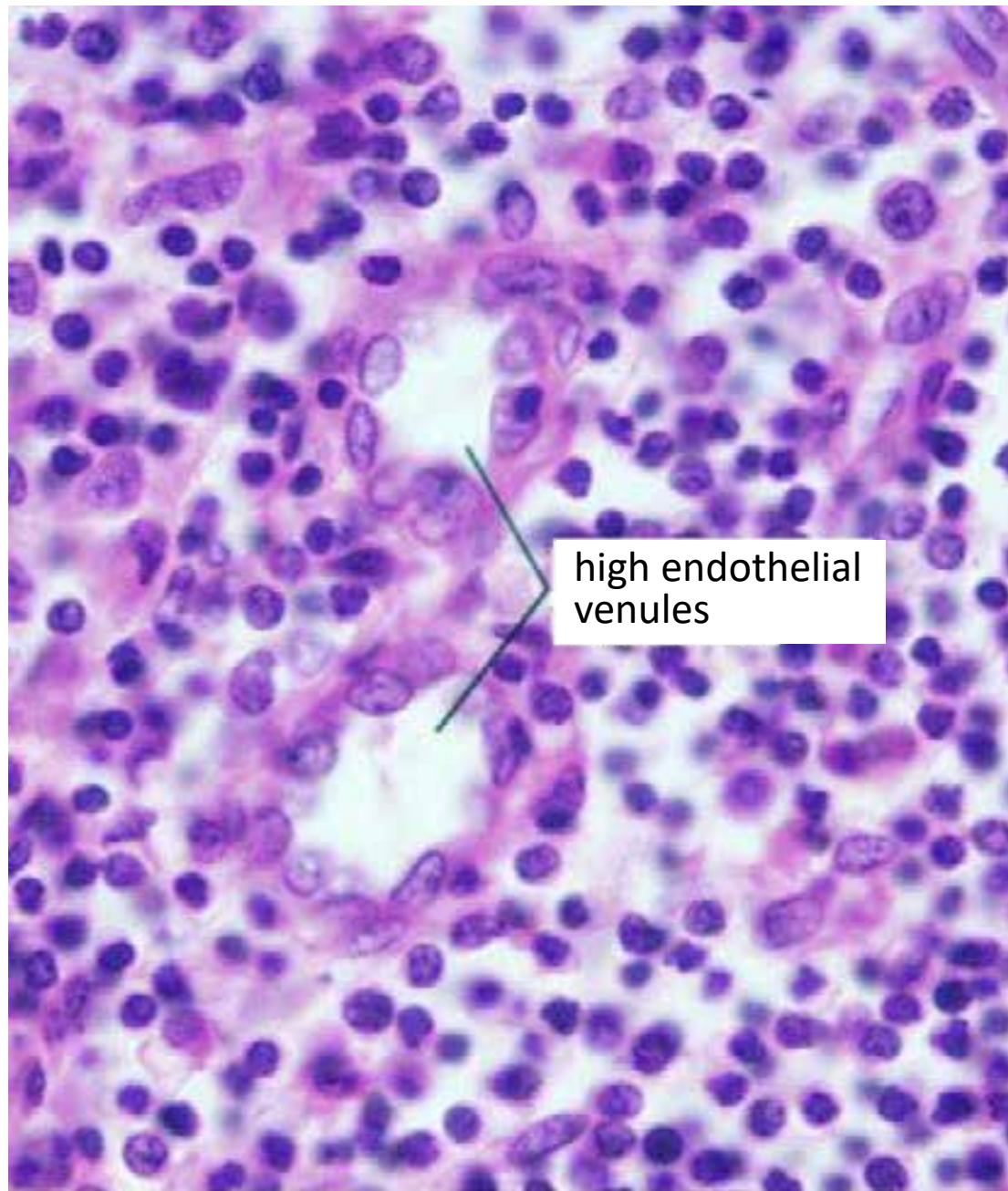


*Slide №118. Section of a lymph node
Hematoxylin-eosin staining*



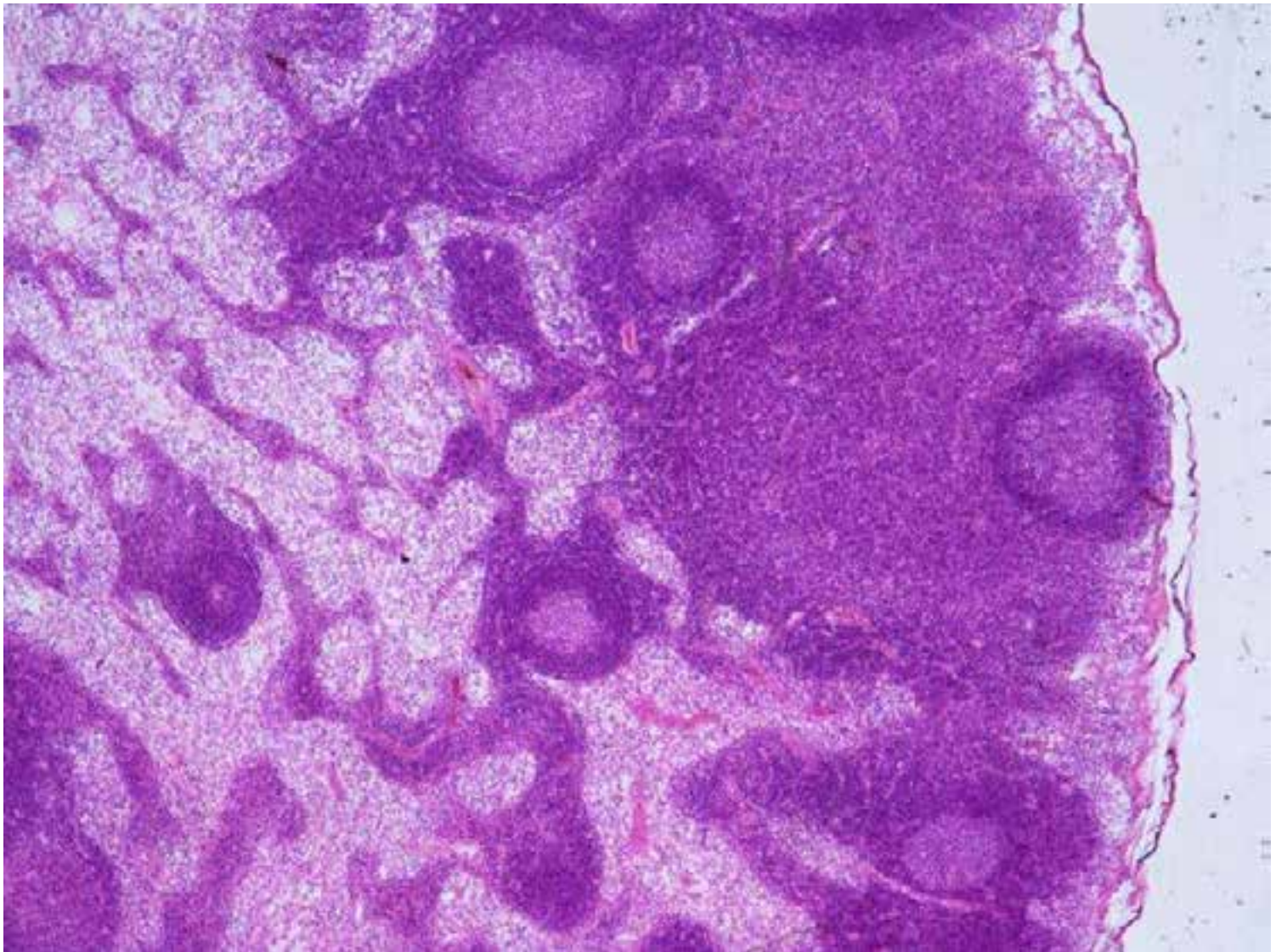
*Slide №118. Section of a lymph node
Hematoxylin-eosin staining*



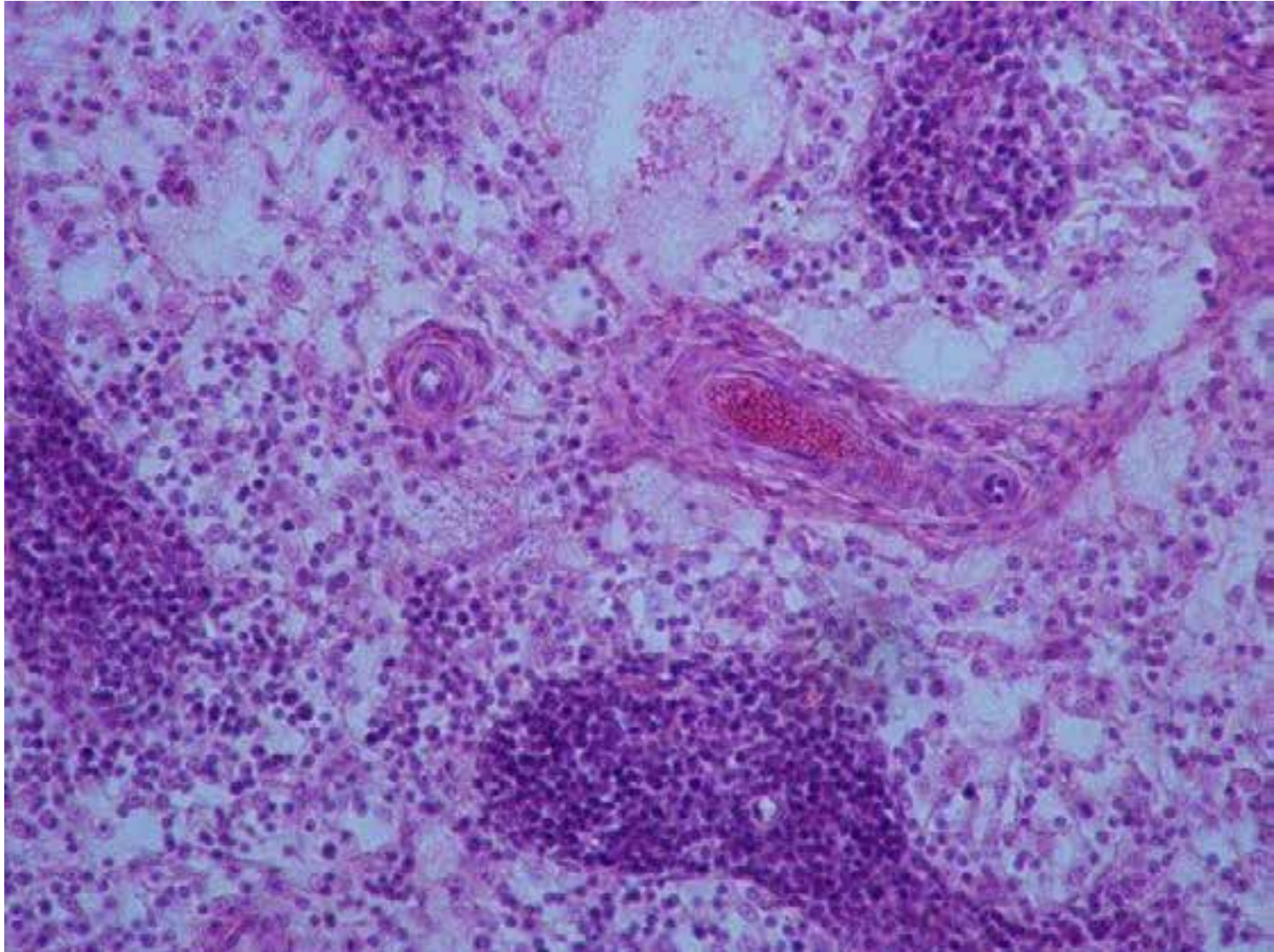


high endothelial
venules

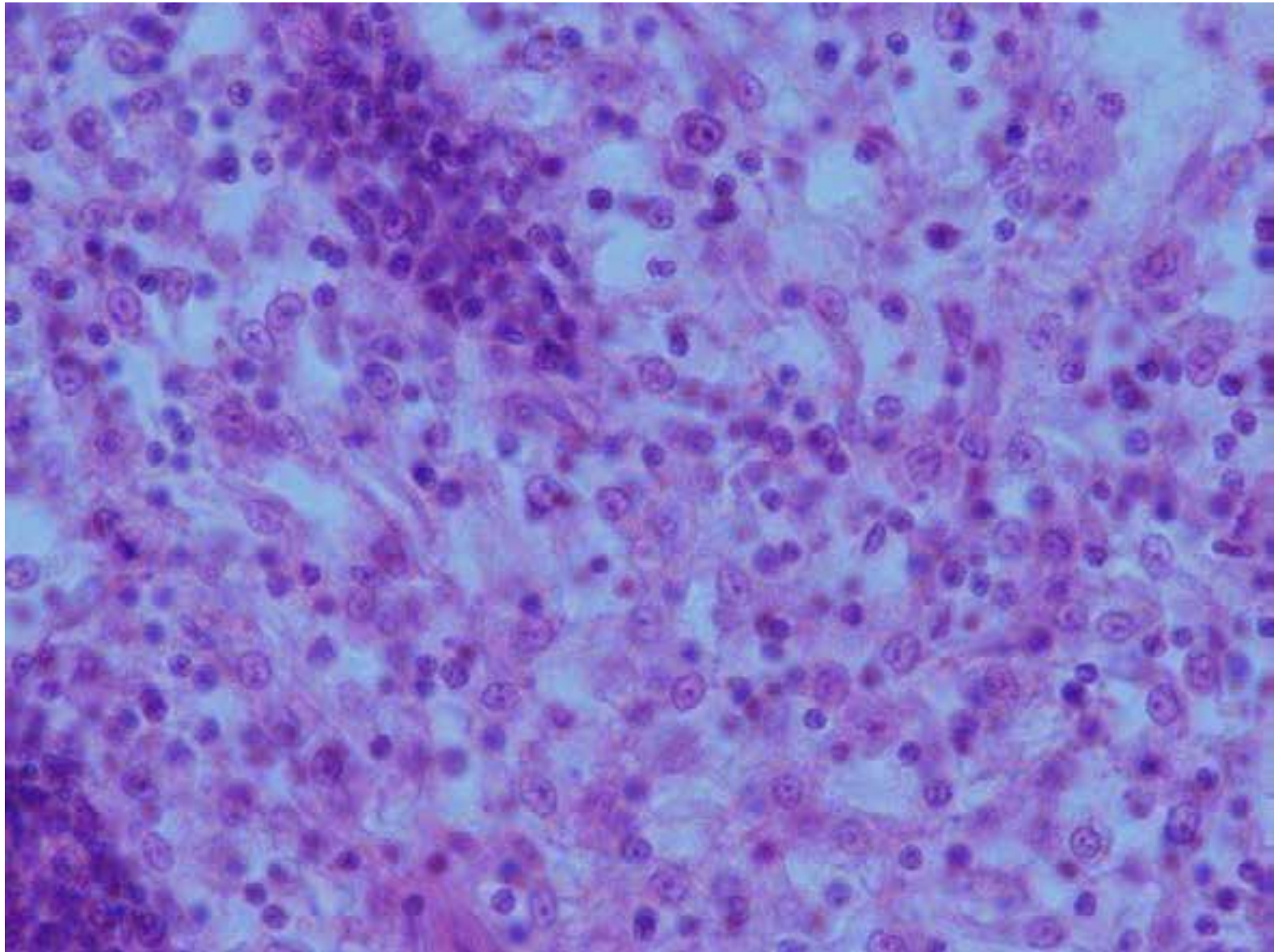
*Slide №118. Section of a lymph node
Hematoxylin-eosin staining*



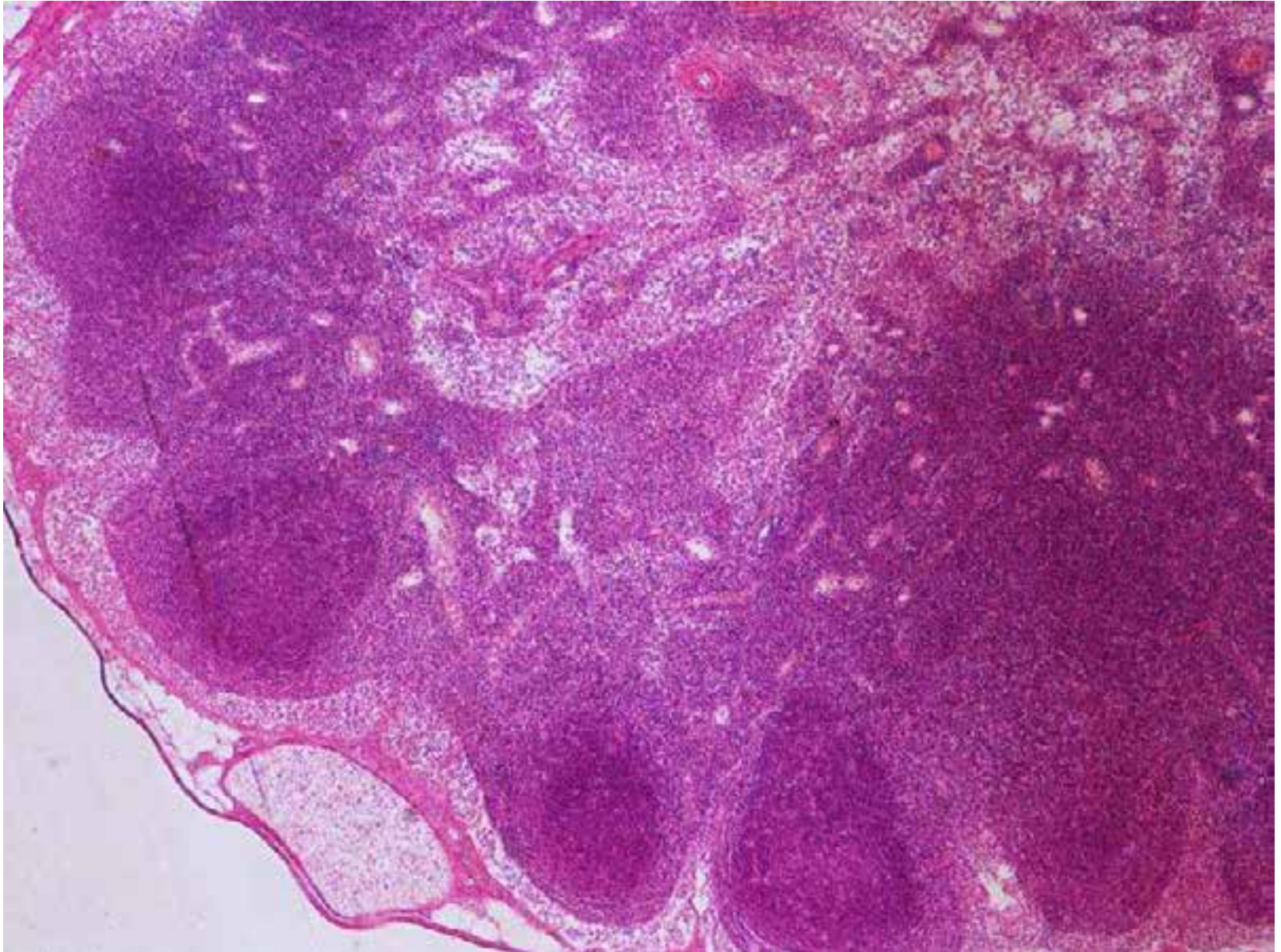
*Slide №118. Section of a lymph node
Hematoxylin-eosin staining*



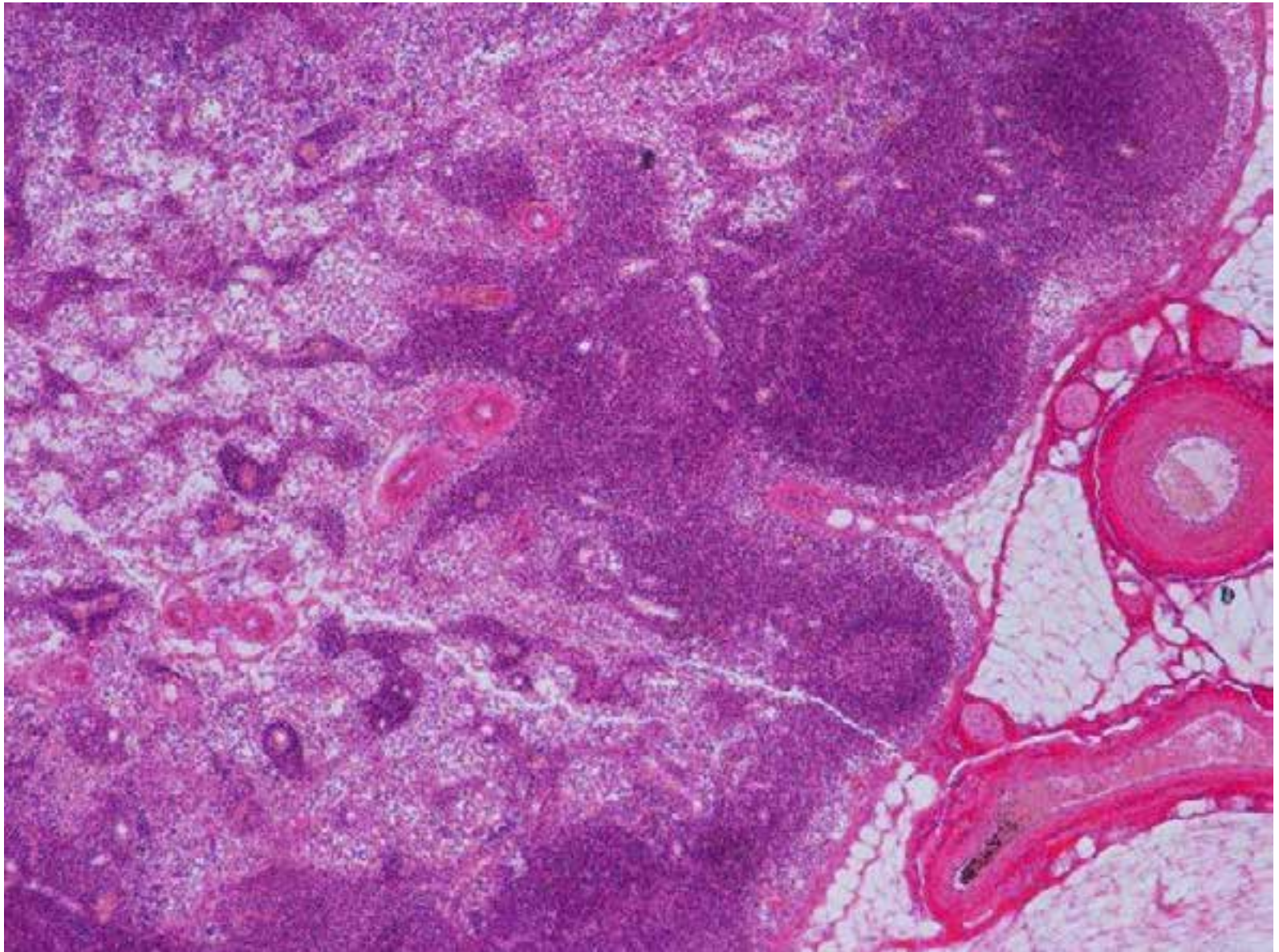
*Slide №118. Section of a lymph node
Hematoxylin-eosin staining*



