



Professor V.F. Voino-Yasenetsky Krasnoyarsk State Medical University
Department of Pathological Anatomy Named After Professor P.G.Podzolkov

Lecture 2.

Hemodynamic Disorders, Thromboembolism, and Shock

Contents:

Part 1.

HYPEREMIA AND CONGESTION
BLEEDING & HEMORRHAGE

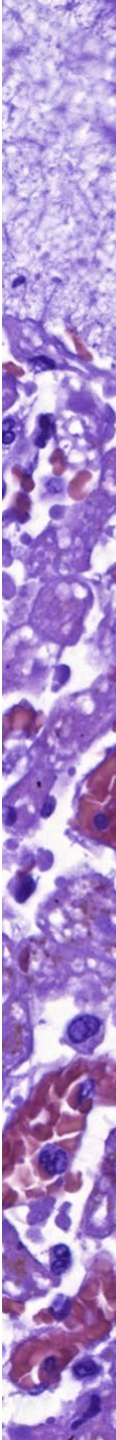
Part 2.

THROMBOSIS
EMBOLISM

Lecturer: Vladimir A. Khorzhevskii

Candidate of Medical Science (PhD),

Head of the Department of Pathological Anatomy named after Professor P.G. Podzolkov



Photography and video recording are prohibited.

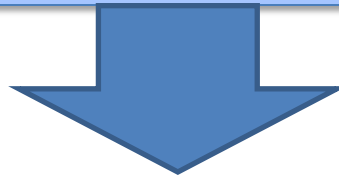
Materials are provided for educational purposes only and may not be acceptable for public display outside the University.



HYPEREMIA AND CONGESTION

Hyperemia is an active process resulting from arteriolar dilation and increased blood inflow, as occurs at sites of inflammation or in exercising skeletal muscle.

Congestion is a passive process resulting from impaired outflow of venous blood from a tissue.



- parenchymal cell death and secondary tissue fibrosis
- elevated intravascular pressure may cause edema
- Rupture of capillaries, producing focal hemorrhages.

Hyperemia

(Rus.: Arterial hyperemia)

Physiological

Physical factors

Chemical factors

Emotions (blush in the cold, shame...)

Increased organ function

Hyperemia

(Rus.: Arterial hyperemia)

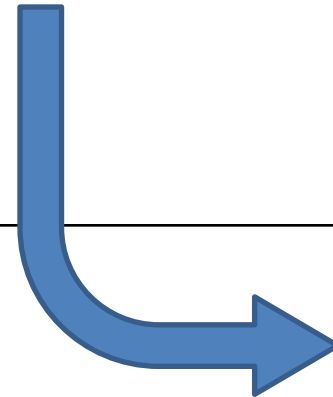
Pathological

General	Local
↑↑ volume of circulating blood (polycythemia vera, plethora)	Angioneurotic hyperemia
	Collateral hyperemia
	Inflammatory hyperemia
	Post-anemic hyperemia
↑↑ number of red blood cells (erythrocytosis).	Decompression (vacate) hyperemia
	Hyperemia due to arteriovenous shunt

Congestion

(Rus.: venous hyperemia)

Local	General
Thrombosis	<pre>graph TD; A[General] --> B[Acute]; A --> C[Chronic];</pre>
Embolic obstruction	
Tumoral compression	
Inflammation	



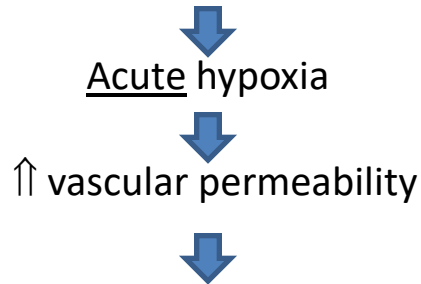
**Next
slide**
😊

General Congestion

(*Rus.: venous hyperemia*)

Acute

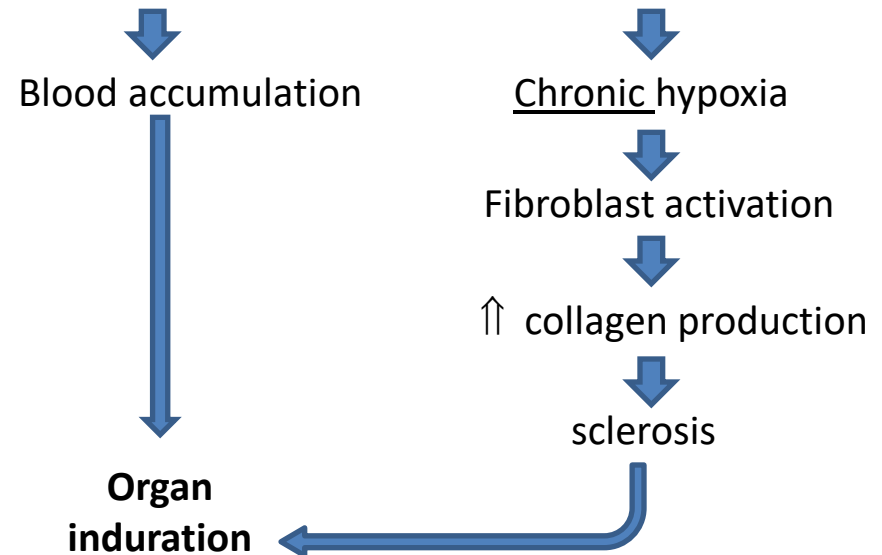
- result of asphyxia, acute myocardial infarction



- **plasma impregnation** of the vessel walls;
- **edema**,
- **blood stasis** in the capillaries and multiple **diapedetic hemorrhages**;
- **Injury** (*rus.: dystrophic*) and **necrotic changes** in the parenchymal organs

Chronic

- result of chronic heart failure (cardiosclerosis, heart valve defects, etc.)



thickening of the
basement membranes
of the endothelium and
epithelium

capillary-
parenchymal
block

- Atrophy
- Injury (*rus.: dystrophy*)
- Venous infarction

Liver in Chronic General Congestion

(Rus.: chronic venous hyperemia)

«Nutmeg liver»

1.

The central vein and sinusoids are distended with blood
(may even be necrosis of centrally located hepatocytes).

2.

The periportal hepatocytes, better oxygenated because of their proximity to hepatic arterioles, experience less severe hypoxia and **may develop only reversible fatty change.**

Liver in Chronic General Congestion

(*Rus.: chronic venous hyperemia*)

The **central** regions of the hepatic lobules, viewed on gross examination, are red-brown and slightly depressed (owing to cell loss) and are accentuated against the surrounding zones of uncongested tan, sometimes fatty, liver (**nutmeg liver**)



Key points:

Macro:

1. Enlarged
2. Indurated
3. “Nutmeg” view on section

Micro:

1. Centrilobular hemorrhages
2. Fatty injury and sclerosis on peripheral zones



Liver in Chronic General Congestion

(*Rus.: chronic venous hyperemia*)

The **central** regions of the hepatic lobules, viewed on gross examination, are red-brown and slightly depressed (owing to cell loss) and are accentuated against the surrounding zones of uncongested tan, sometimes fatty, liver (**nutmeg liver**)

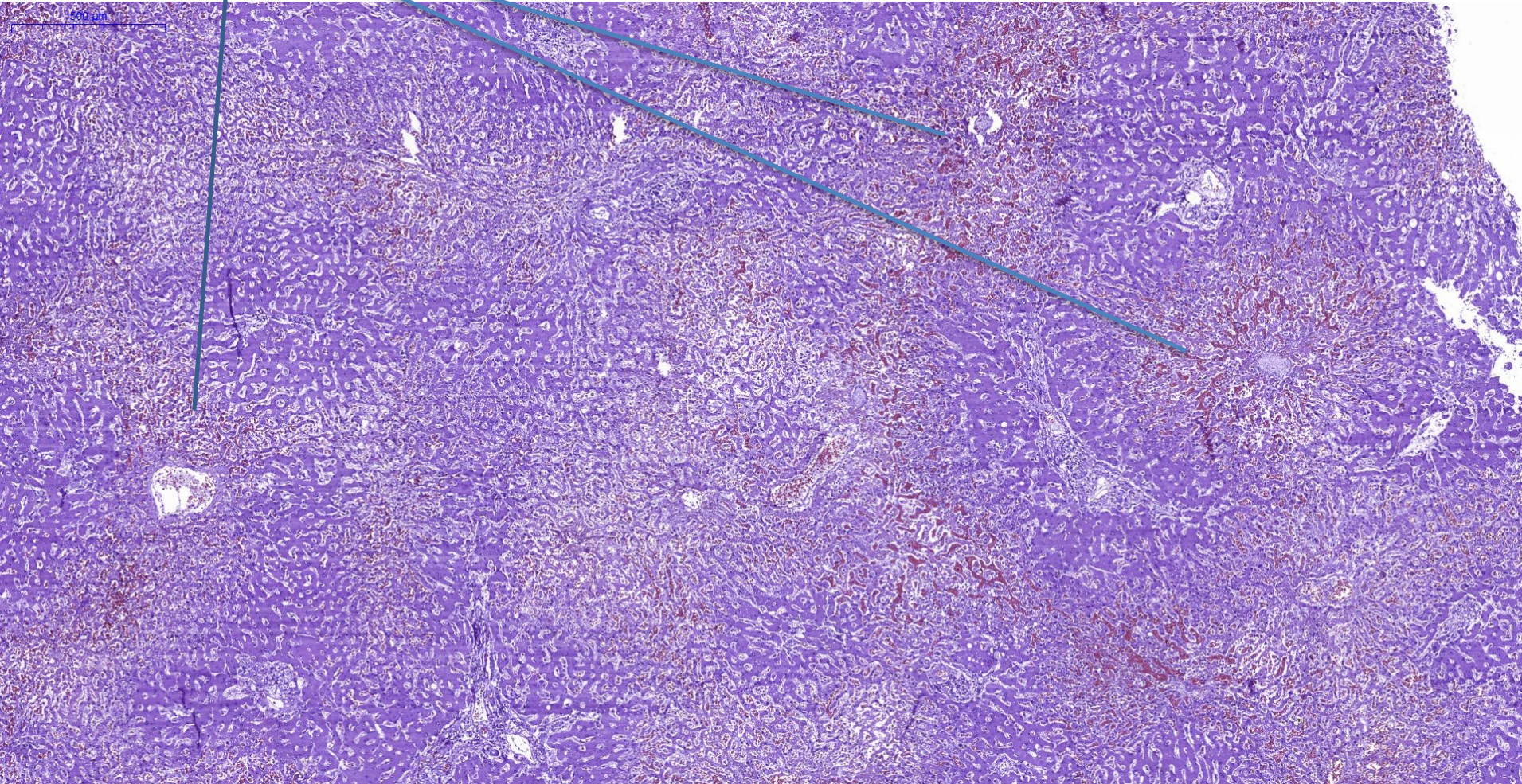


Liver in Chronic General Congestion

(Rus.: *chronic venous hyperemia*)

H

«nutmeg liver»

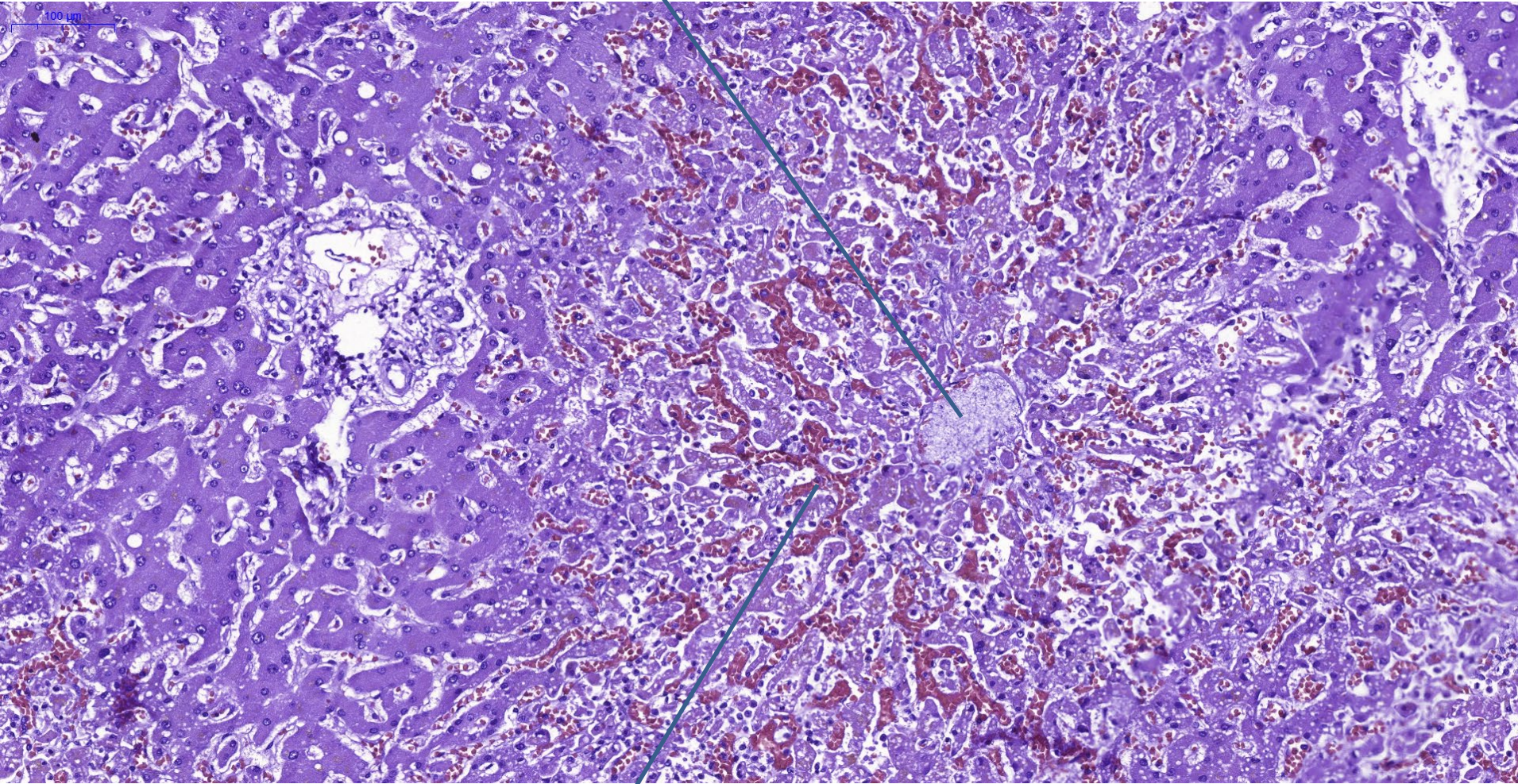


Liver in Chronic General Congestion

(Rus.: chronic venous hyperemia)

«nutmeg liver»

