CIRCULATORY DISTURBANCES

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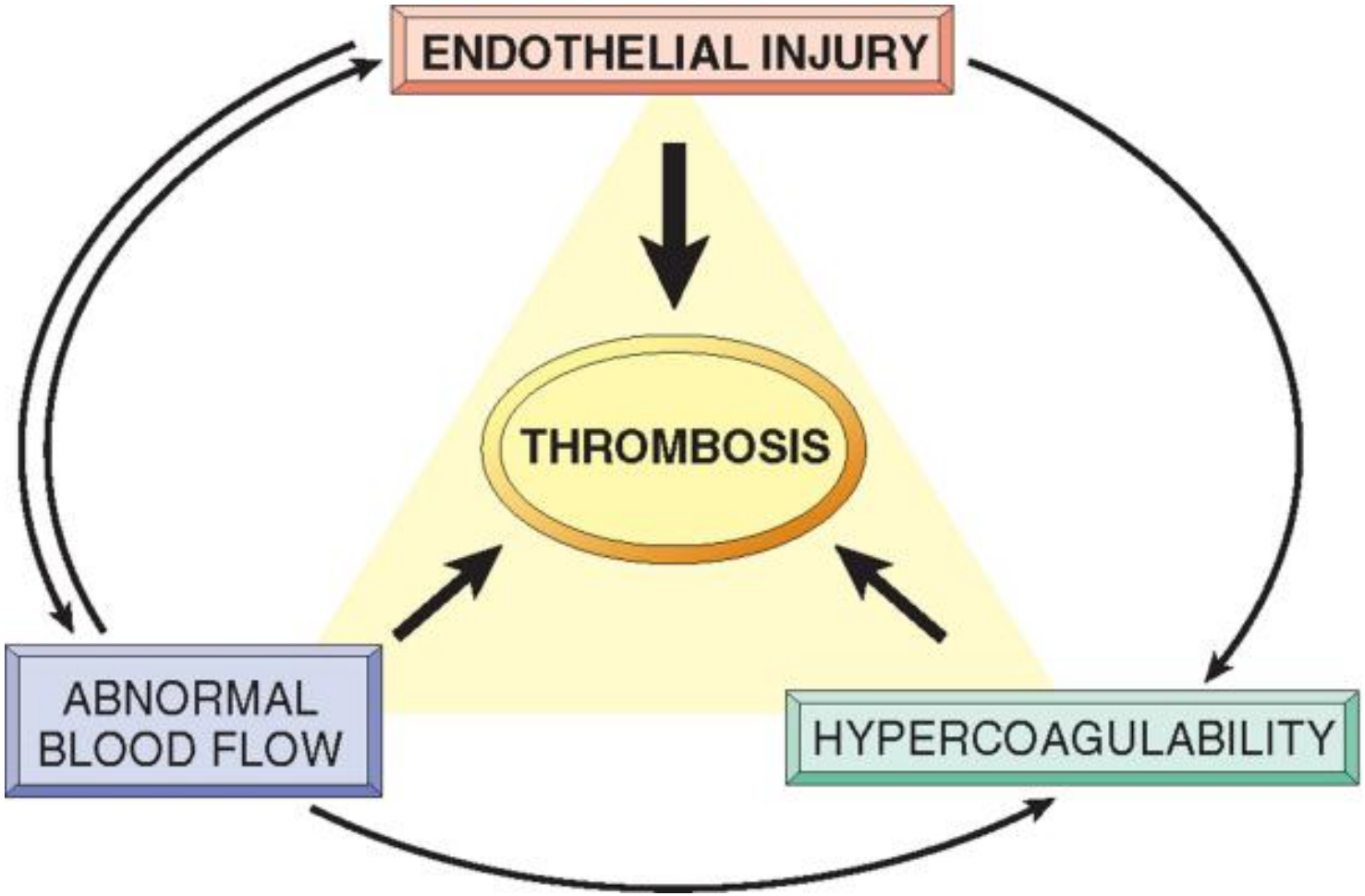
THROMBOSIS

- **Definition of thrombosis:**
- Formation of a compact mass composed of the elements of the circulating blood inside a vessel or a heart cavity during life. This compact mass is called **thrombus**.
- **Thrombus:**
- It is a solid mass made up of blood elements that develops within the cardiovascular system (CVS) during life.

Causes of Thrombosis:

- The primary influences predispose to thrombus formation, the so called **Virchow's triad**:
  1. Endothelial injury.
  2. Stasis or turbulence of the blood flow.
  3. Blood hypercoagulability.

Pathogenesis of Thrombosis



I. **Damage to the vascular endothelium:**

A. Mechanical e.g. trauma, pressure and ligature.

B. Inflammatory e.g. phlebitis, arteritis and endocarditis.

C. Degenerative e.g. atheroma, aneurysm and myocardial infarction.

- The platelet adhere to the damaged endothelium.

II. Stasis or turbulence of the blood flow:

- In normal blood stream, the cells occupy the central part and the plasma occupies the peripheral part.
- In stasis the platelets cross the plasmatic zone and come in contact to the vascular endothelium.

A. Slowing of blood stream (stasis):

- Slowing occurs in the following conditions:
  - (a) In heart failure specially in the leg veins.
  - (b) In the auricles of the heart in association with valvular diseases.
  - (c) In aneurysmal sacs, varicose veins and in the portal vein secondary to liver cirrhosis.
  - (d) In the tissues showing acute inflammation.

B. **Disorders of blood stream or turbulence of the blood flow:**

- Turbulence of the blood flow occurs in the following conditions:
- Distortion of the vascular lumen as in aneurysm, atheroma, varicose veins and compression of the vessel from outside allows the platelets to come in contact with the vascular endothelium thus initiating thrombosis.

III. **Blood hypercoagulability or changes in blood composition:**

A. After operations the platelets increase in number and become more sticky.
   - They agglutinate in small masses and adhere to the vascular endothelium.
   - Platelet lysis releases thromboplastin which starts thrombosis.

B. Increased fibrinogen during pregnancy and in lobar pneumonia leads to increased thrombosis.

C. Increased red blood cells in polycythemia causing increased blood viscosity and stasis.

D. White blood cells increased in leukemia causing increased viscosity and stasis.

E. Decreased plasma volume as in dehydration increases tendency to thrombus formation.

- More than one of the above factors may be the cause of thrombosis.

Mode of Formation and Types of Thrombi:

1. ***Pale thrombus (platelet thrombus):***

- The initial thrombus is composed of platelets only.
- The platelets deposit on the site of endothelial damage.
- They adhere to the exposed subendothelial collagen by the help of von-Willebrand factor (factor VIII).

- This factor is produced by endothelial cells and acts as a bridge between platelet surface receptors and collagen.
- The adherent platelets release adenosine diphosphate (ADP) and serotonin which promote further aggregation and adhesion of platelets forming a small white amorphous mass.
- Such platelet thrombus is fragile and can be washed away by the blood stream except if stasis is present.

2. *Mixed thrombus:*

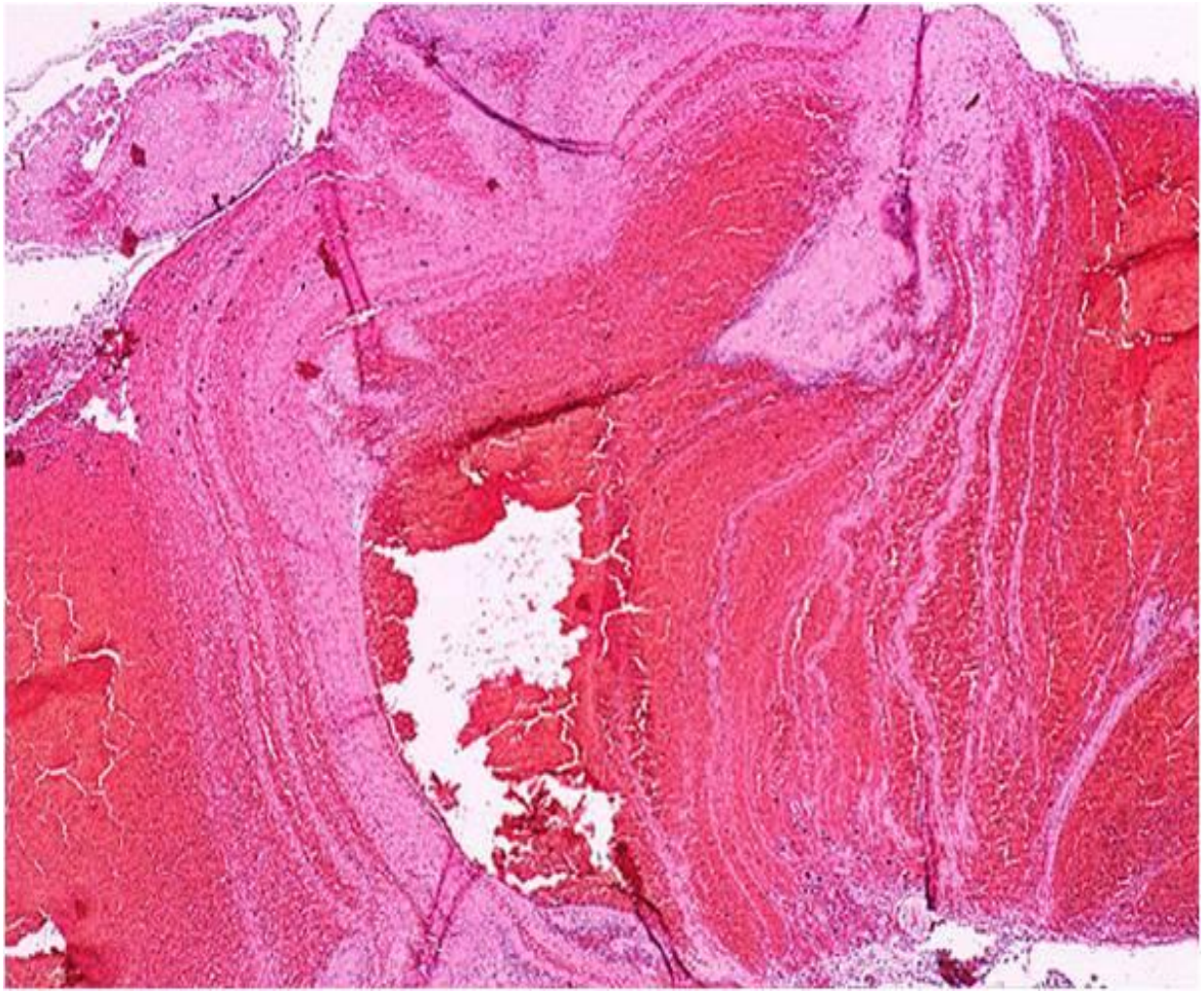
- Stasis allows clotting factors to accumulate in the area.
- Thromboplastin released from the platelets and damaged tissue promotes fibrin formation which deposits on the primary platelet thrombus.
- Next the deposited fibrin encourages further platelet accumulation.
- The platelets deposit as laminae at right angle to the blood stream.
- Between the laminae there is complete blood stasis and fibrin is deposited entangling the red and white blood cells.

- The formed thrombus is a mixed one as it is composed of both platelet masses and blood clots.
- In paraffin section it shows alternate layers of fused platelets, and fibrin with entrapped blood cells.
- The fused platelets appear as homogenous reddish violet streaks called ***lines of Zahn***.
- If the resulting thrombus occludes the vessel partially it is called **mural thrombus**.
- If the thrombus occludes the vessel completely it is called **occluding thrombus**.