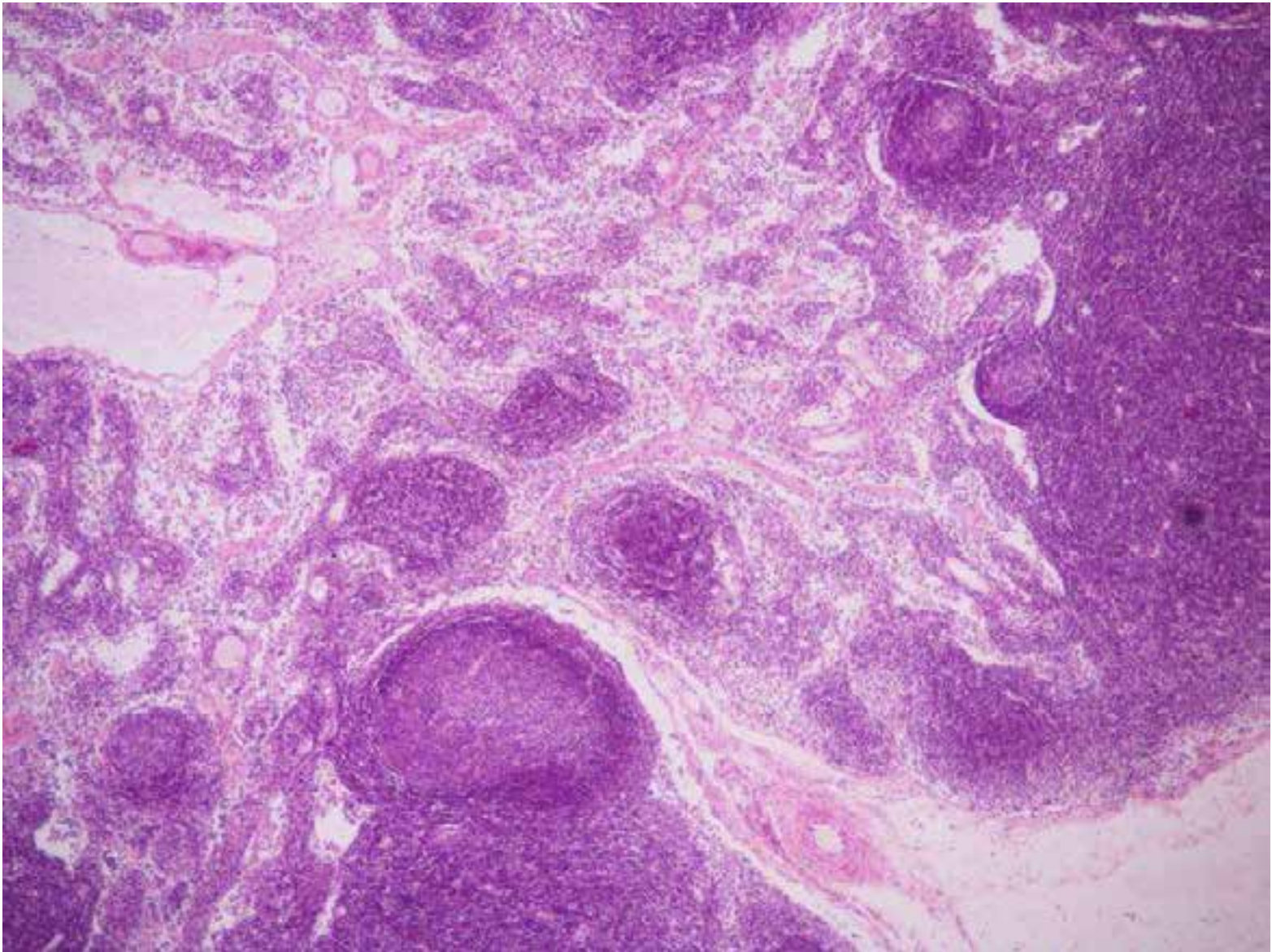
*Slide №118. Section of a lymph node
Hematoxylin-eosin staining*



*Slide №118. Section of a lymph node
Hematoxylin-eosin staining*



*Slide №118. Section of a lymph node
Hematoxylin-eosin staining*



DEVELOPMENT OF THE SPLEEN

5th week of the intrauterine life

Splenic anlage segregates inside the mesenchyme of the dorsal mesentery A portion of the cells differentiate into reticular tissue

12th week

B cells emerge

3rd month

Sinusoidal capillaries emerge

5th month

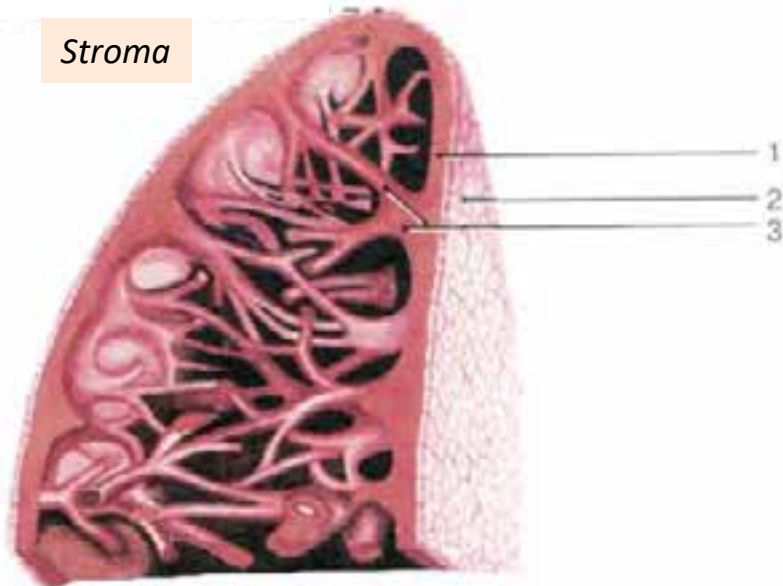
T and B zones are demarcated (respectively, lymphatic nodules and the red pulp)
Splenic myelopoiesis reaches its maximum

from the 6th month

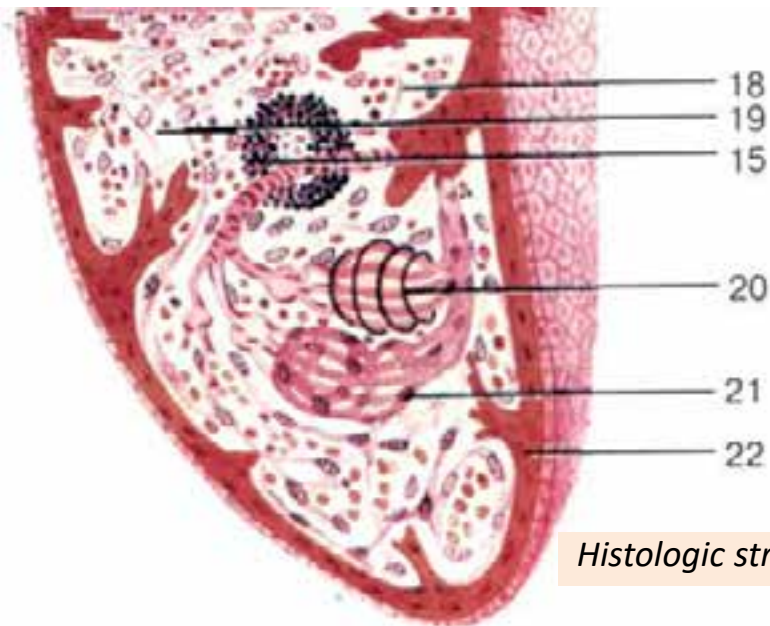
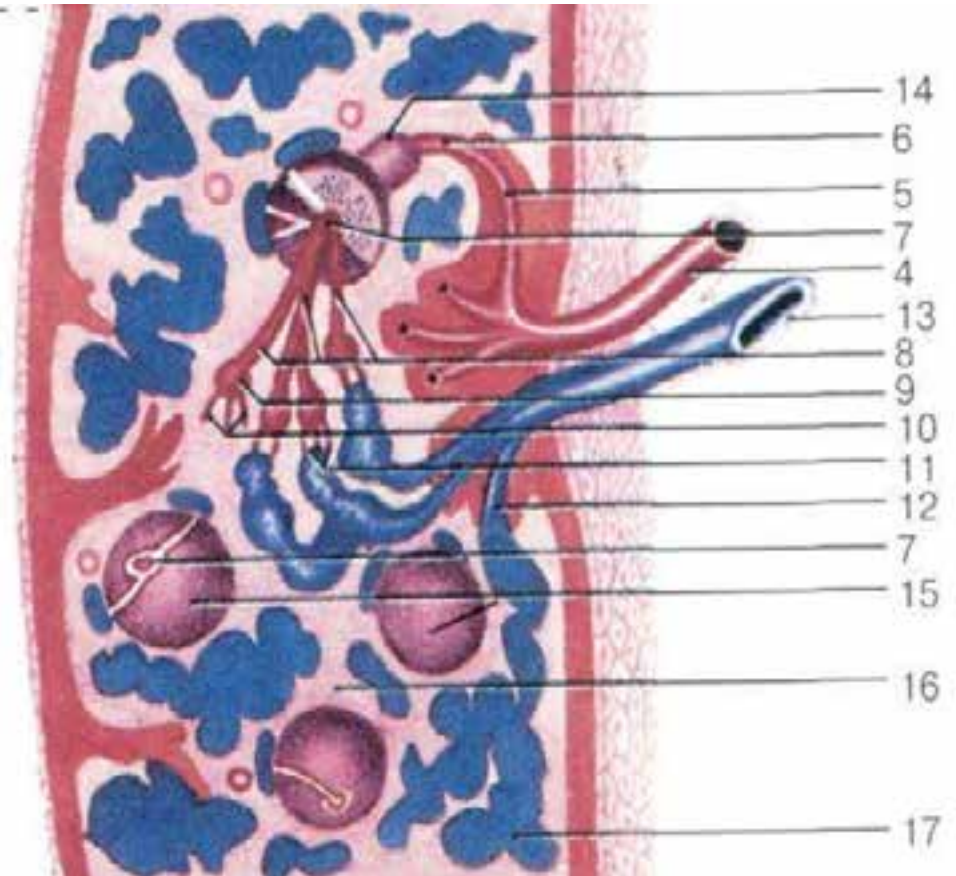
The spleen acquires its definitive structure

STRUCTURE OF THE SPLEEN

Stroma

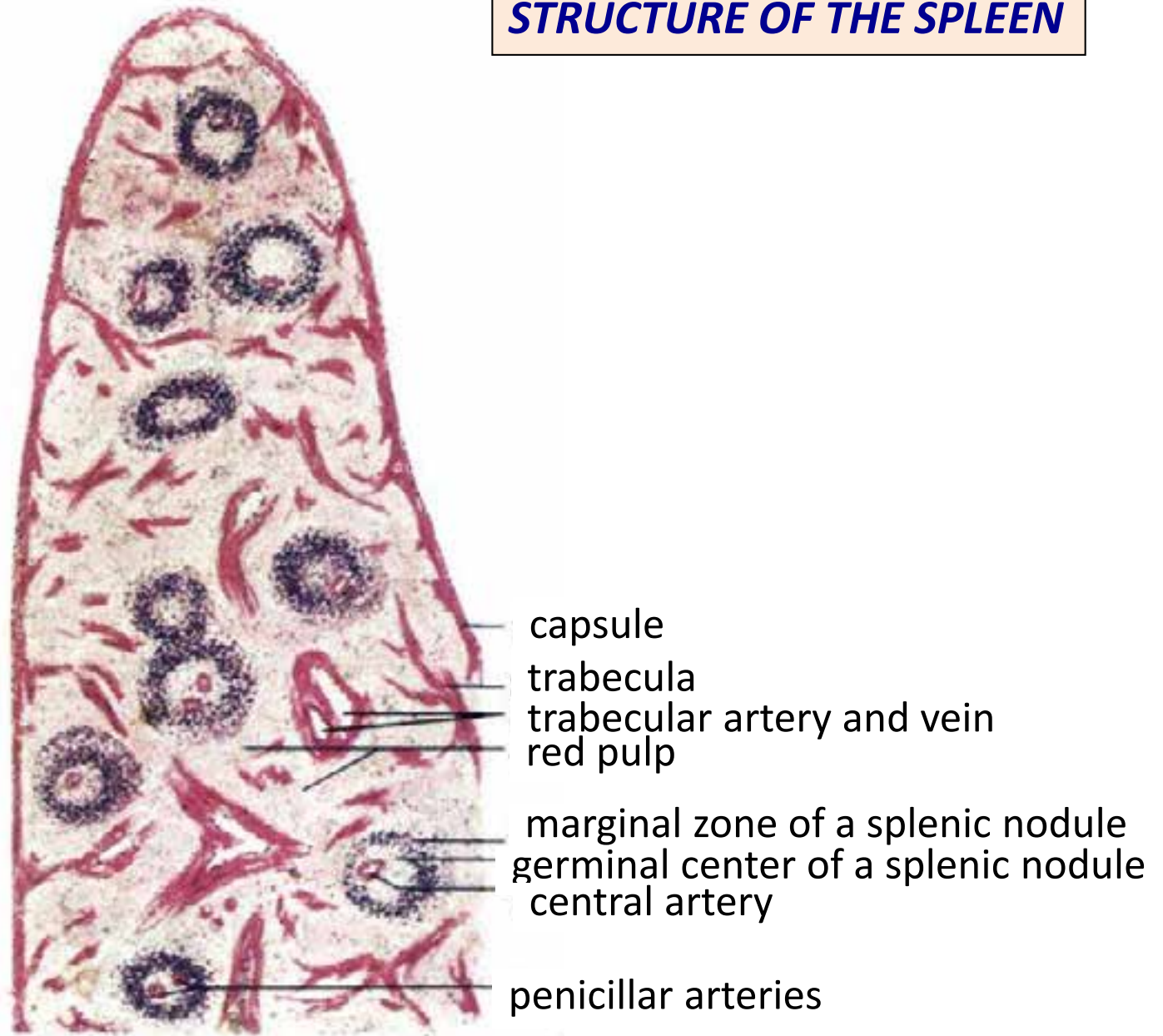


Vascular system

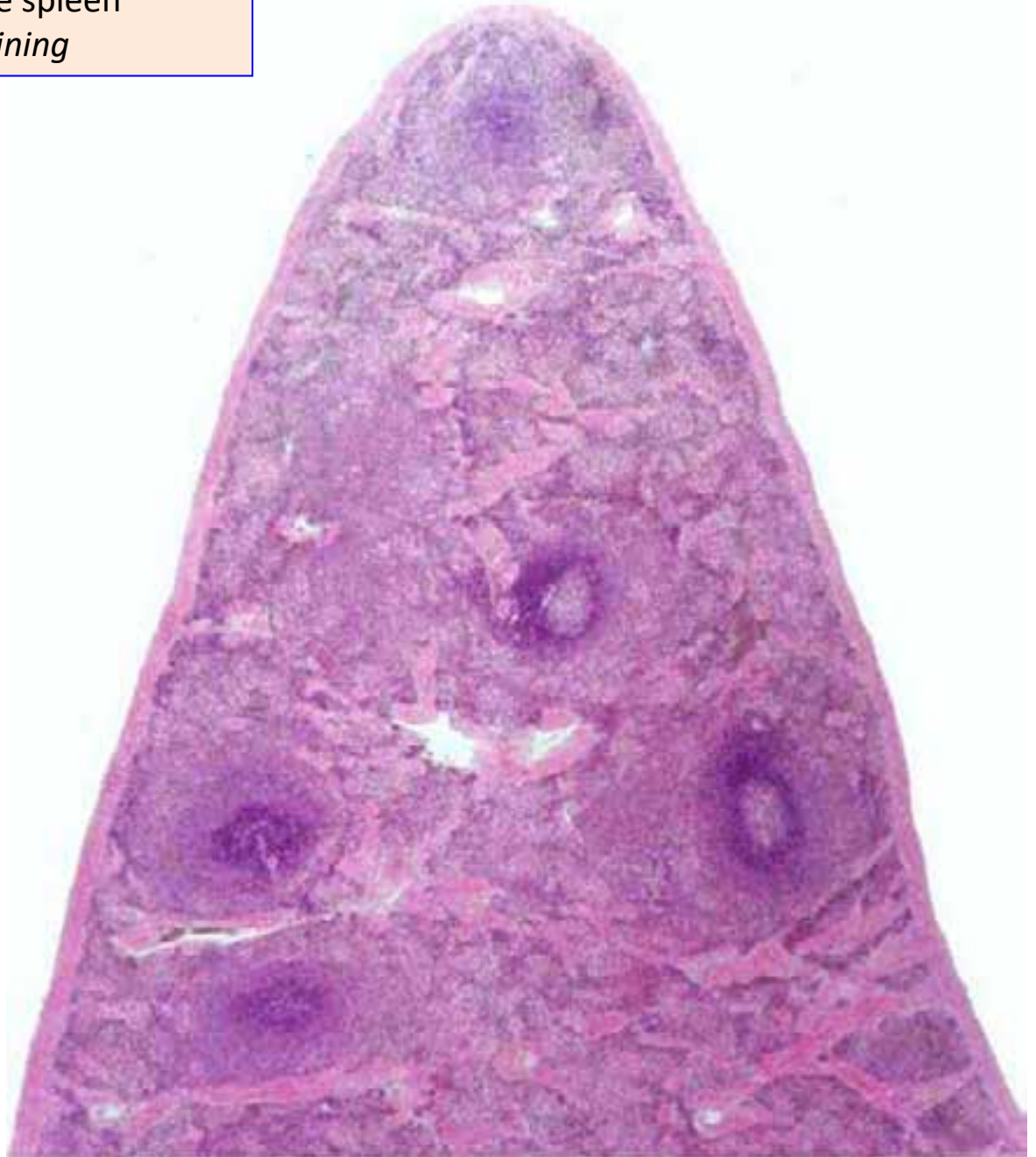


Histologic structure

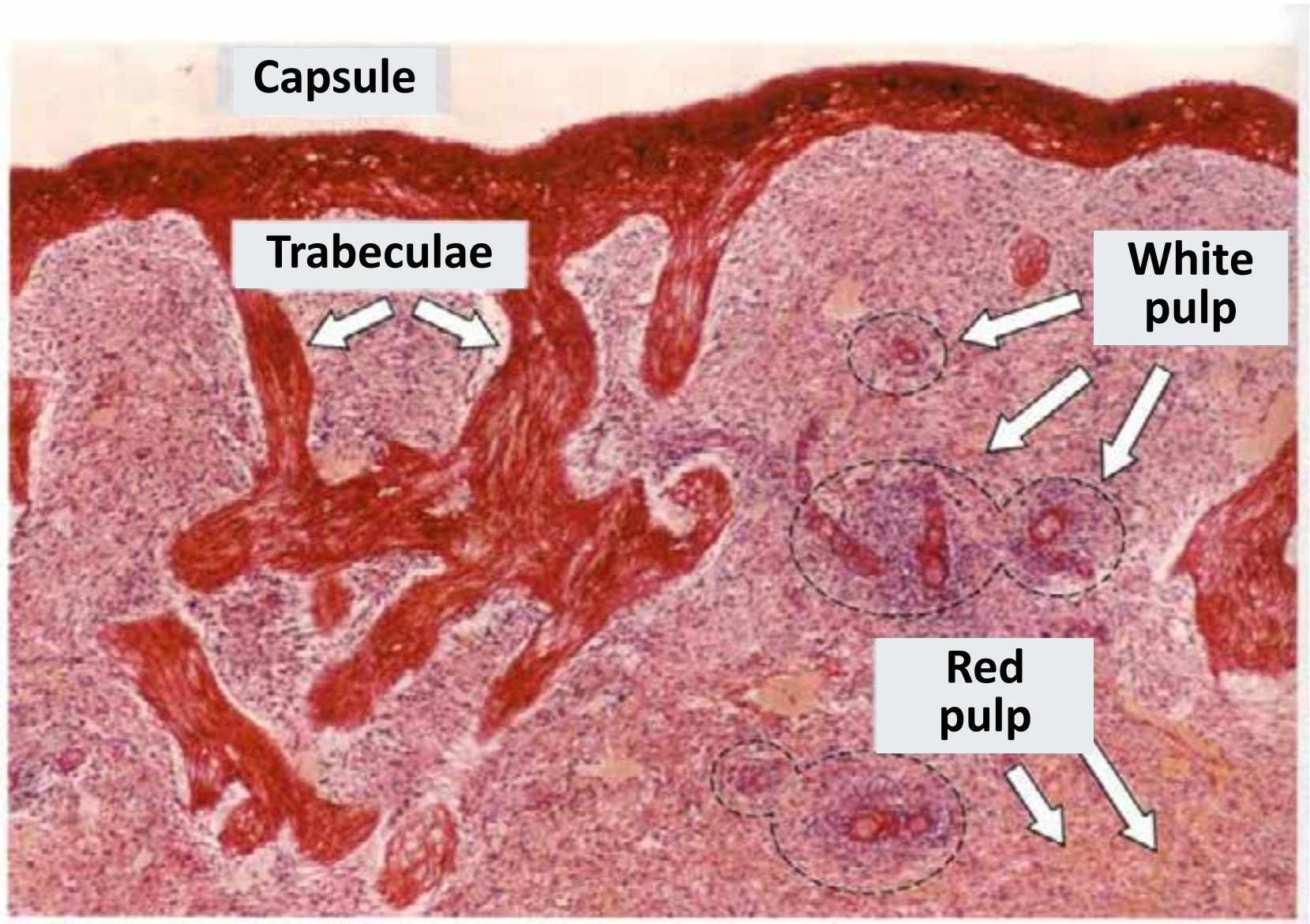
STRUCTURE OF THE SPLEEN



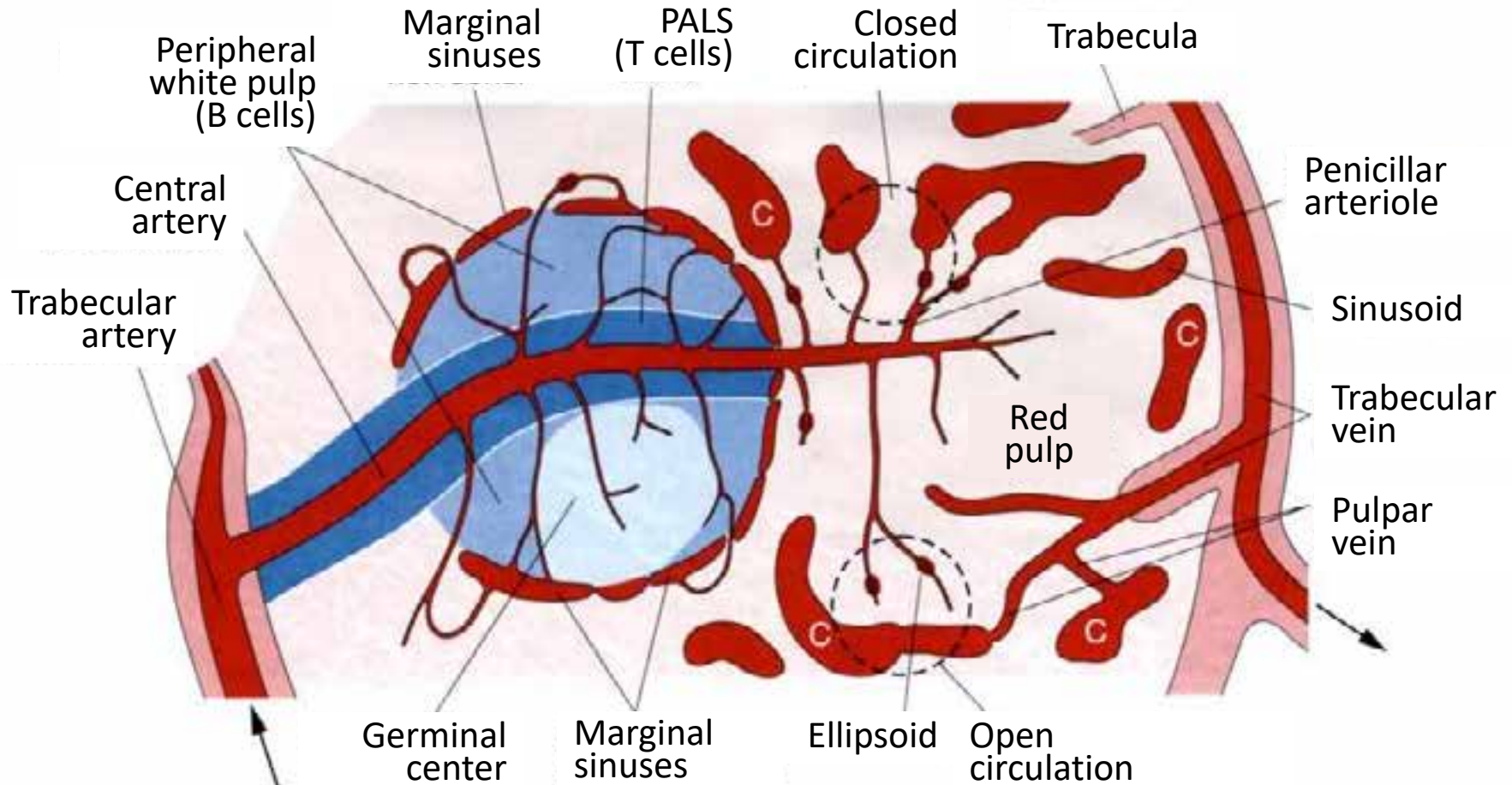
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