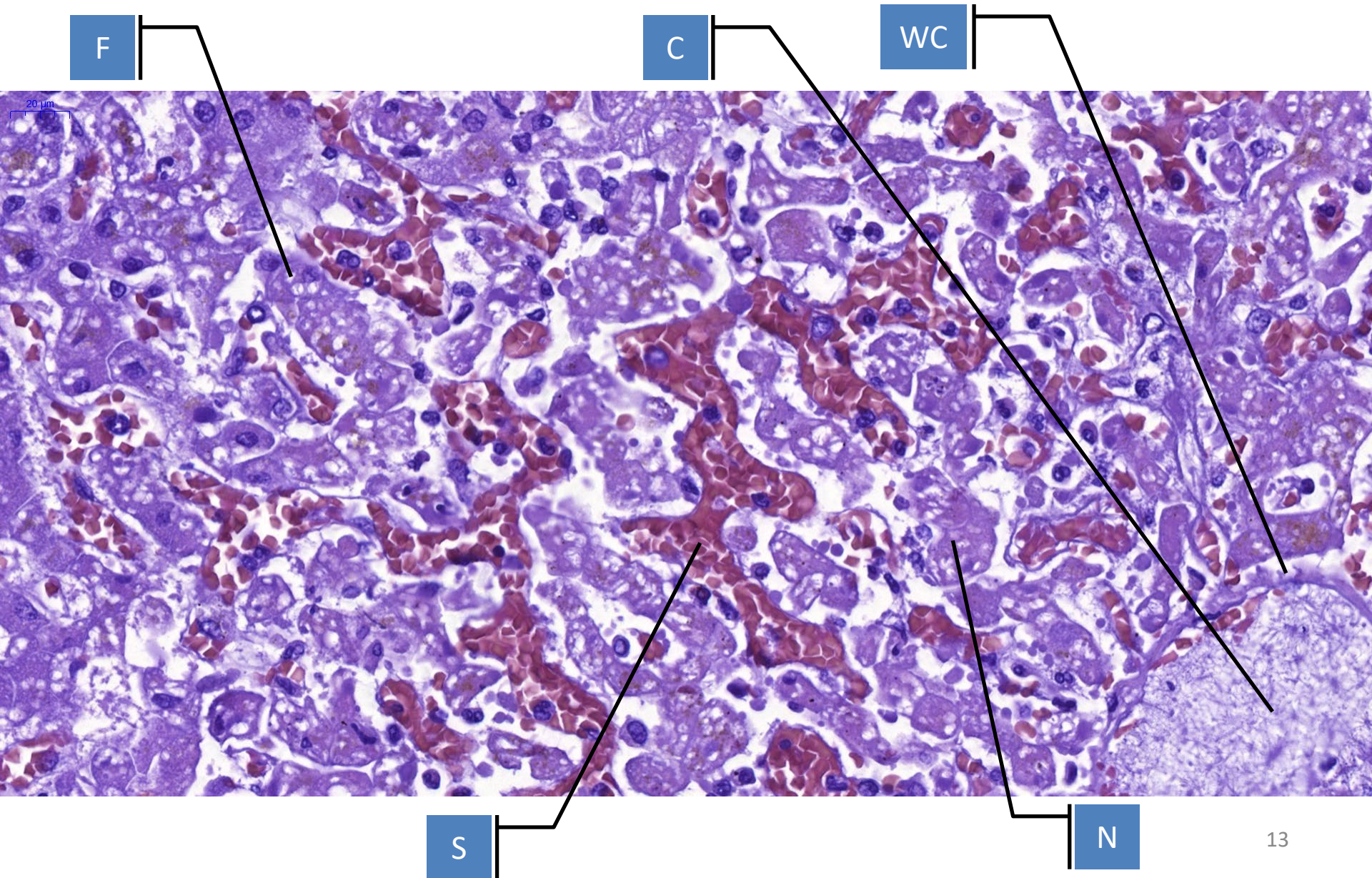
C



S

Liver in Chronic General Congestion

(Rus.: chronic venous hyperemia)
«nutmeg liver»



Lung in Chronic General Congestion

(Rus.: chronic venous hyperemia)

“Brown induration of the lung”

1.

A lot of diapedetic hemorrhages

(as a result of increased blood pressure in the microcirculatory vessels).

2.

Haemosiderosis

(accumulation of haemosiderin → Brownish color)

3.

Sclerosis

(that leads to parenchyma induration)



Lung in Chronic General Congestion

(*Rus.: chronic venous hyperemia*)

“Brown induration of the lung”



Key points:

Macro:

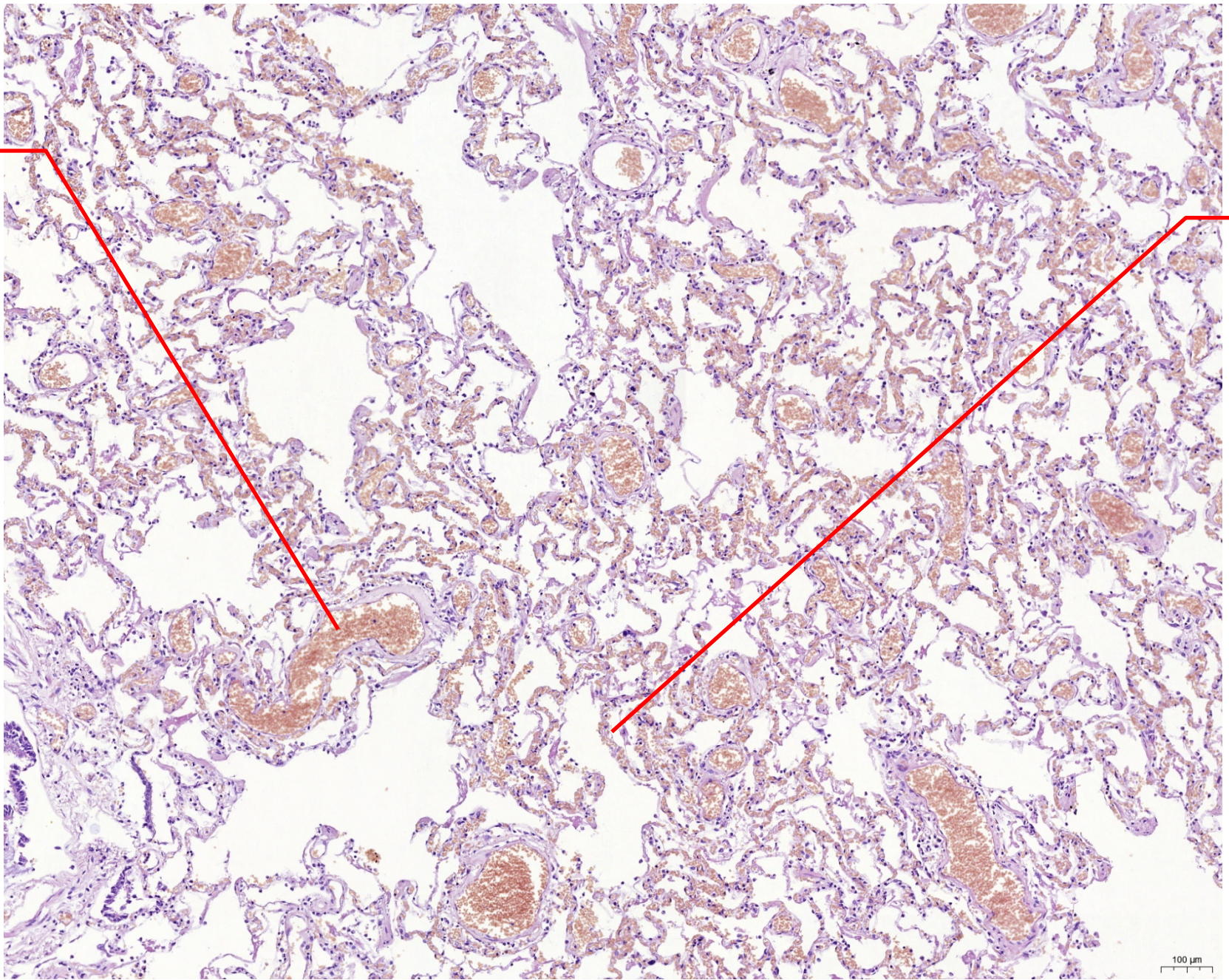
1. Enlarged
2. Indurated
3. “Brounish” view on section

Micro:

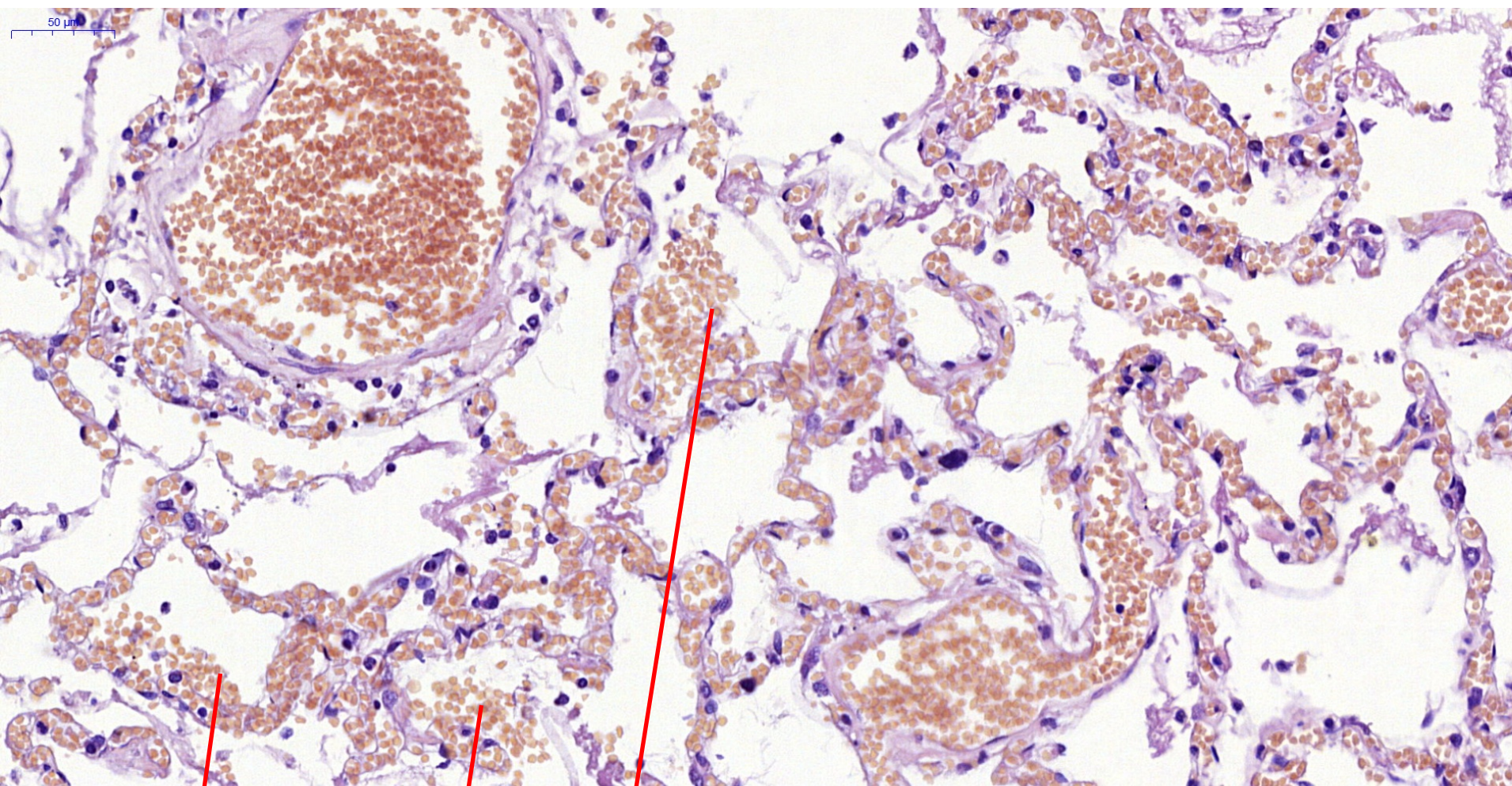
1. Diapedetic hemorrhages
2. A lot of haemosiderin

V

A



100 μm

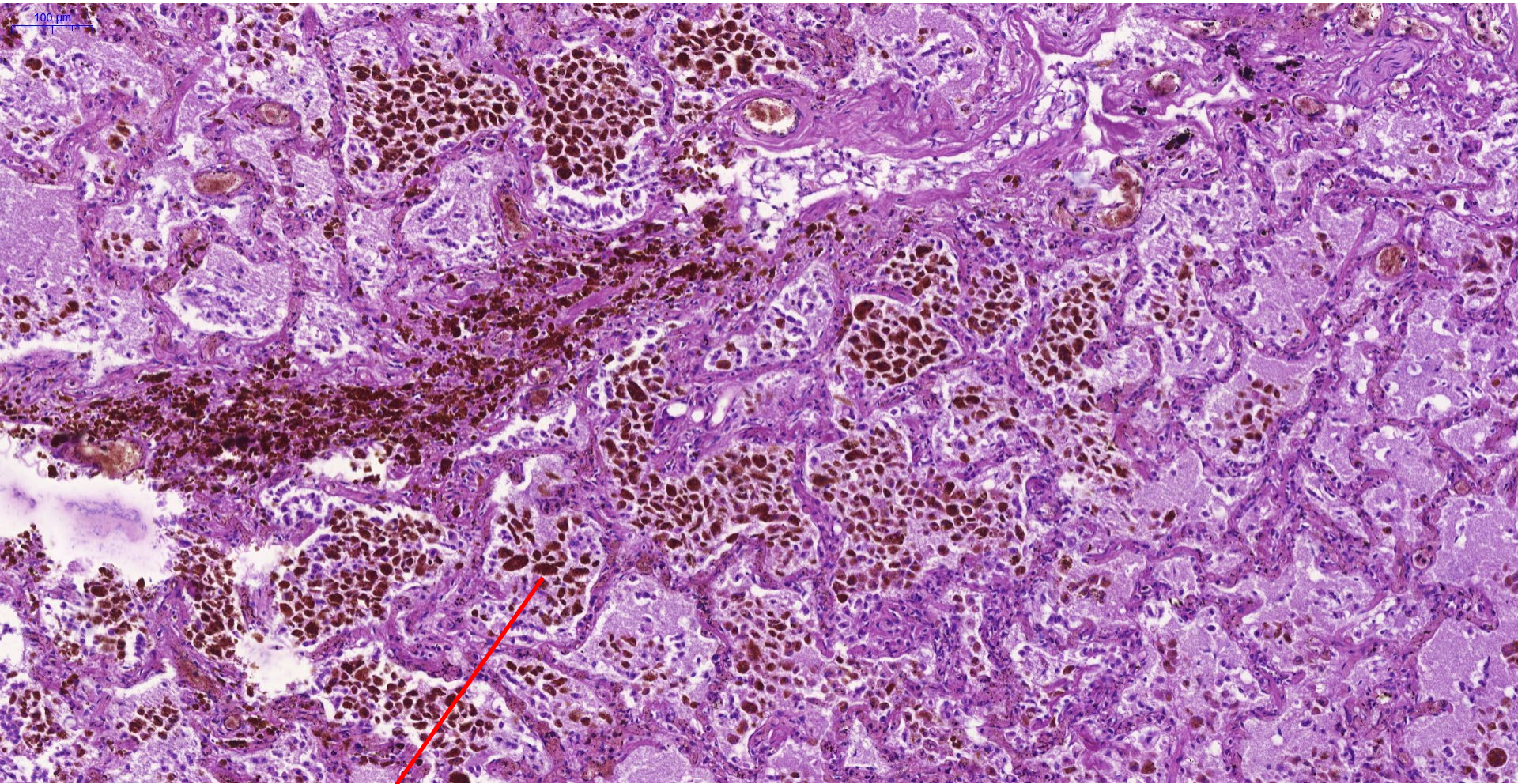


E

E

E

Hemosiderin-laden macrophages are called **hemosiderophages**



M

Kidneys and spleen in Chronic General Congestion

(Rus.: chronic venous hyperemia)

Cyanotic induration of the kidneys and spleen



Key points:

Macro:

1. Enlarged
2. Indurated
3. “Cyanotic” view on section

Micro:

1. Diapedetic hemorrhages
2. Overflowing with blood

Chronic General Congestion

(*Rus.: chronic venous hyperemia*)

↑↑ Hydrostatic blood pressure + Hypoxia

Plasmorrhagy (plasma extravasation)

Extravascular fluid accumulation

pleural cavity
(*hydrothorax*)

+

pericardial cavity
(*hydropericardium*)

+

peritoneal cavity
(*hydroperitoneum, or ascites*)

=

Anasarca

BLEEDING & HEMORRHAGE

Bleeding

- extravasation of blood from vessels or heart cavities, is most often the result of damage to blood vessels or defective clot formation.

