General Pathology

Hemodynamic Disorders

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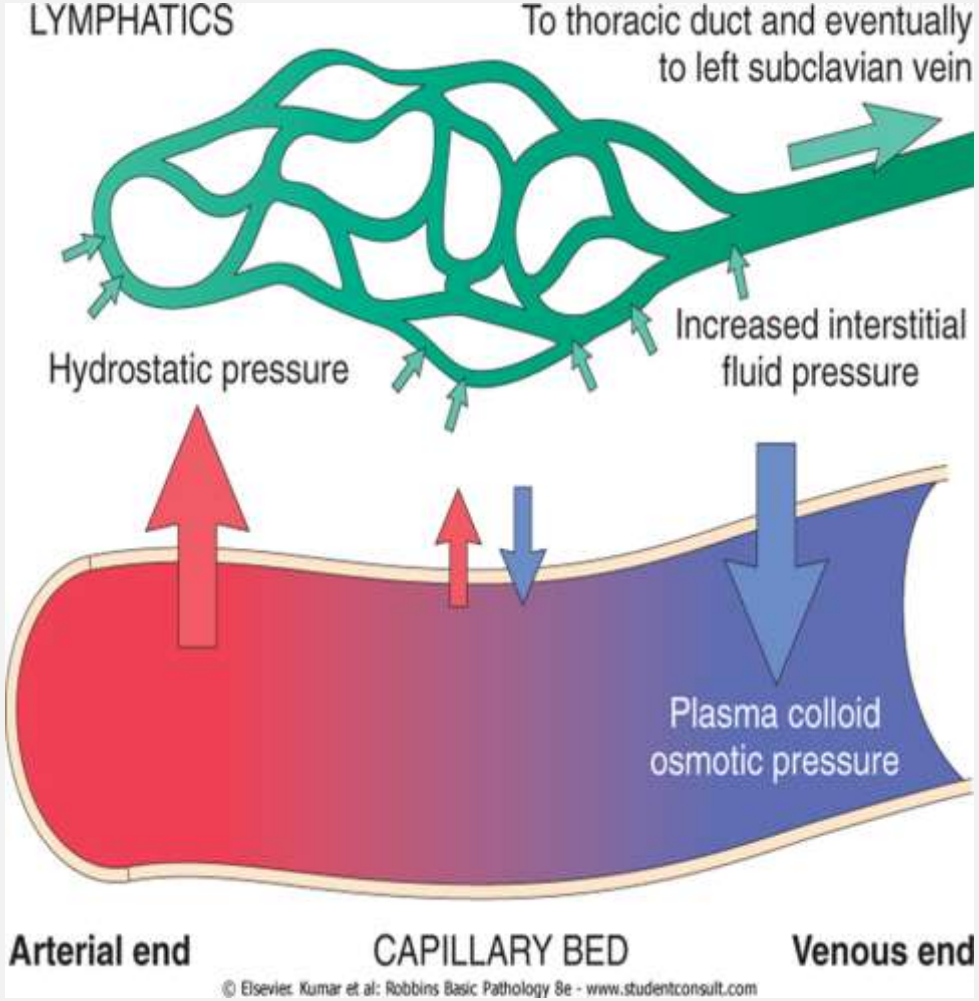
Lecture Outline

- Oedema
- Hyperemia & Congestion
- Haemorrhage
- Thrombosis
- Embolism
- Infarction
- Shock



Introduction

- The health of cells and tissues depends on an intact blood circulation and normal fluid homeostasis.
- Increases in vascular volume or pressure, decreases in plasma protein content, or alterations in endothelial function can result in a net outward movement of water across the vascular wall (***oedema***).
- Absence of clotting after vascular injury results in ***haemorrhage*** and more extensive hemorrhage can result in hypotension (***shock***) and death.
- Conversely, inappropriate clotting (***thrombosis***) or migration of clots (***embolism***) can obstruct tissue blood supplies and cause cell death (***infarction***).