STRUCTURE OF THE SPLEEN



SPLenic CIRCULATION



**Closed circulation is a fast route,
ensures nutrition and oxygenation
of splenic tissues**

splenic artery
trabecular arteries
pulpar arteries
central artery
penicillar arterioles
sheathed arterioles
arteriolar sphincters

blood capillaries

closed circulation

venous sinusoids
venous sphincters
trabecular veins
splenic vein

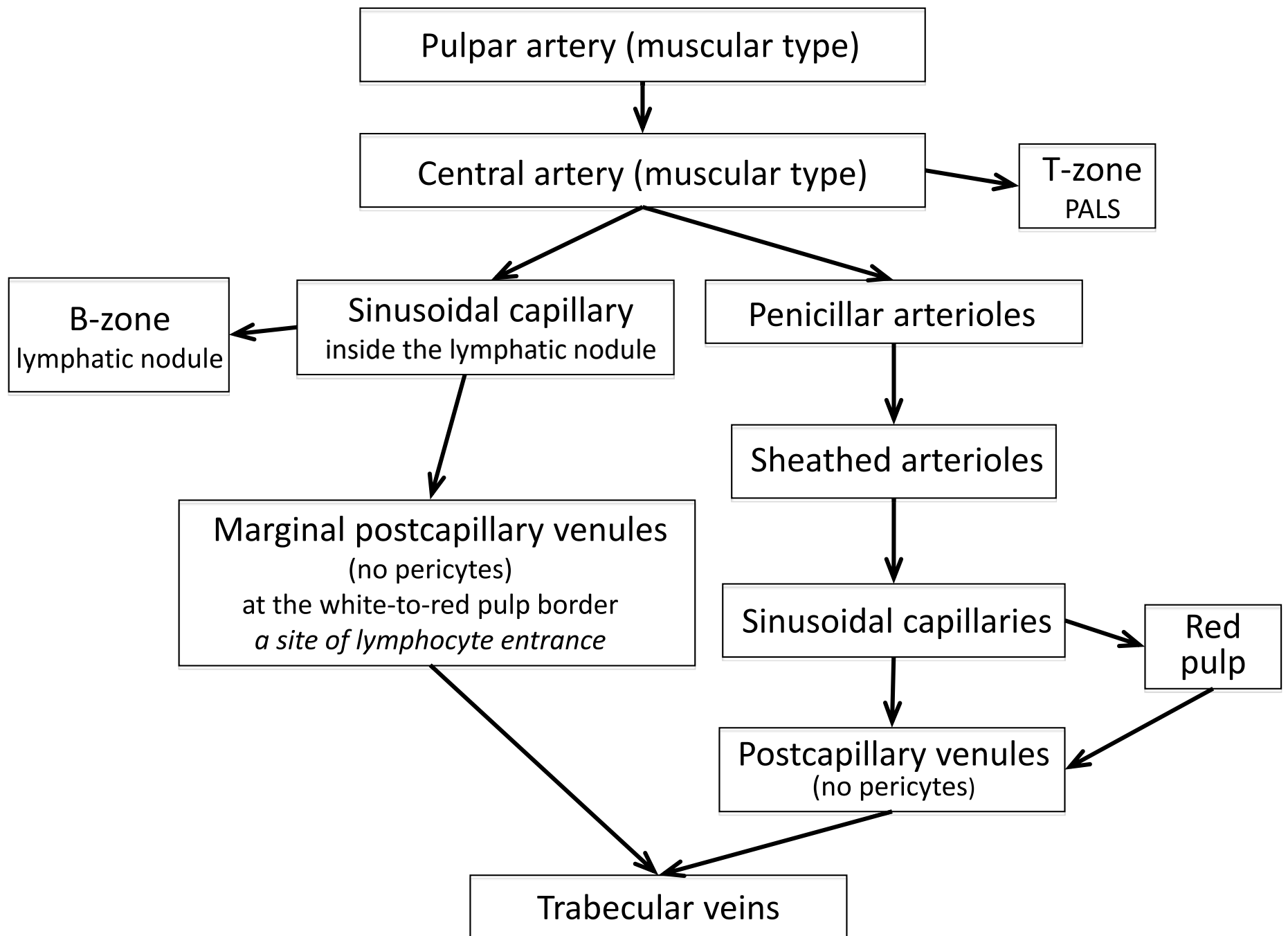
SPLENIC CIRCULATION

**Open circulation is slow, ensures
contacts of formed elements with
macrophages,
and contacts of macrophages with antigens**

open circulation

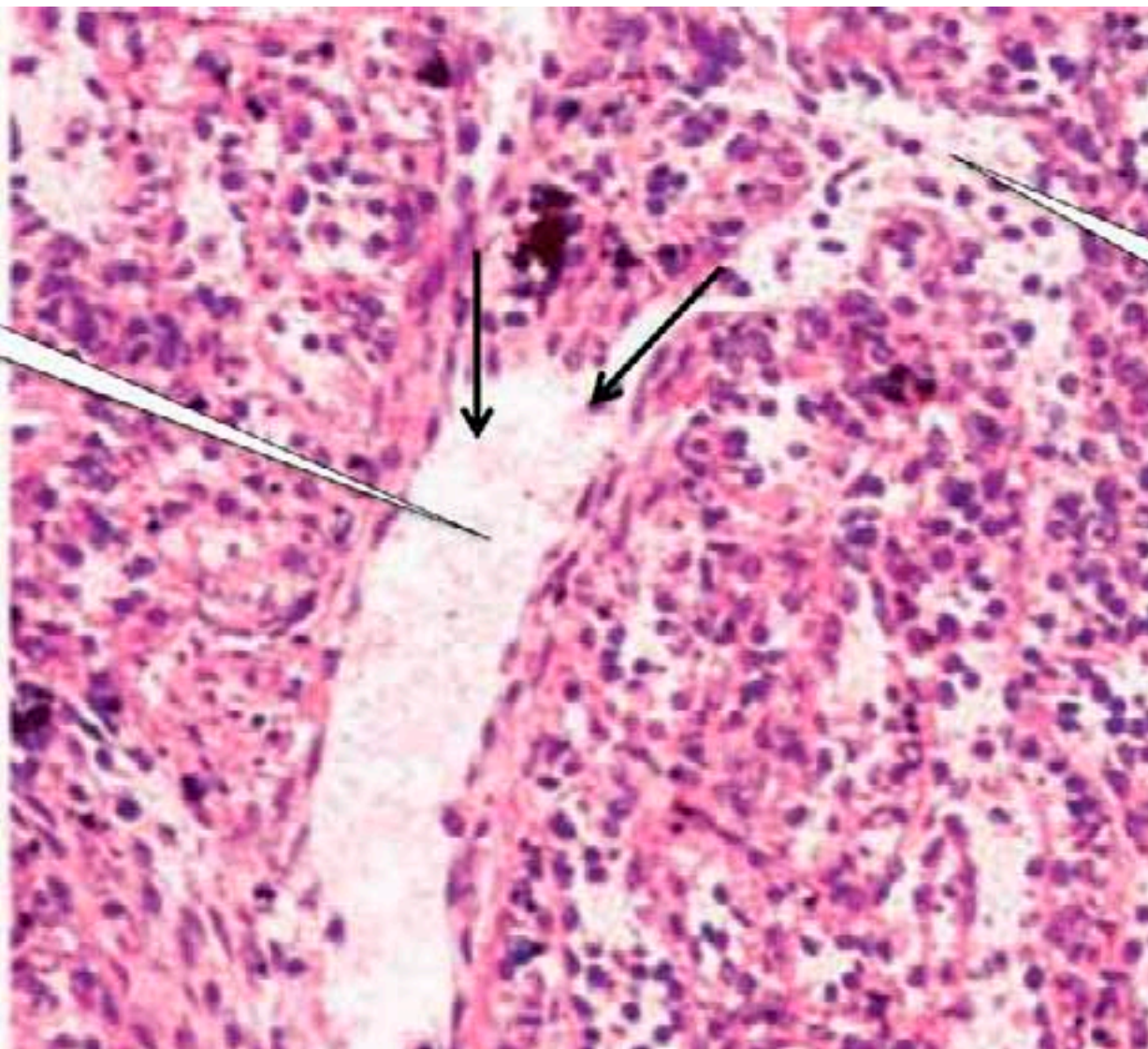
red pulp

venous sinusoids
venous sphincters
trabecular veins
splenic vein

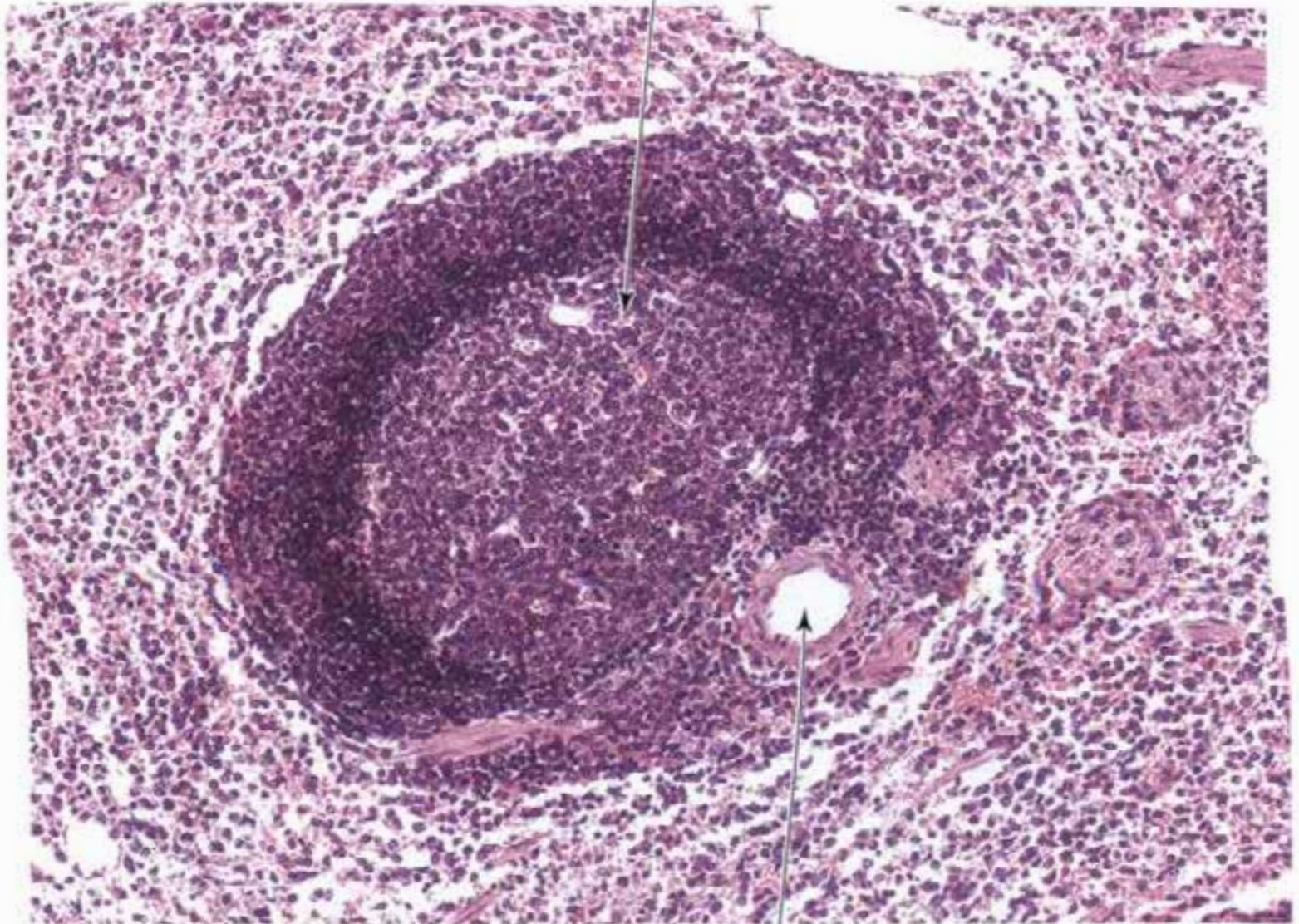


trabecular
vein

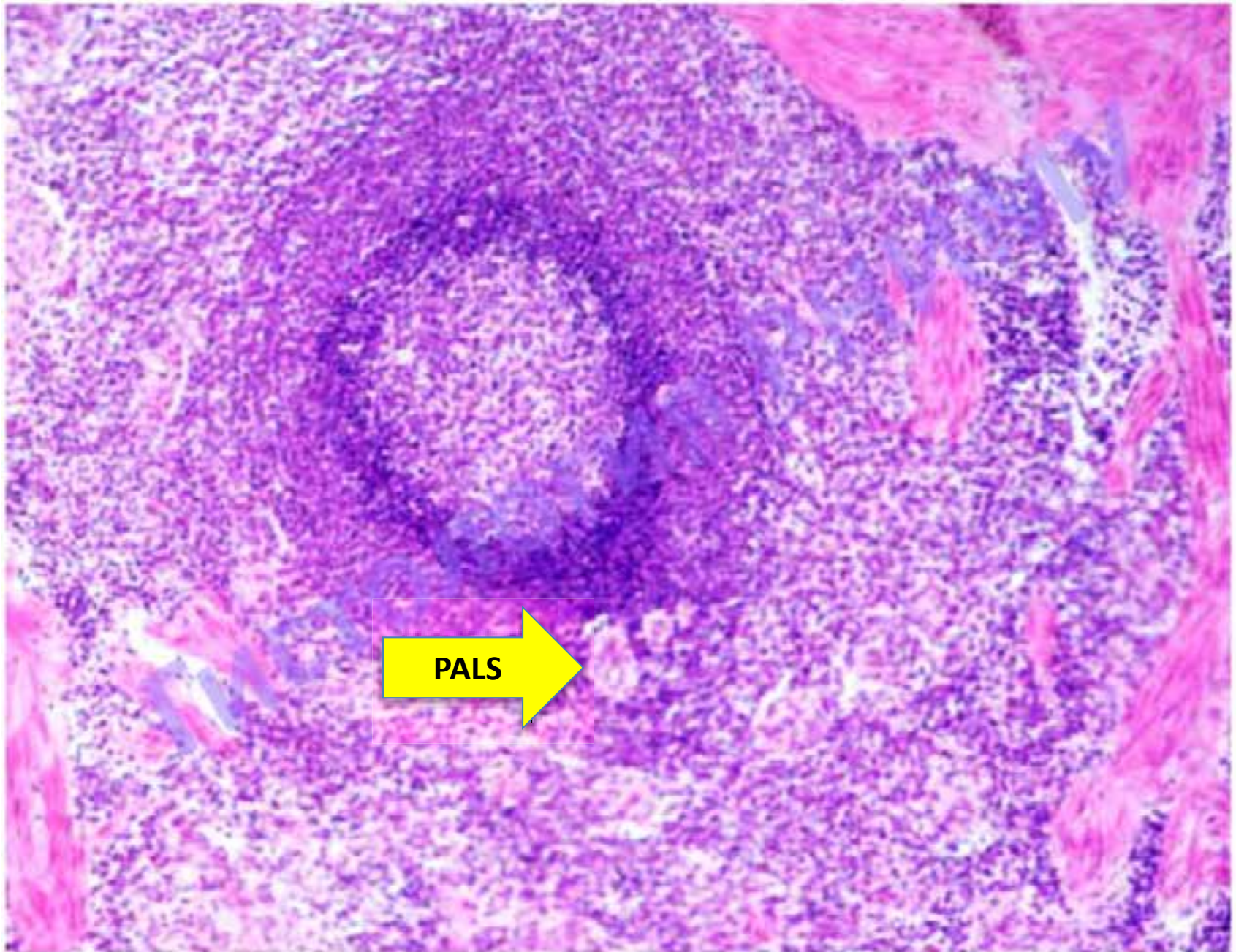
venous
sinus



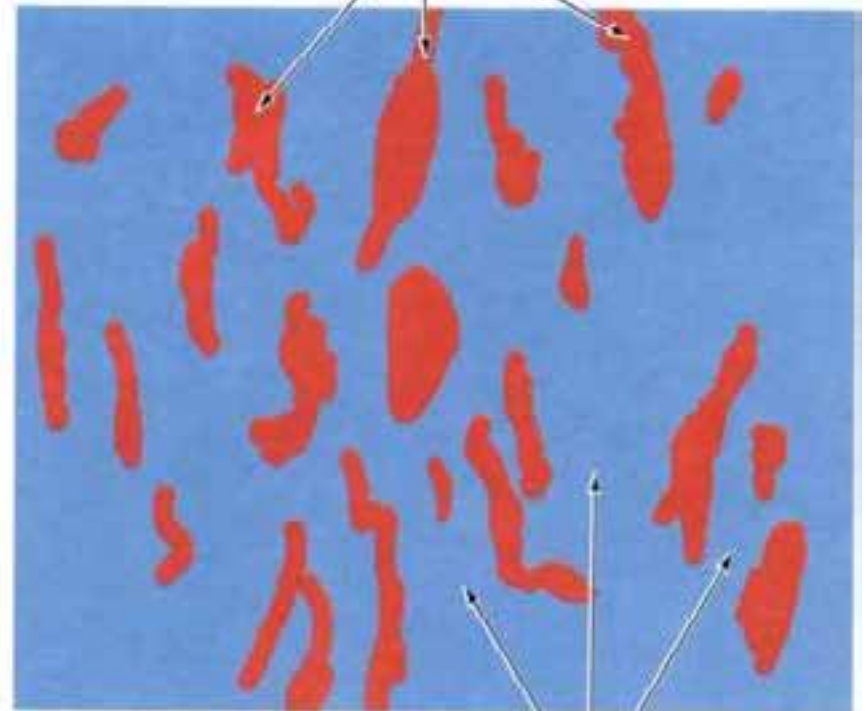
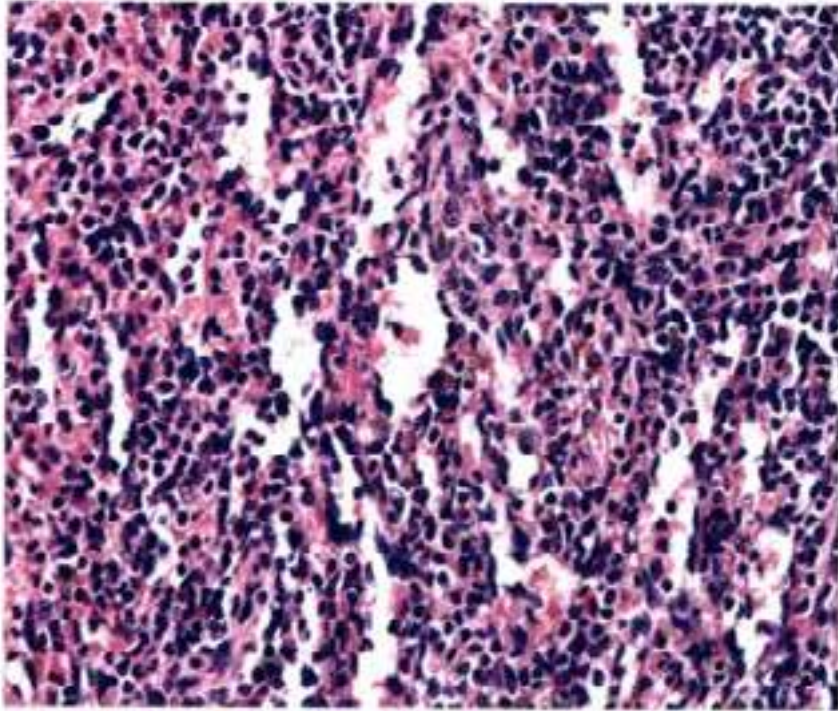
germinal center



central artery (*located excentrically*)



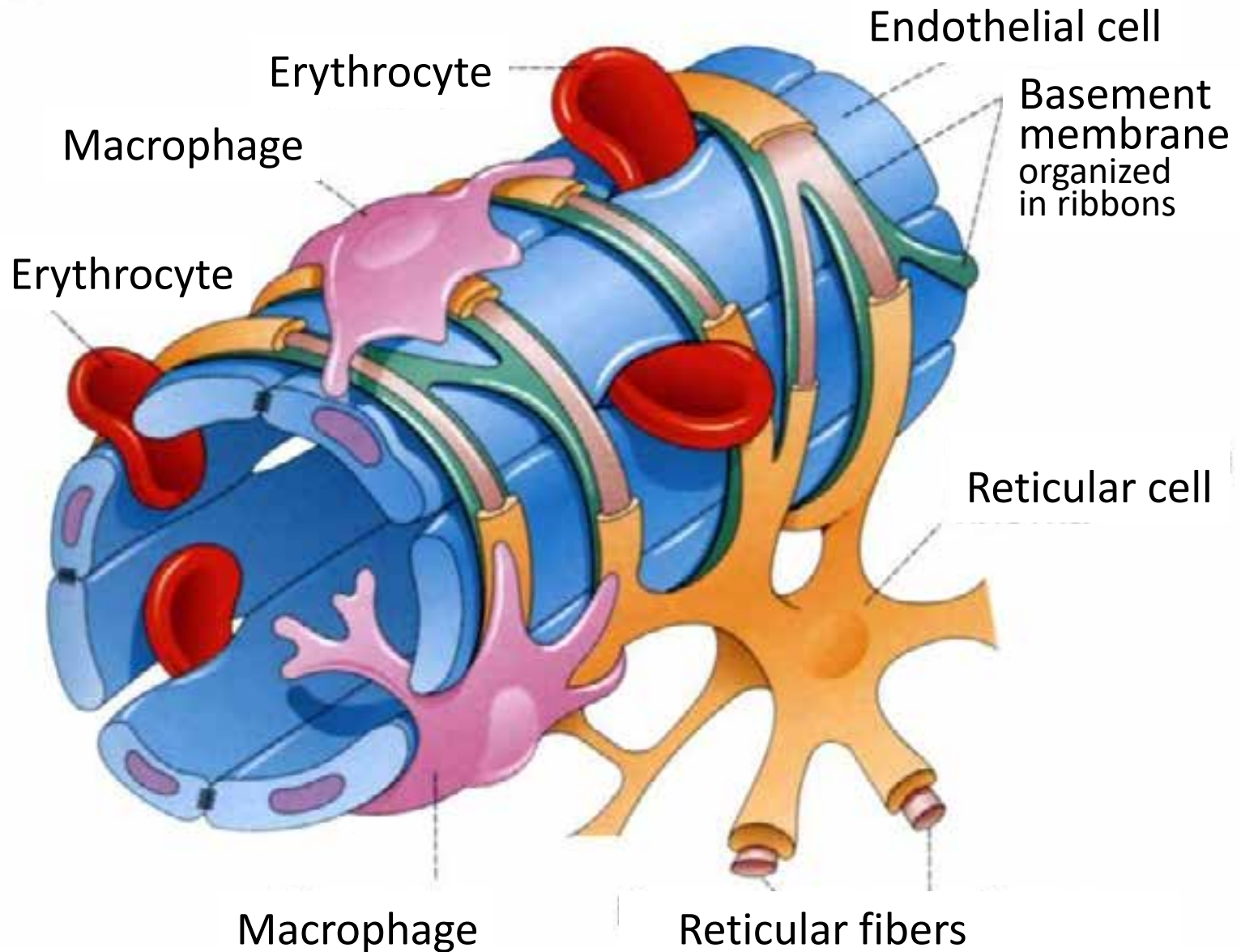
splenic sinusoids



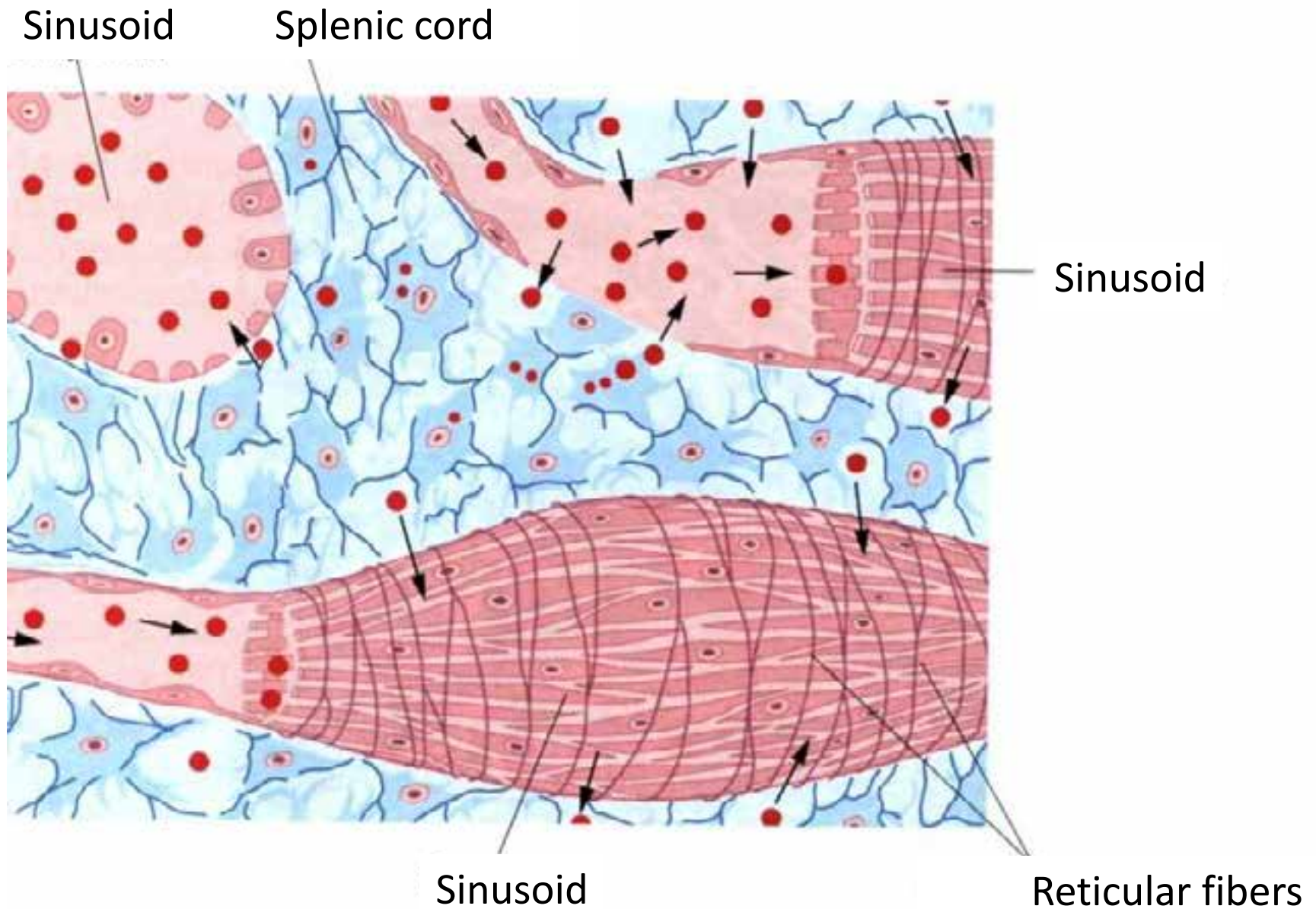
Sinusoid (venous sinus) is a type of postcapillary venule