External
(into the environment)

- **hemoptysis** (haemoptoe),
- **nosebleeds** (epistaxis),
- **vomiting with blood** (haematemesis),
- **discharge of blood in the feces** (melaena),
- **bleeding from the uterus** (metrorrhagia).

Internal
(into the cavity)

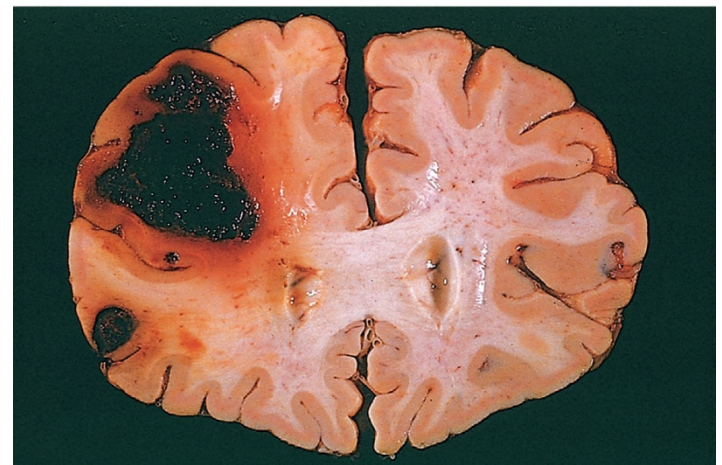
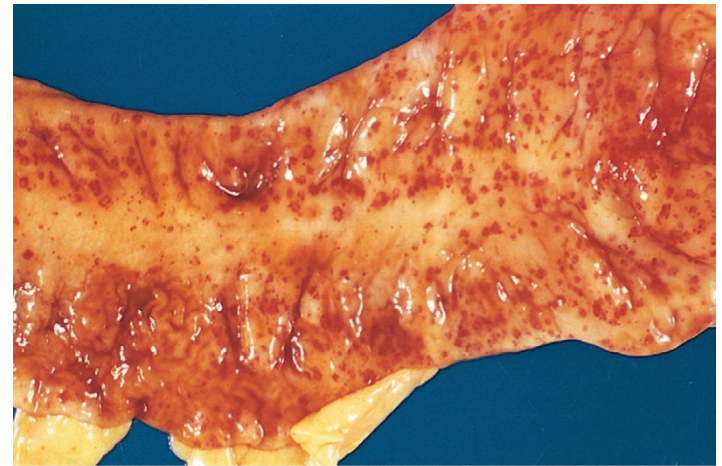
- **pericardial cavity** (hemopericardium),
- **pleura** (hemothorax),
- **abdominal cavity** (hemoperitoneum).

Hemorrhage

- When blood accumulates in the tissues

Hematoma - the accumulation of blood in a tissue with a violation of its integrity, and if tissue elements are preserved, it is called **hemorrhagic impregnation** (hemorrhagic infiltration).

Flat hemorrhages, are called **bruises**,
Small punctate hemorrhages are called **petechiae**,
Larger hemorrhages are called **ecchymosis**.



Causes of bleeding (hemorrhage)

rupture of the vessel wall (heart)

- as a result of rupture of the wall of the heart or vessel occurs when injured, including surgical trauma, with inflammation or sclerosis.

erosion of the vessel wall

- as a result of erosion of the vessel wall (arrosive bleeding), occurs more often with inflammation (erosion of the vessel wall by proteolytic enzymes), caseous necrosis (in the wall of the tuberculous cavity), in the zone of a malignant tumor, at the bottom of a stomach ulcer (erosion by gastric juice) and ectopic (tubal) pregnancy.

increased permeability

due to increased permeability of the vessel wall, or diapedetic hemorrhage is observed with angioneurotic disorders, tissue hypoxia (arterial hypertension, vasculitis, infectious diseases, diseases of the blood system (hemoblastosis and anemia).

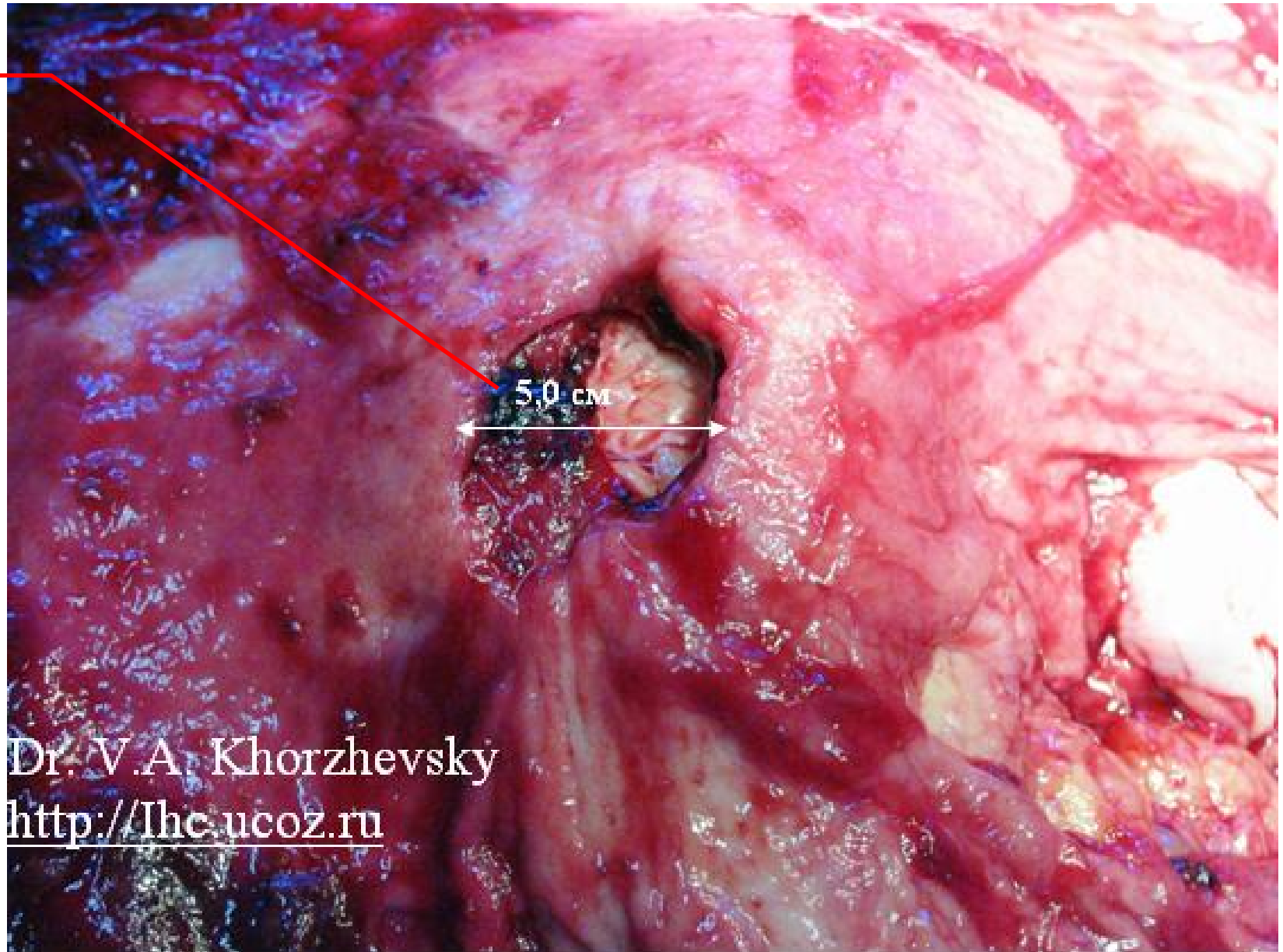
Outcome: resorption of blood, formation of a cyst at the site of hemorrhage, encapsulation or replacement of hematoma with connective tissue, suppuration