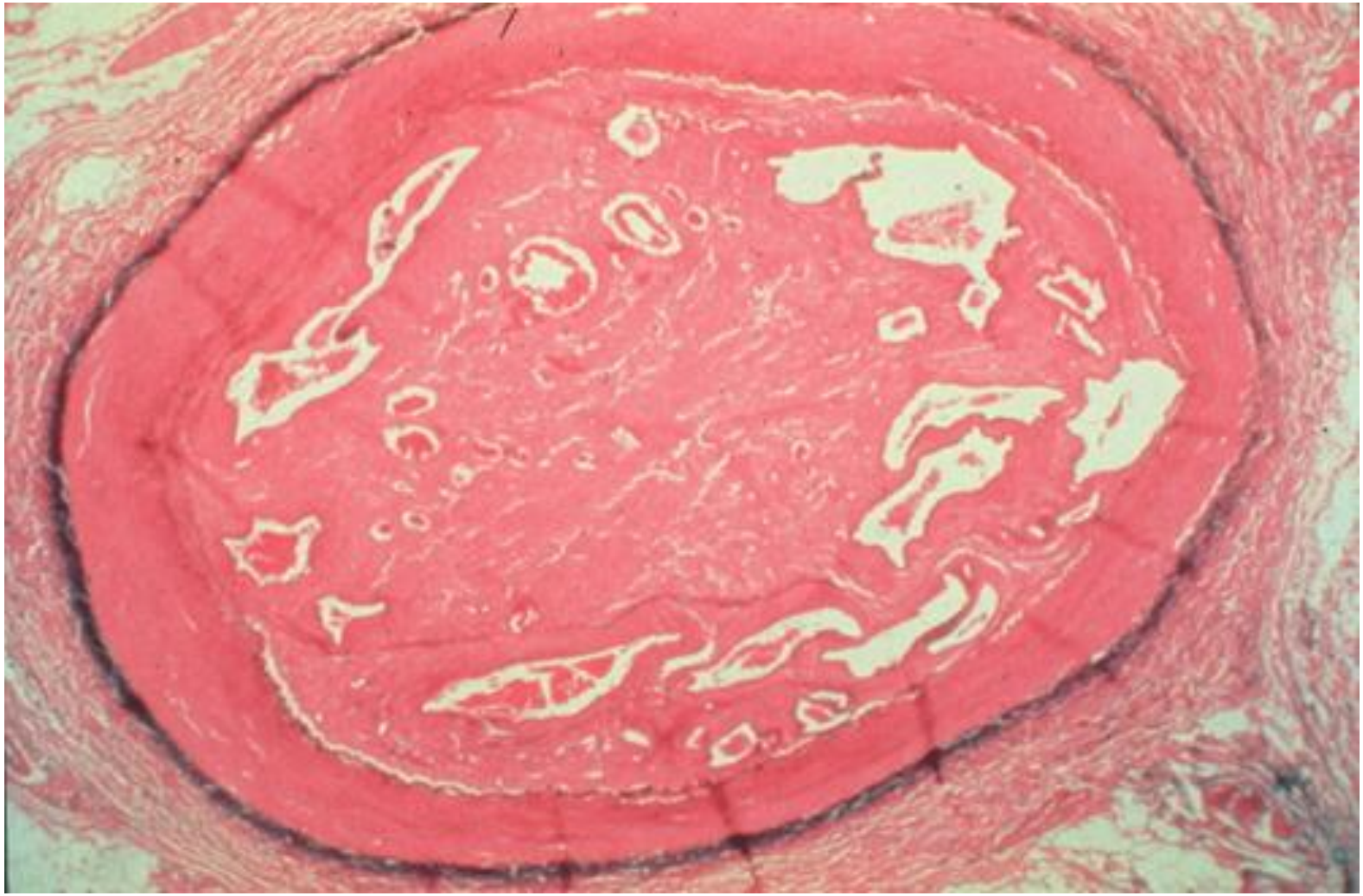
3. *Propagating thrombus:*

- If the formed thrombus occludes a vein completely, proximal to occlusion the blood will be stagnant and it clot
- The clot is soft, red and fixed to the original thrombus but not to the vascular wall.
- When this propagating thrombus reaches a level at which a tributary or a branch joins the affected vein, thrombosis starts again as the blood once more will be in motion.
- Thrombosis occurs in moving blood, whereas clotting occurs in stagnant blood.
- The process can be repeated and the propagating thrombus extends in the direction of the heart.

Lines of Zhan



Thrombus; organized & re-canalized



Classification of Thrombi:

- Thrombi are classified according to the color and the presence or absence of bacteria.

1) **Color:**

A. ***Pale thrombus:***

- Formed mainly of platelets and fibrin.
- It is greyish white, firm and adherent to the intima e.g. cardiac vegetations.

B. ***Red thrombus:***

- Formed mainly of red cells and fibrin.
- It is dark, red, soft and loosely attached to the vessel wall.
- It is very rare.

C. ***Mixed thrombus:***

- Most thrombi has pale and red components.

2) **Presence or absence of bacteria:**

A. ***Septic thrombus (Infected):***

- The thrombus contains bacteria.
- If the bacteria are pyogenic the thrombus is called septic thrombus.

B. ***Aseptic thrombus (Non-infected):***

- It contains no bacteria or low virulent bacteria.

Sites of Thrombus Formation:

A. **Thrombosis in Veins:**

- More common because of their slow blood, and thin wall.
- Two types occur:

I. ***Thrombophlebitis:***

- Thrombosis is initiated by inflammation in the venous wall.

- Two types occur:

a) ***Septic thrombophlebitis:***

- Occurs in veins draining septic lesions as in appendicular vein in case of acute appendicitis and in pelvic veins in case of puerperal sepsis.

b) ***Aseptic thrombophlebitis:***

- Inflammation is caused by factors other than bacteria as trauma and radiations.
- A small fixed aseptic thrombus occurs.

II. ***Phlebothrombosis:***

- Thrombosis caused by factors other inflammation e.g:

a) Occurs in the veins of the feet and calf in chronic cardiac patients confined to bed due to:

- Stasis caused by the heart lesion and the absence of muscular movements.
- Compression of the calf muscles against the bed mattress.
- The thrombus may propagate to the femoral and iliac veins and may fragment causing pulmonary embolism.

b) In the femoral and pelvic veins after labor or abdominal operations.

- The factors responsible are:
  1. Platelets increase in number and become more sticky.
  2. Prolonged bed rest leads to stasis.
  3. Mild inflammation at the operation site.

c) Thrombosis in varicose veins due to stasis.

B. Thrombosis in Arteries:

- Less common than venous thrombosis because of the rapid blood flow in the arteries and the thick elastic arterial wall which resists injury.
- Thrombosis occurs in arteries affected by:

(a) Atheroma, polyarteritis nodosa, thromboangitis obliterans due to roughness of the intima.

(b) Aneurysms due to stasis, disordered blood stream and roughness of the intima.

- Arterial thrombosis causes ischemia.

C. Thrombosis in the Heart:

- More common in the left side.
- The following types occur:

1. *Mural thrombi:*

- Occur over infarcts, commonly on the endocardial surface of the left ventricle near the apex.

2. *Vegetations:*

- Pale thrombi over the valves in rheumatic and bacterial endocarditis.

3. ***Auricular thrombi:***

- Develop in the atrial appendages in heart failure due to stasis.
- Commonly in the left auricle in mitral stenosis.
- They are commonly adherent to the wall.
- Rarely the thrombus detach and remains in the dilated atrial cavity and is called ***ball thrombus***.

4. ***Agonal thrombi:***

- Red thrombi occurring in the ventricles commonly the right at the time of death specially caused by lobar pneumonia.

D. Thrombosis in capillaries:

- Capillary thrombosis rarely occurs in acute inflammation, severe cold and frost bite.
- They are due to stasis, endothelial damage and hemoconcentration.

Fate of the Thrombus:

1. **Septic thrombus:**

- Fragments by the proteolytic enzymes into septic emboli causing pyemic abscesses.

2. **Aseptic thrombus:**

- Its elements disintegrate and form a pale structureless mass.
- If the mass is small it dissolves by fibrinolysis.
- If the mass is large it undergoes:

(a) *Organization:*

- The thrombus is invaded by capillaries and fibroblasts from the vascular wall and change to a fibrous mass.
- This causes permanent vascular occlusion.

(b) *Organization and canalization:*

- Occasionally some of the capillaries dilate and allow passage of blood through the thrombus or the fibrosed thrombus shrinks from the vascular wall leaving a space which gets lined by endothelium.

(c) *Dystrophic calcification:*

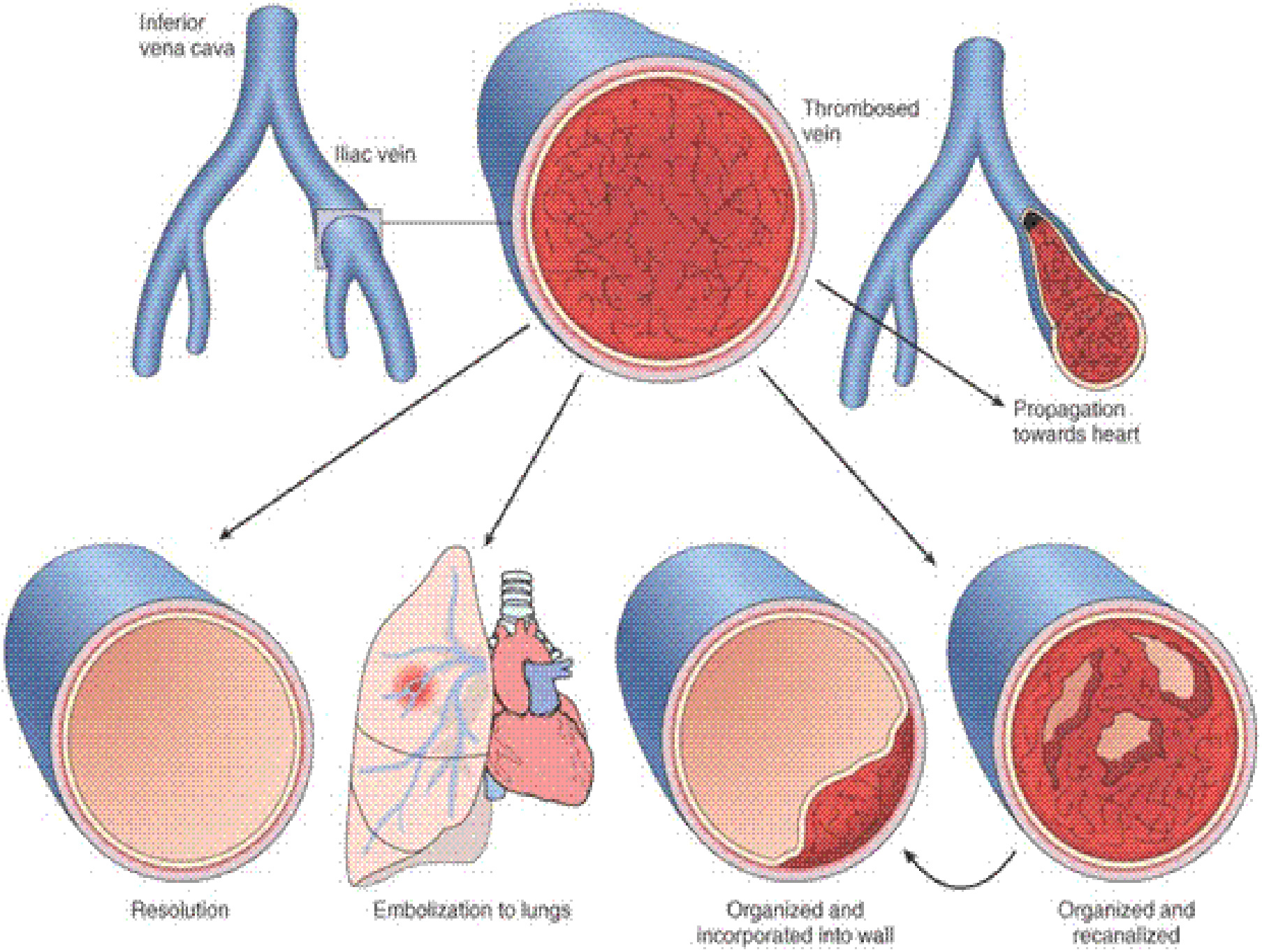
- May occur giving a phlebolith.