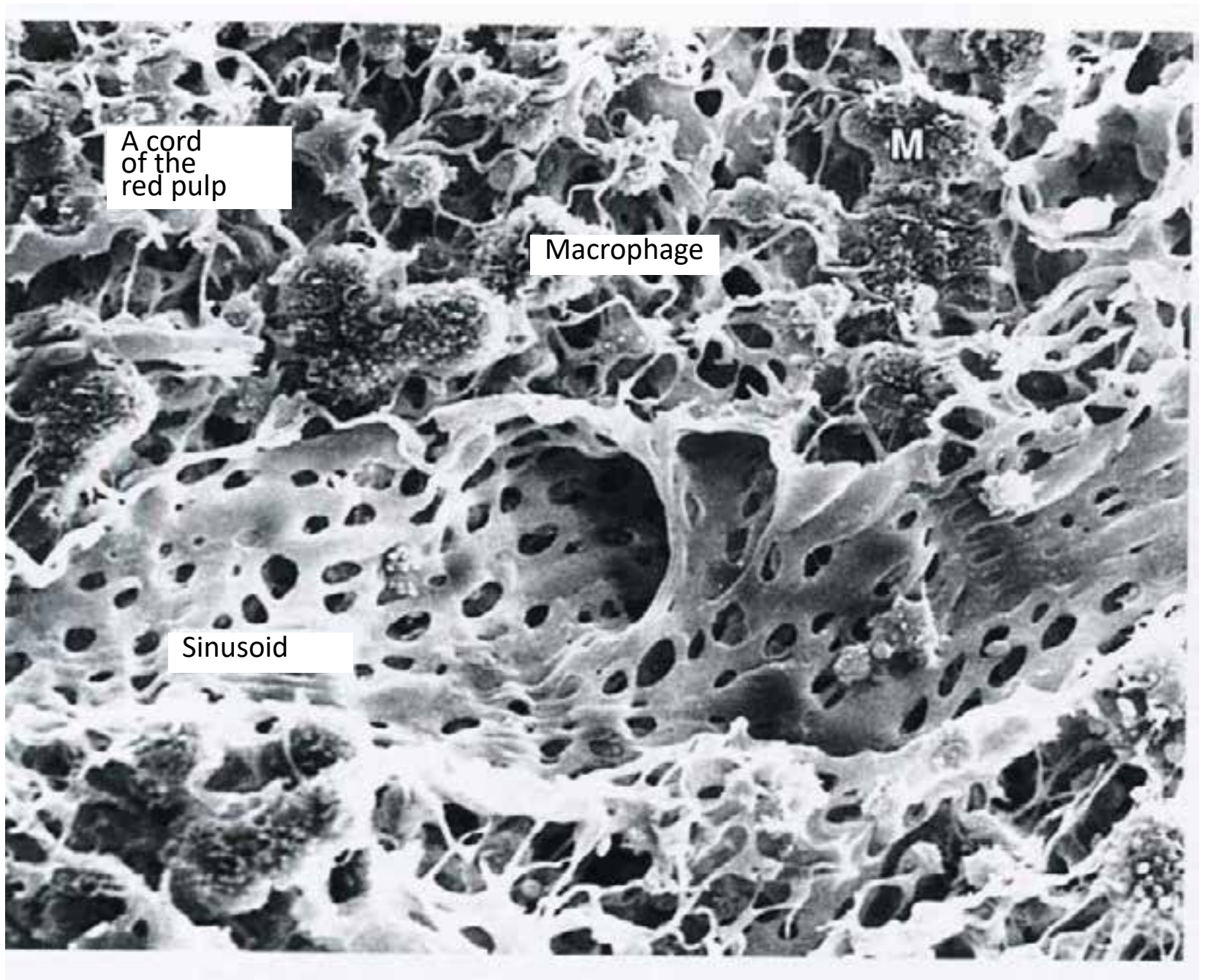
splenic cords

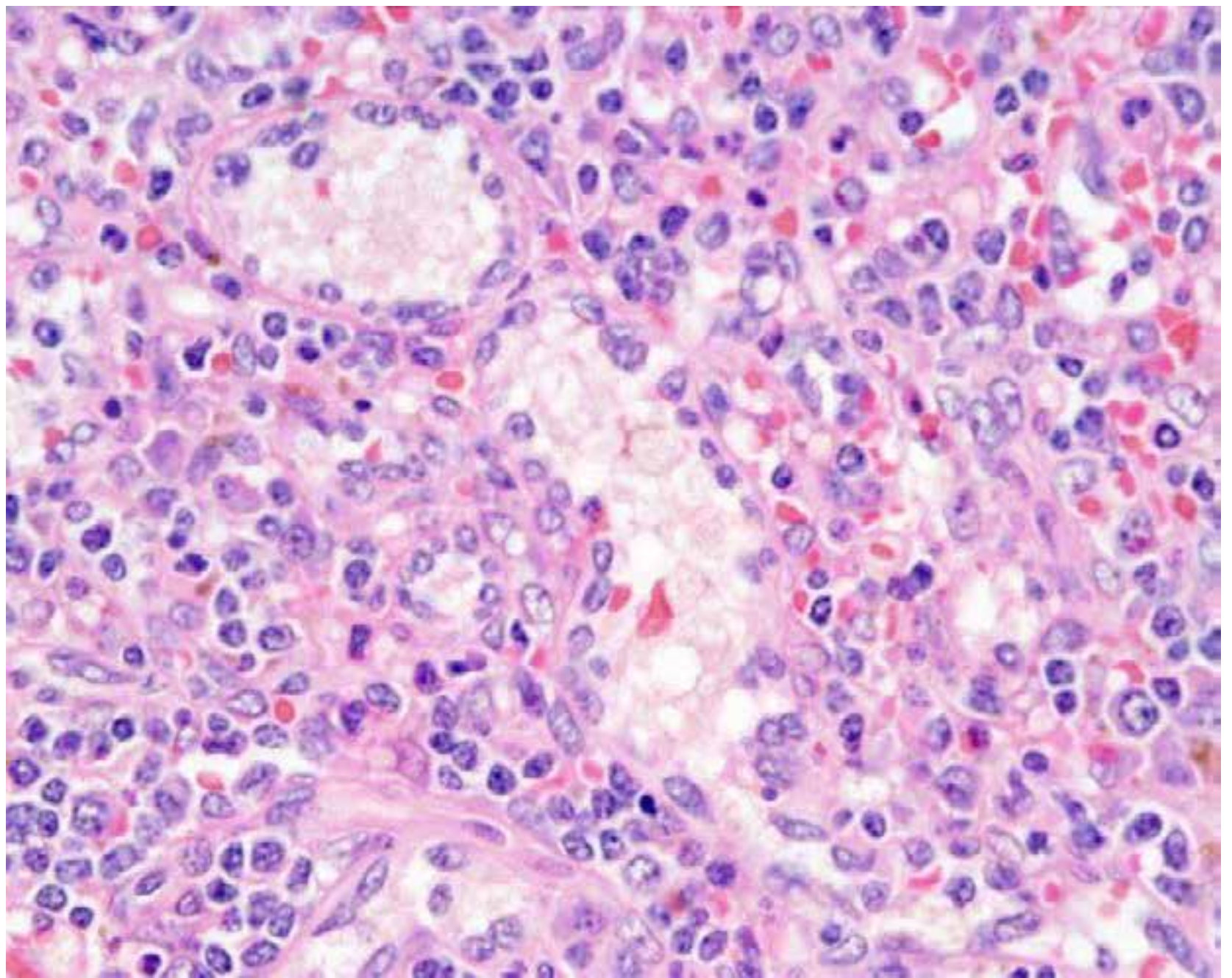
STRUCTURE OF SPLENIC SINUSOIDS

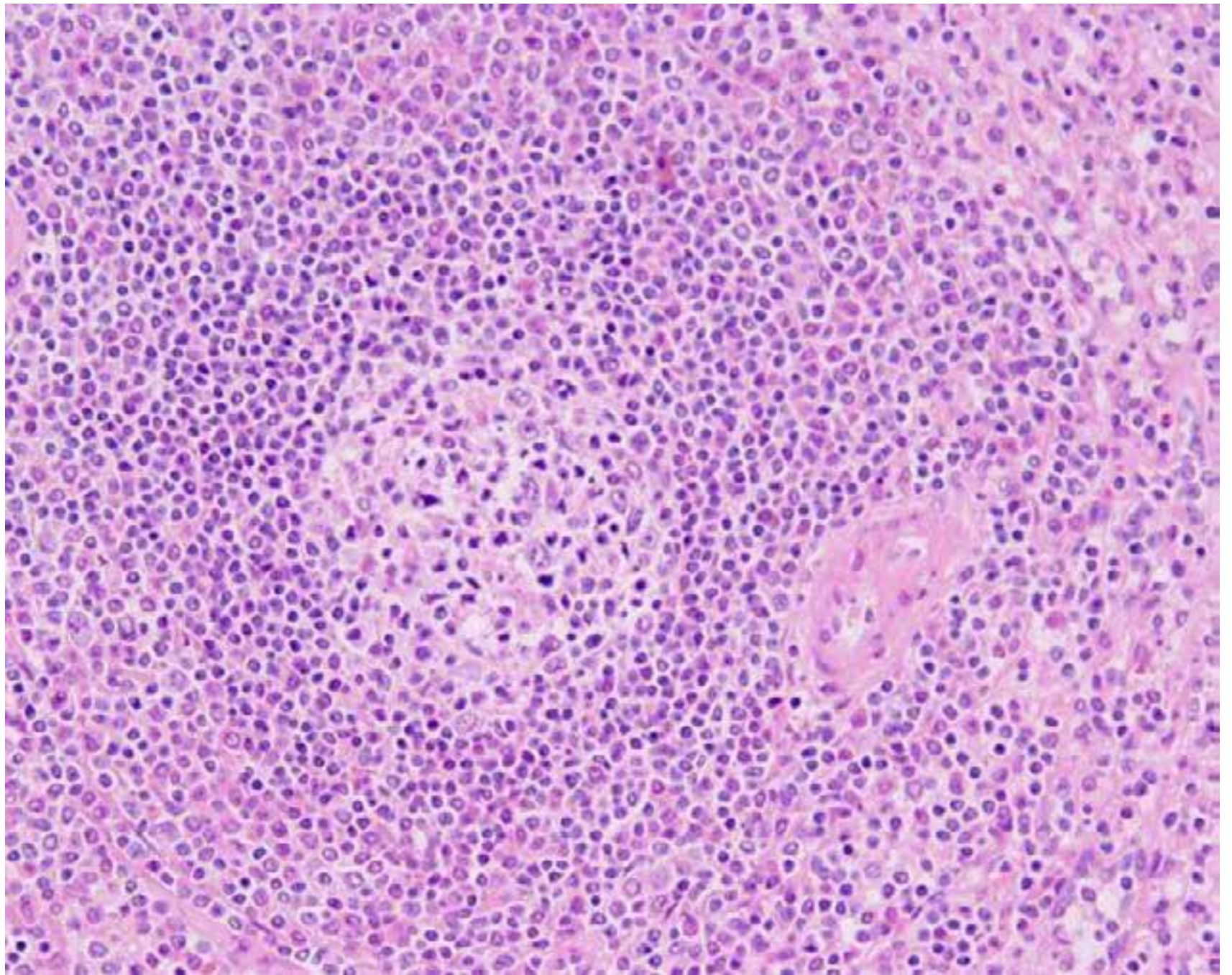


STRUCTURE OF THE RED PULP

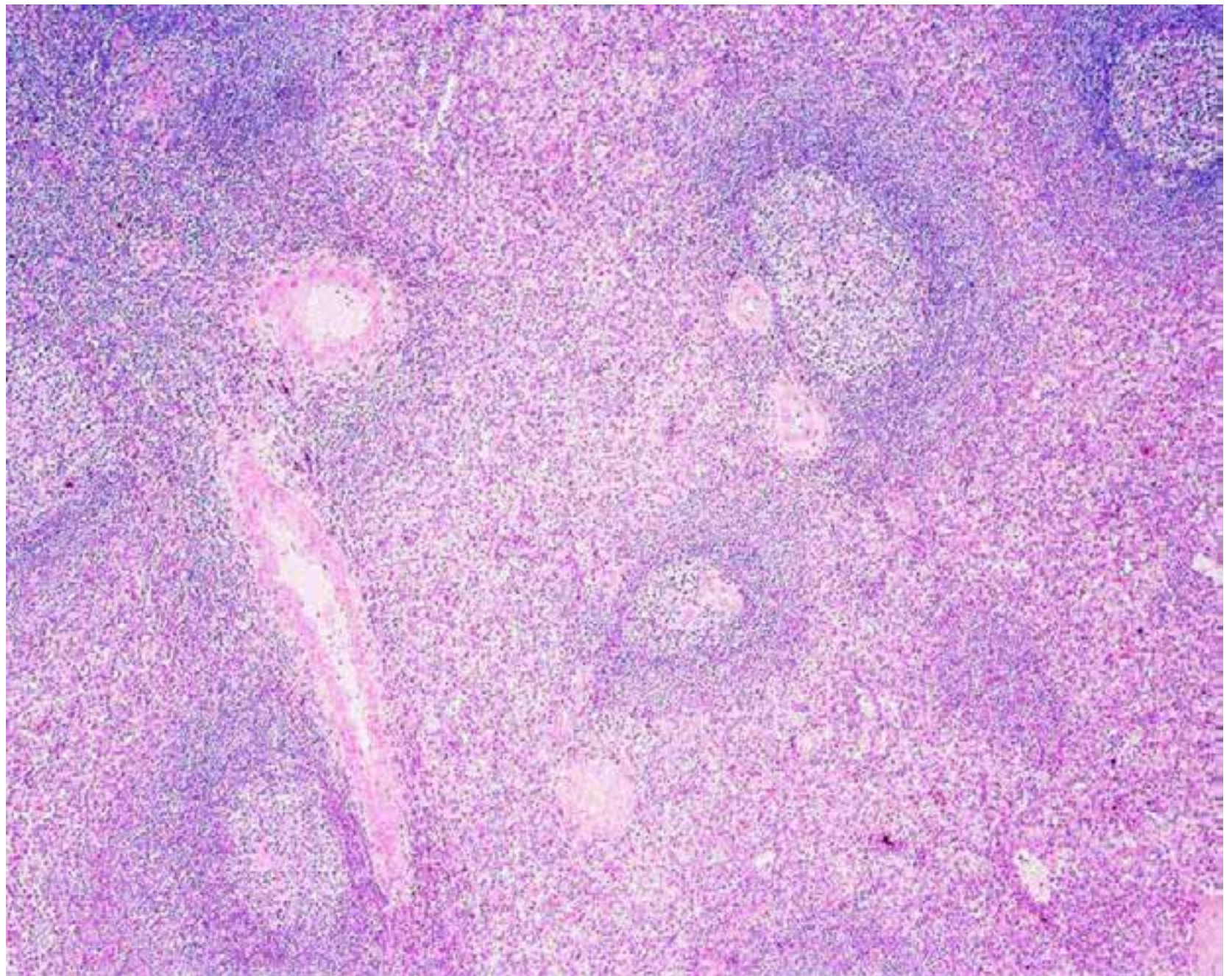




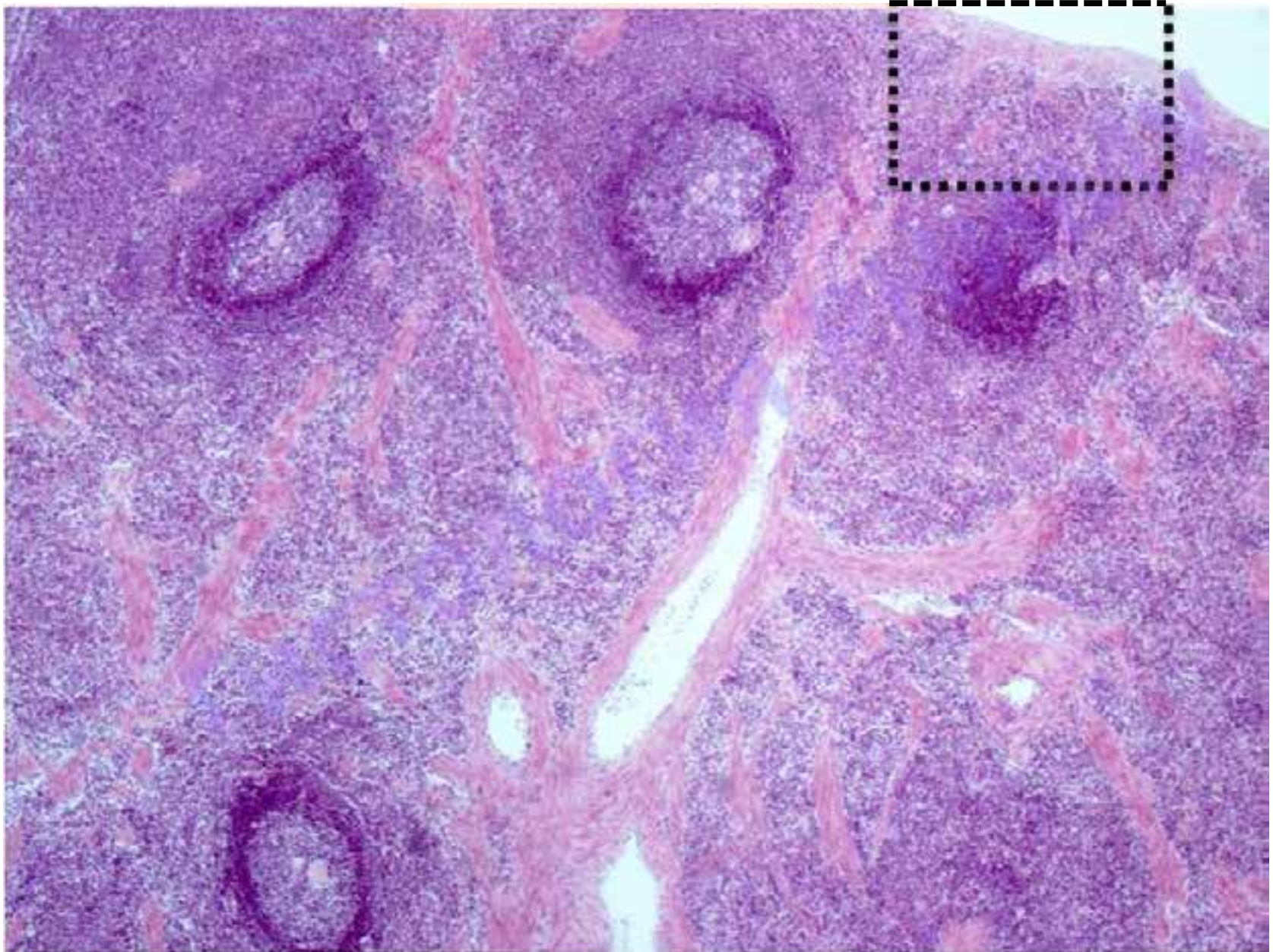




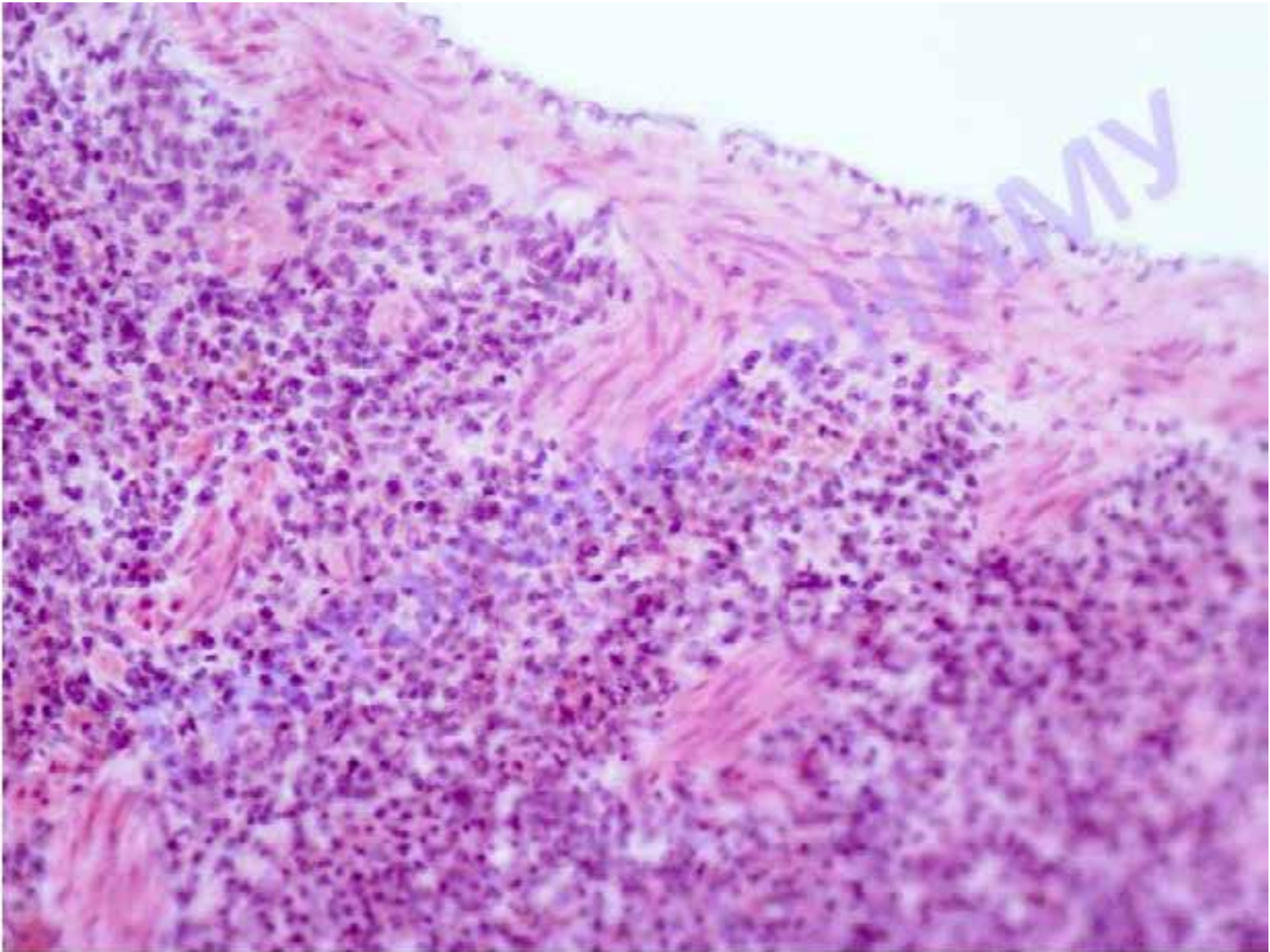




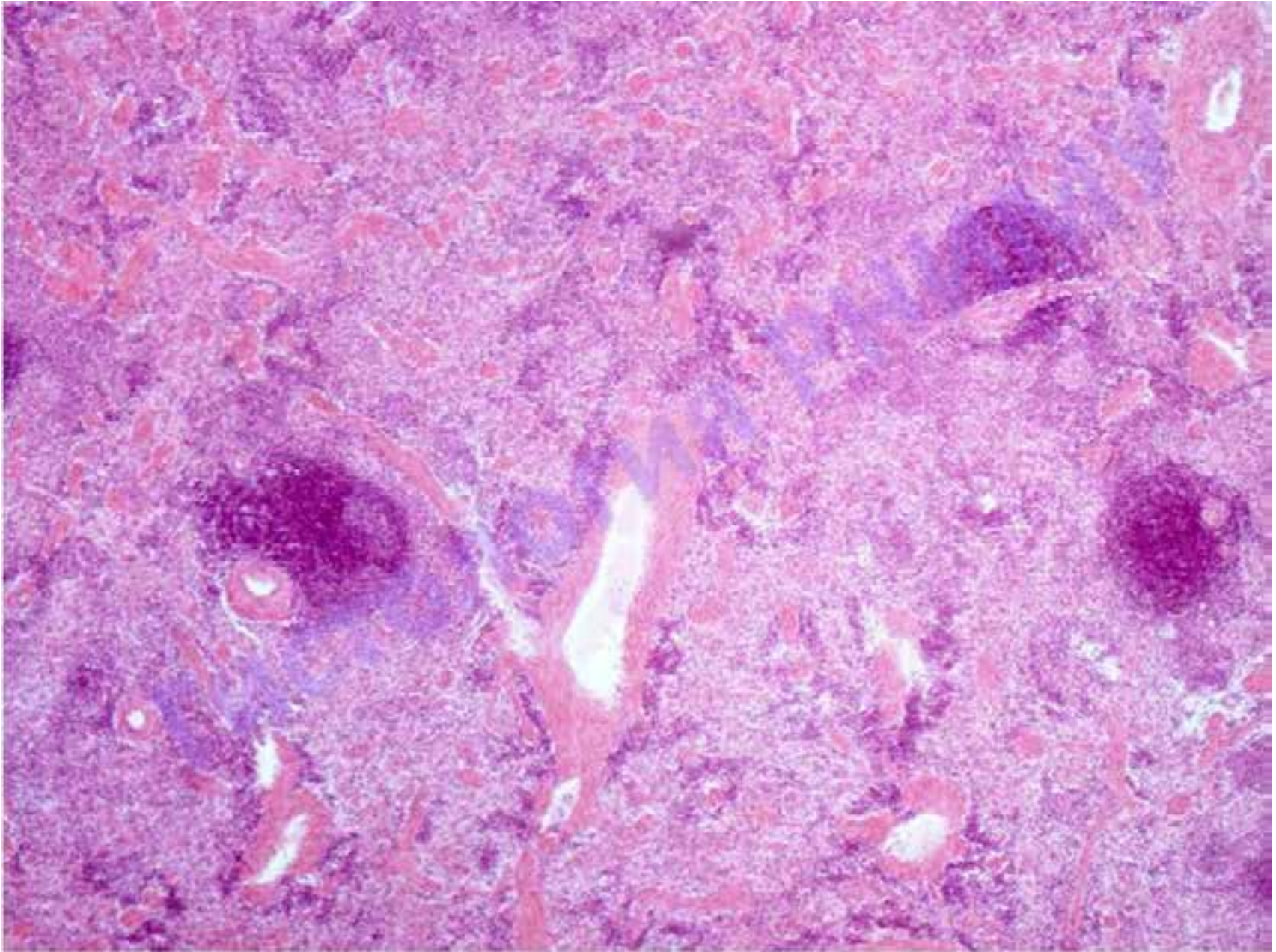
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



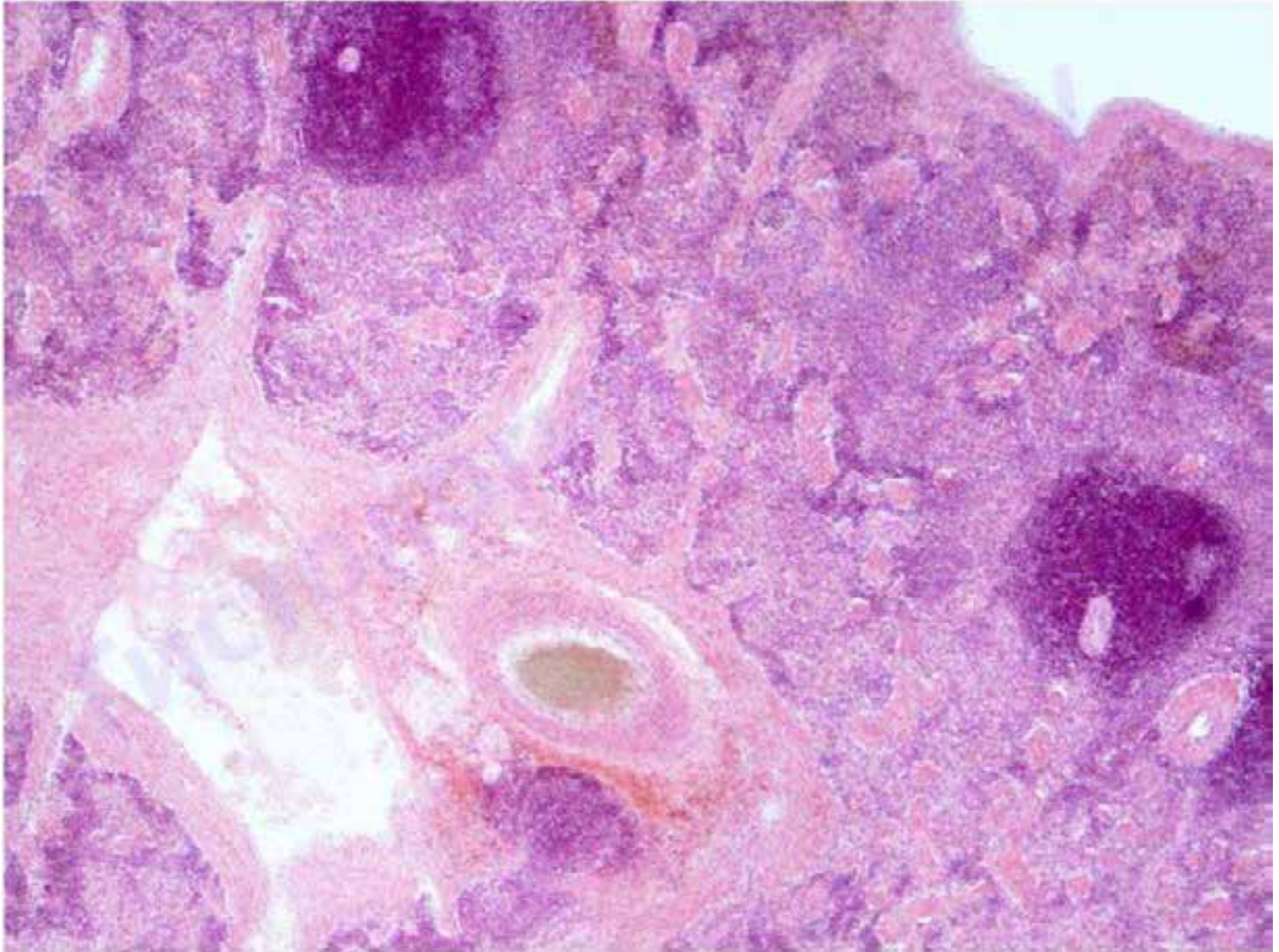