Cardiac Rupture After Catheter Ablation Procedure



Erosion of the vessel wall in the bottom of gastric ulcer

H

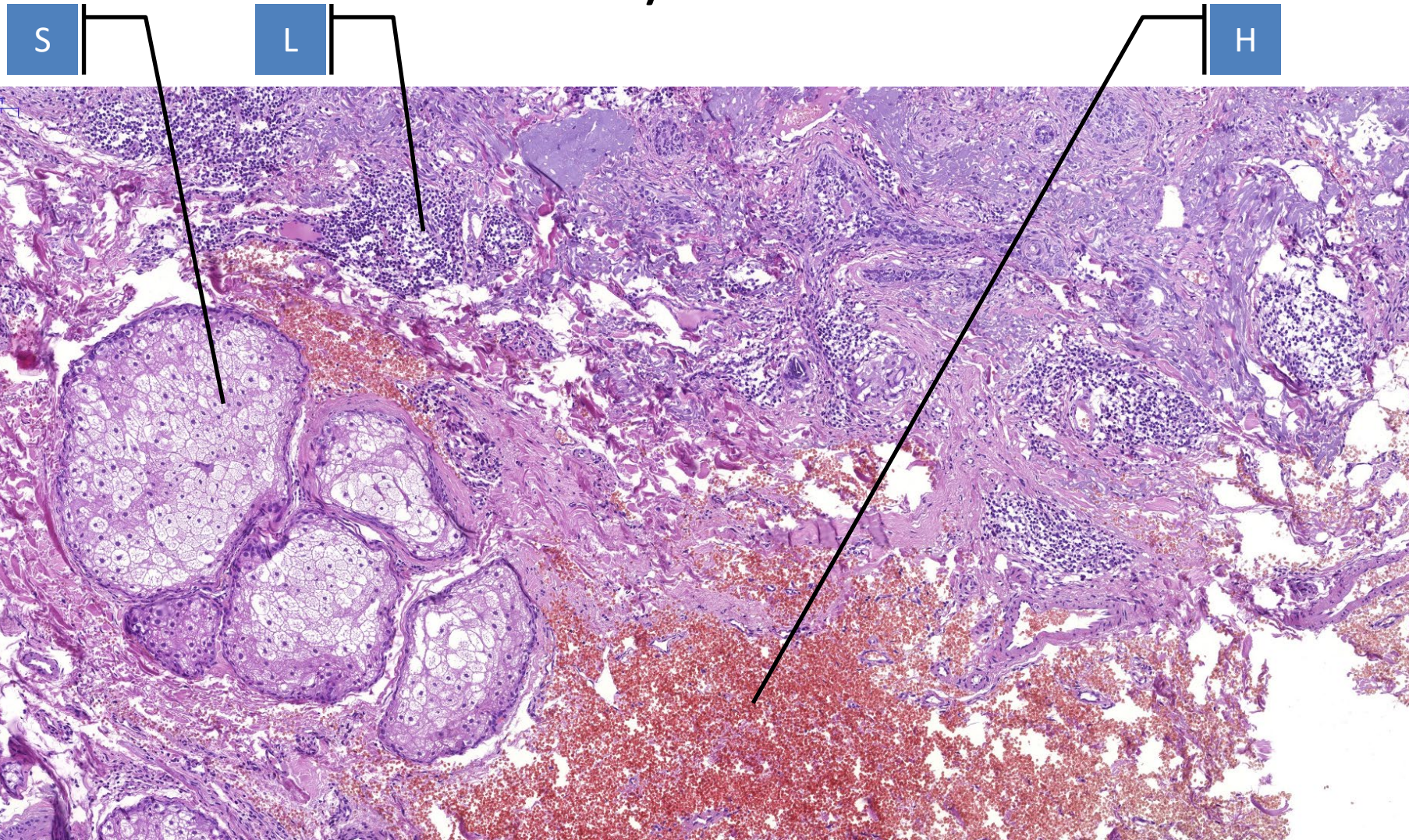


Dr. V.A. Khorzhevsky
<http://lhc.ucoz.ru>

Due to increased permeability of the vessel wall in case of systemic vasculitis

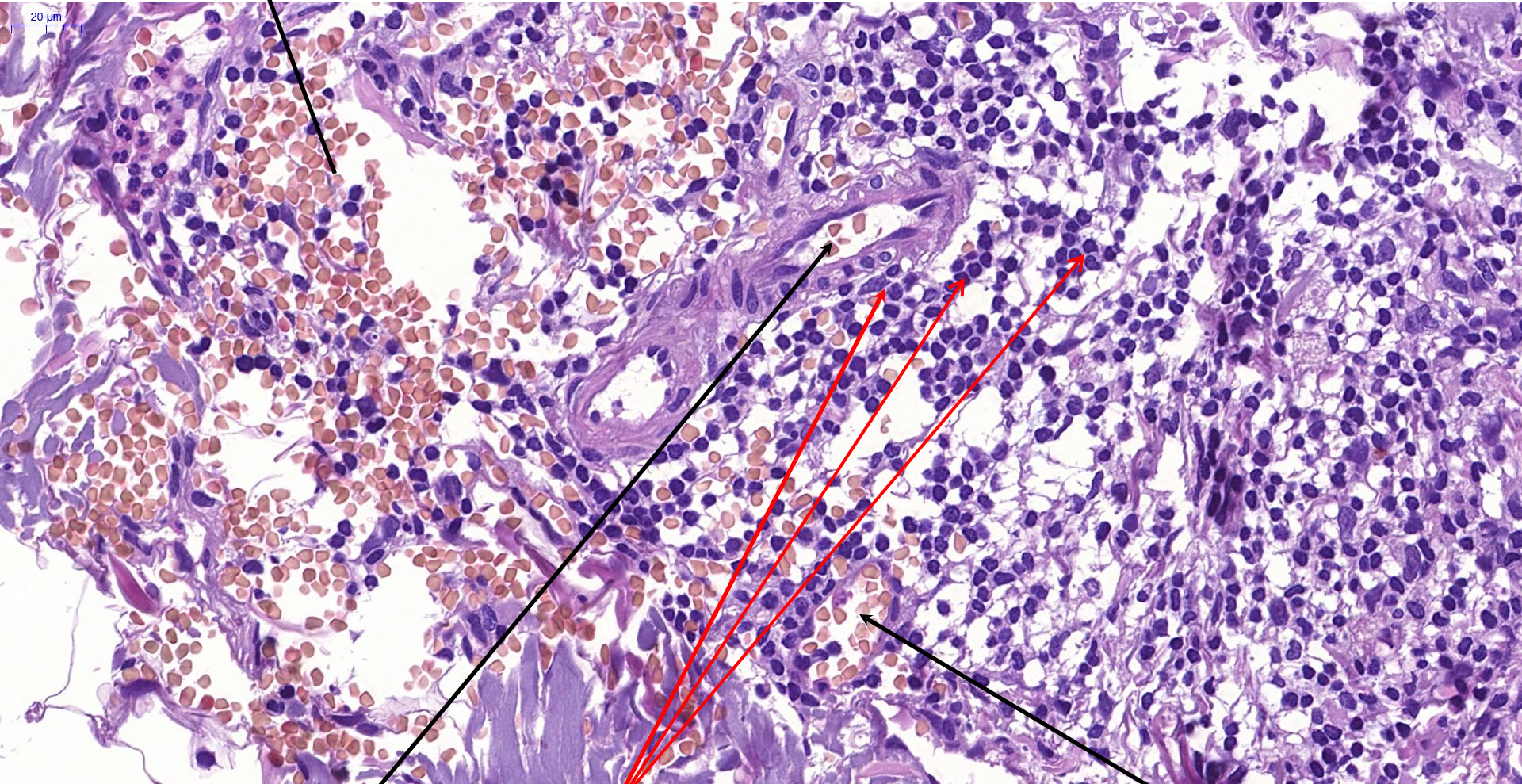


Due to increased permeability of the vessel wall in case of systemic vasculitis



Due to increased permeability of the vessel wall in case of systemic vasculitis

H

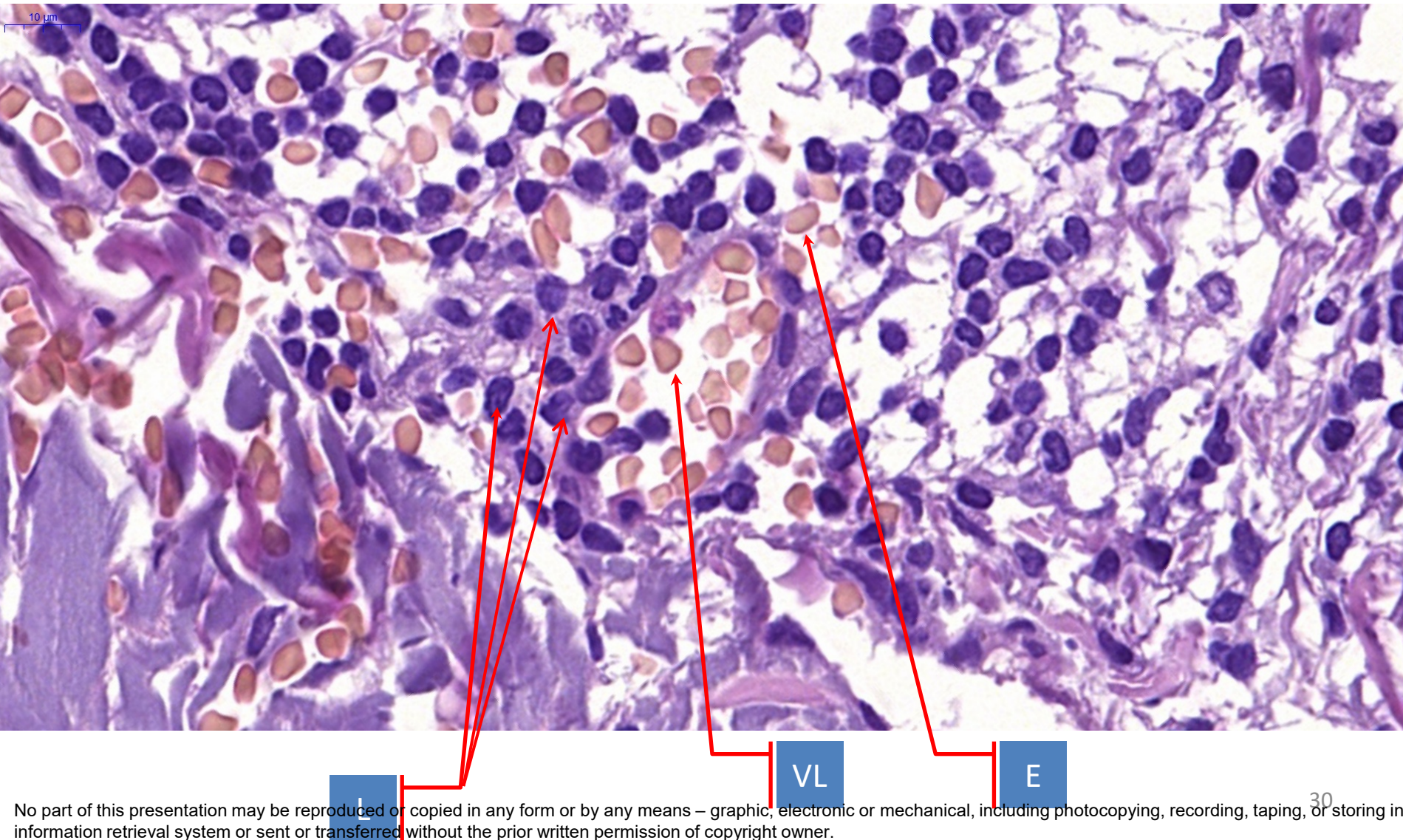


CV




L

CV

Due to increased permeability of the vessel wall in case of systemic vasculitis



Sizes of the hemorrhage

Name		
Petechiae	Purpura	Ecchymoses
<i>1 to 2 mm in diameter</i>	<i>are slightly larger (3 to 5 mm)</i>	<i>are larger (1 to 2 cm)</i>
		

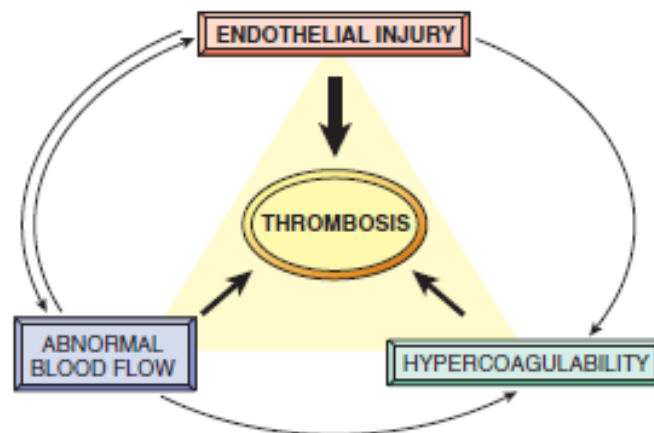
Thrombosis

Thrombosis

- lifetime coagulation of blood in the lumen of the blood vessels, in the cavities of the heart, or in places of hemorrhages.

Virchow's triad:

- endothelial injury,
- stasis or turbulent blood flow,
- hypercoagulability of the blood



1. Endothelial injury

- leading to platelet activation almost inevitably underlies thrombus formation in the heart and the arterial circulation, where the high rates of blood flow impede clot formation.
- severe endothelial injury may trigger thrombosis by exposing **VWF and tissue factor**. However, **inflammation** and other noxious stimuli also promote **thrombosis by shifting the pattern of gene expression in endothelium** to one that is “prothrombotic.”
 - physical injury,
 - infectious agents,
 - abnormal blood flow,
 - inflammatory mediators,
 - metabolic abnormalities (hypercholesterolemia or homocystinemia),
 - toxins absorbed from cigarette smoke.

2. Abnormal Blood Flow

Turbulence (chaotic blood flow) contributes to arterial and cardiac thrombosis by causing endothelial injury or dysfunction, as well as by forming countercurrents and local pockets of stasis.

Stasis is a major factor in the development of venous thrombi.

Stasis and turbulence have the following deleterious effects:

- Both promote endothelial cell activation and enhanced procoagulant activity.
- Stasis allows platelets and leukocytes to come into contact with the endothelium when the flow is sluggish.
- Stasis also slows the washout of activated clotting factors and impedes the inflow of clotting factor inhibitors.

3. Hypercoagulability

Hypercoagulability refers to an abnormally high tendency of the blood to clot, and is typically caused by alterations in coagulation factors.

→	Primary (Genetic)
	Common (>1% of the Population)
	Factor V mutation (G1691A mutation; factor V Leiden) Prothrombin mutation (G20210A variant) Increased levels of factor VIII, IX, or XI or fibrinogen
	Rare
	Anti-thrombin III deficiency Protein C deficiency Protein S deficiency
	Very Rare
	Fibrinolysis defects Homozygous homocystinuria (deficiency of cystathione β -synthetase)
→	Secondary (Acquired)
	High Risk for Thrombosis
	Prolonged bed rest or immobilization Myocardial infarction Atrial fibrillation Tissue injury (surgery, fracture, burn) Cancer Prosthetic cardiac valves Disseminated intravascular coagulation Heparin-induced thrombocytopenia Anti-phospholipid antibody syndrome
	Lower Risk for Thrombosis
	Cardiomyopathy Nephrotic syndrome Hyperestrogenic states (pregnancy and postpartum) Oral contraceptive use Sickle cell anemia Smoking

Morphology of the thrombus

thrombi typically have firm, crumbling consistency, they are focally attached to vessel walls and contain gray strands of deposited fibrin.

At autopsy, **postmortem clots can sometimes be mistaken** for venous thrombi. However, the former are gelatinous and because of red cell settling they have a dark red portion and a yellow “chicken fat” upper portion; they also are usually not attached to the underlying vessel wall.

Thrombi can have grossly (and microscopically) apparent laminations called **lines of Zahn**; these represent pale **platelet** and fibrin layers alternating with darker **red cell**–rich layers.

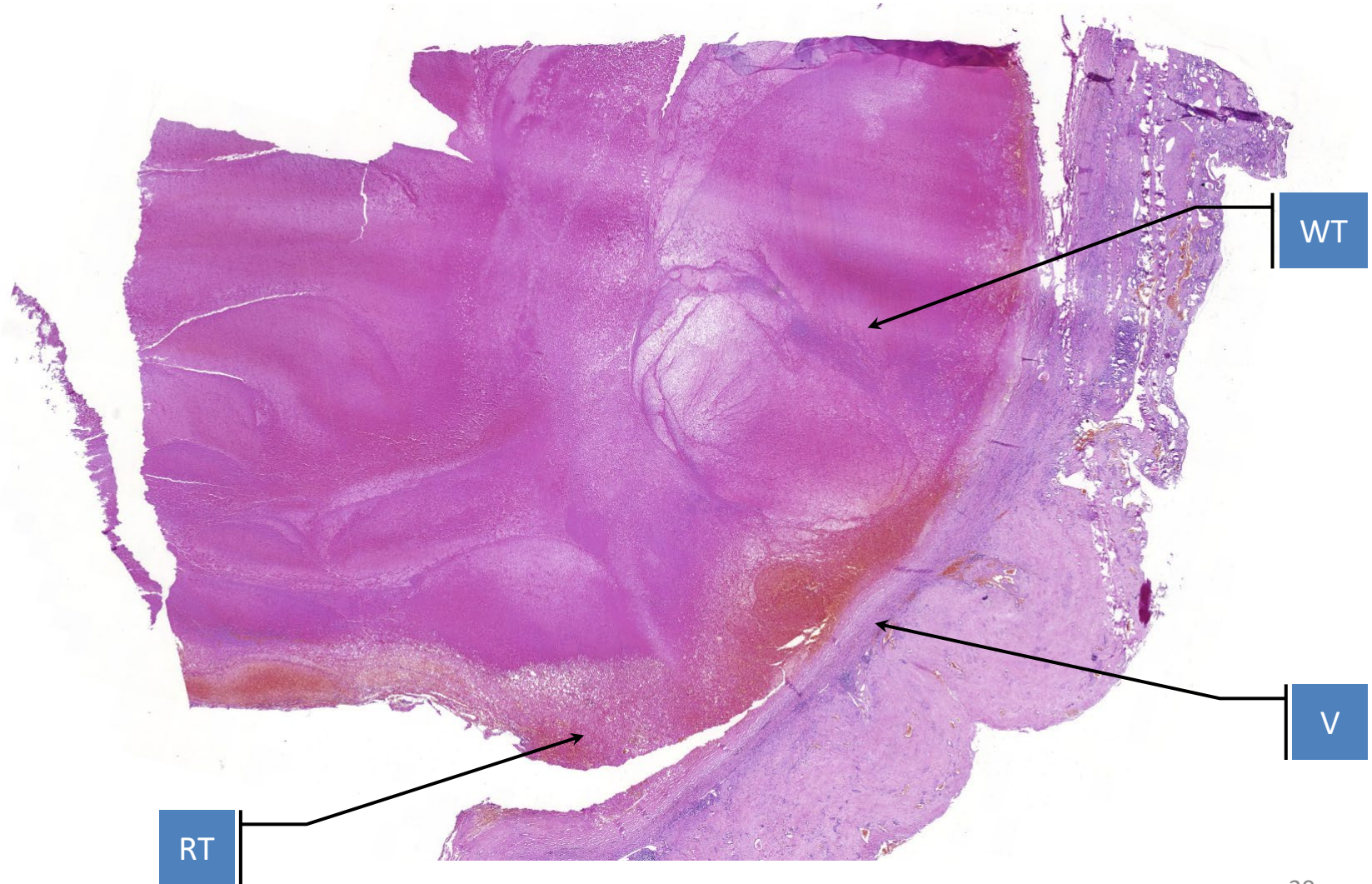
Morphology of the thrombus

White clot	Red clot	Mixed clot
↑↑ platelet	↑↑ Erythrocytes	platelet / Erythrocytes / platelet ...
Fibrin	Fibrin	Fibrin
Leukocyte	Leukocyte	

Macroscopic picture		
Head	Body	Tail
Connected with vessel wall (intima)	Free in vessel lumen	Free in vessel lumen
= White clot	= Mixed clot	= Red clot

Mixed thrombus (microscopy)