(d) *Detachment and embolization:*

- Forming aseptic emboli causing infarcts.

(e) *Propagating thrombus:*

- Due to spread of venous thrombosis.


Inferior
vena cava
Iliac vein
Thrombosed
vein
Propagation
towards heart
Resolution
Embolization to lungs
Organized and
incorporated into wall
Organized and
recanalized

Clot

- A mass of blood elements formed in stagnant blood.
- The clot is dark red with a glistening smooth surface.
- The clot is not adherent to the vessel wall.
- **Post-mortem clots:**
- Occur in the cardiac chambers after death.

- There are two types:

(1) *Red or current jelly clot:*

- Occurs with rapid blood clotting.
- It is formed of a fibrin network entangling red and white blood cells.

(2) *Yellow or chicken fat clot:*

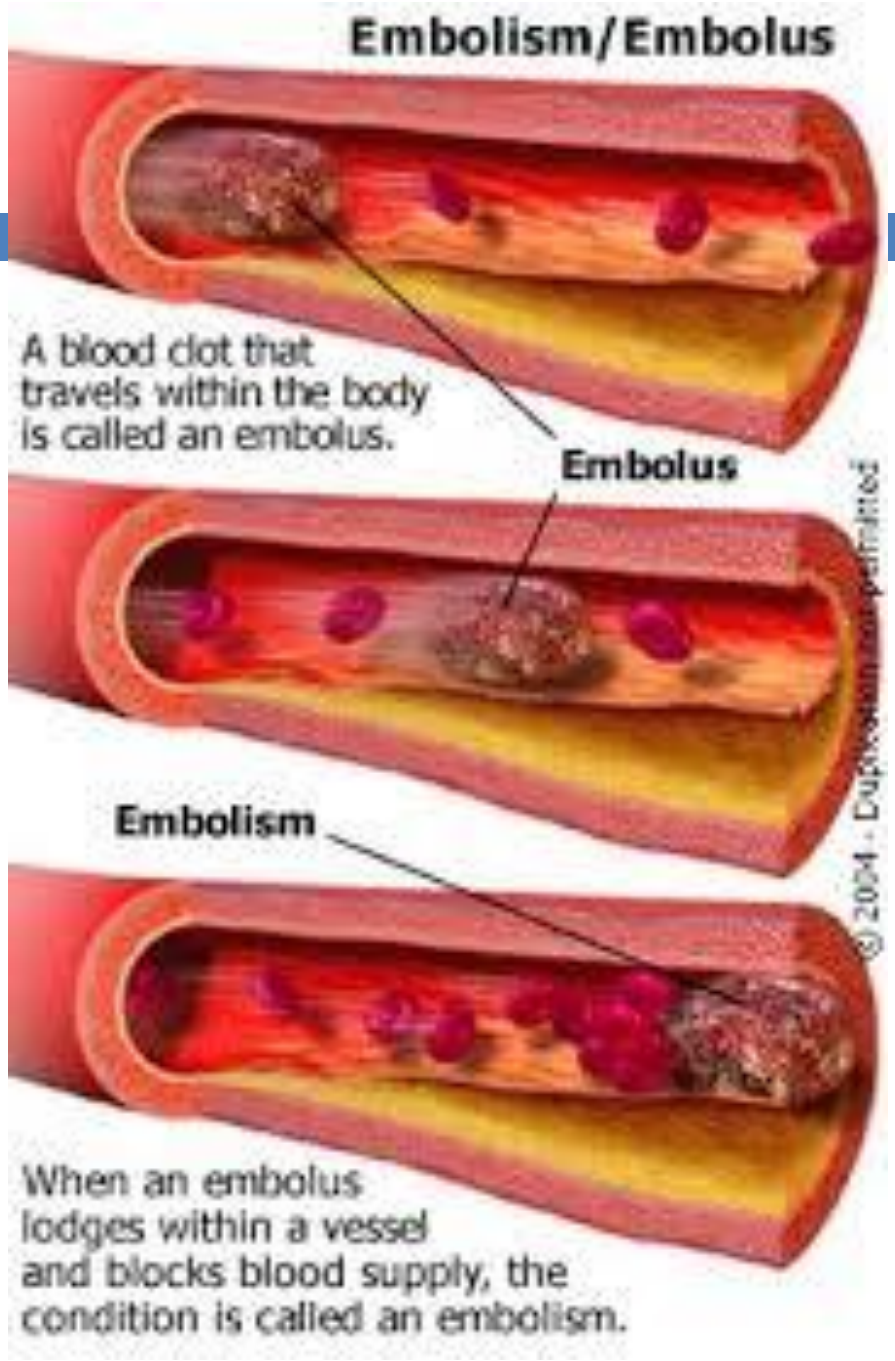
- Occurs with slow blood clotting.
- This allows sedimentation of the red cells in the dependent part with plasma, and white cells above.
- Slow clotting occurs with anticoagulant or with deficient coagulation factors as in hemophilia.

Difference between thrombus and clot:

Thrombus	Clot
1. Occurs in circulating blood 2. Firmly attached 3. Friable and dry 4. Pale, pale red or red 5. Show's lines of Zhan's	1. Occurs in stagnant blood 2. Loosely attached 3. Soft and moist 4. Red and yellow 5. No lines of Zhan's

EMBOLISM

- **Embolus:**
- It is an insoluble solid, liquid or gaseous mass circulating in the blood stream.
- **Embolism:**
- It is the process of impaction of the embolus in a narrow vessel.


Embolism/Embolus
A blood clot that travels within the body is called an embolus.
Embolus
Embolism
When an embolus lodges within a vessel and blocks blood supply, the condition is called an embolism.

Sites of Embolism:

- **Embolism occurs at many Sites:**
  1. Systemic arteries.
  2. Pulmonary arteries.
  3. Intrahepatic branches of the portal vein.

Types of Emboli:

- **Emboli are many types:**
  1. Detached thrombi and vegetations.
  2. Tumor emboli.
  3. Parasitic emboli as bilharzial ova.
  4. Air emboli.
  5. Fat emboli.
  6. Clumps of bacteria.
  7. Amniotic fluid emboli.

Course of emboli of thrombotic origin (thrombo-embolism):

- An embolus from a systemic vein or the right side of the heart passed through the pulmonary artery to be impacted in the lung.
- An embolus from the left side of the heart or the aorta gets impacted in systemic artery e.g. cerebral, renal, splenic ... etc.
- An embolus from the portal radicles becomes impacted in the intra hepatic branches of the portal vein.

- An embolus from the systemic veins can by-pass the lung through patent foramen oval or interventricular septal defect to be arrested in systemic artery, called ***paradoxical embolism***.
- Another explanation for paradoxical embolism is that the embolus is so small that it can pass through the pulmonary capillaries.

Effect of Emboli of Thrombotic Origin:

- **Depends upon:**
  1. Size of the embolus.
  2. Nature of the embolus, septic or aseptic.
  3. State of the collateral circulation in the affected organ. So:

(a) ***Aseptic embolism:***

- Produces transient ischemia if the collateral circulation is good and infarction when poor.

(b) ***Septic embolus:***

- Produces pyemic abscess at the site of it impaction

Air Embolism:

- Rare and may result from:

(1) Injury to the large neck veins. Air is sucked by the negative pressure in the thorax.

(2) Faulty technique in doing artificial pneumothorax and in transfusion.

(3) Air passes into the uterine veins in criminal abortion.

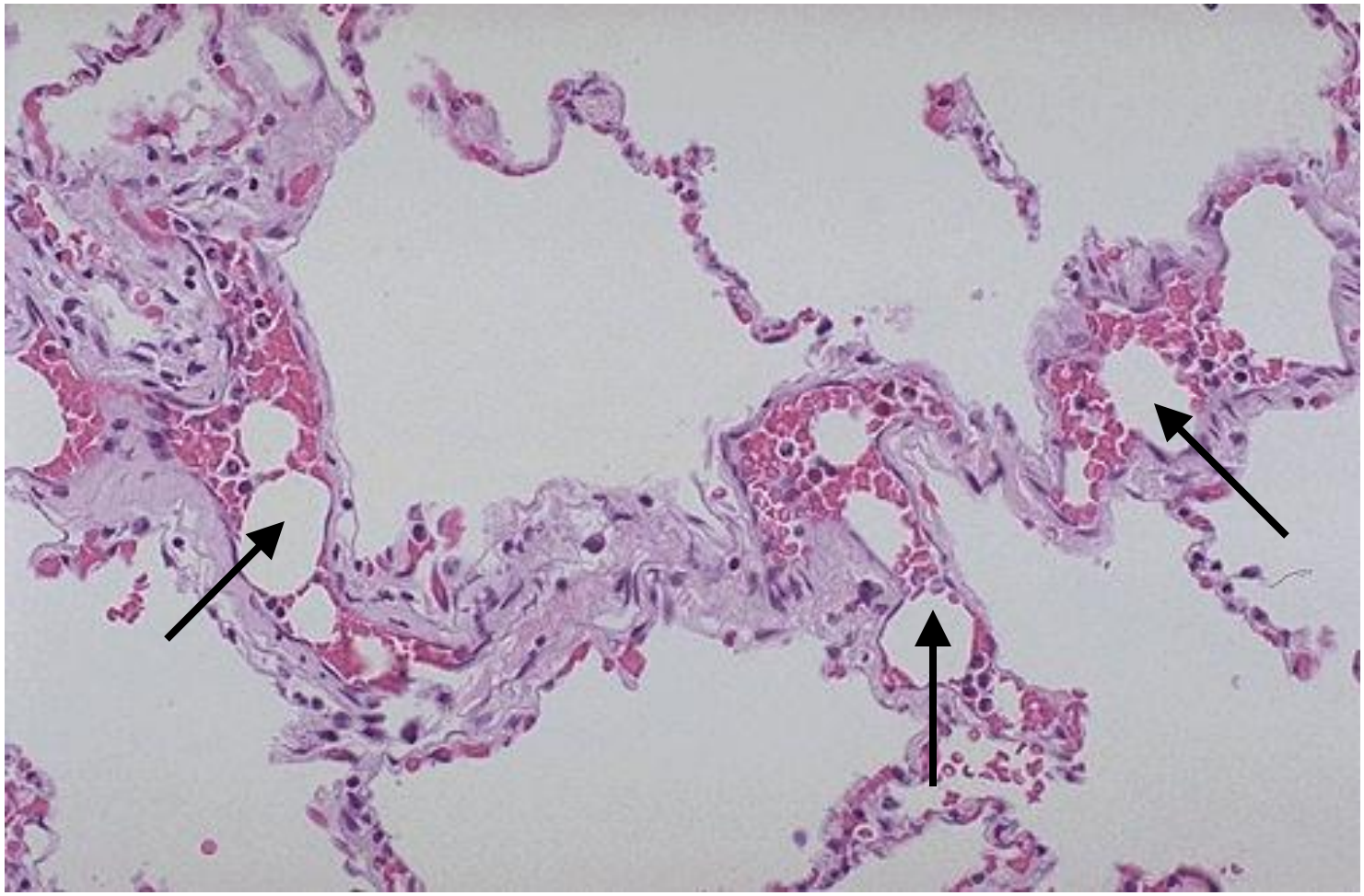
(4) Caisson's disease (decompression sickness): In deep dives compressed gases are inhaled.