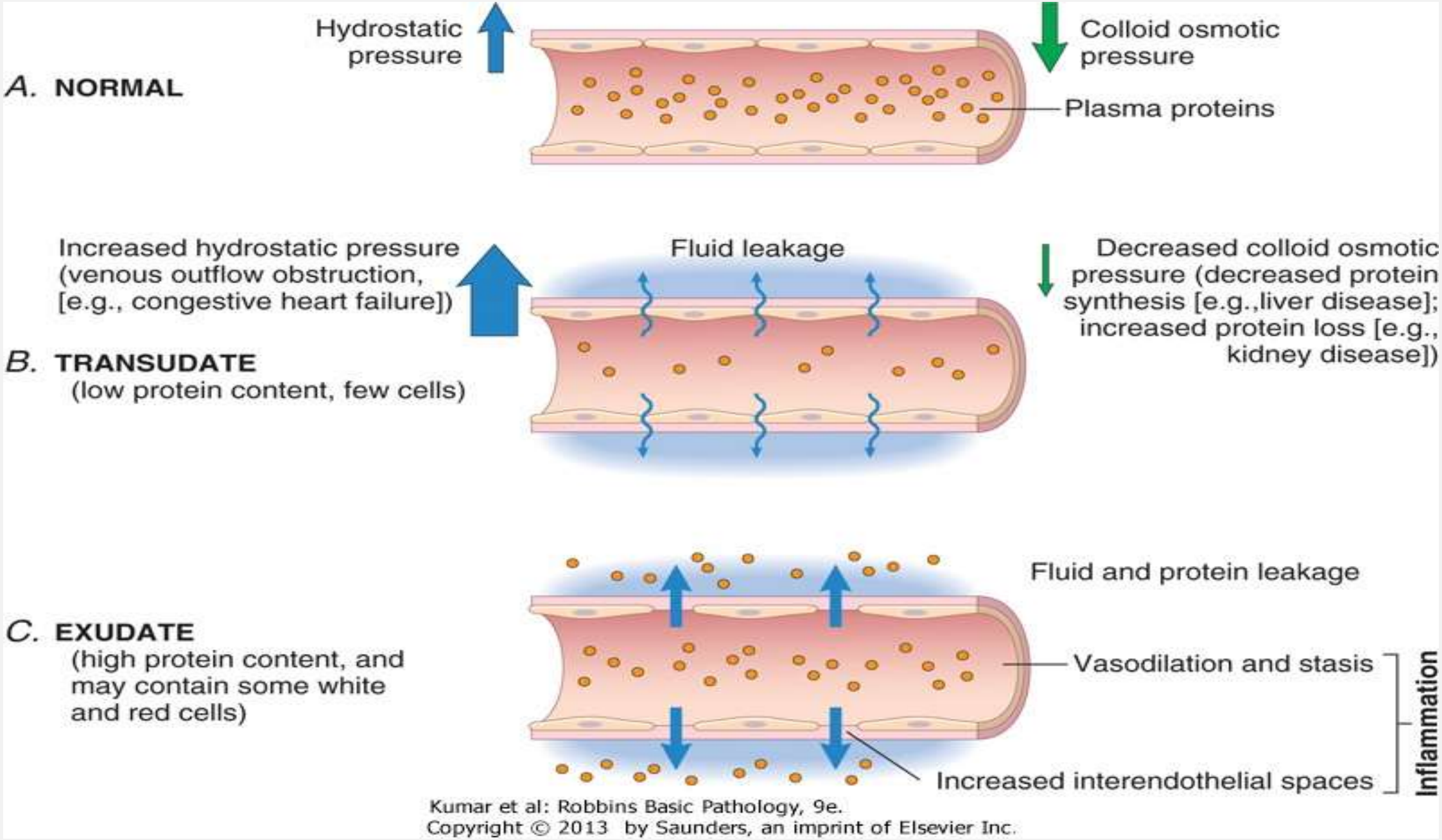
Oedema

- **Signifies abnormal increase of fluid in the interstitial tissue spaces**
- Can either be inflammatory or Non-inflammatory oedema
- The mechanism of inflammatory oedema mostly involves increased vascular permeability.
- The movement of fluid between vascular and interstitial spaces is controlled mainly by the opposing effects of vascular hydrostatic pressure and plasma colloid osmotic pressure.
- **Aetiology**: increased hydrostatic pressure, reduced plasma osmotic pressure, lymphatic obstruction and increased sodium and water retention.