1000 μ m

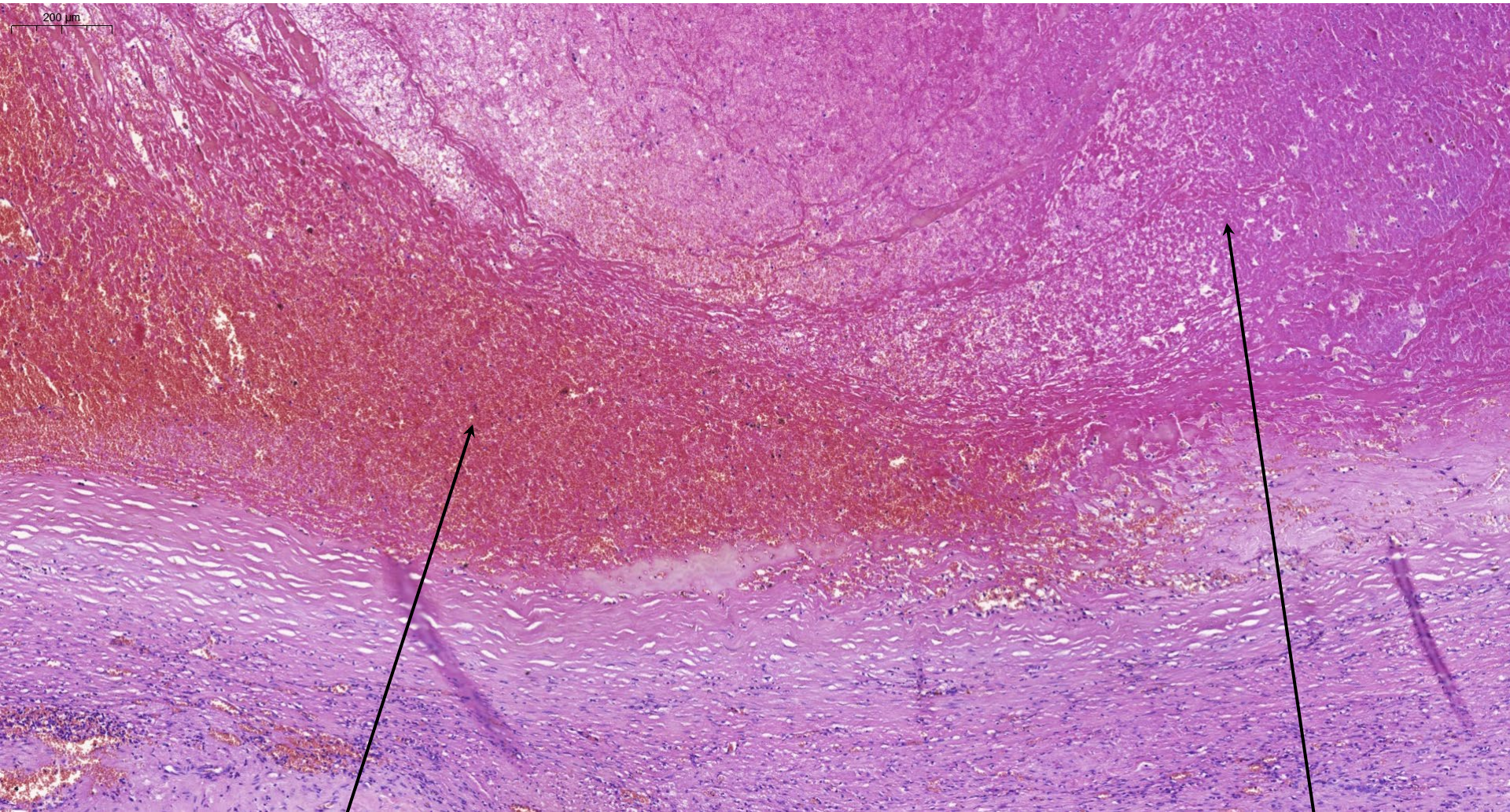


WT

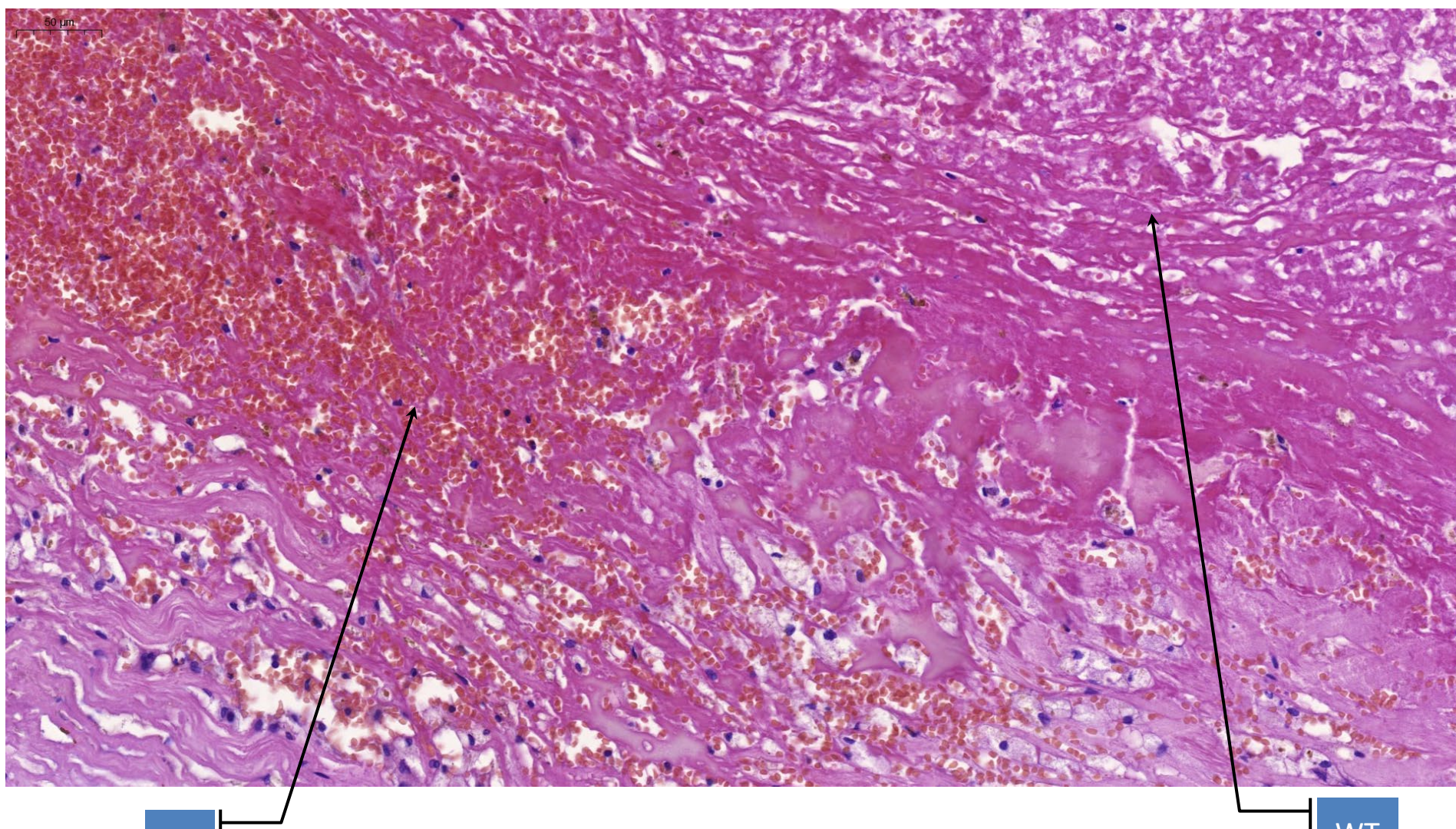
V

RT

Mixed thrombus (microscopy)



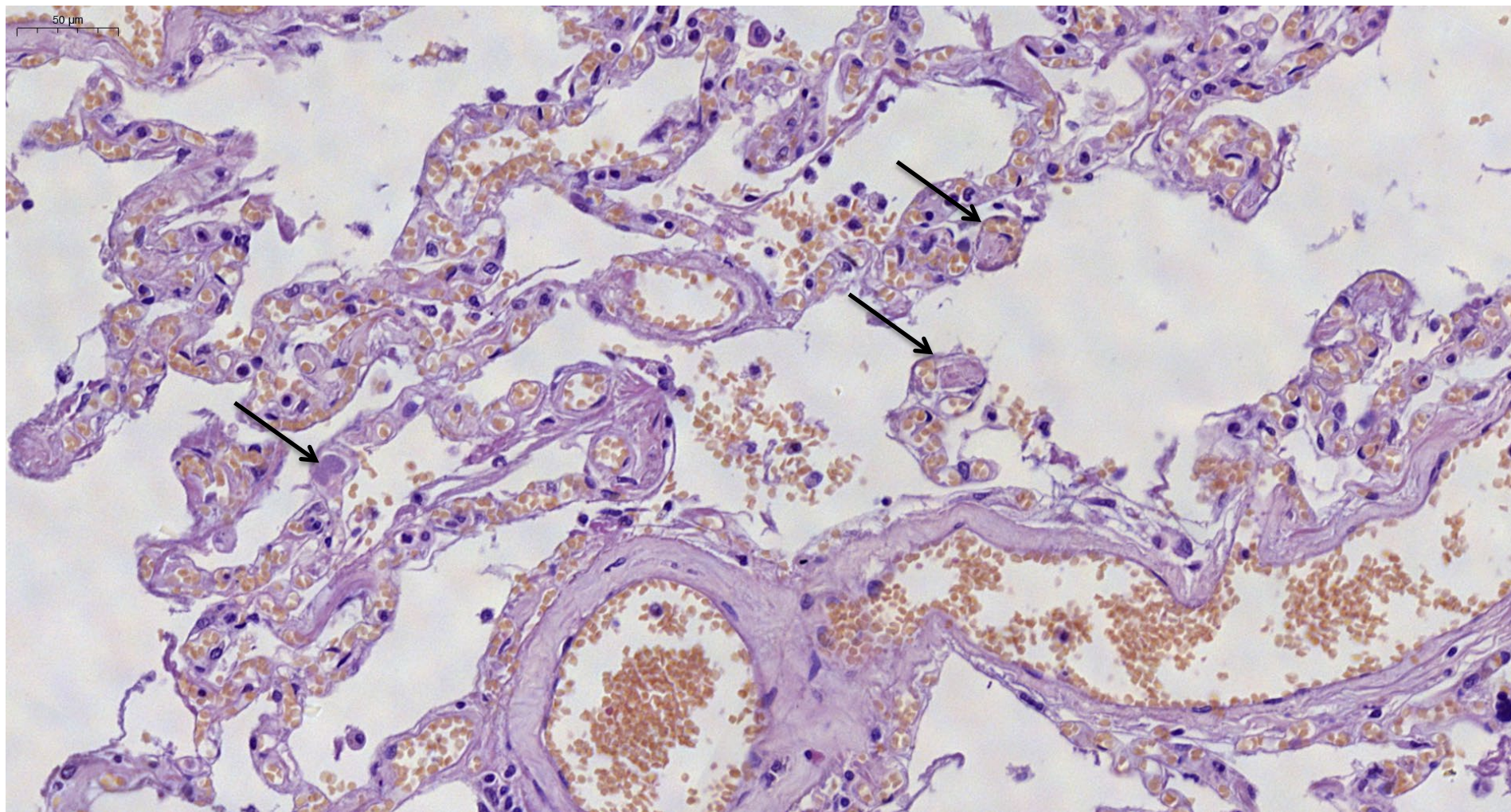
Mixed thrombus (microscopy)



RT

WT

Hyaline clots in case of SARS-Cov-2019 pneumonia



- Microscopically looks like hyaline

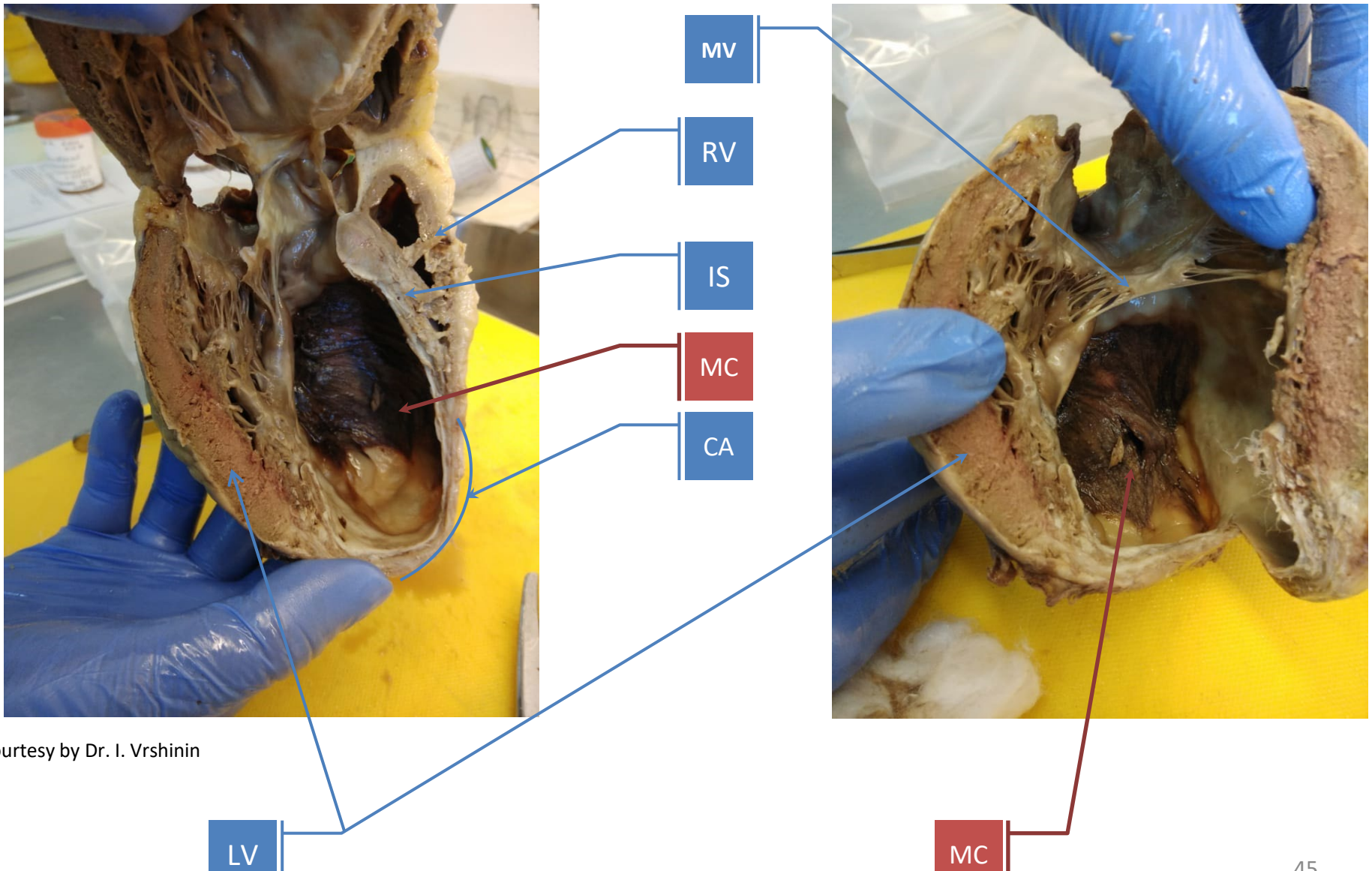
Location of the clot in relation to the vessel (heart) wall

- Thrombi occurring in heart chambers or in the aortic lumen are designated as **mural** thrombi.
- **Obturing** thrombi
- **Spherical** thrombi

Causes of a thrombus formation

in the veins	In the arteries	In the cavities of the heart
chronic heart failure	atherosclerosis	heart failure with hemodynamic disturbances and expansion of the chambers
physical inactivity	arterial aneurysms	myocardial infarction that reaches endocardium
immobility after an acute disorder of blood circulation	inflammation of the arteries (arteritis)	inflammation of the valves (endocarditis) in rheumatic diseases and sepsis
long duration of a surgery		heart rhythm disturbances
long-term serious condition of the patient		
inflammation of the veins (phlebitis)		