- The high pressure increases the amount of gasses dissolved in the blood.
- If decompression is done rapidly gases specially nitrogen form emboli in the blood vessels.
- Small amount of air is harmless, but 50-100 cc interferes with cardiac contraction and causes acute heart failure.

Fat Embolism:

- Rare and caused by:
  (1) Bone fractures and crush limb injuries.
  (2) Cutaneous burns.
  (3) Inflammation of fatty tissues.
  (4) Severe fatty changes in the liver.
- The fat globules enter through the ruptured veins and produce pulmonary or systemic embolism.

Fat embolism



Fat emboli in the lung

Amniotic Fluid Embolism:

- Rare condition in which strong contractions cause a tear in the fetal membranes and the amniotic fluid pushed in an opened vein.
- The condition results in a fatal pulmonary embolism to the mother.

PULMONARY EMBOLISM

- **Sources of the Embolus:**
- The embolus arises from:
  (1) Recent thrombi in the veins of the lower limbs e.g. after prolonged rest due to bone fracture.
  (2) Thrombi in the iliac and pelvic veins e.g. after labor or operations.
  (3) Thrombi in the right side of the heart e.g. in cases of right sided heart failure.

Effects:

(1) *Big embolus:*

- Occludes the pulmonary artery or one of branches.
- Serotonin released in big amounts from the platelets of the embolus causes bilateral vasoconstriction of the pulmonary arterioles.
- Death occurs in seconds to minutes due to acute right sided heart failure.
- There is no time for an infarct to occur.

(2) *Medium sized embolus:*

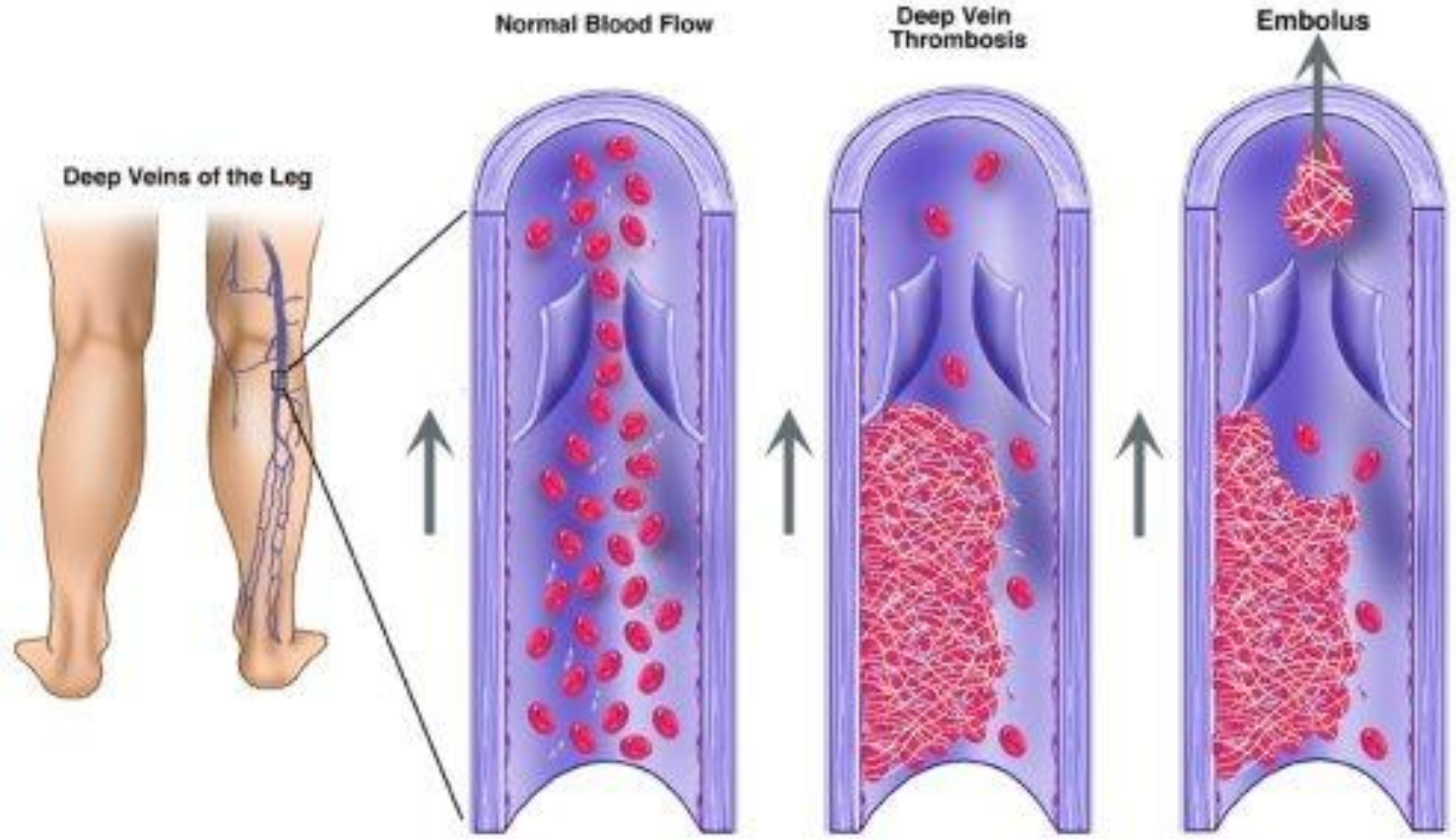
(a) If the lung is healthy no effect will occur as the lung has a double blood supply (pulmonary and bronchial arteries).

(b) If the lung is suffering from chronic venous congestion with blood stagnation, lung infarct occurs.

(3) *Small sized emboli:*

- No effect.

Thrombotic emboli



ISCHAEMIA

- **Definition:**
- Decrease blood supply to a part of tissue due to occlusion of its artery.
- Ischemia may be sudden or gradual.

Types:

I. **Acute ischemia (Sudden ischemia):**

- ***Causes:***
- Sudden complete arterial occlusion by:

1. Thrombosis or embolism.
2. Surgical ligature of the artery.
3. Twisting of the pedicle of a movable organ e.g. intestinal loop.
4. Arterial spasm as in ergot poisoning.

- **Effects:**

(a) Sudden occlusion of end arteries or arteries with inefficient collaterals causes infarction or gangrene.

(b) Sudden occlusion of arteries with efficient collaterals may not cause tissue damage.

- **Chronic ischemia (Gradual ischemia):**
  Incomplete arterial occlusion by:

(a) Atherosclerosis.

(b) End arteritis as in syphilis.

(c) Pressure on the artery by enlarged lymph node, tumor ... etc.

- The gradual occlusion gives chance for the collaterals to open up so:

(a) With inefficient collaterals, cellular degeneration, atrophy and replacement fibrosis occur e.g. atherosclerosis of the coronary branches causes myocardial fibrosis.

(b) With efficient collaterals no tissue damage occurs.

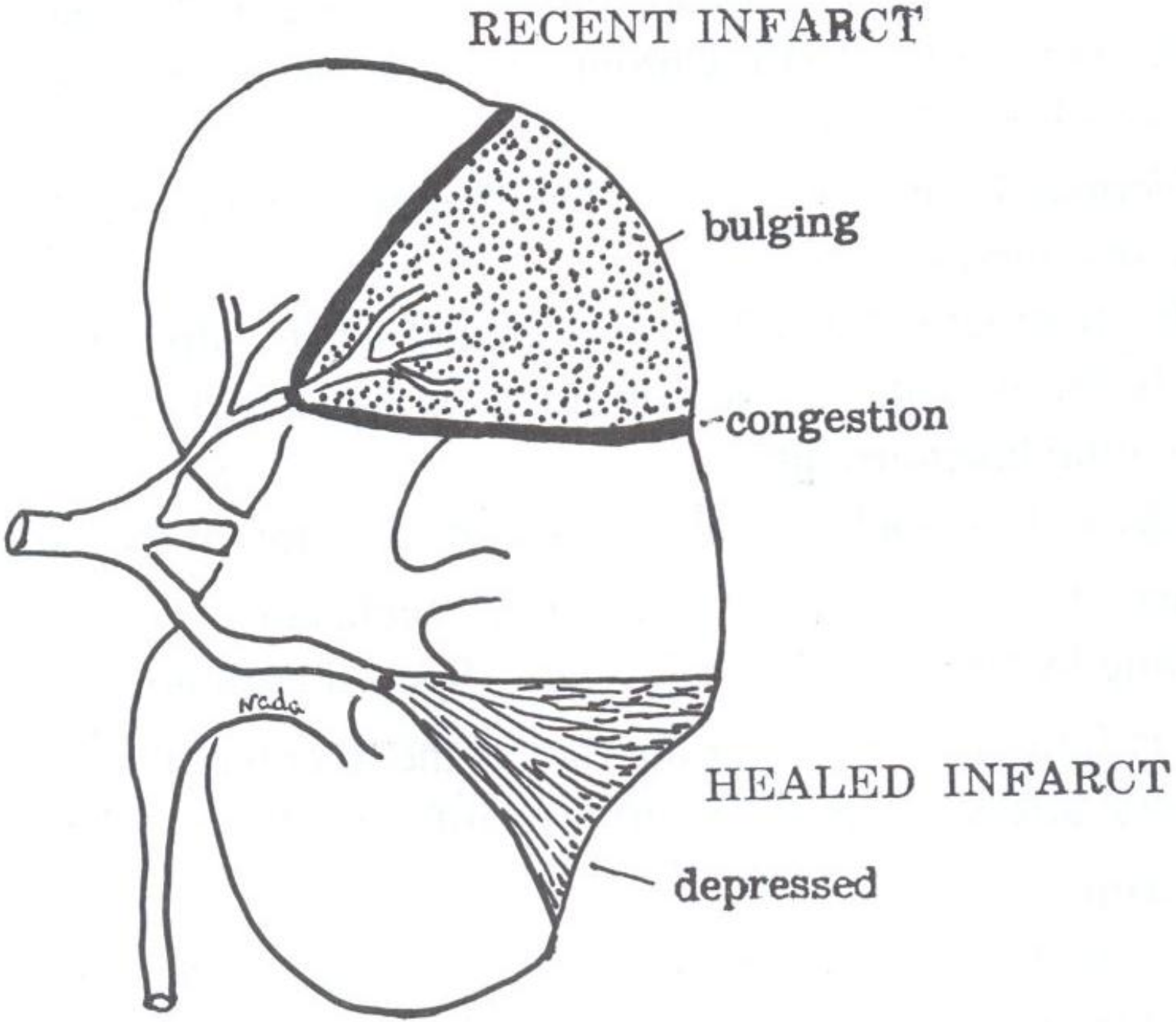
INFARCTION

- **Definition:**
- Infarct is an area of coagulative necrosis (liquefactive in the brain) caused by sudden ischemia produced by occlusion of either arterial supply or venous drainage.
- Nearly 99% of infarcts are the result of arterial occlusion.
- Infarctions caused by venous thrombosis are likely to occur in organs having single venous outflow channels as testis and ovary.