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



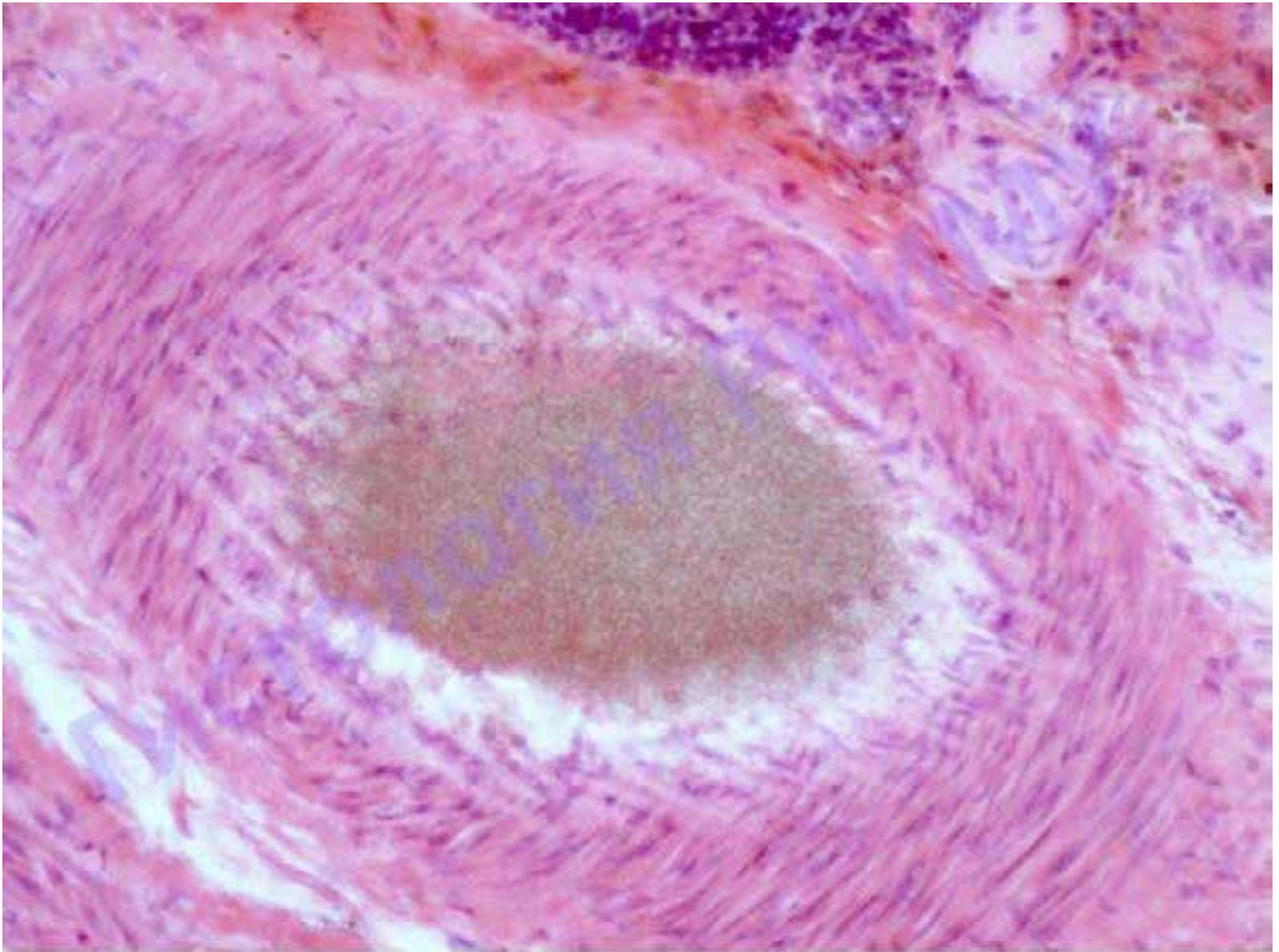
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



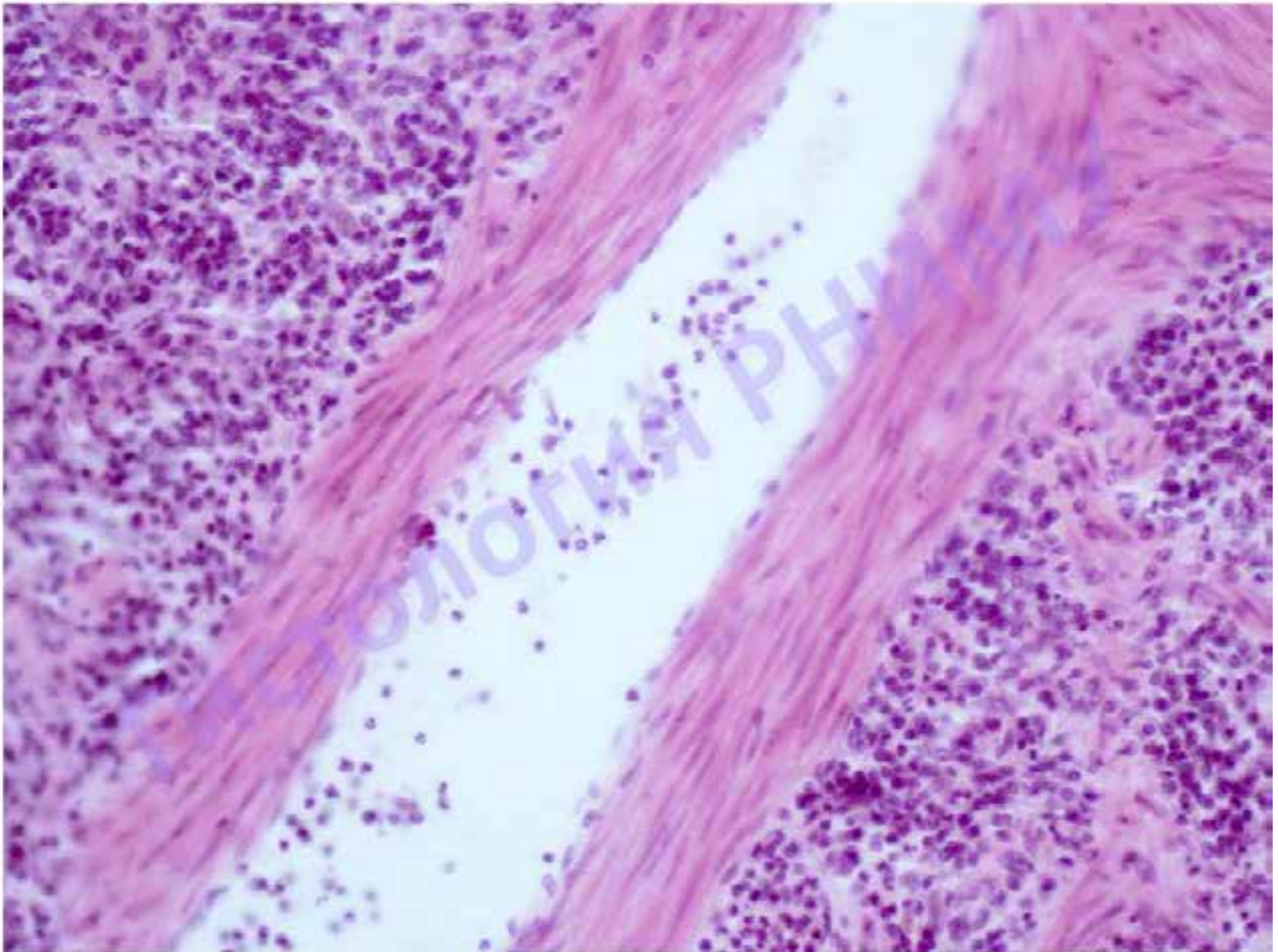
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



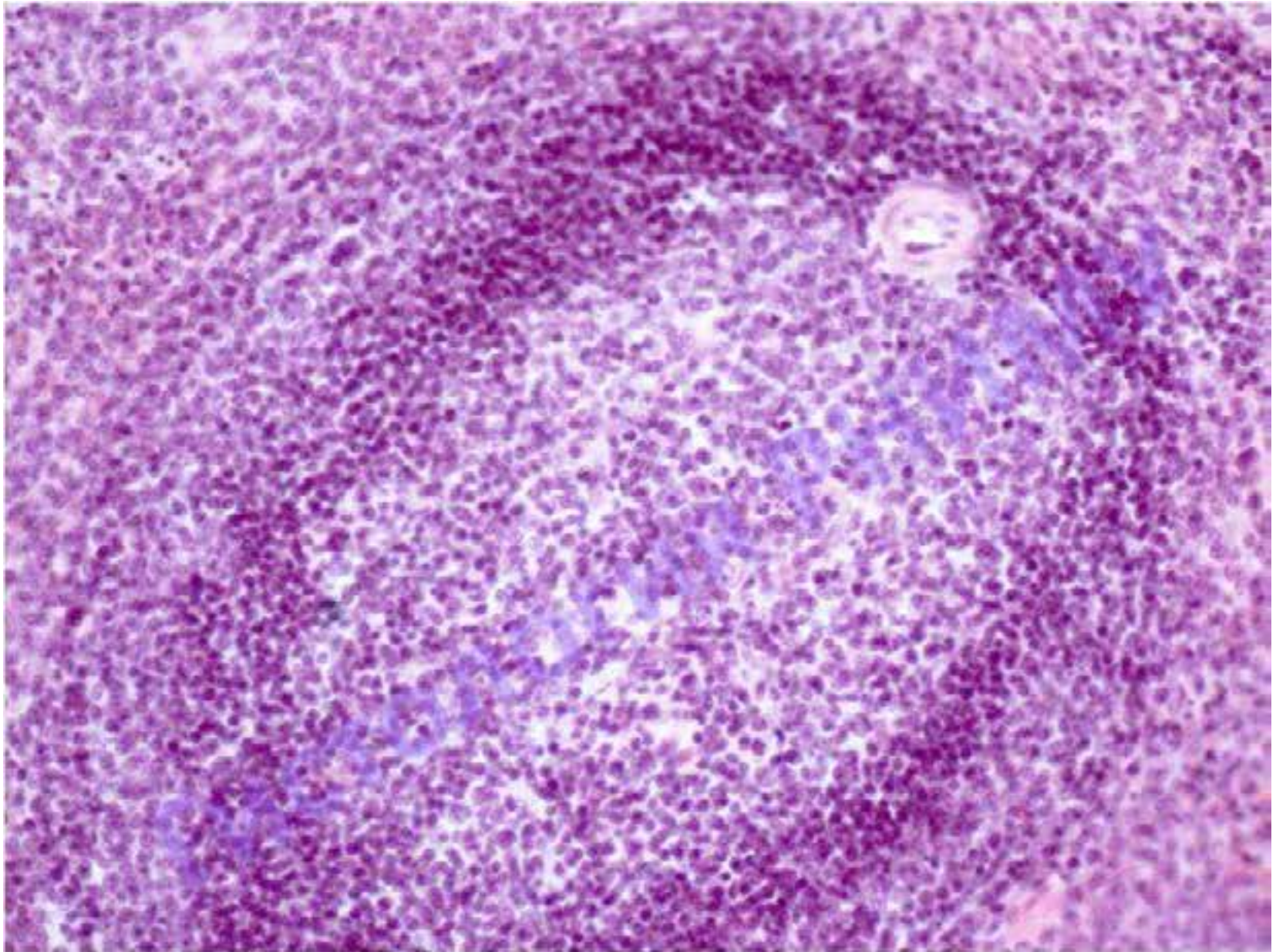
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



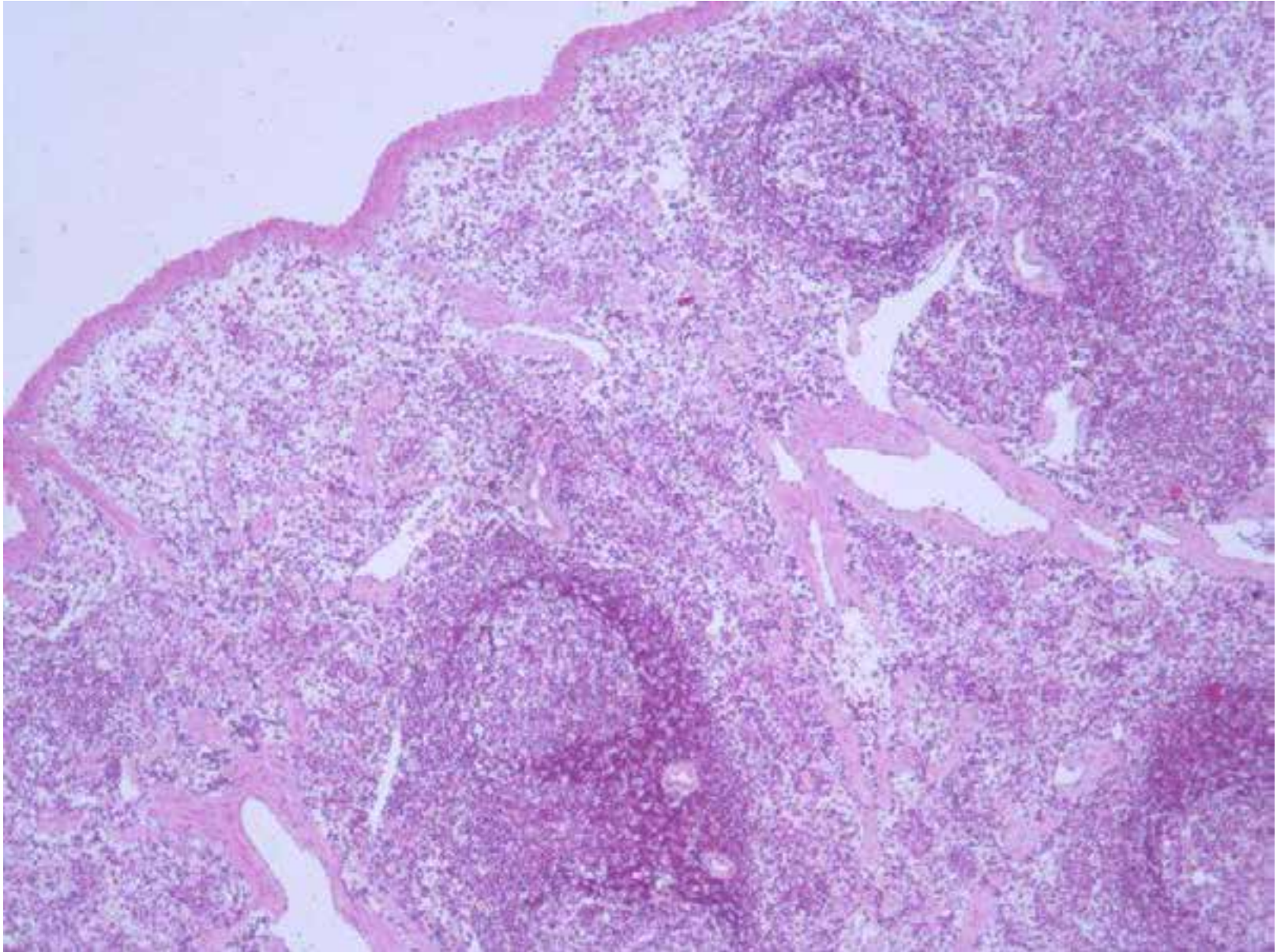
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