Mural heart thrombi in case of post-infarction chronic aneurysm



Courtesy by Dr. I. Vrshinin

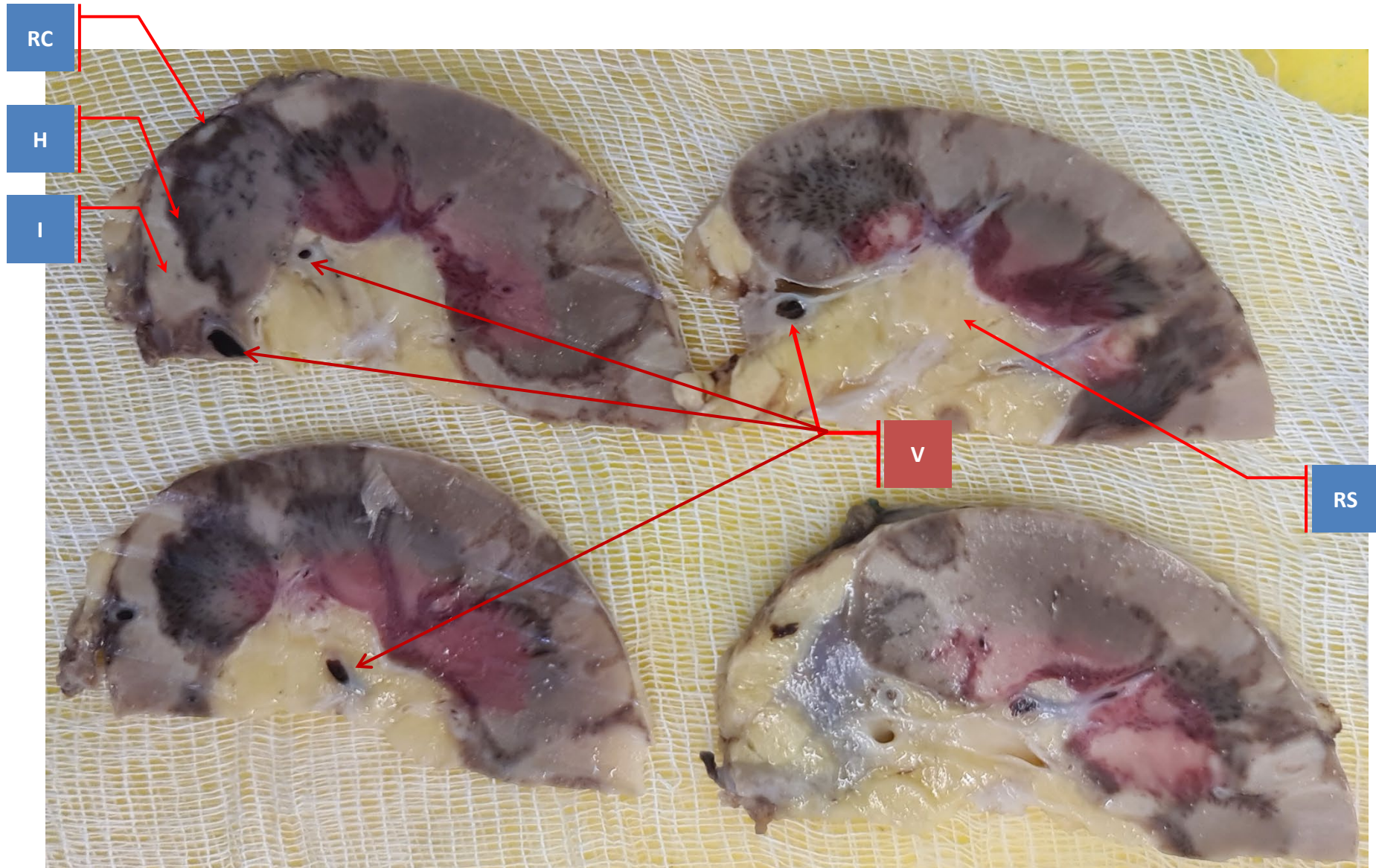
Courtesy by Dr. I. Vrshinin



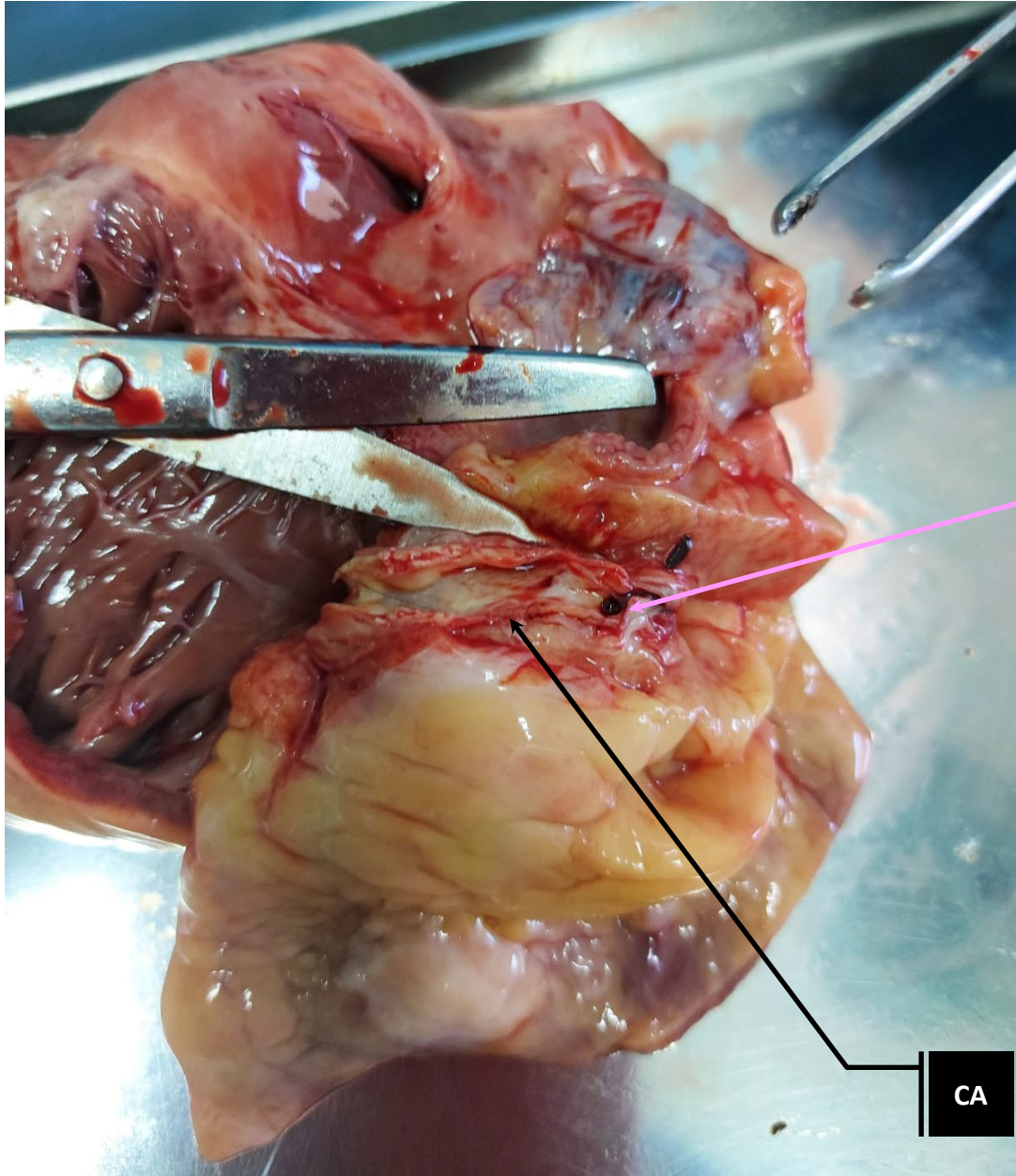
RC

WC

Obturator red thrombus of the renal vein



Coronary artery thrombosis

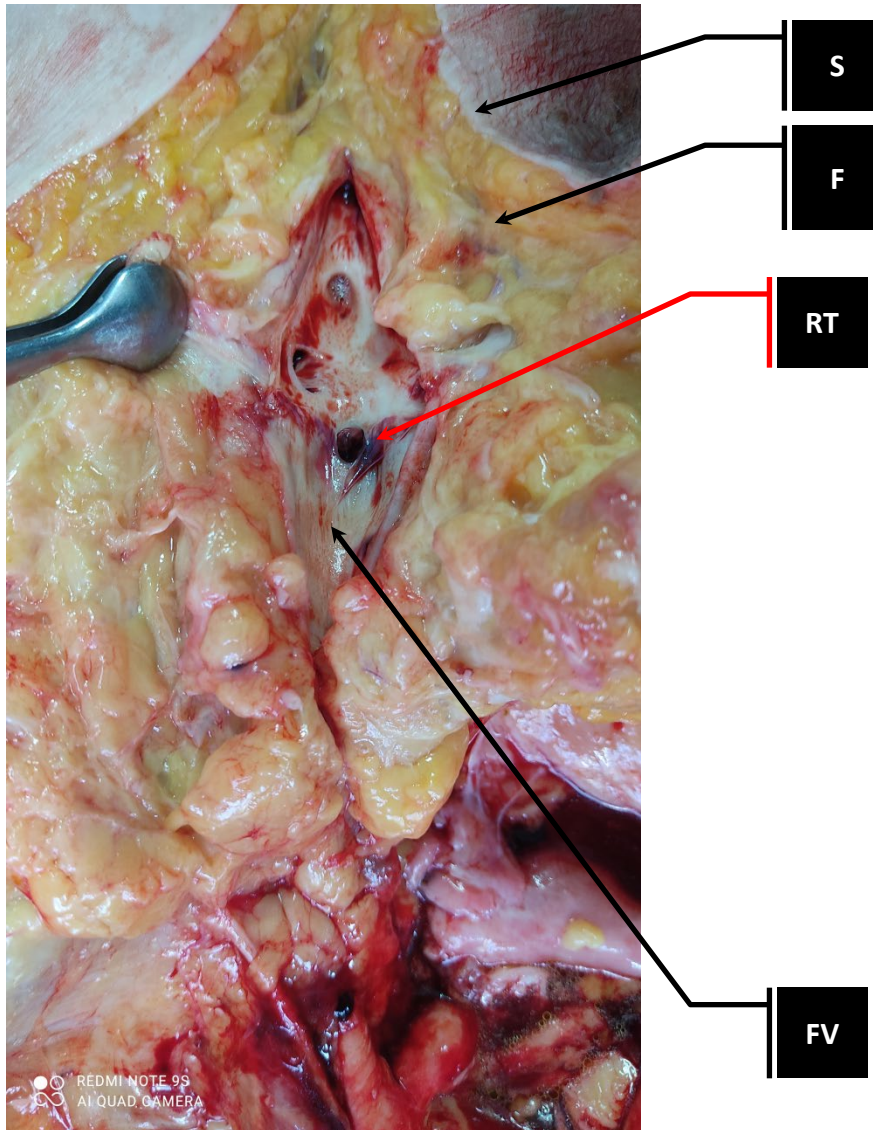


Courtesy by Dr. Y. Zhukov

RT

CA

Femoral vein thrombosis



Courtesy by Dr. A. Kotikov

Predisposing factors are:

- prolonged immobilization (for example, after surgery)
- chronic heart failure
- varicose veins of the lower extremities.

Fate of the Thrombus

Favorable outcome	Unfavorable outcome
Dissolution (aseptic lysis)	Propagation
Organization and Recanalization	Embolization
Calcification (or petrification) of a thrombus	Septic lysis

EMBOLISM

An embolus is a detached intravascular solid, liquid, or gaseous mass that is carried by the blood from its point of origin to a distant site, where it often causes tissue dysfunction or infarction.

Orthograde embolism (emboli move through the bloodstream):

- from the inferior or superior vena cava to the lungs;
- from the left half of the heart and aorta into the arteries of the heart, brain, kidneys, spleen, intestines, limbs, etc.
- from the vessels of the portal system into the portal vein of the liver.

Retrograde embolism:

- embolus, due to its severity, moves against the bloodstream

Paradoxical embolism

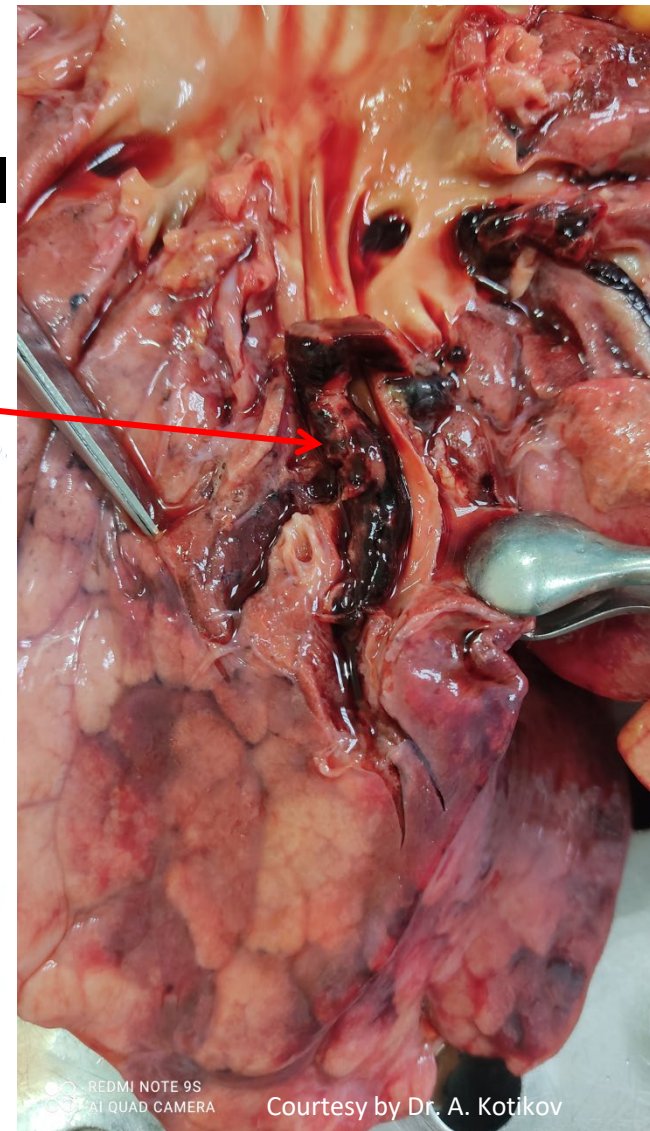
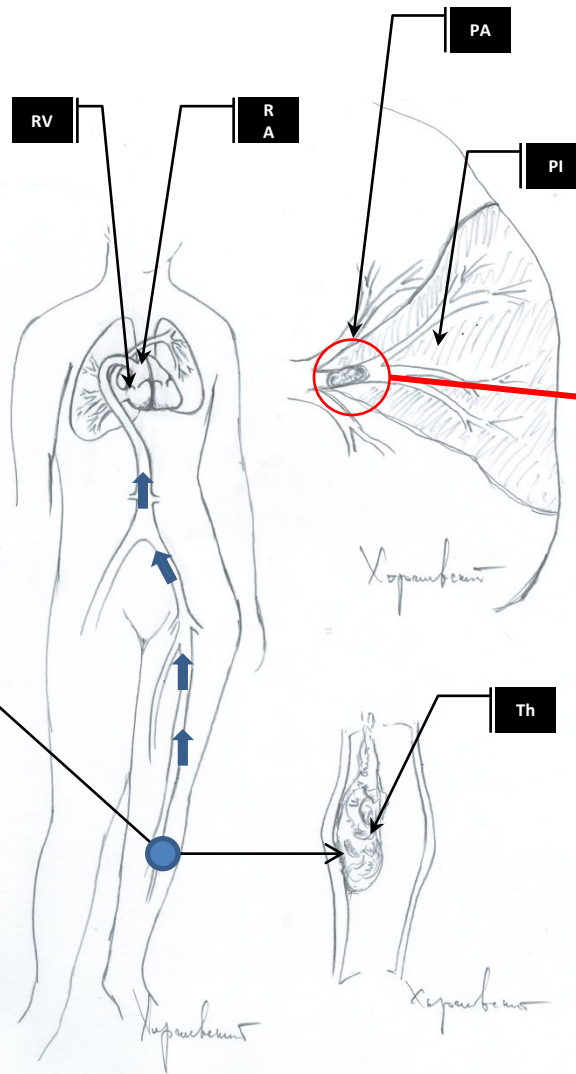
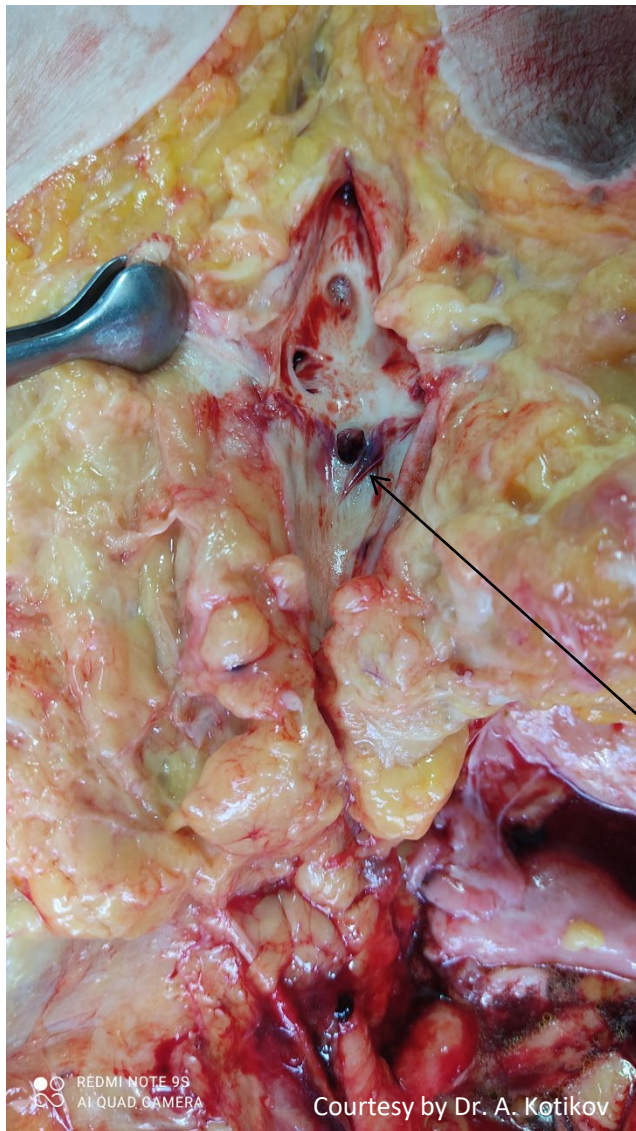
- from the veins of the great circle to arteries (in case of defects of the atrial or interventricular septum).