- **Causes of infarction:**
- Infarction is caused by sudden ischemia.
- Thrombosis and embolism are the main causes.
- The affected area appear pale red at first due to cutting of the blood supply.
- Later the color deepens when the collateral circulation opens, still nutrition is inadequate and degeneration begins and proceeds to necrosis which is completed in two days.
- Parenchymatous cells undergo necrosis earlier than the fibrous stroma.

General features of the infarct:

- ***Gross picture:***
- The infarct is wedge shaped or pyramidal as the arteries have a fan like distribution.
- The base is directed towards the surface of the organ.
- The infarct is subcapsular, raised when recent due to edema and depressed when healed due to fibrosis.
- It is surrounded by a red zone of inflammatory hyperemia as the necrotic tissue irritate the surrounding living tissue.
- The infarct is firm in consistency.
- The size depends on the size of the occluded vessel.
- Infarcts are of two types; red and pale.


RECENT INFARCT
bulging
congestion
HEALED INFARCT
depressed

- ***Red infarcts (hemorrhagic):***
- Occur in soft and vascular organs as the lung, liver and intestine.
- The red color is due to hemorrhage in the substance of the infarct.
- When hemolysis occurs the liberated red cells and its products are removed, the infarct may become pale.

- ***Pale infarcts:***
- Are more common and occur in firm and less vascular organs as the kidney, heart and spleen.
- ***Liquefactive infarcts:***
- Occur in the brain and spinal cord.

- ***Microscopic picture:***
- Early the cells show various post-necrotic changes.
- Next structural details are lost but the outlines are preserved.
- Lastly necrotic tissue appears as granular pink debris.
- The infarct is surrounded by a zone of inflammation.

- ***Fate:***

(a) Small infarct:

- Necrotic tissues are removed by macrophages, granulation tissue fills the defect followed by fibrosis.

(b) Large infarct:

- Gets surrounded by a fibrous capsule and its substance may show dystrophic calcification.

General reactions:

- Infarcts are associated with general reactions in the form of:
- Fever
- Leucocytosis
- Increased sedimentation rate; ESR
- Elevation of certain serum enzymes as transaminase in myocardial infarction.

Infarcts in different organs:

A. **Kidney:**

- ***Causes:***

(a) Thrombosis of a branch of the renal artery usually caused by atherosclerosis.

(b) Rarely emboli from the left side of the heart.

- ***Gross picture:***
- Pale infarct appears on the convex border of the kidney as a pale red cuboidal area.
- It affects the cortex and a part of the medulla.
- The shape of the infarct as described before.

- ***Microscopic picture:***

(a) Early the cells show various post-necrotic changes.

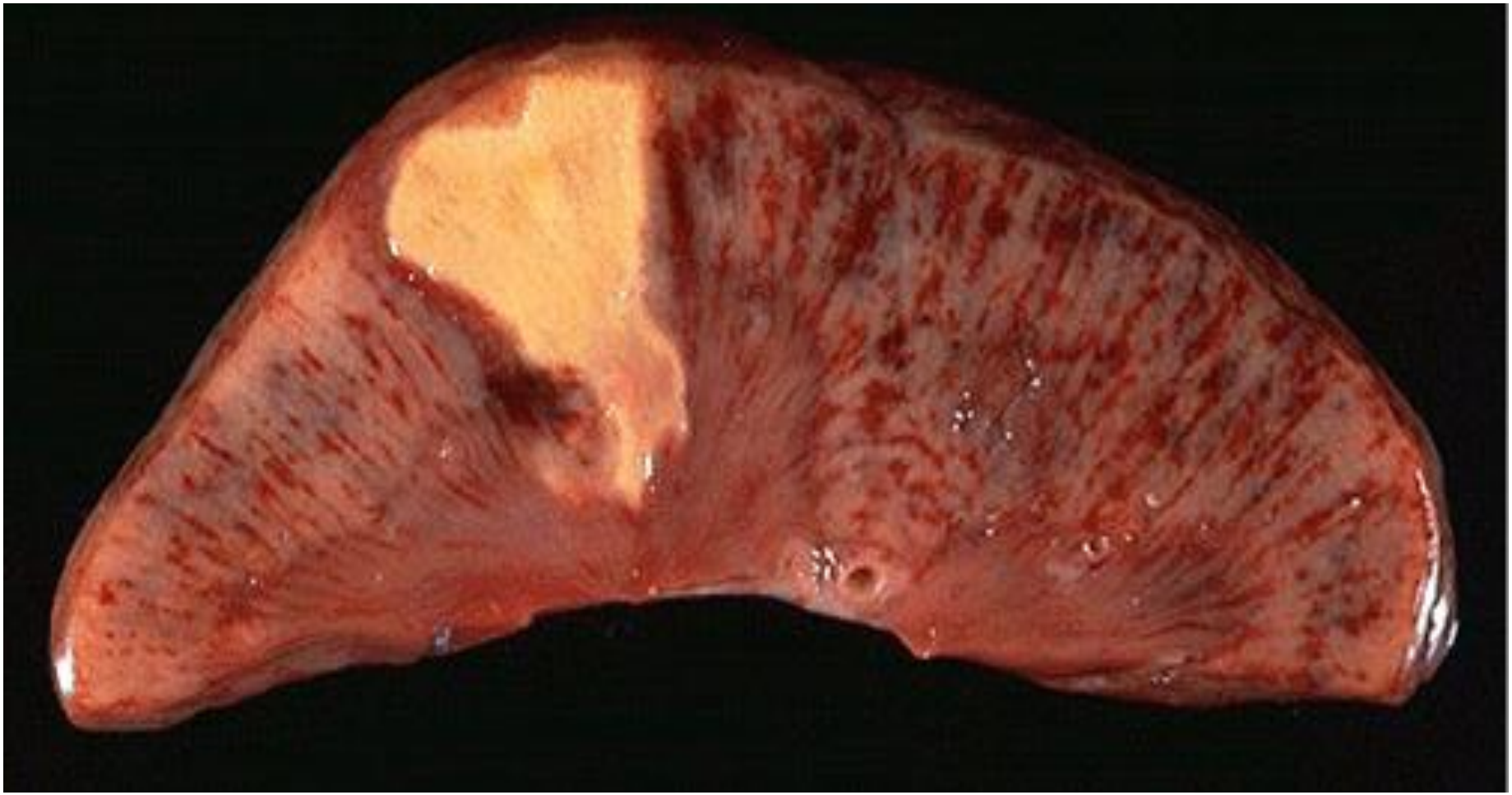
(b) Later on all structural details are lost, but the outlines of the glomeruli, tubules and vessels appear as homogenous pink shadows for sometime.

(c) Lastly the necrotic tissue appears as granular red debris.

(d) The margin of the infarct is hyperemic and infiltrated by neutrophils and macrophages.

- **Clinically:**
- Hematuria.
- No pain as the kidney capsule is not affected (has a different blood supply).

Infarction of the kidney



Infarction of the kidney

B. **Spleen:**

- ***Causes:***

(a) Emboli originating from the left side of the heart as in bacterial endocarditis.

(b) Chronic myeloid leukemia causes increased blood viscosity and thrombosis.

- ***Gross picture:***
- Usually pale, occasionally red infarct.

- ***Microscopic picture:***

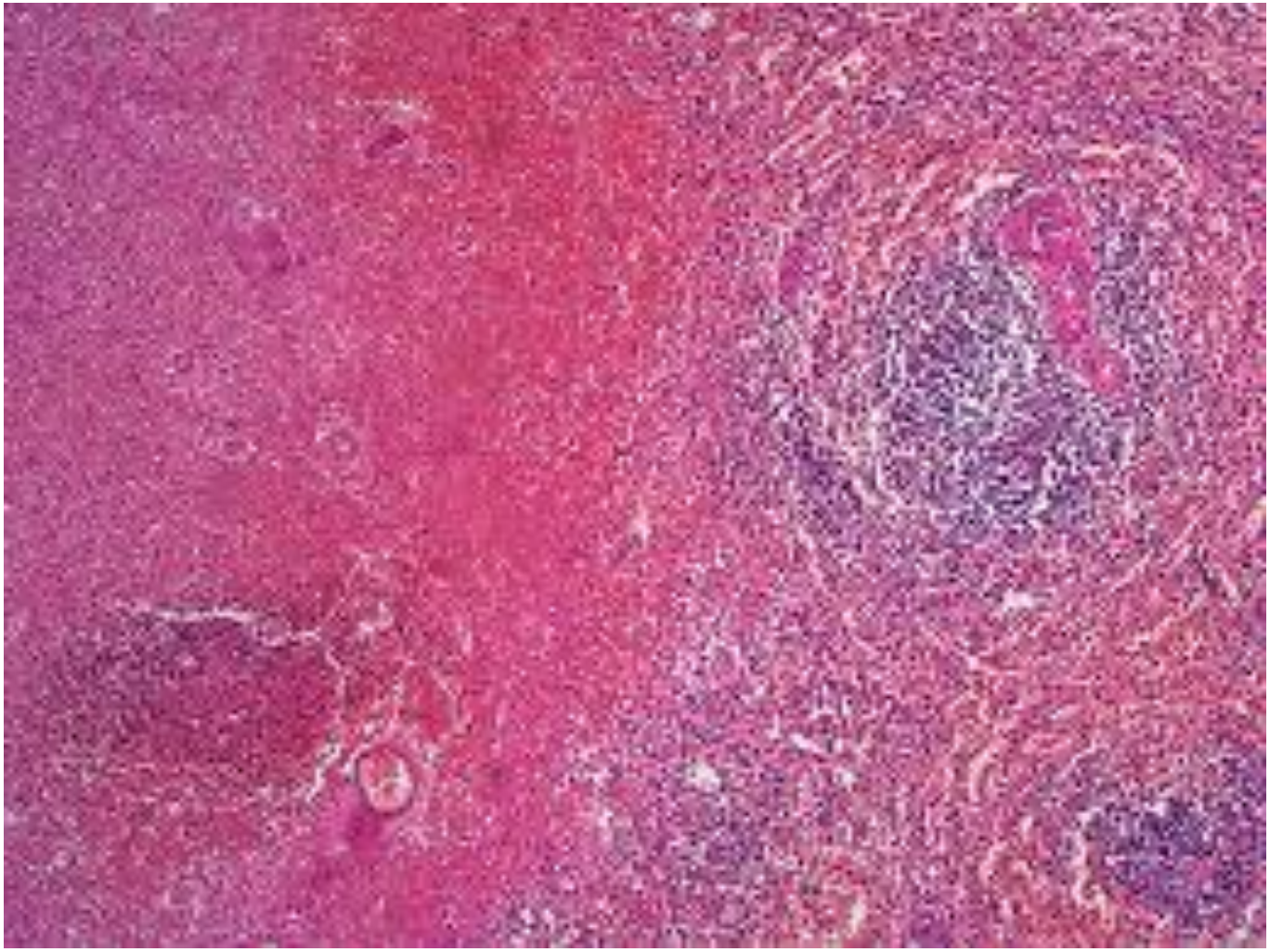
(a) Early all structural details of the red and white pulp are lost.