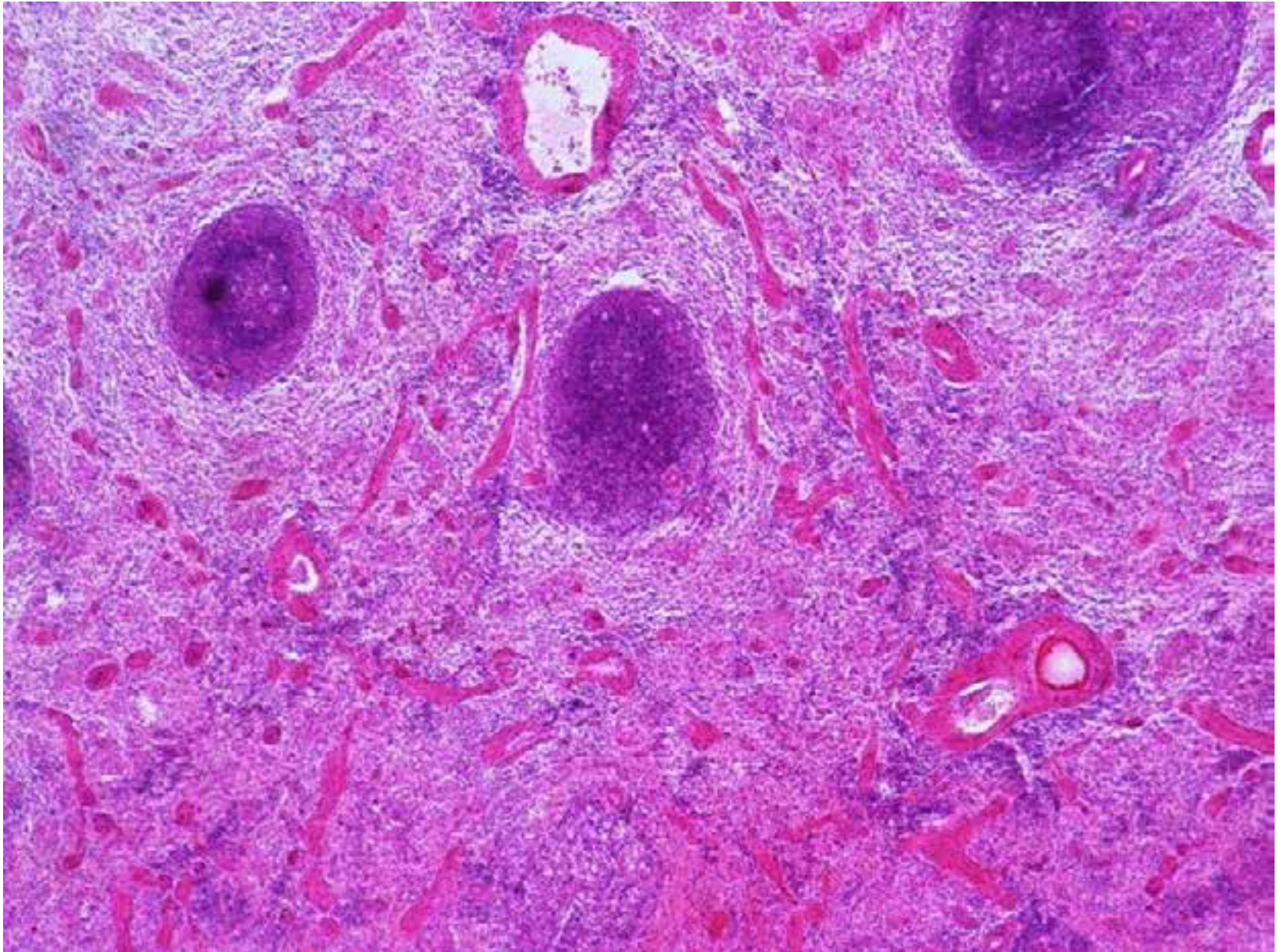
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



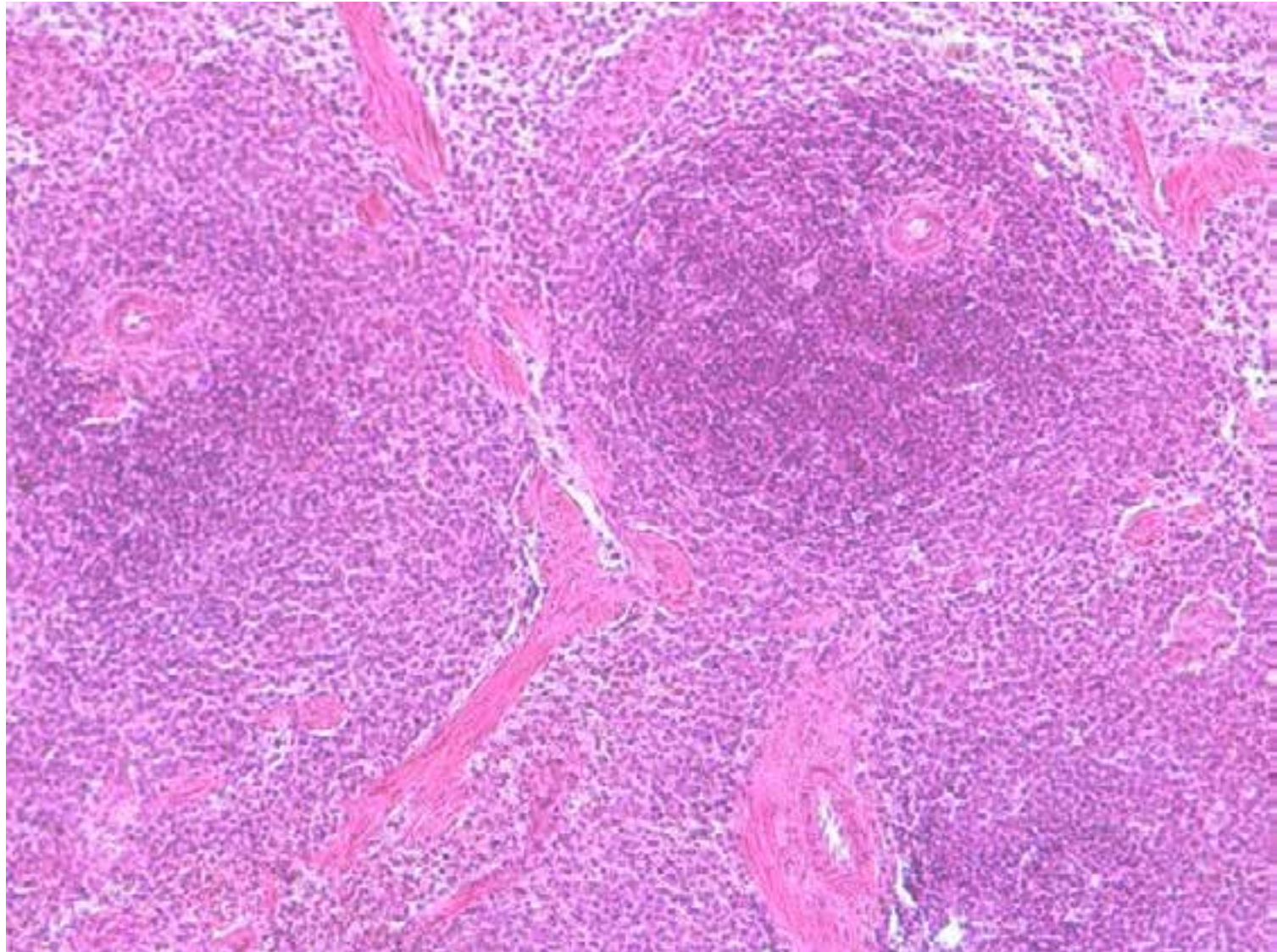
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



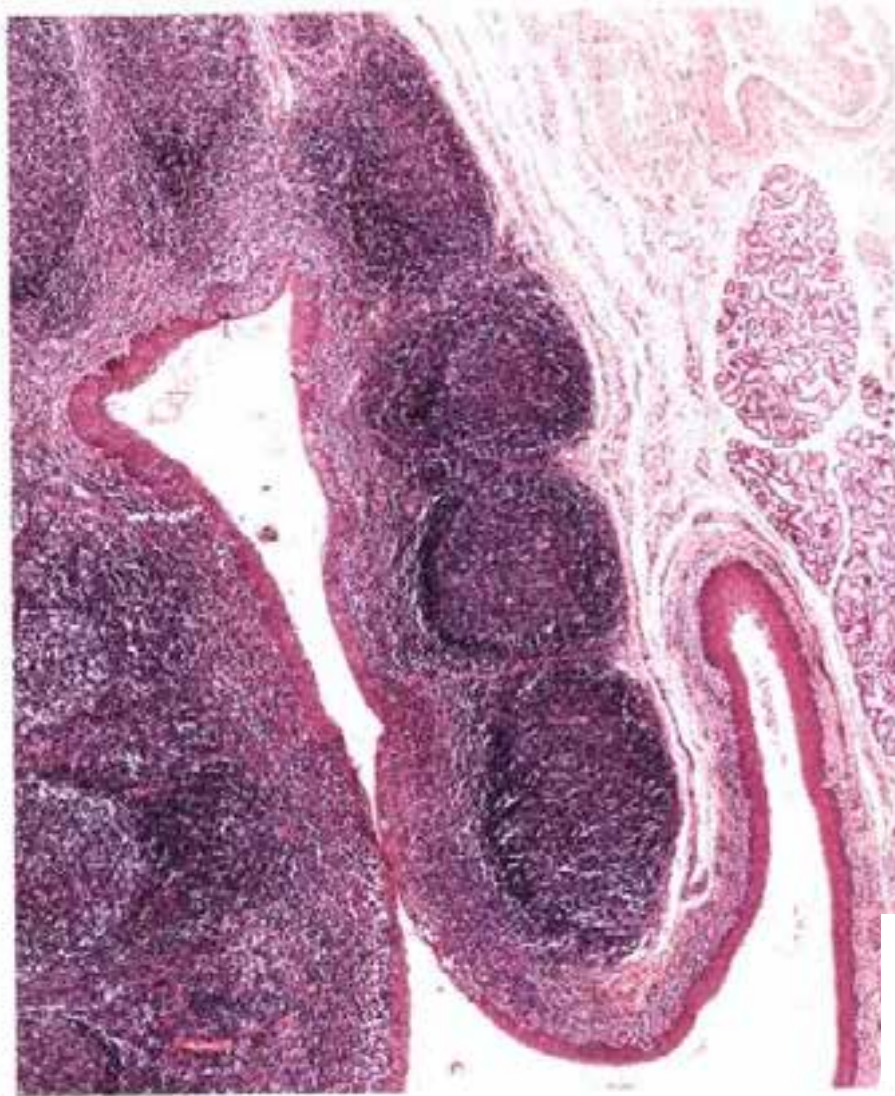
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



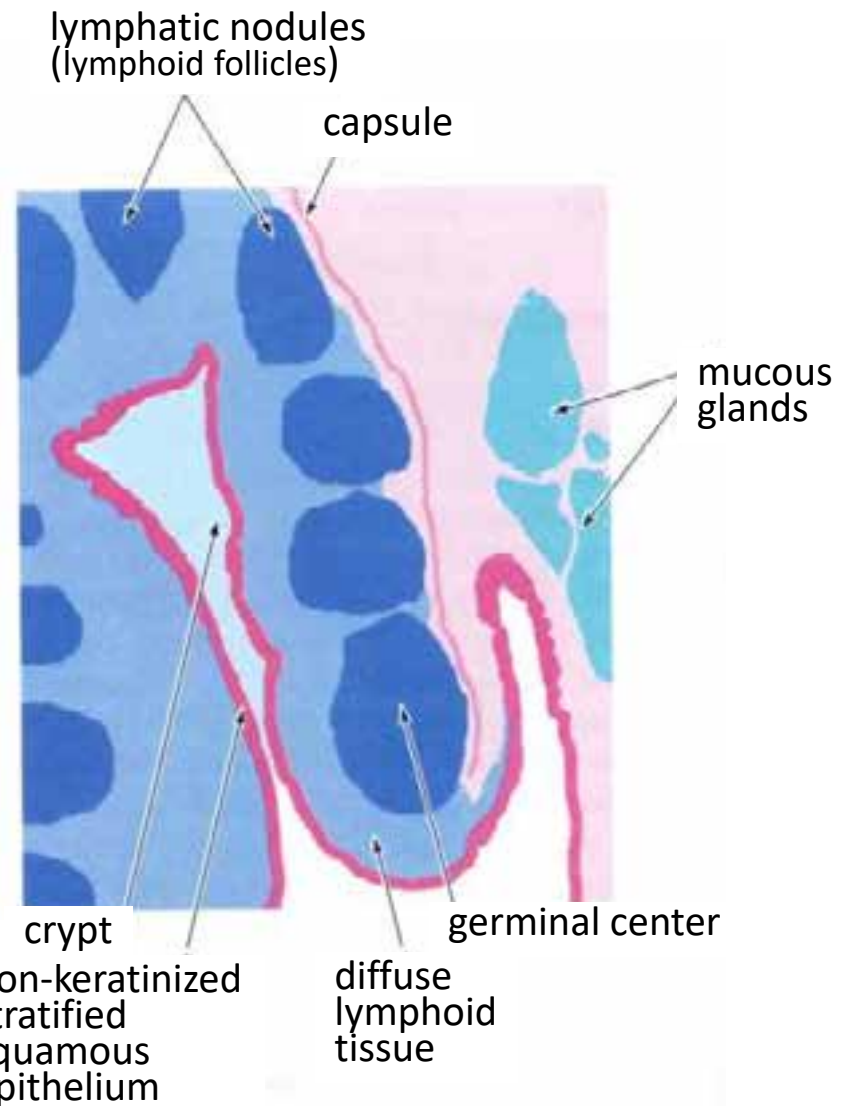
*Slide №119. Section of the spleen
Hematoxylin-eosin staining*



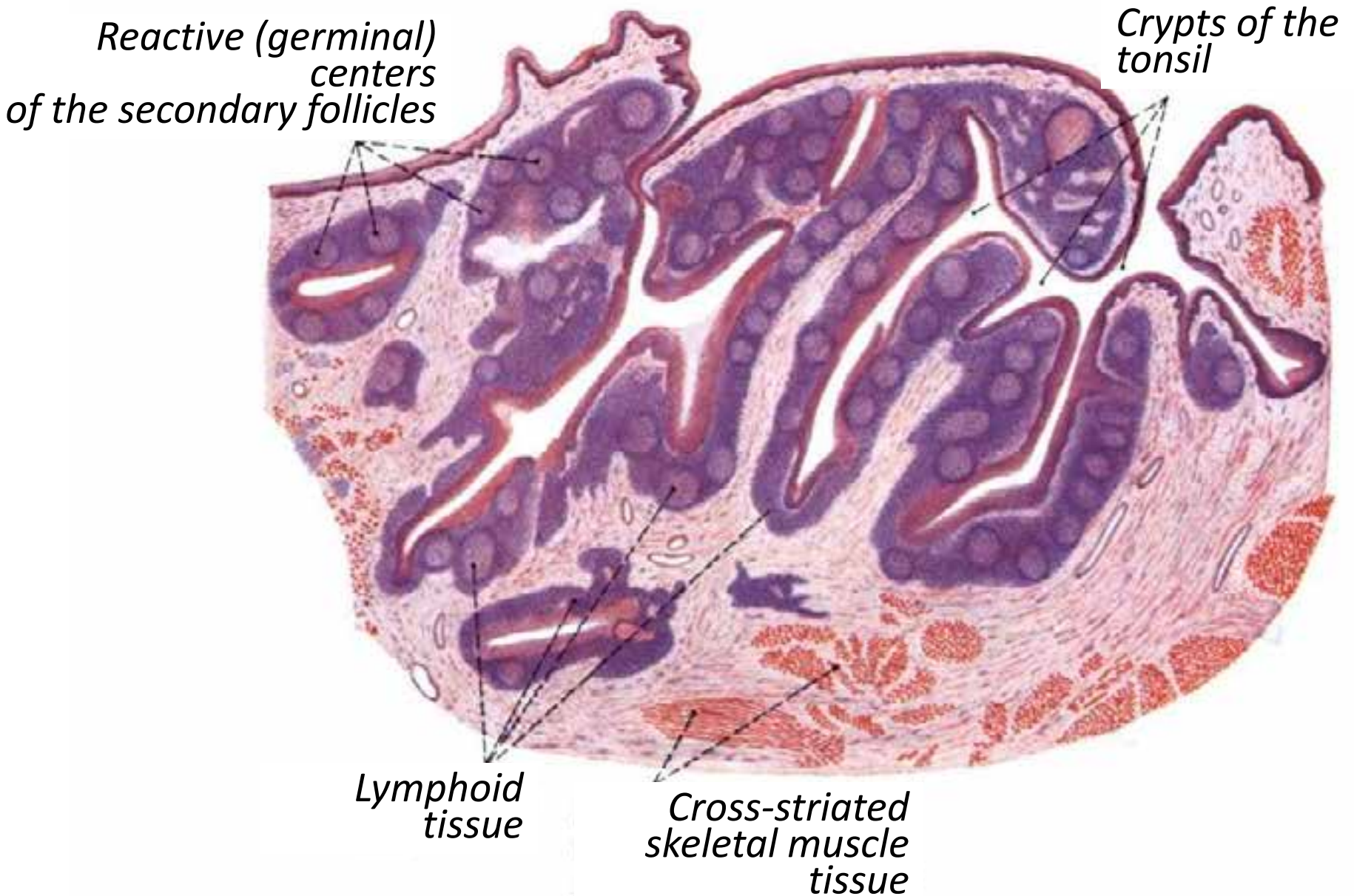
STRUCTURE OF THE PALATINE TONSIL



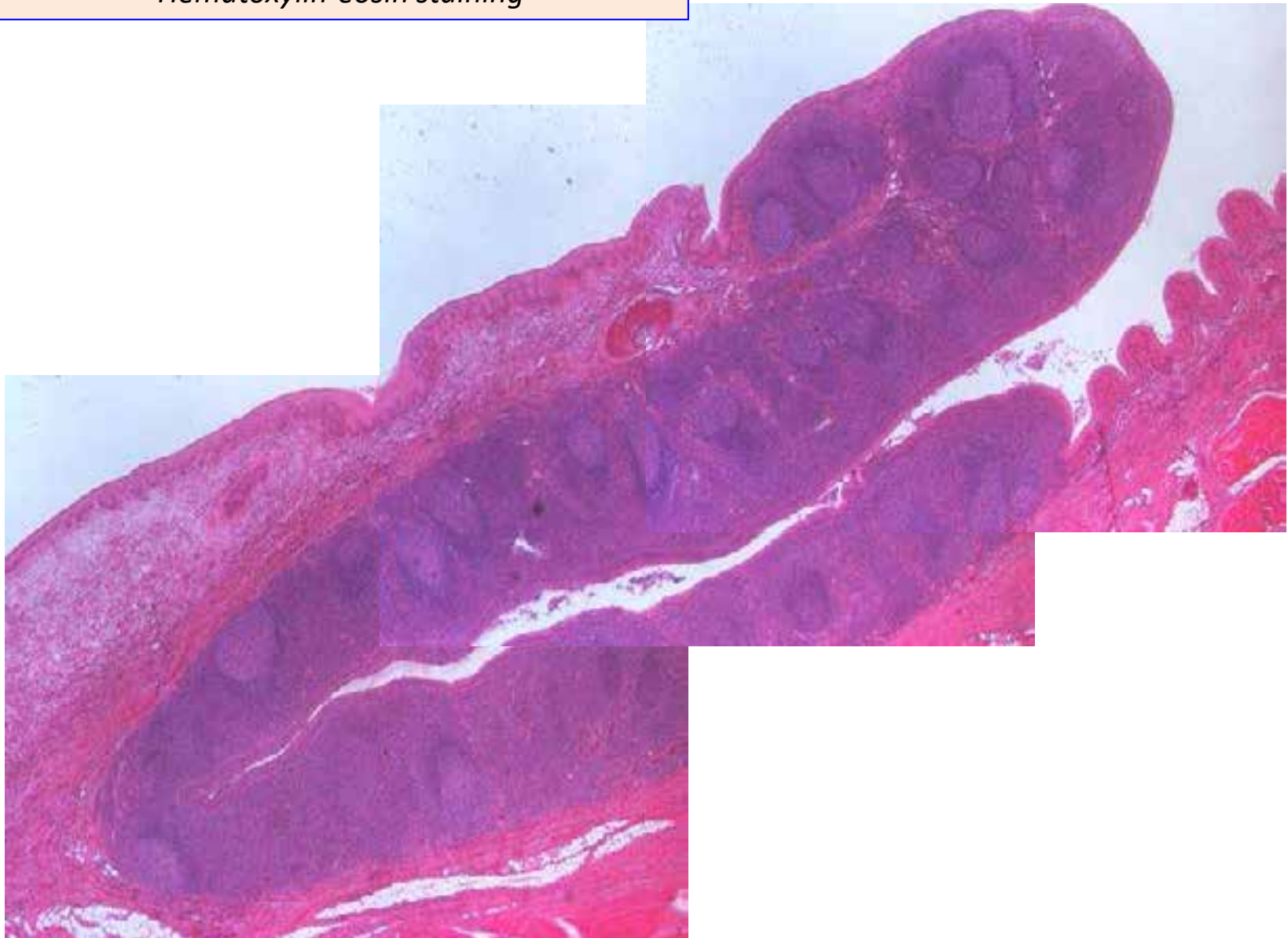
A



STRUCTURE OF THE PALATINE TONSIL



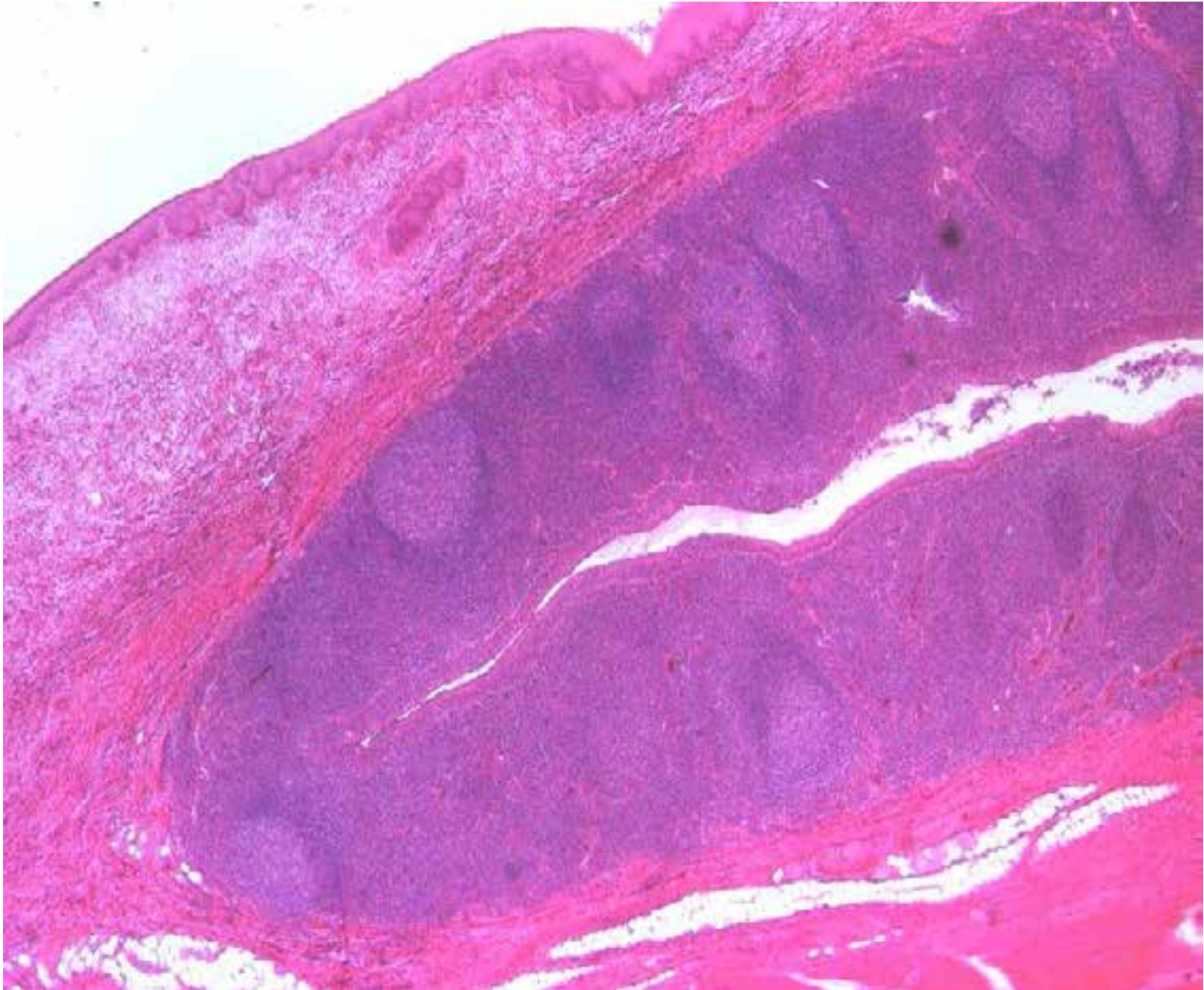
*Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining*