Nature of emboli

Depending on the nature of emboli, the following types of embolism are distinguished:

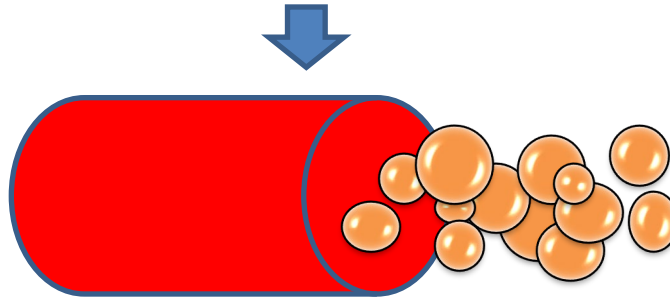
- **Thromboembolism**
- **fatty**
- **air**
- **gas**
- **tissue (cellular)**
- **microbial**
- **embolism by foreign bodies**

Femoral vein thrombosis and Pulmonary Thromboembolism



Fat Embolism

Soft tissue crush injury or rupture of marrow vascular sinusoids (due to the long bone fracture)

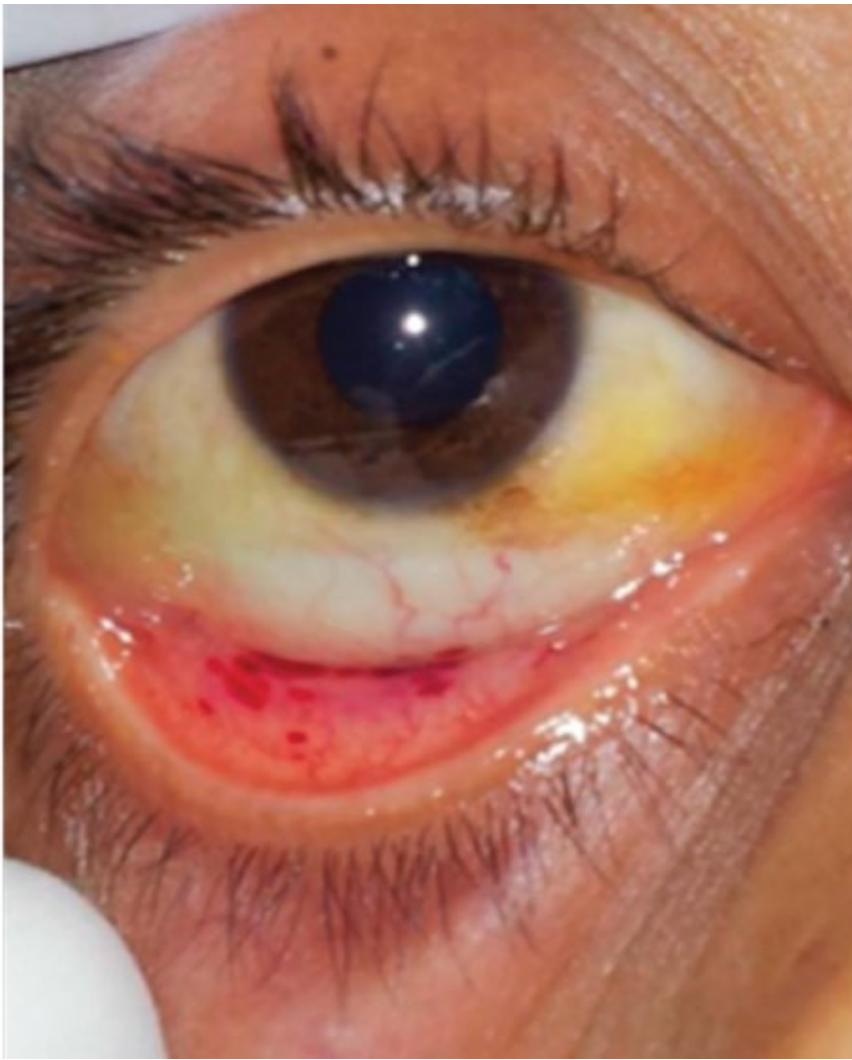


microscopic fat globules in the circulation



1-3 days

tachypnea, dyspnea, tachycardia, irritability, restlessness,
which can progress rapidly to coma.



Diffuse petechial rash

Maghrebi S, Cheikhrouhou H, Triki Z, Karoui A: Transthoracic Echocardiography in Fat Embolism: A Real-Time Diagnostic Tool. J Cardiothorac Vasc Anesth 2017;31[3]:e47-e48.)

Air Embolism

- air trapped in a coronary artery during bypass surgery or introduced into the cerebral arterial circulation by neurosurgery;
- obstetric or laparoscopic procedures or as a consequence of a chest wall injury



Air bubbles within the circulation



distal ischemic injury

very large venous emboli may arrest in the heart and cause death

lethal dose for humans is the amount air within 17-100 cubic centimeters

Gas Embolism

decompression sickness is caused by sudden changes in atmospheric pressure
(divers, underwater construction workers, and persons in aircraft)



Gas bubbles within the circulation

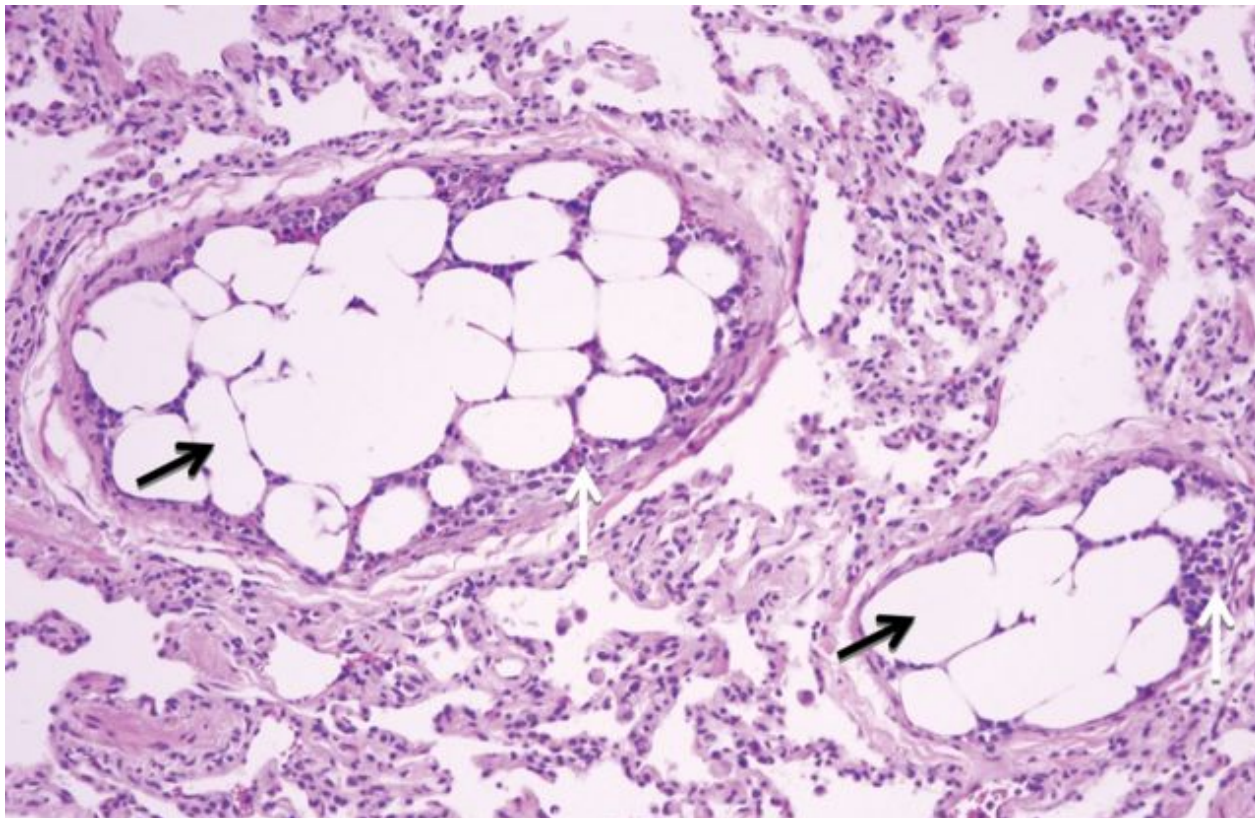


Gas bubbles in the pulmonary vasculature cause edema, hemorrhages, and focal atelectasis or emphysema, leading to respiratory distress.

Bubbles in the central nervous system can cause mental impairment and even sudden onset of coma.

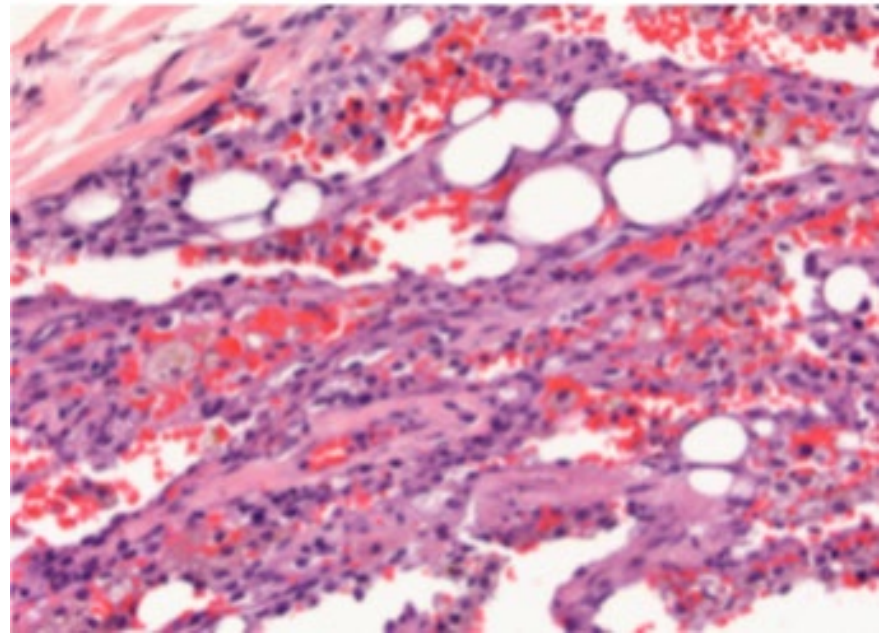
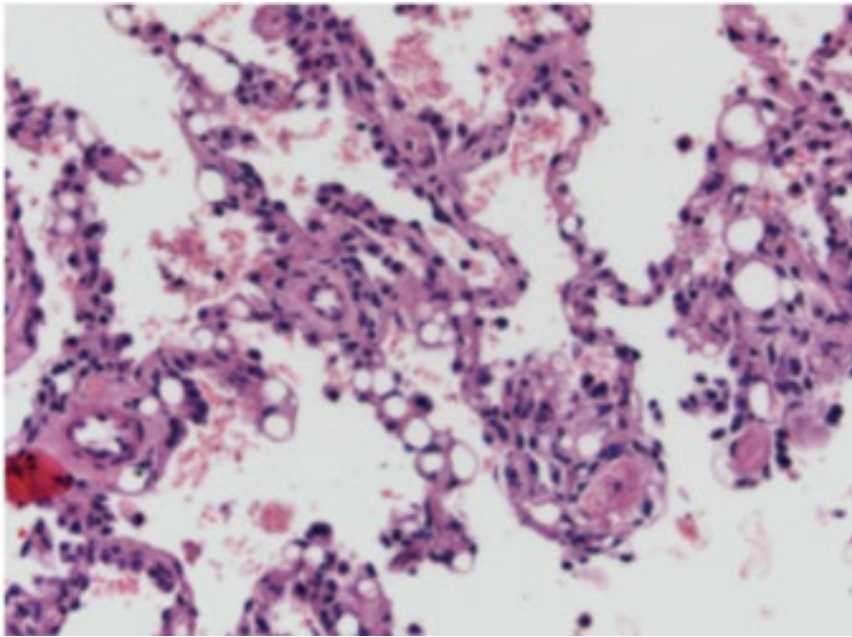
Tissue (cellular) Embolism

- Tissue (cellular) embolism underlies the development of metastases of malignant tumors.
- In addition to tumors, detached pieces of heart valves in endocarditis, fragments of brain tissue in trauma can act as tissue emboli.
- Tissue embolism also includes amniotic fluid embolism.



Embolism by foreign bodies

silicone injections for cosmetic purposes with silicone pulmonary embolism



- Kirill Lyapichev, Felix Manuel China, Julio Poveda, Jeniffer Pereda, Pablo A. Bejarano, Monica T. Garcia-Buitrago, "Pulmonary Empty Spaces: Silicone Embolism—A Decade of Increased Incidence and Its Histological Diagnosis", *Case Reports in Pathology*, vol. 2016, Article ID 3741291, 5 pages, 2016. <https://doi.org/10.1155/2016/3741291>

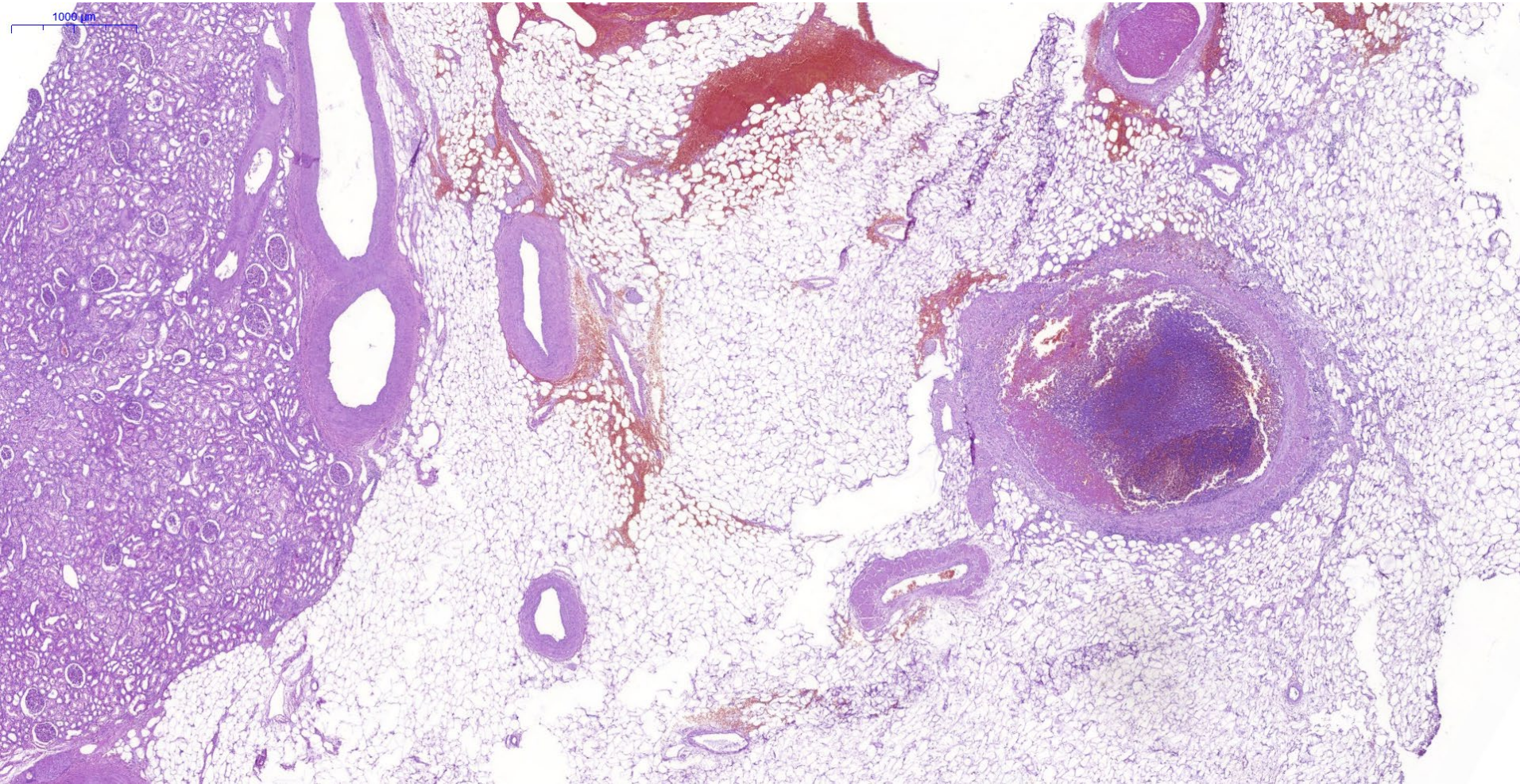
Microbial Embolism

bacterial colonies, fungi, protozoa or parasites circulating in the bloodstream obstruct the lumen of the capillaries.