(b) Lately the necrotic tissue appears as granular red debris with extensive interstitial hemorrhage.

- ***Clinically:***
- Left hypochondrial pain due to affection of the capsule.

Infarction of the spleen

Infarction of the spleen



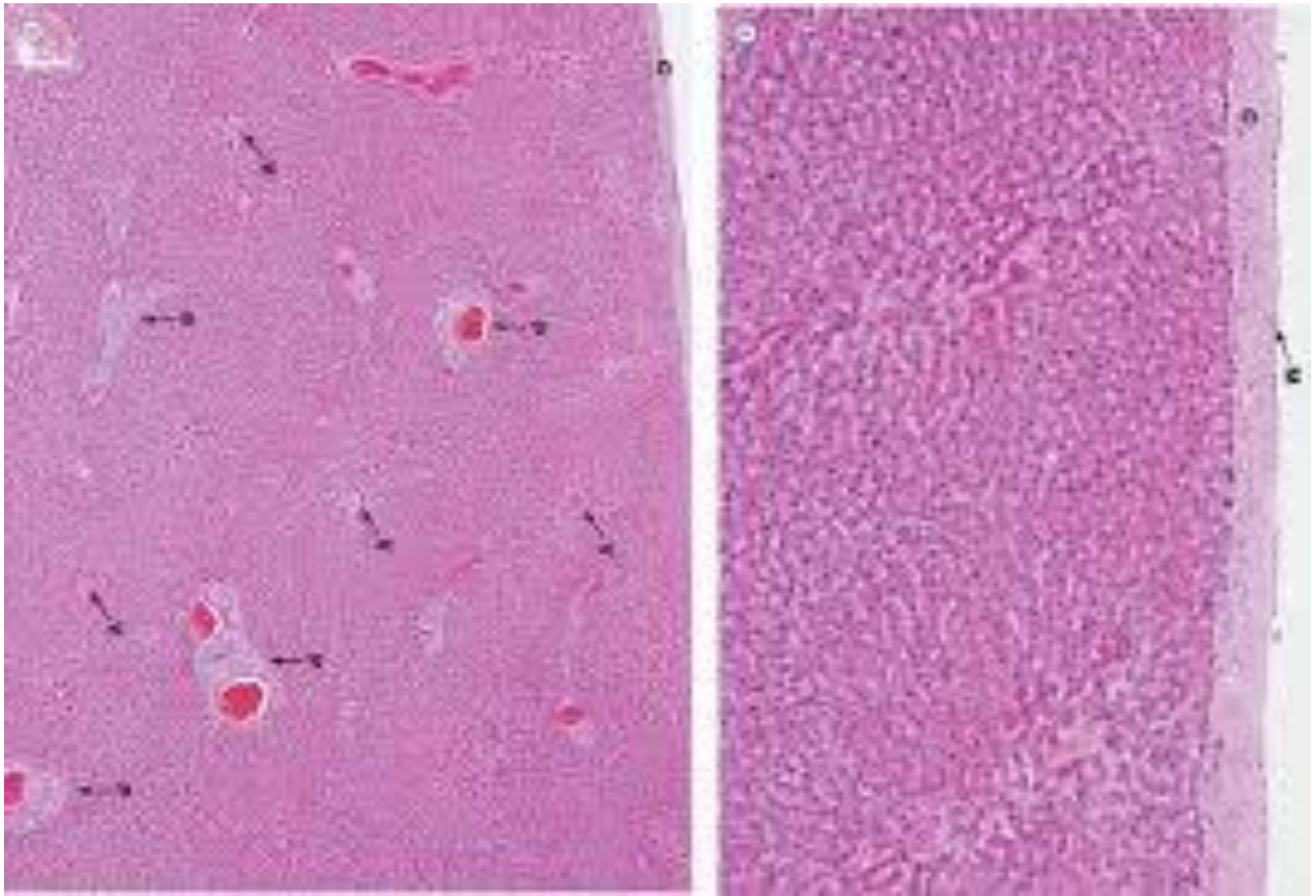
C. **Heart:**

- Pale infarct resulting from occlusion of a coronary branch.
- Healing by fibrosis takes 4-8 weeks.

D. **Liver:**

- Infarcts of the liver are rare as the liver has a double blood supply (hepatic artery and portal vein).
- The infarct is hemorrhagic.

Liver infarction



E. **Intestine:**

- ***Causes:***

(a) Emboli originating from the left side of the heart.

(b) Thrombosis of the superior mesenteric artery due to atherosclerosis.

(c) Strangulated hernia, intussusception and volvulus.

- ***Gross picture:***

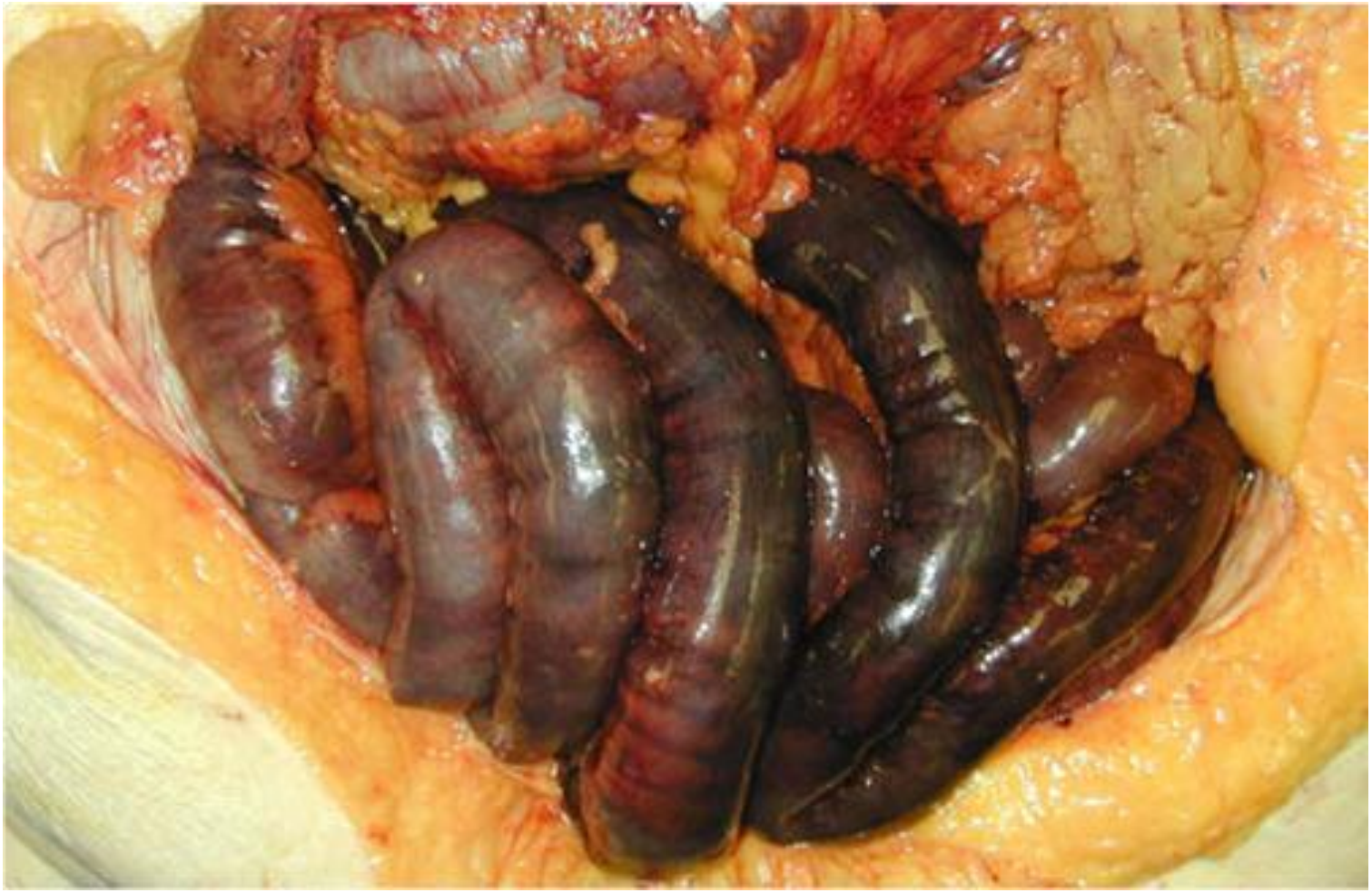
- The affected loop appears dark red, thick and edematous.
- The serous coat is covered by fibrinous exudate.
- The intestinal wall, lumen and peritoneal cavity show hemorrhages.

- ***Clinically:***

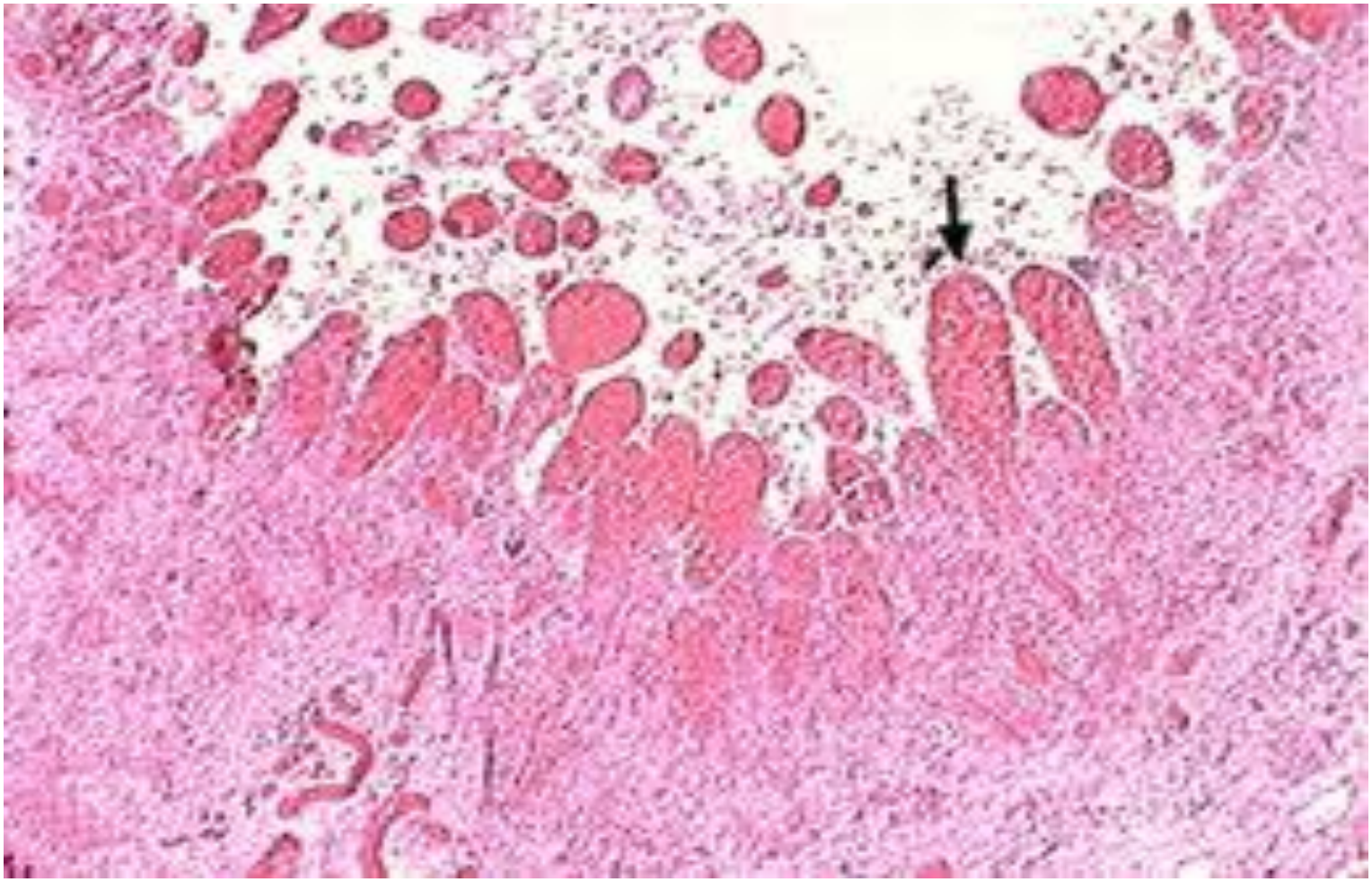
(a) Functional acute intestinal obstruction.