Peripheral Edema - Differential Diagnosis

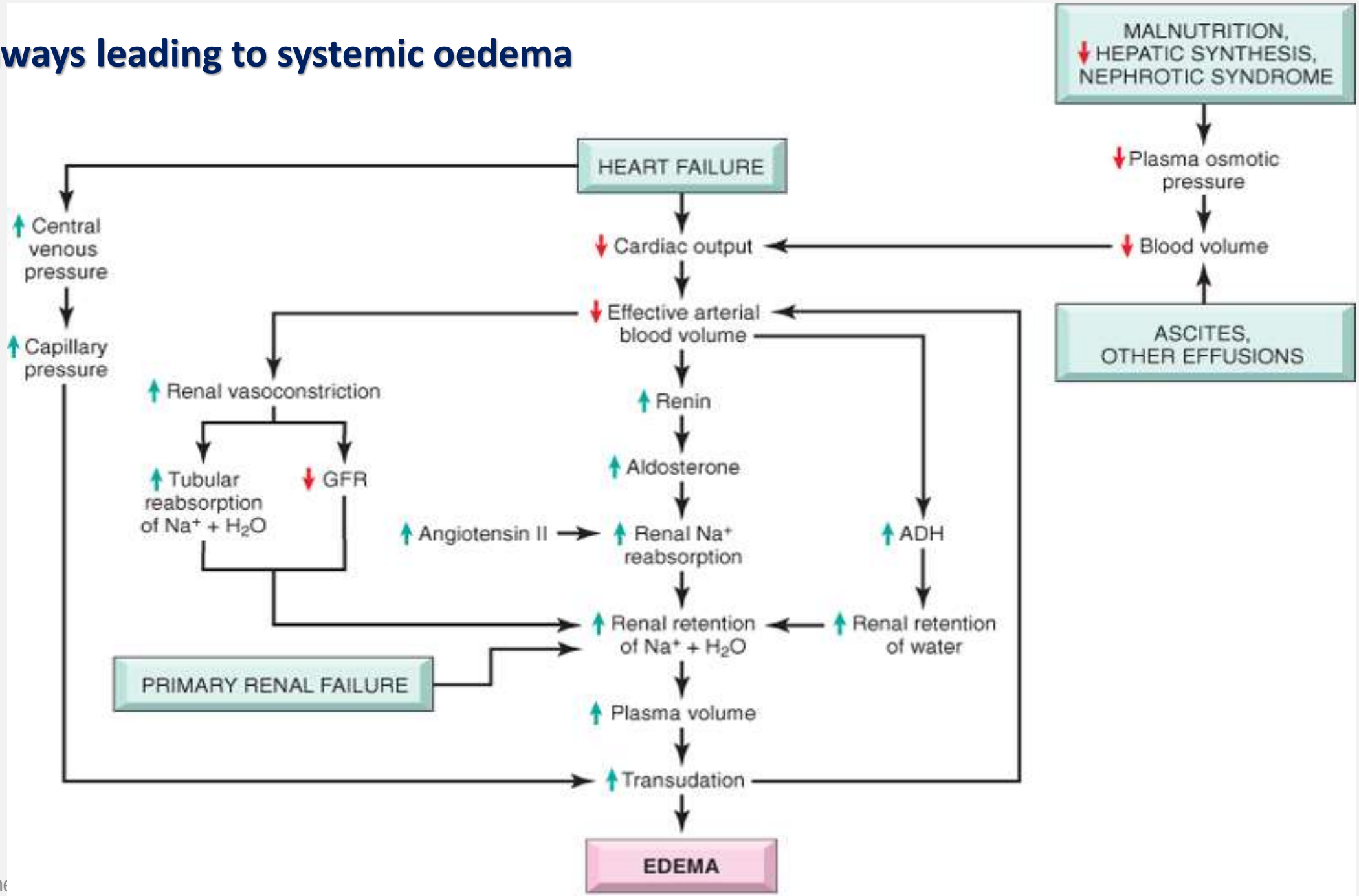
Increased Hydrostatic Pressure	Decreased Oncotic Pressure (Hypoalbuminemia)	Increased Capillary Permeability	Lymphatic Obstruction (Lymphedema)	Miscellaneous
<u>Volume Expansion</u> • Kidney failure* • Pregnancy • Medication side effect* (e.g. prednisone, NSAIDs) • Acute salt load • Heart failure* <u>Venous Obstruction/ Insufficiency</u> • Heart failure* • Pulmonary hypertension • Cirrhosis* • Deep vein thrombosis* • Chronic venous stasis* <u>Arteriolar vasodilation</u> Dihydropyridine Ca^{2+} channel blockers	Malnutrition Cirrhosis* Nephrotic syndrome	Sepsis Cellulitis*	<u>Malignancy</u> • Lymph node dissection • Infiltration of lymphatics • Extrinsic compression of lymphatics Filariasis (e.g. *Wuchereria bancrofti, Brugia malayi*)	Hypothyroidism

* Most common causes of acute edema in US
* Most common causes of chronic edema in US