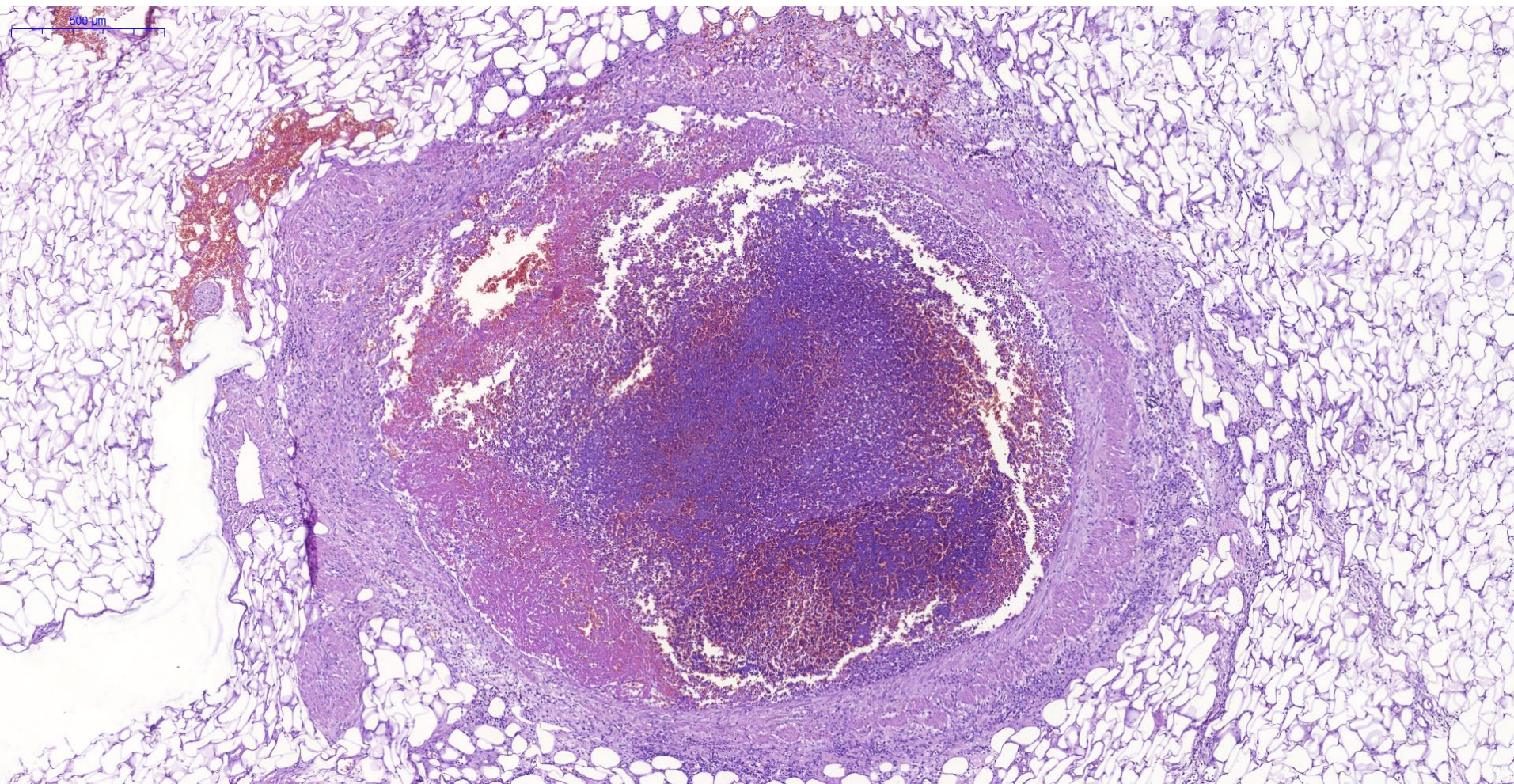


metastatic abscesses
(Sepsis)

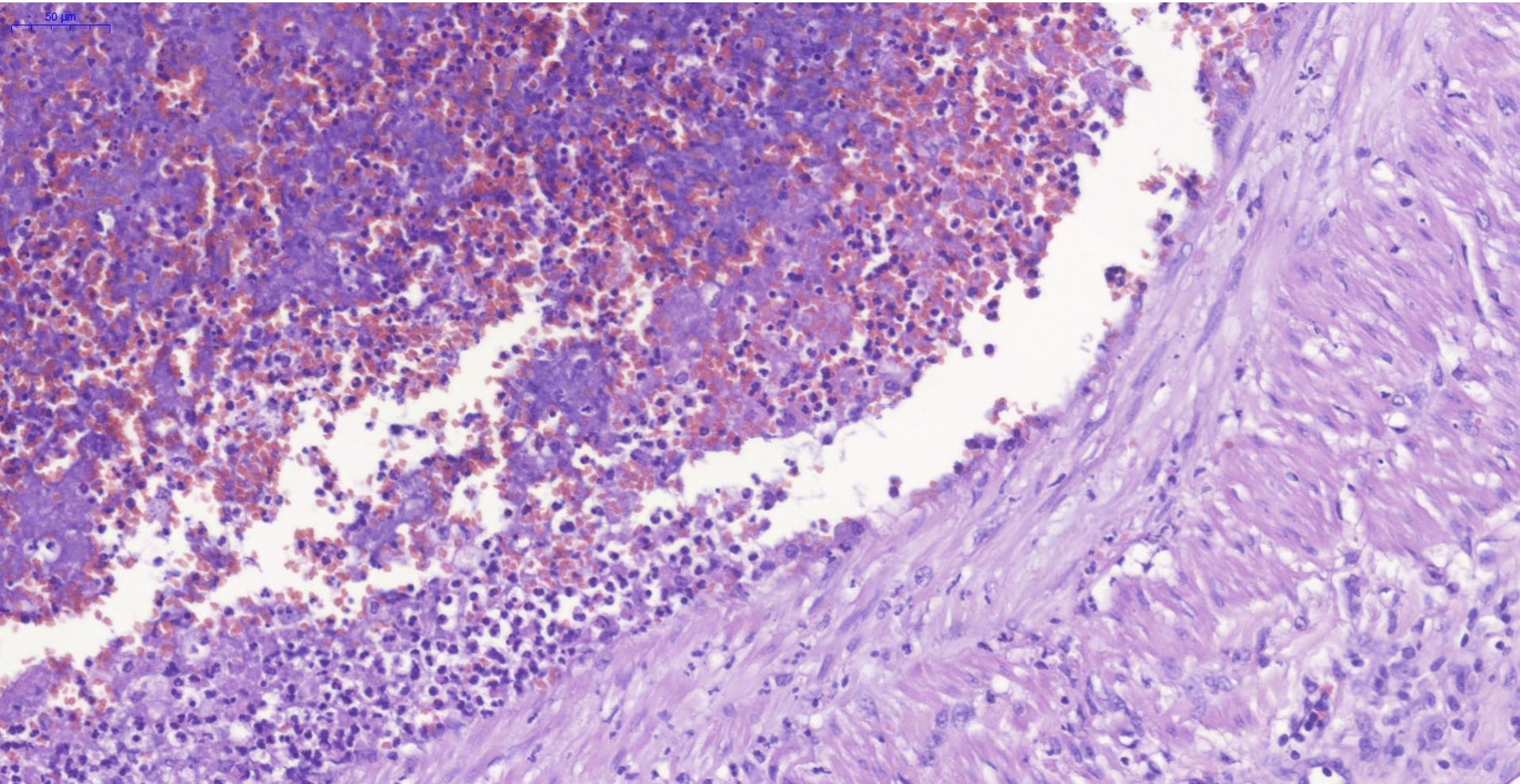
Microbial Embolism



Microbial Embolism

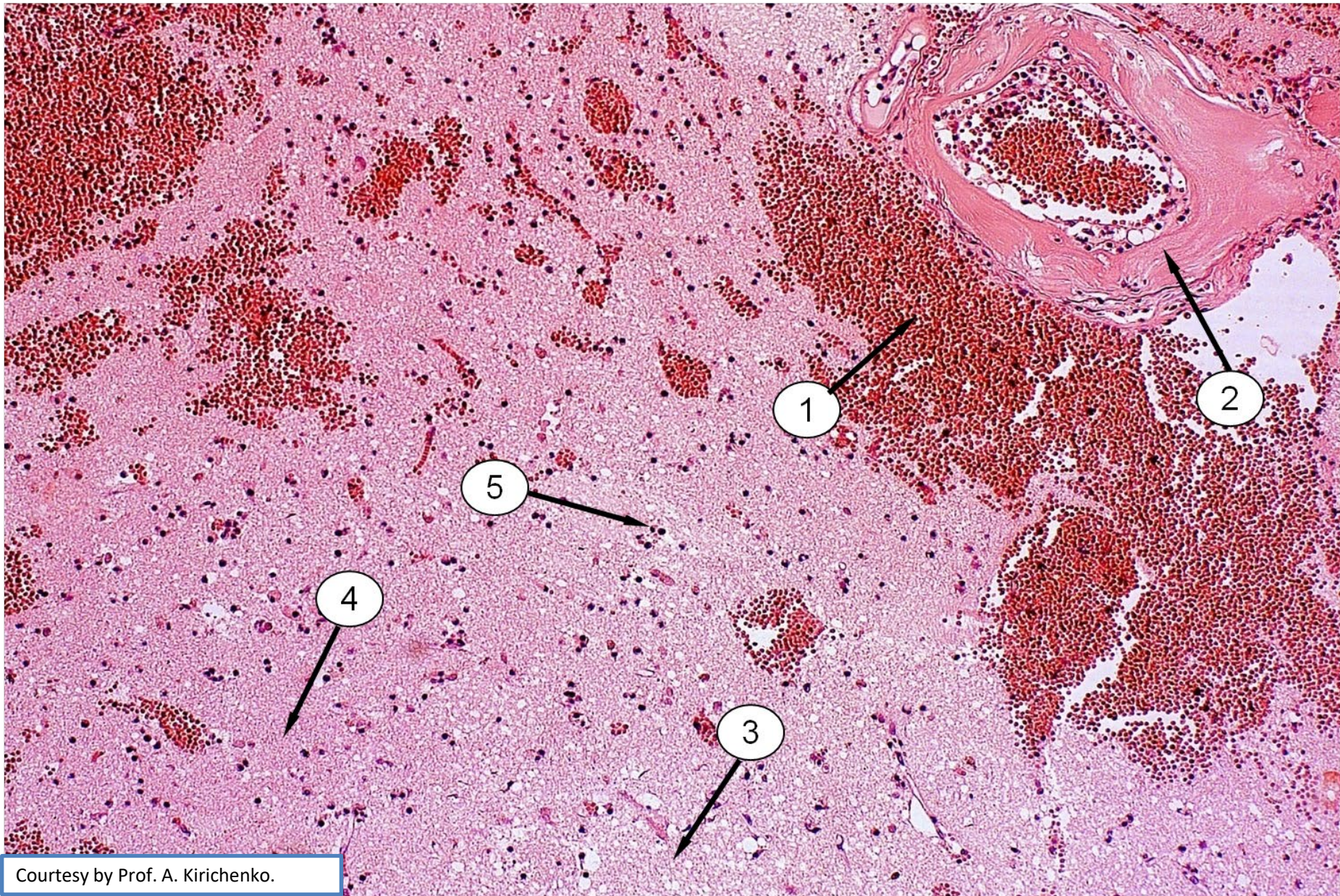


Microbial Embolism

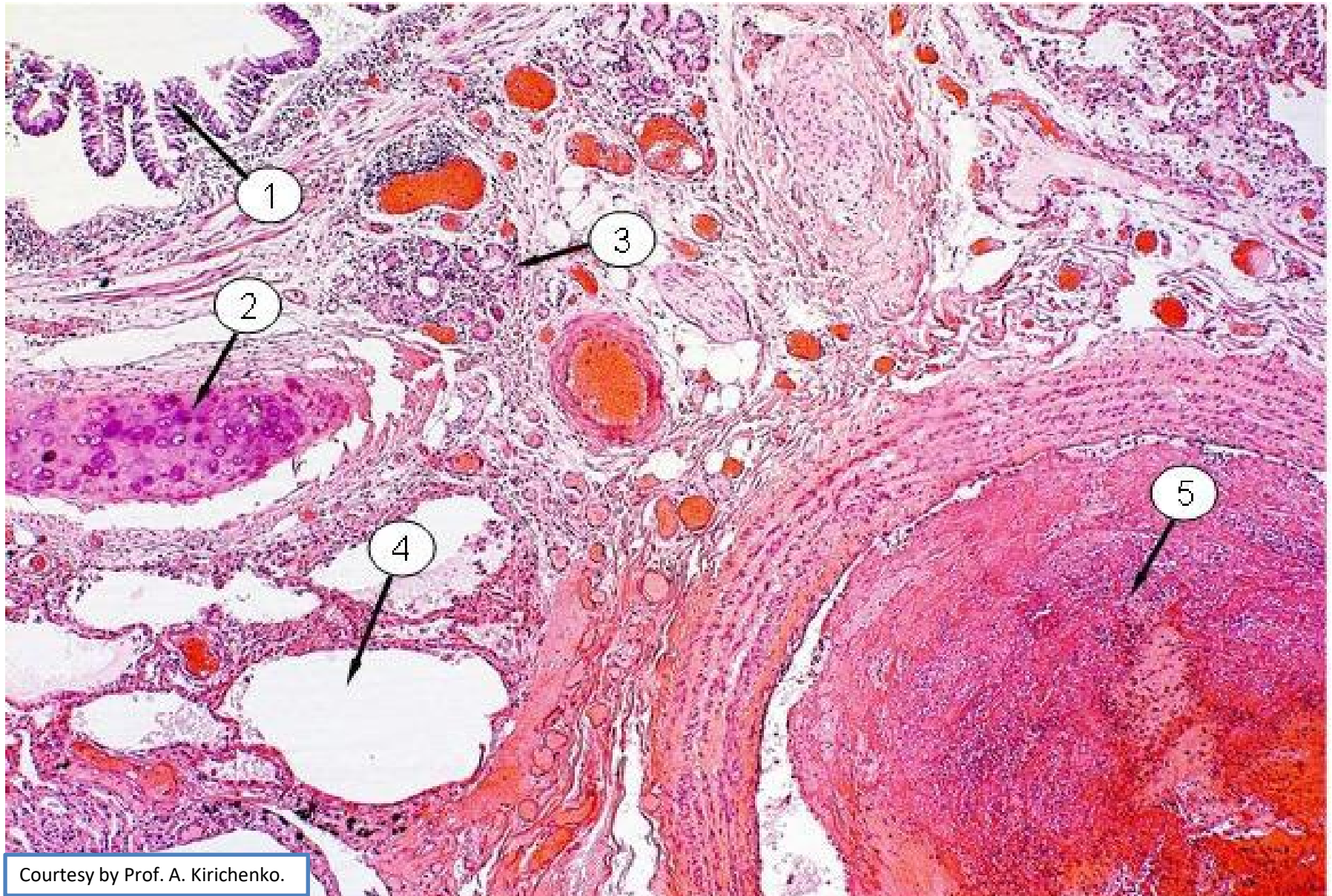


Histology microscope slides for practical classes

Intracerebral (brain) hemorrhage.



Microscopy: pulmonary Thromboembolism



Thank you for your attention!

If study to remember, you will forget, but if study to understand you will remember.