(b) Gangrenous peritonitis due to bacterial invasion.

Intestinal infarction → Gangrene



Intestinal infarction



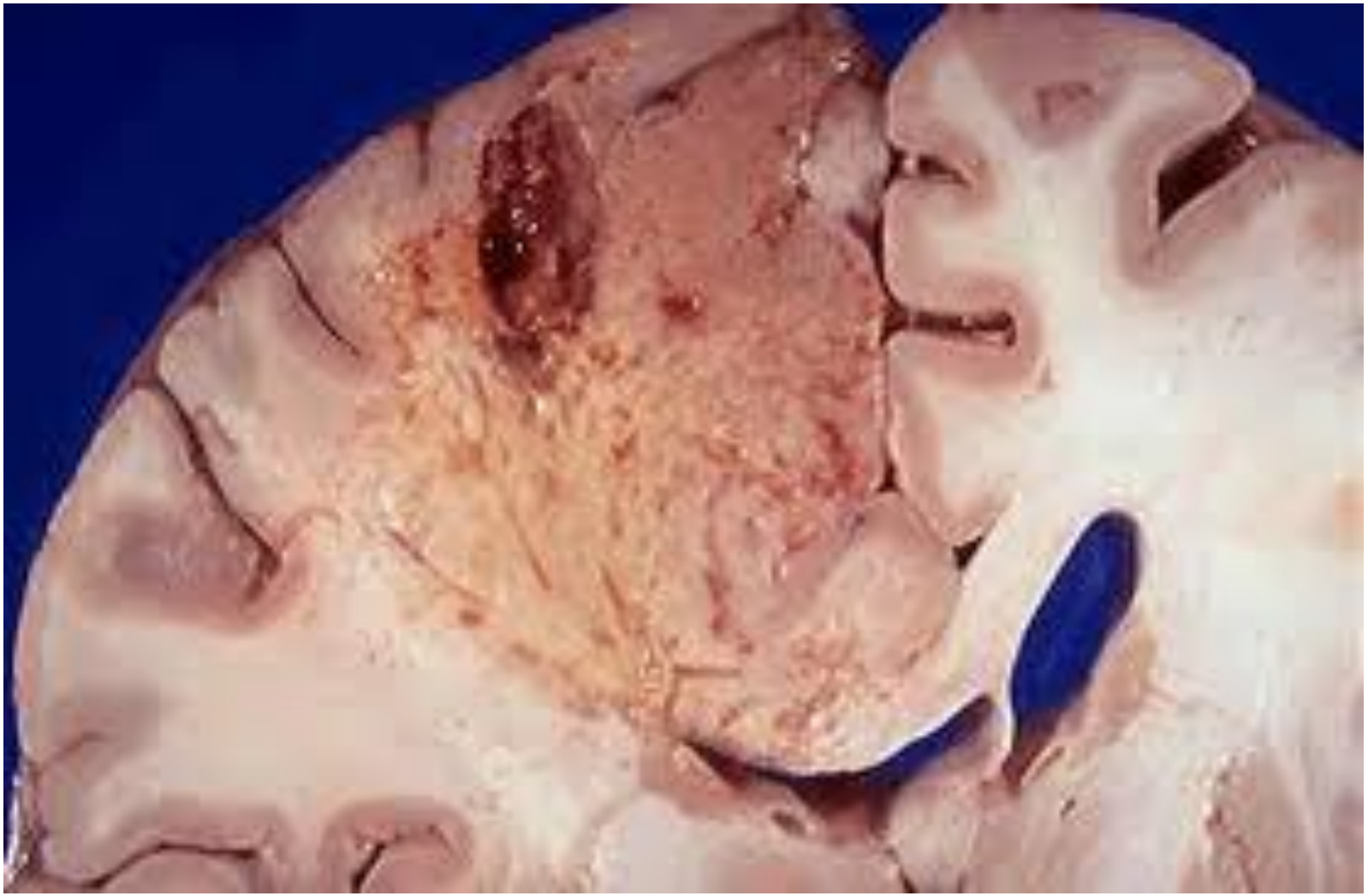
6. **Brain:**

- ***Causes:***
  - (a) Thrombosis of the cerebral arteries due to atherosclerosis, commonly the middle and posterior cerebral.
  - (b) Embolism to the cerebral arteries.
- The embolus is derived from vegetations in the left side of the or atherosclerotic lesion in the aorta.

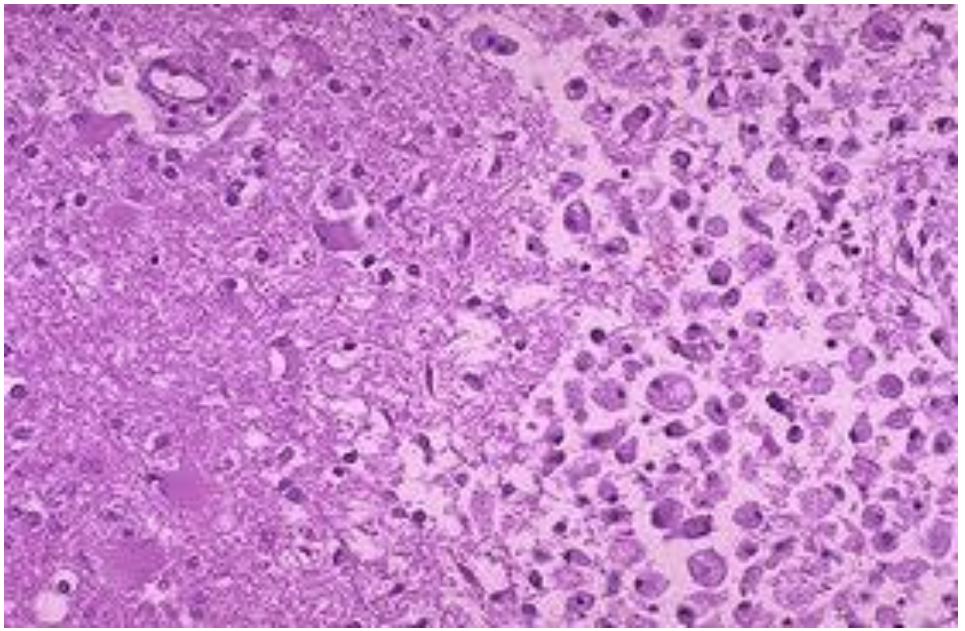
- ***Gross picture:***
- The infarct is wedge shaped with the base at the surface of the brain.
- Early the infarct is pale red, edematous with petechial hemorrhage.
- Liquefactive necrosis occurs within 2-3 days and the infarct becomes soft and yellow (cerebral softening).
- When the infarct is in the cortex, the surface becomes depressed because some of the necrotic tissue are removed from the area.
- The meningeal covering of the infarct become thick and adherent.
- Small infarct is replaced by glial tissue, while a large one becomes capsulated by glial wall.

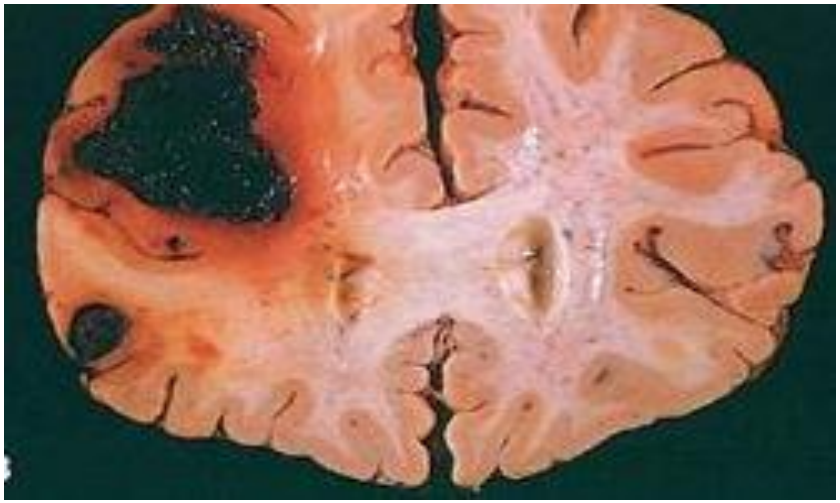
- ***Microscopic picture:***
- The myelin substance of the infarct breaks down to form fat globules which are taken by the microglia cells.
- The cells become distended and their cytoplasm stains faintly "compound granular corpuscles".
- Neutrophilic infiltration is sometimes seen.
- The related nerve tract undergoes degeneration.
- ***Clinically:***
- Hemiplegia when the infarct affects the internal capsule.