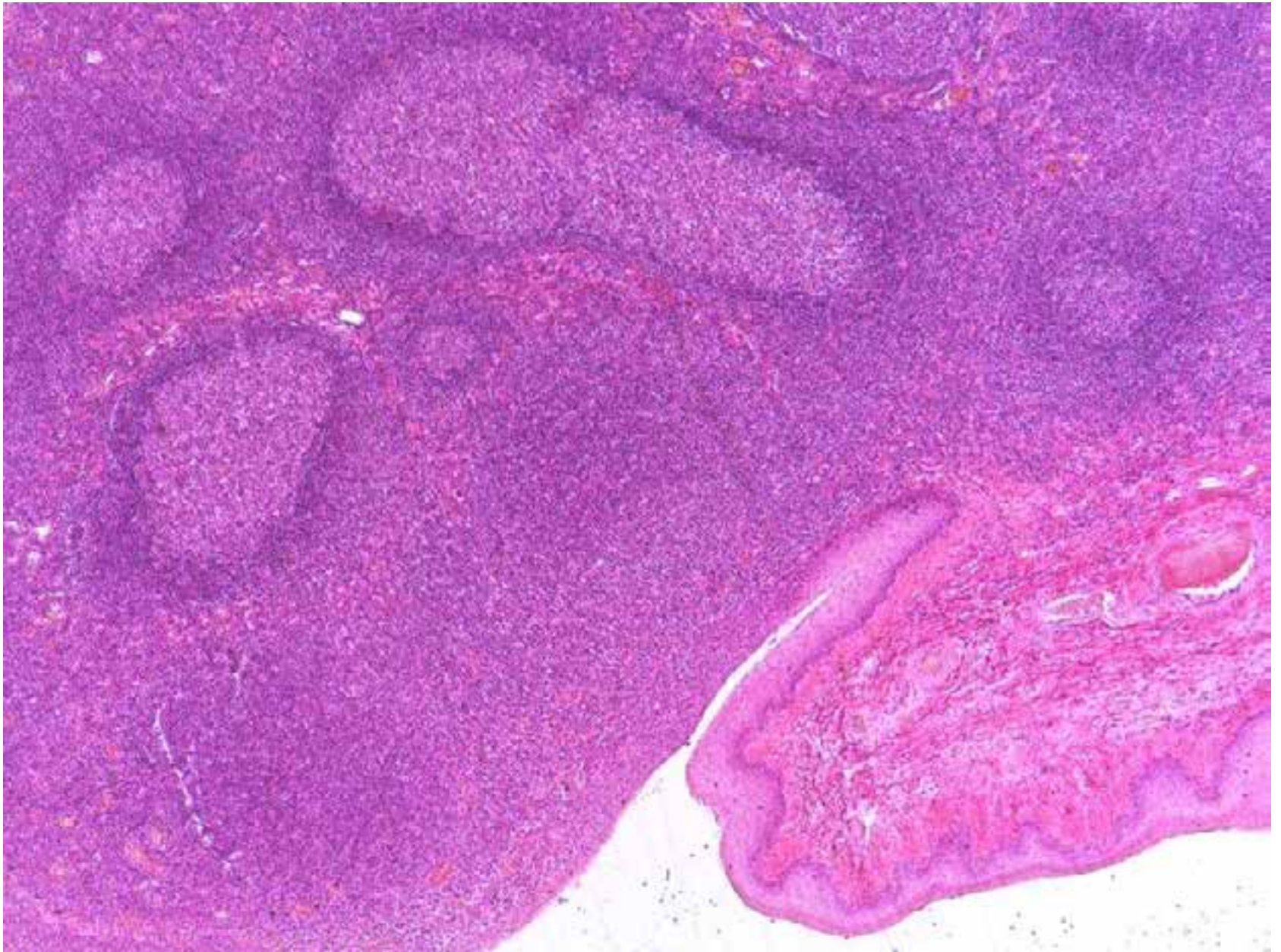
*Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining*



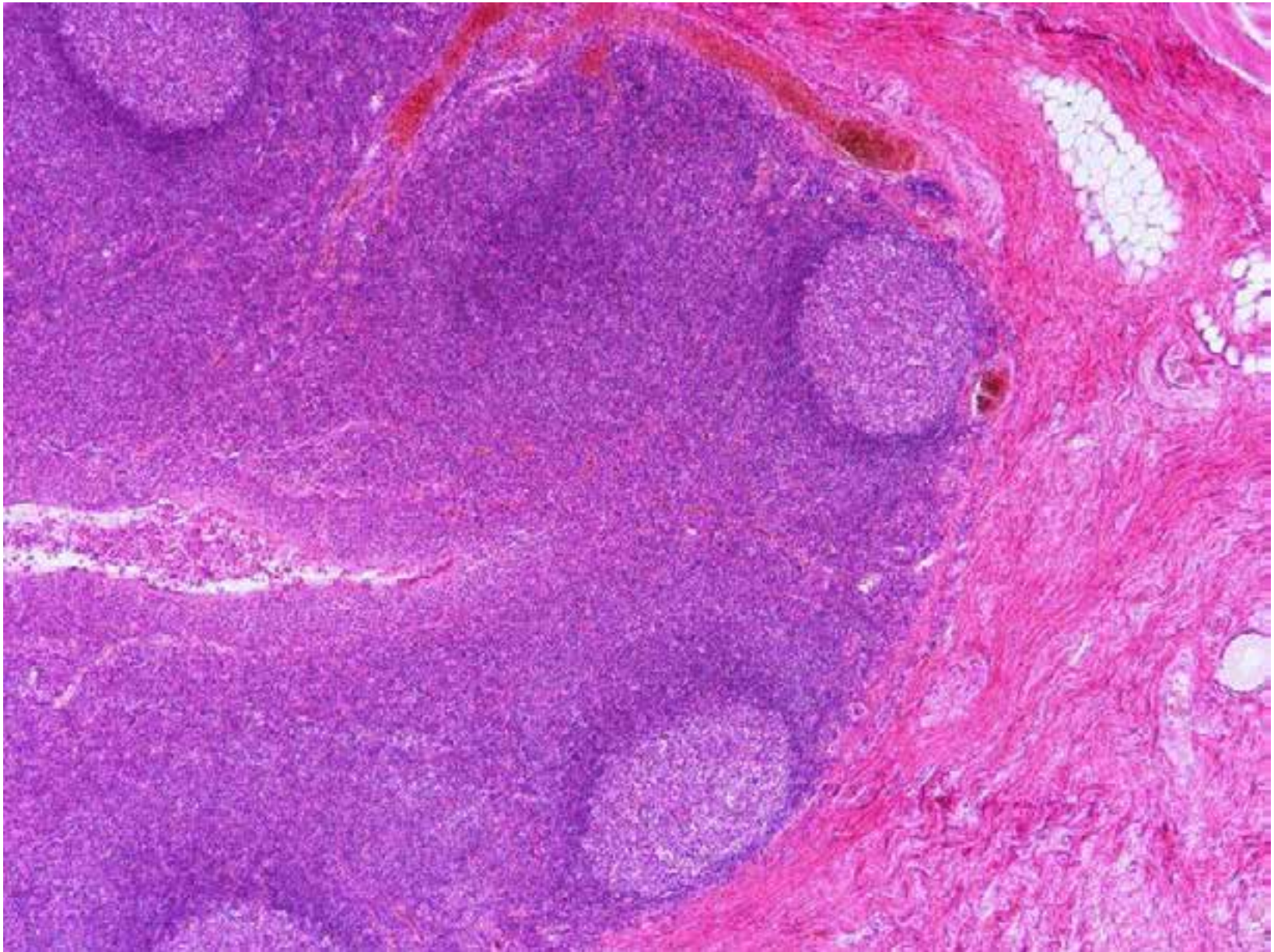
*Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining*



*Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining*



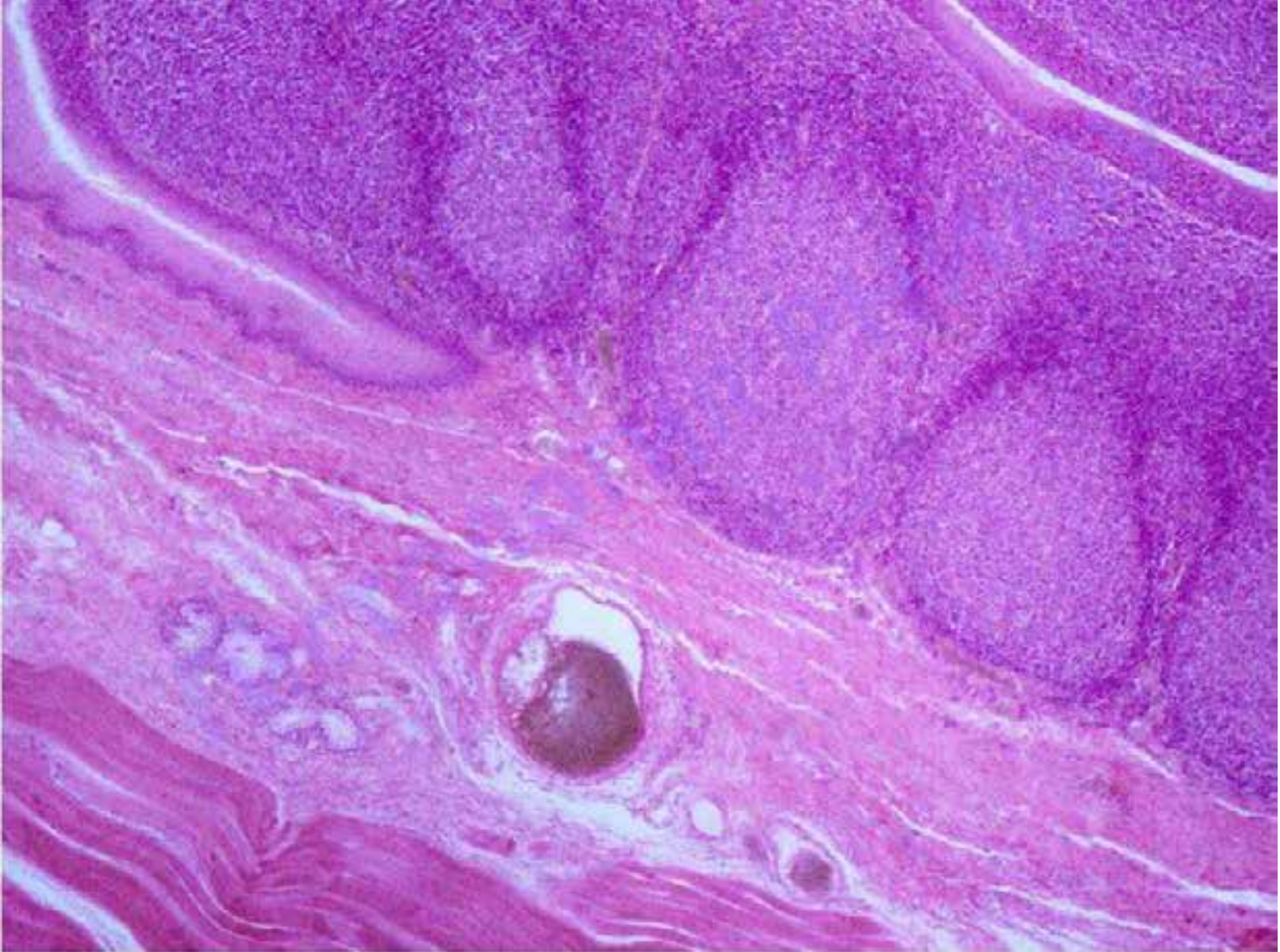
*Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining*



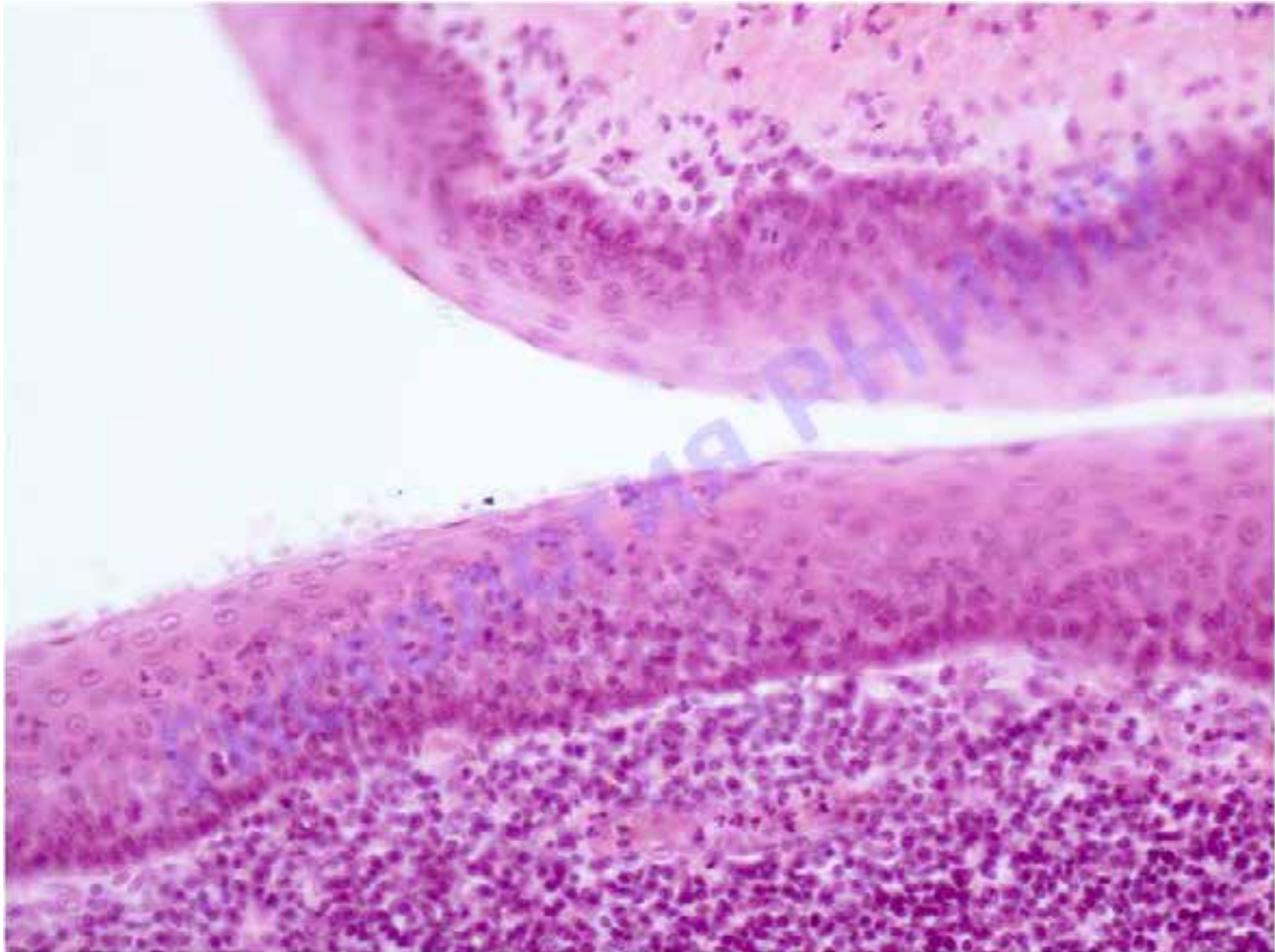
*Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining*



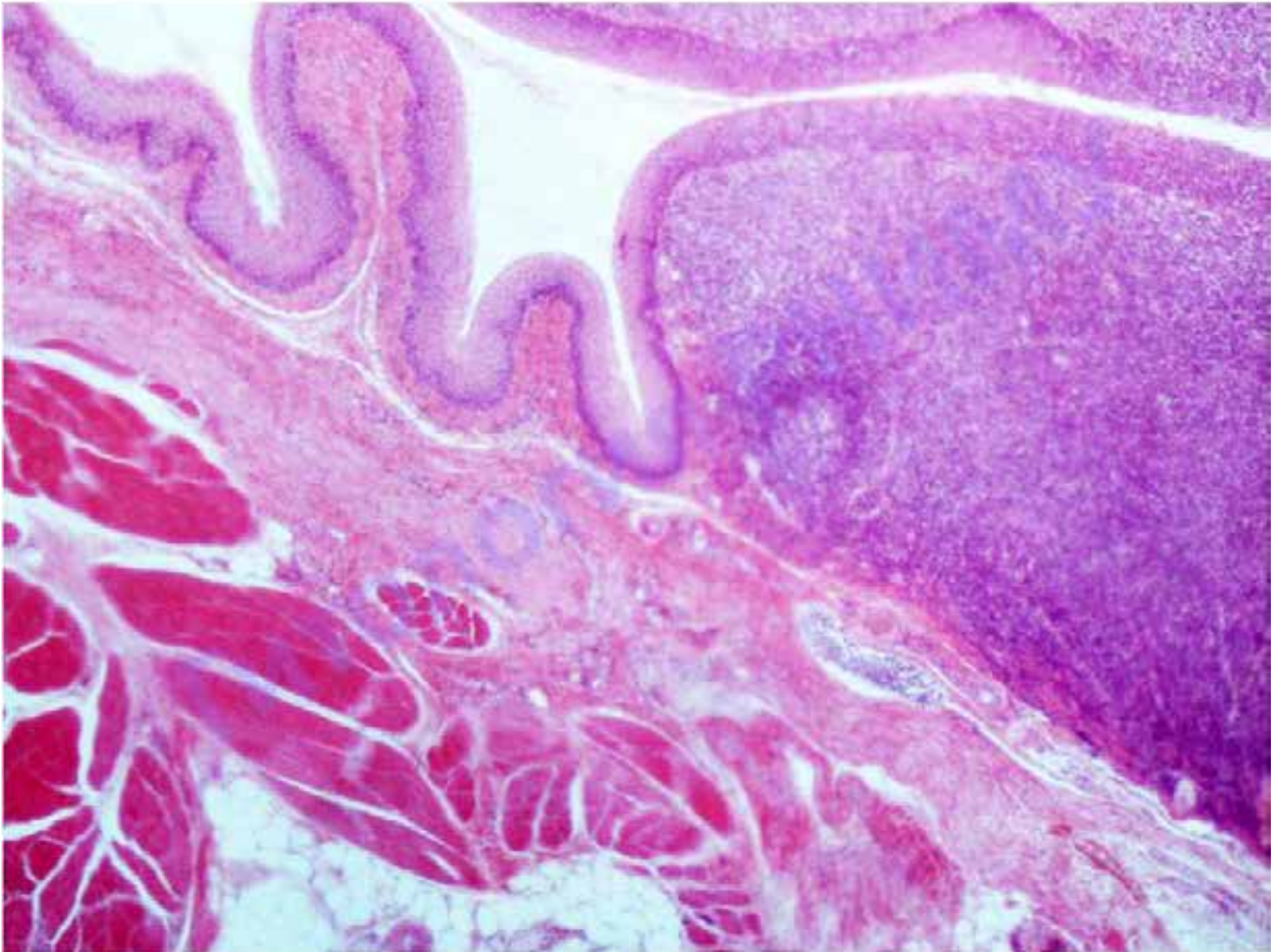
*Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining*



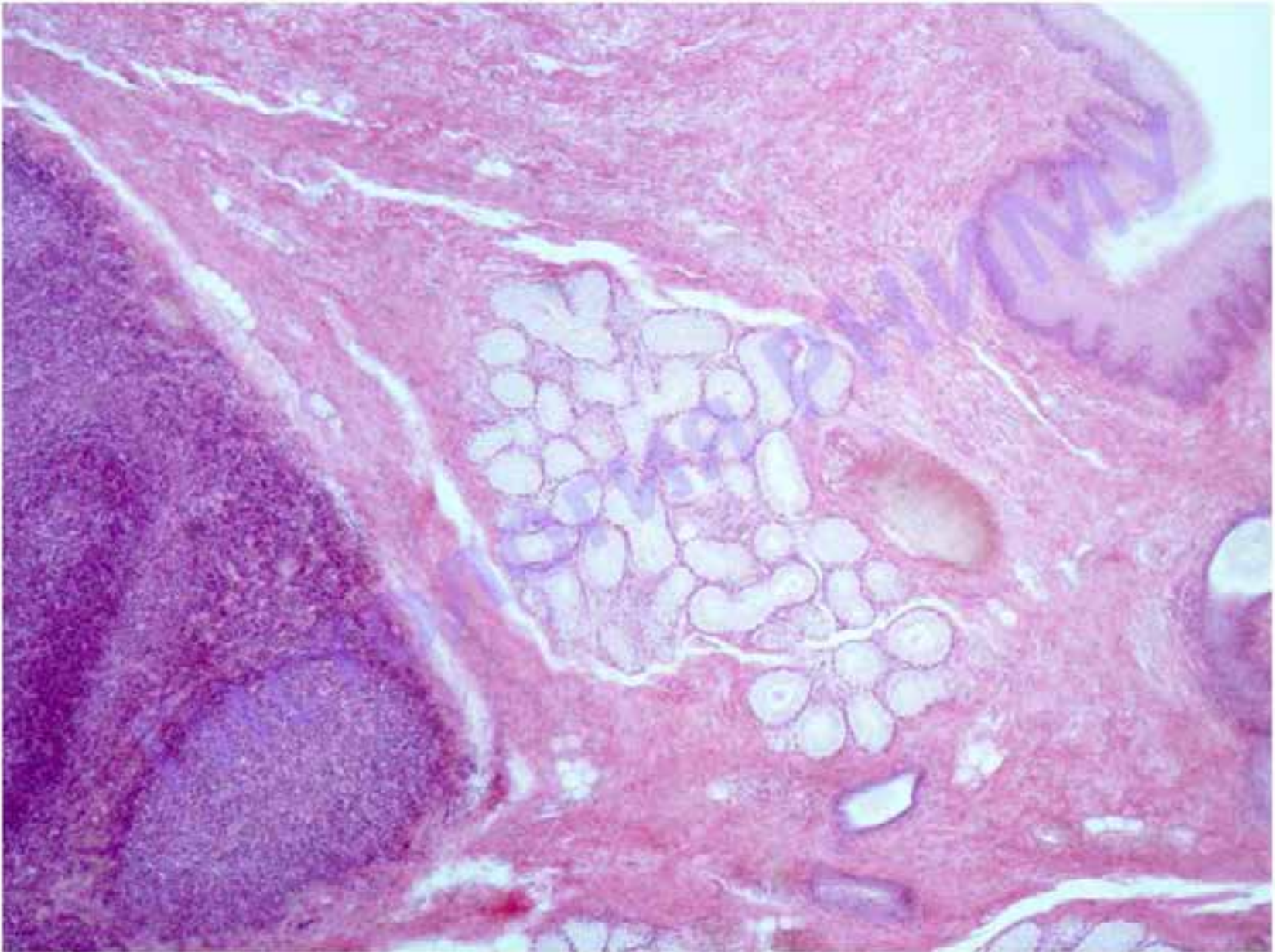
Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining



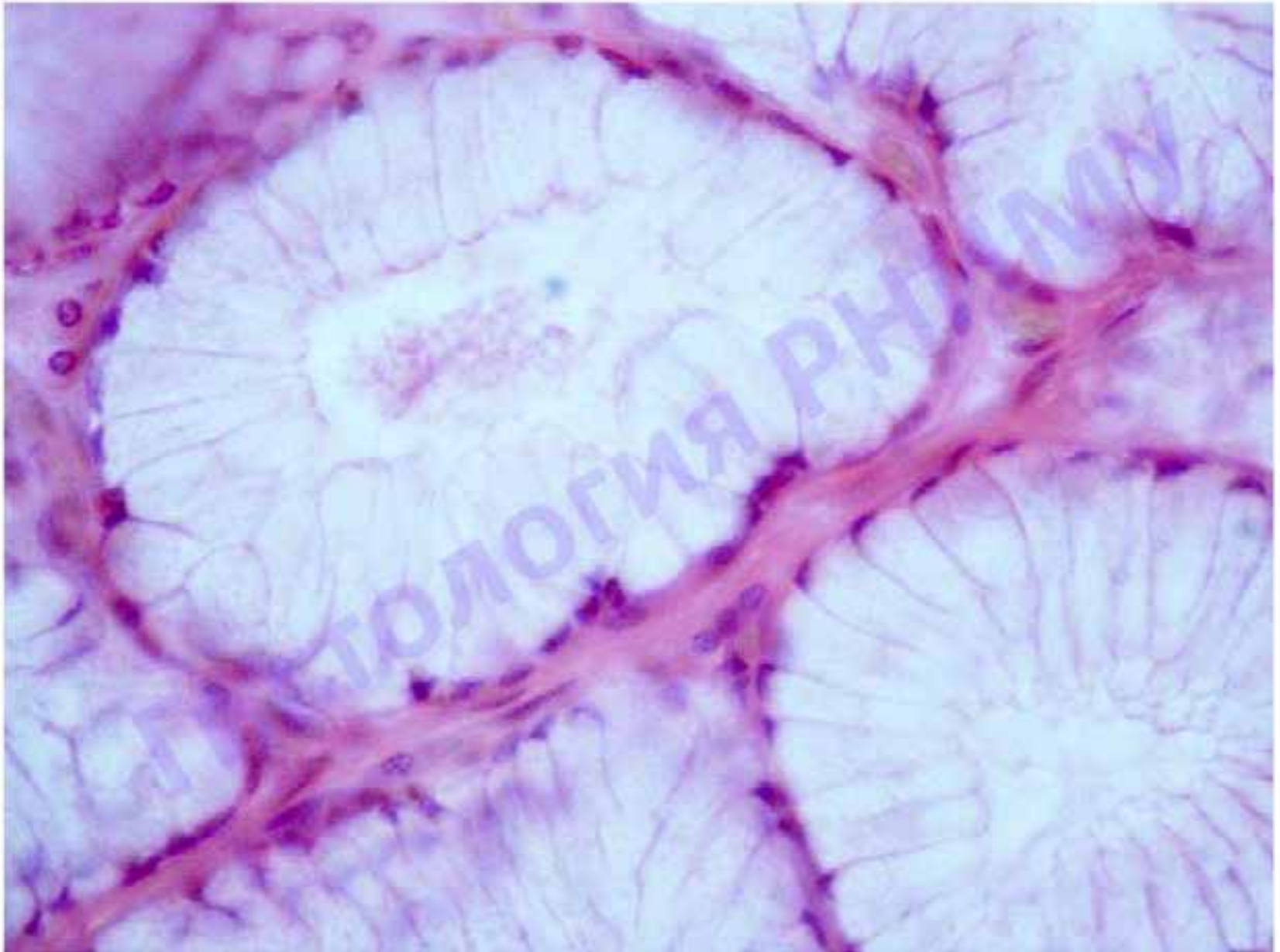
Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining



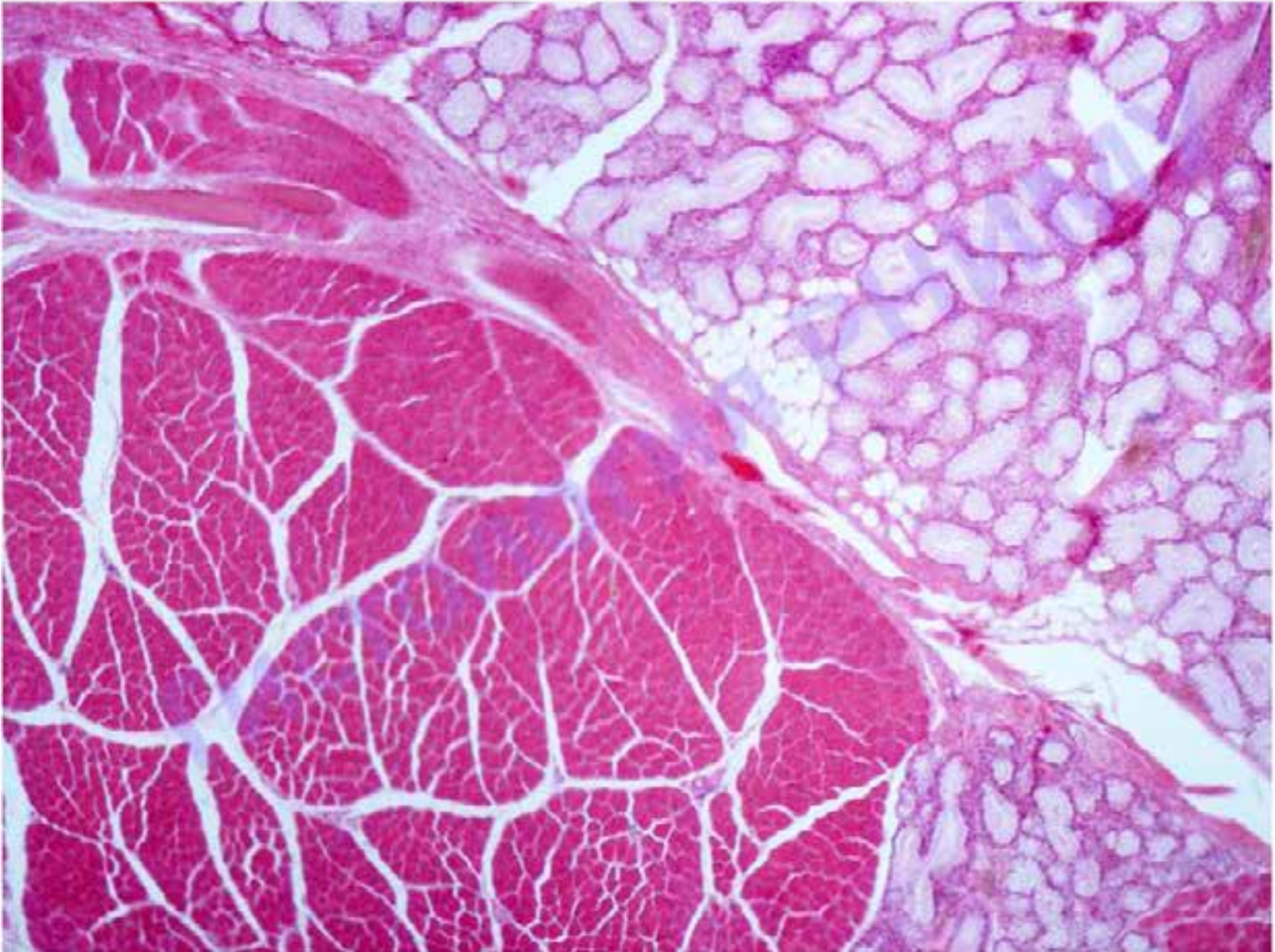
Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining



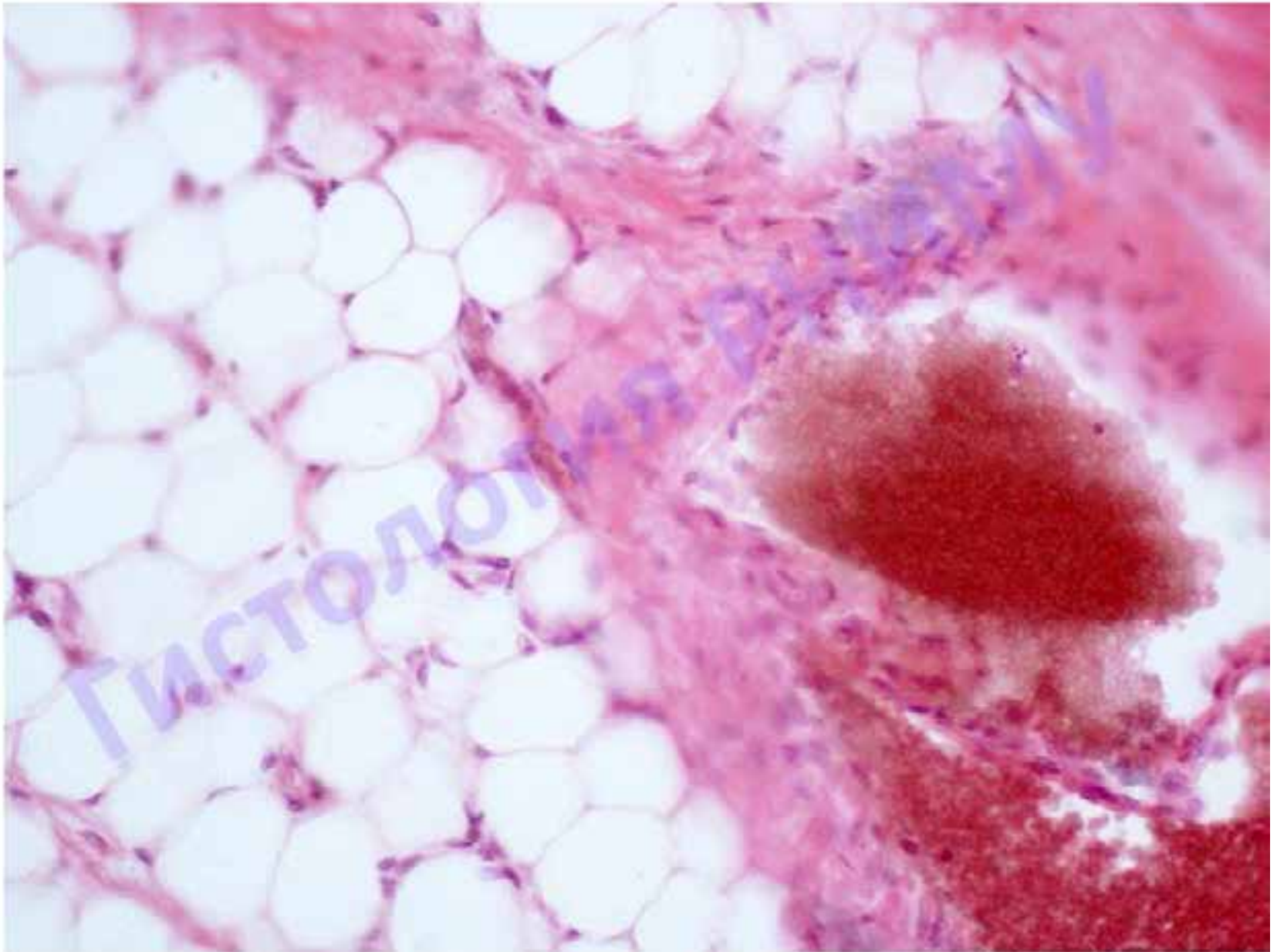
Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining



Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining



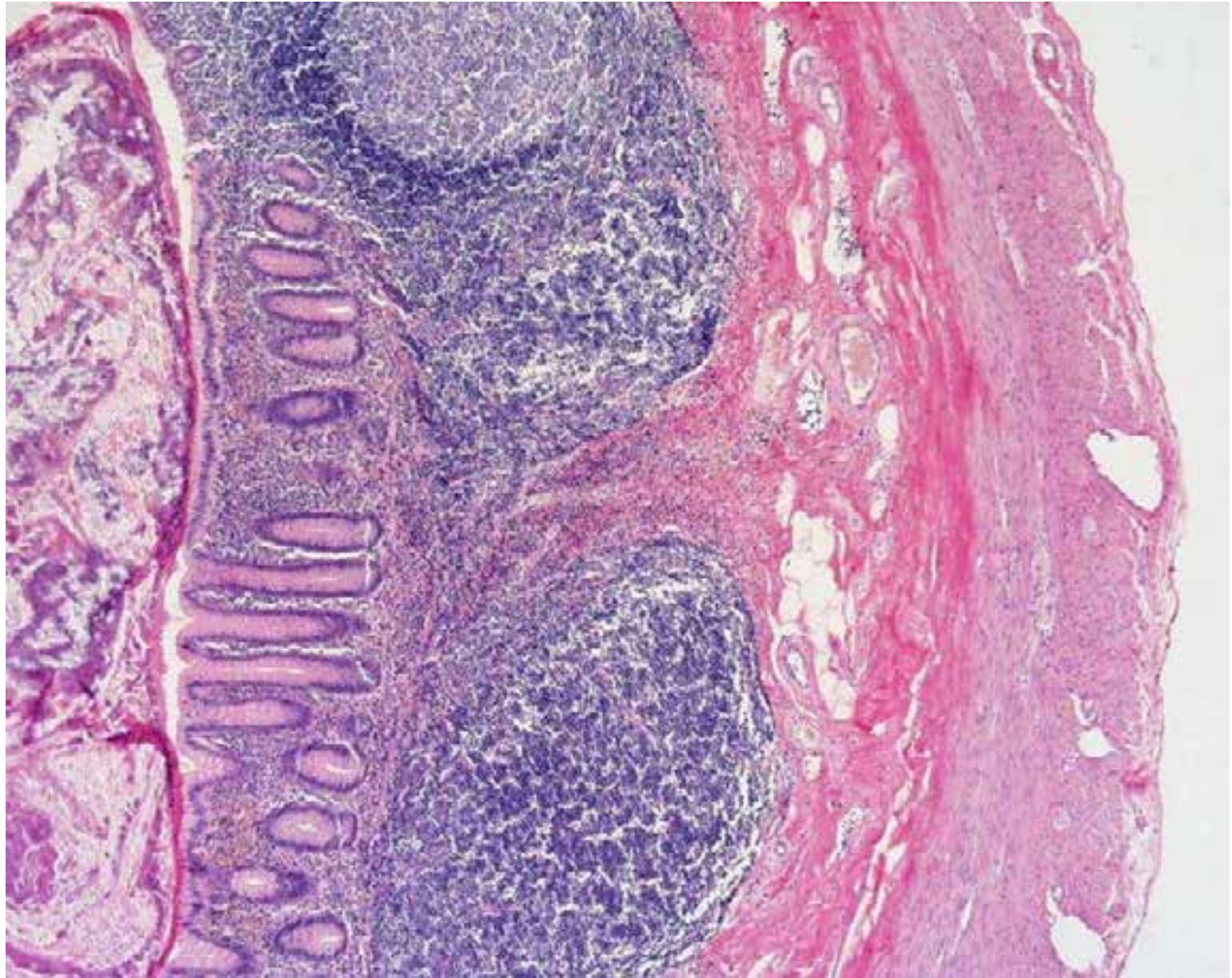
Slide №125. Section of the palatine tonsil
Hematoxylin-eosin staining



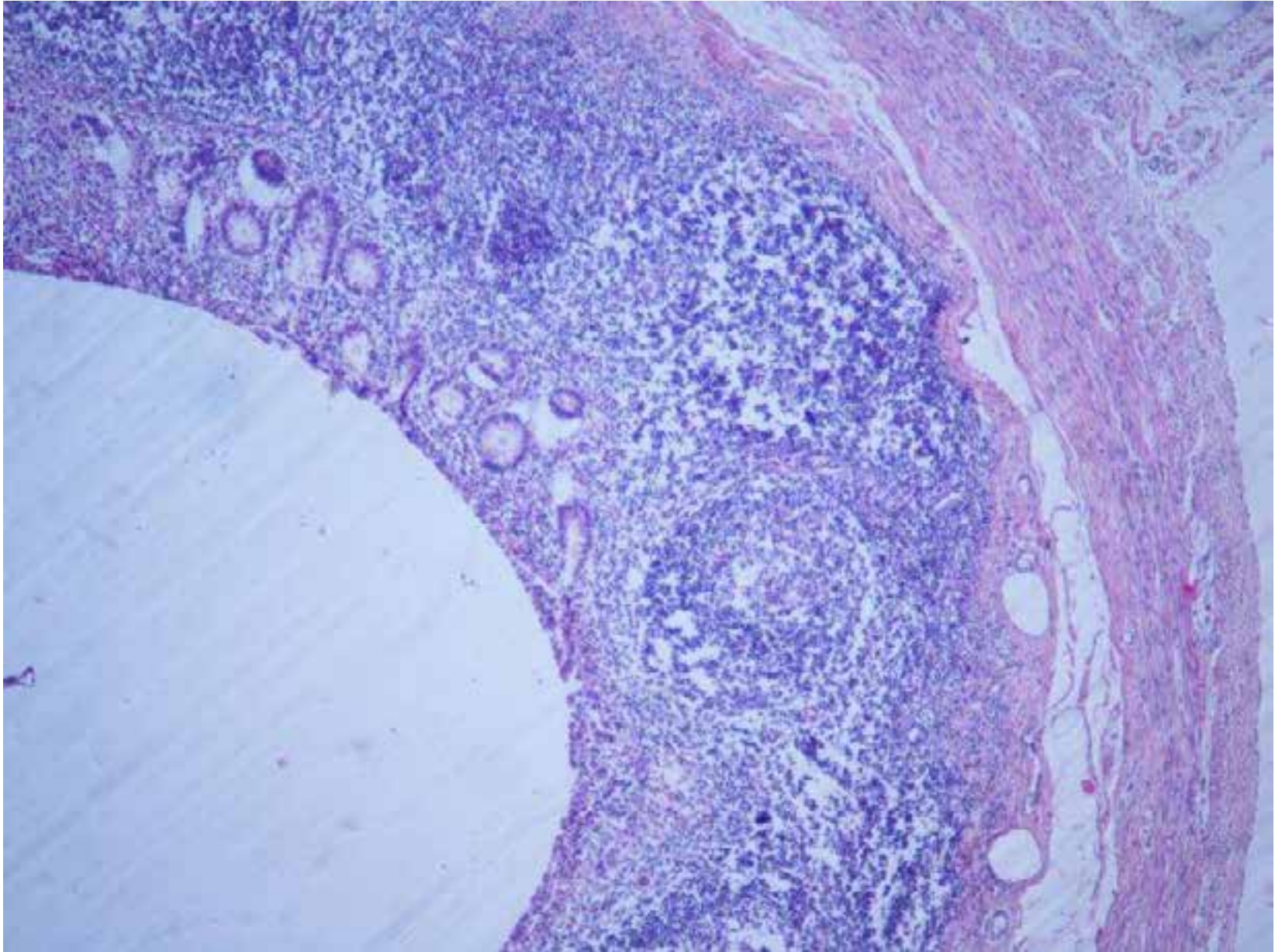
Slide №133. Appendix, cross section
Hematoxylin-eosin staining



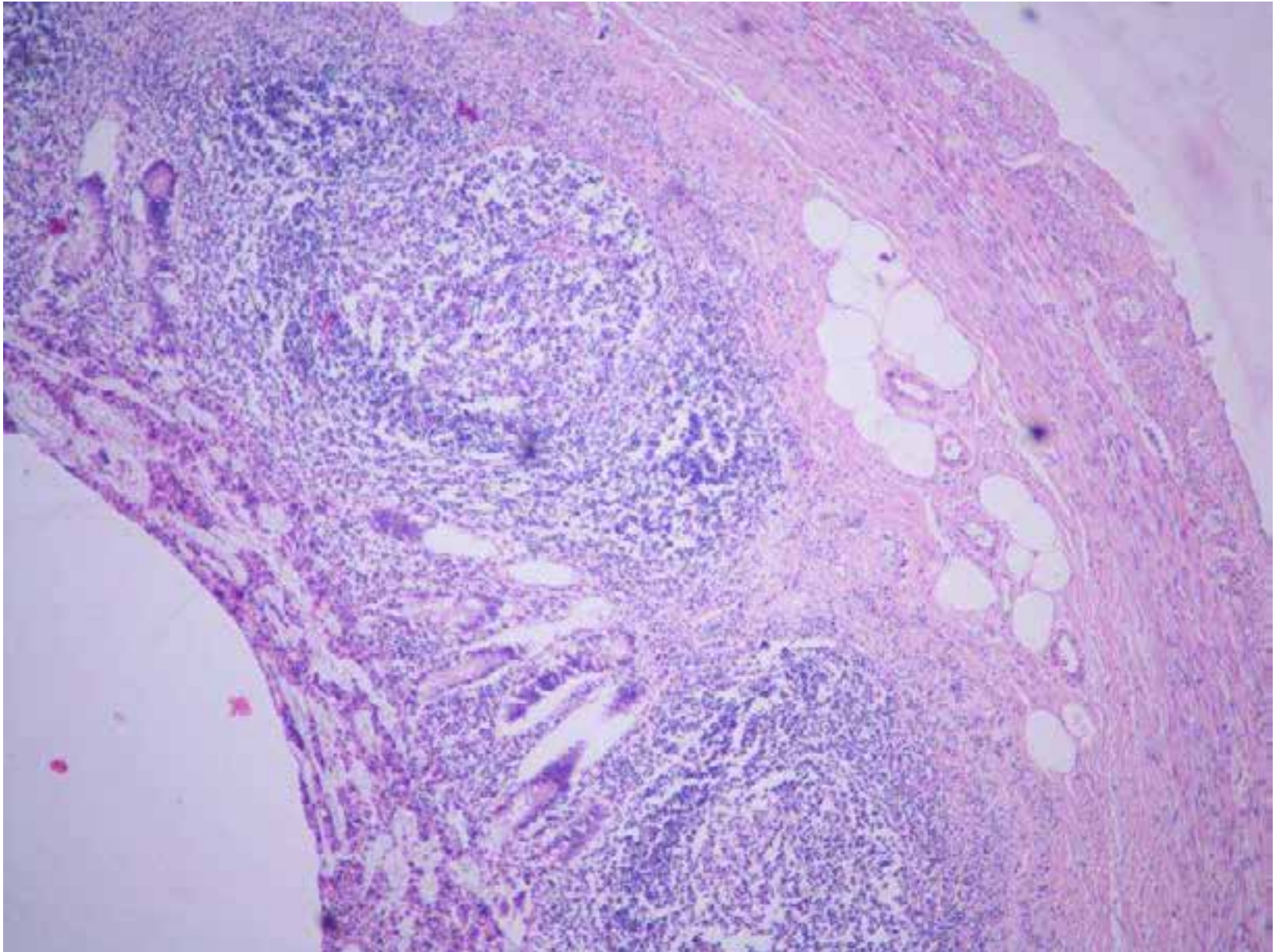
Slide №133. Appendix, cross section
Hematoxylin-eosin staining



Slide №133. Appendix, cross section
Hematoxylin-eosin staining



Slide №133. Appendix, cross section
Hematoxylin-eosin staining



Lymphoid nodules of the gut



Slide №133. Appendix, cross section
Hematoxylin-eosin staining