Brain infarction



Brain infarction





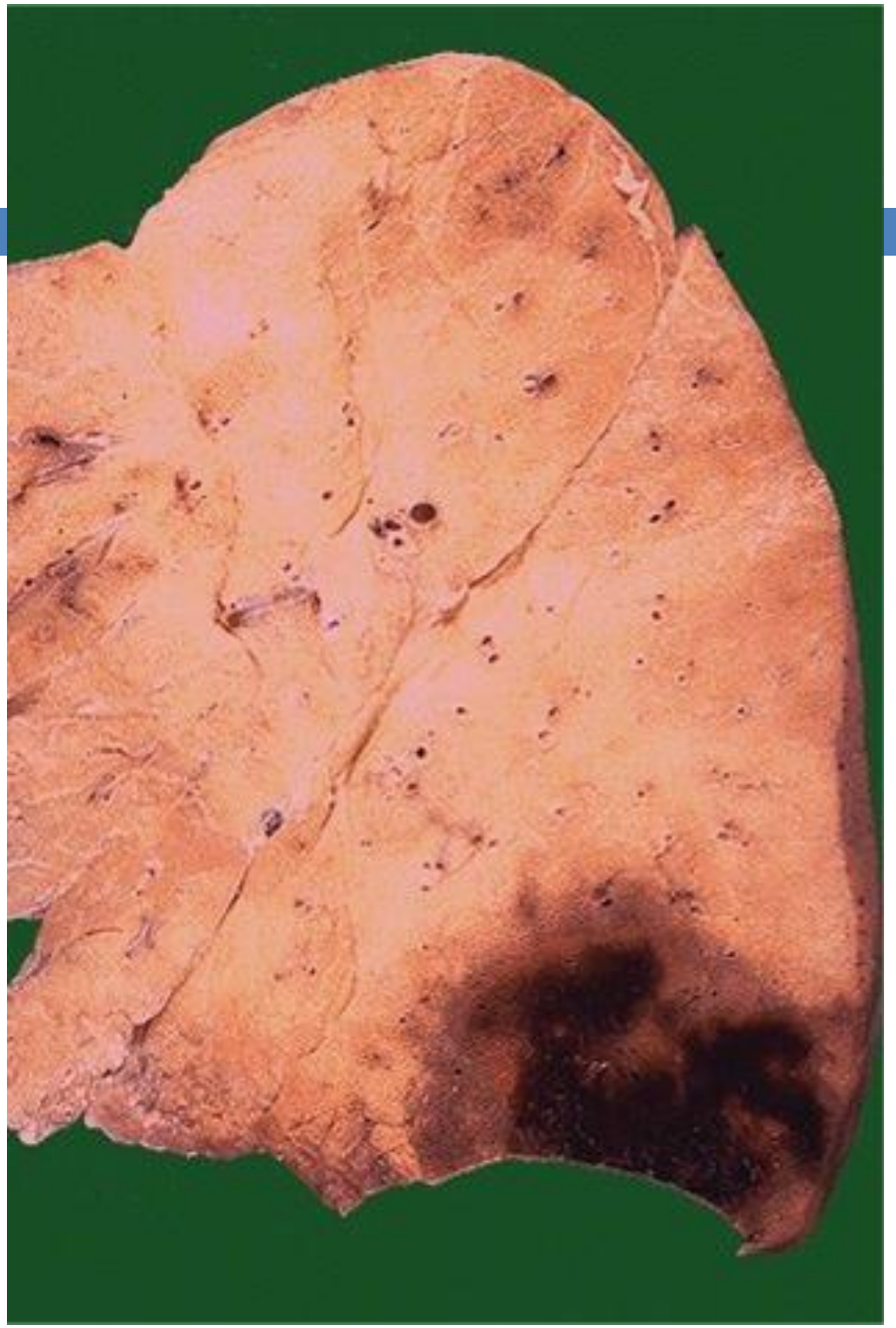
7. Lung:

- ***Causes:***
- Embolism or thrombosis of a small pulmonary artery, when the lung is suffering from chronic venous congestion.
- Experimentally occlusion of a pulmonary branch in a healthy animal does not result in infarction as the lung has a double blood supply (pulmonary and bronchial vessels).

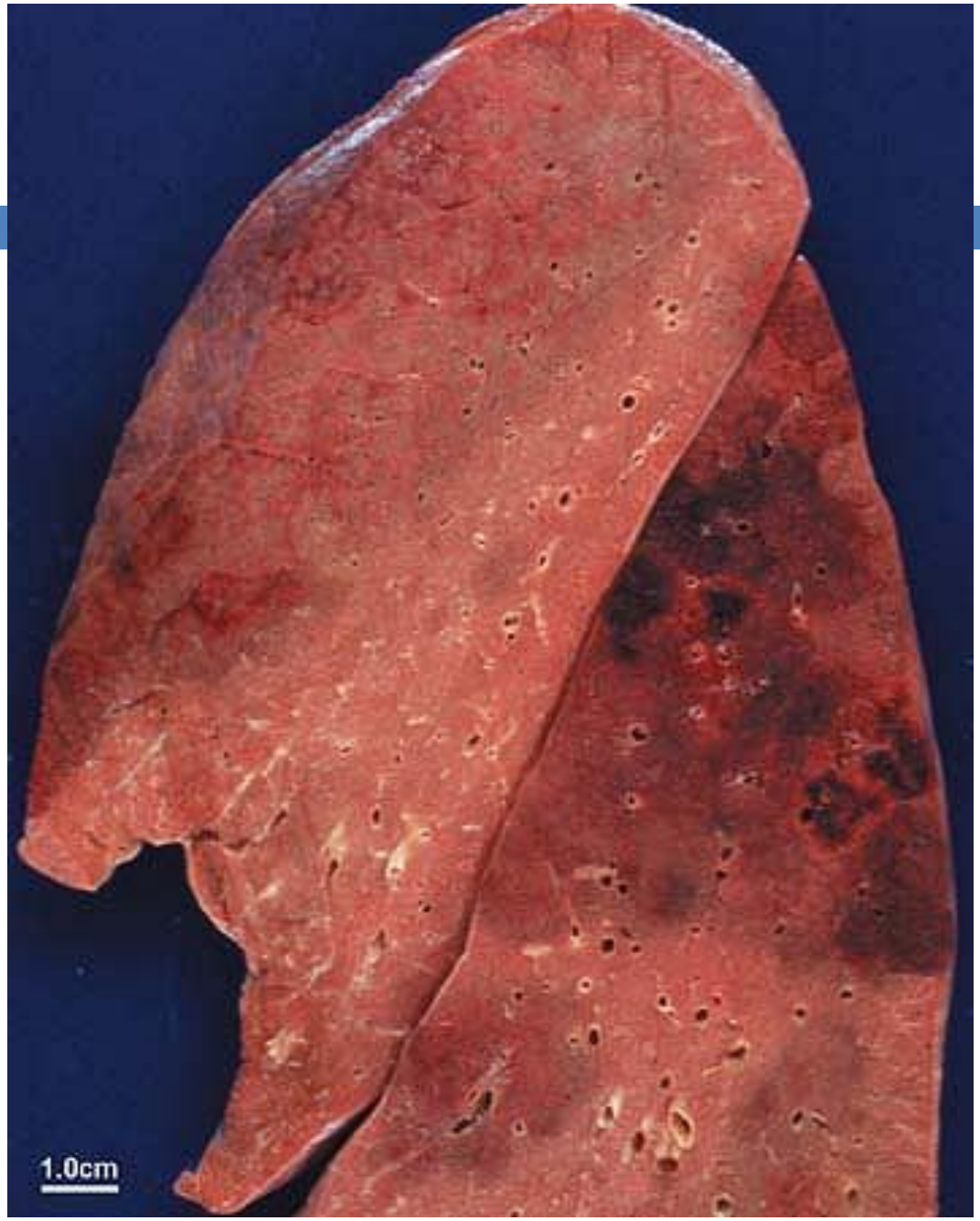
- ***Gross picture:***
- Lung infarcts are wedge shaped, may be single or multiple, variable in size and situated beneath the pleura specially at the lobe margins.
- The covering pleura shows fibrinous pleurisy.
- The infarct is firm in consistency and dark red in color (hemorrhagic infarct).

- ***Microscopic picture:***
- The alveolar walls appear as homogenous red thin lines.
- The alveolar spaces contain many red cells, intact and hemolysed.
- The surrounding lung shows the picture of chronic venous congestion.
- ***Clinically:***
- Hemoptysis and chest pain.

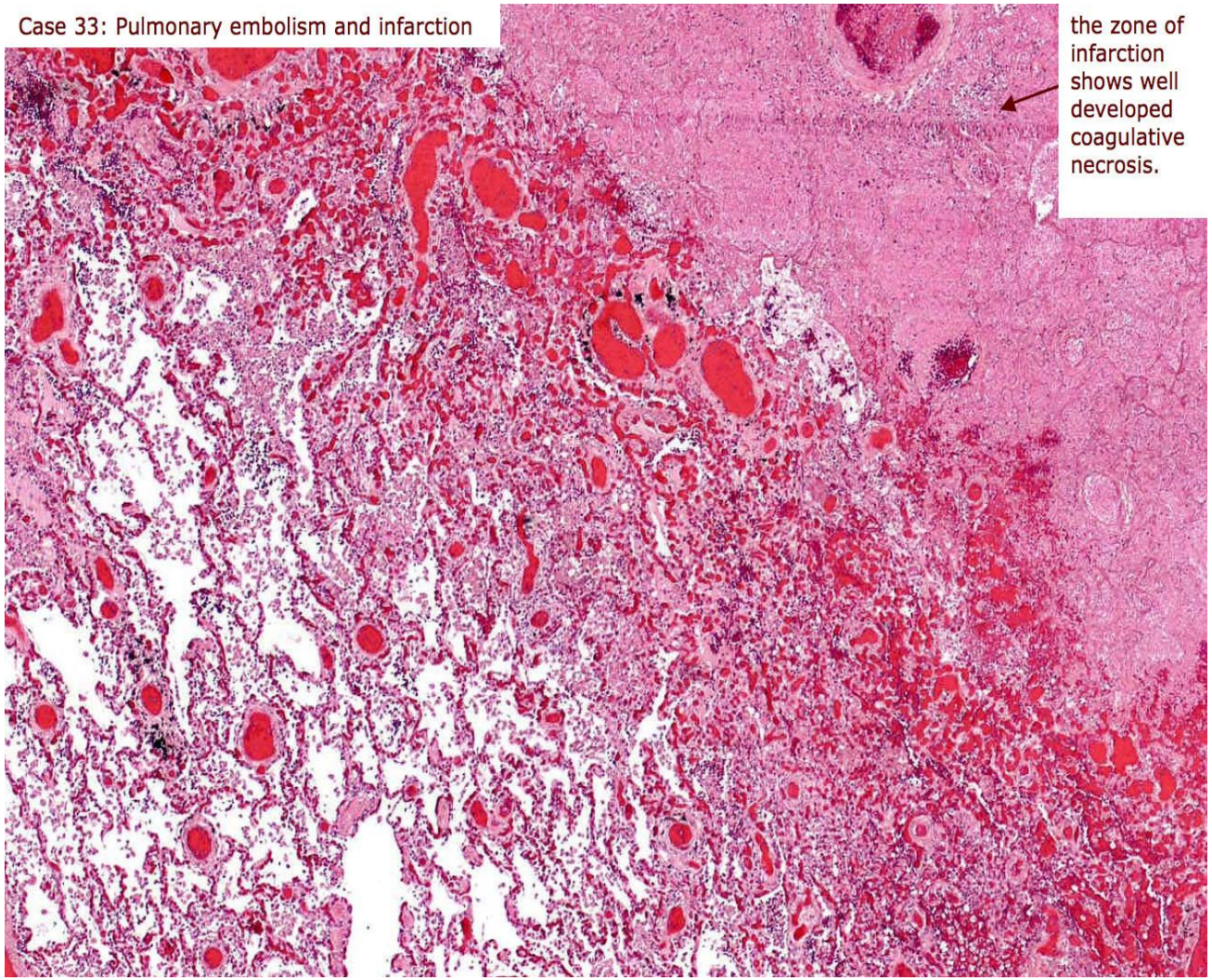
Infarction of the lung (hemorrhagic infarction)



Infarction of the lung (hemorrhagic infarction)



Pulmonary embolism and infarction



THANK YOU