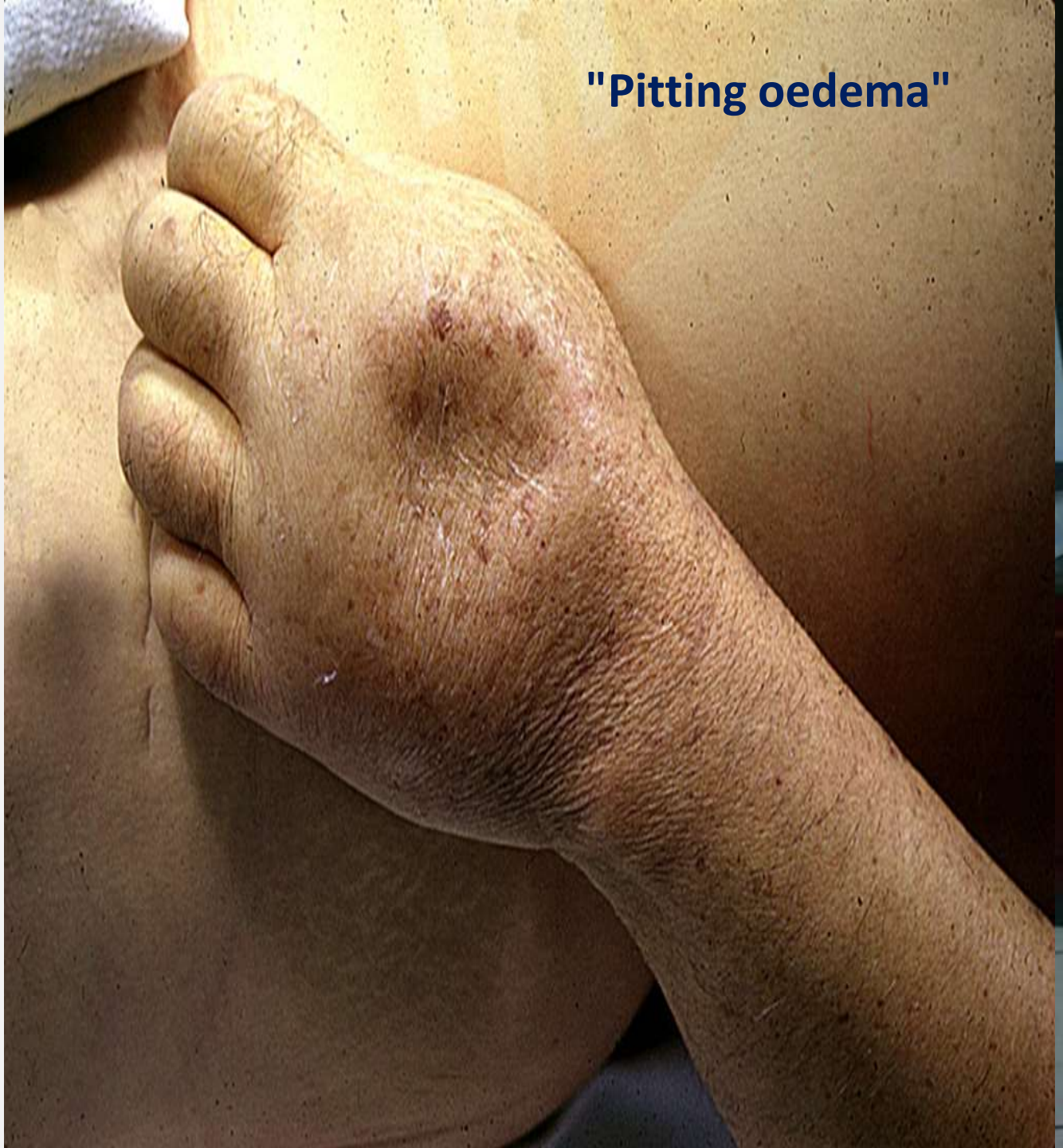
Kumar et al: Robbins Basic Pathology, 9e.

Pathways leading to systemic oedema



Types of edema

- **Localized**
  - In the organ and limb
- **Generalized (anasarca or dropsy)**
  - When it is systemic in distribution, particularly noticeable in the subcutaneous tissues.
- **Pitting**
  - Momentary pressure of finger produces a depression
- **Non-pitting or solid oedema**
  - No depression is produced on pressure e.g. in myxoedema, elephantiasis.
- Oedema accumulation in body cavities gets the prefix **hydro-**


"Pitting oedema"


Ascites

Features	Transudate	Exudate
Cause	Usually develop from imbalances in hydrostatic and oncotic forces in circulation.	Usually develop from increased capillary permeability or decreased lymphatic reabsorption.
Associated with	Congestive heart failure Fluid overload Nephrotic syndrome Hepatic cirrhosis Malnutrition	Microbial infections Membrane inflammations Malignancy Connective tissue diseases.
Appearance	Clear, thin-colored, pale yellow	Turbid, hemorrhagic, straw colored
Fibrinogen	Low content of fibrinogen (low tendency to clot)	High content of fibrinogen (high tendency to clot)
Specific gravity	<1.012	>1.012
pH	>7.3	<7.3
Glucose content	Same as plasma	Low (less than 60 mg/dl)
Total Protein	Less than 3 gm/dl	More than 3 gm/dl
Fluid/Serum Protein	<0.5	>0.5
LDH	<0.67 x UNL Serum	>0.67 x UNL Serum
WBC count	<1000/ul	>1000/ul
Differential count	Mesothelial cells or lymphocytes	Polymorphs, lymphocytes or RBCs
Culture	Sterile	Positive

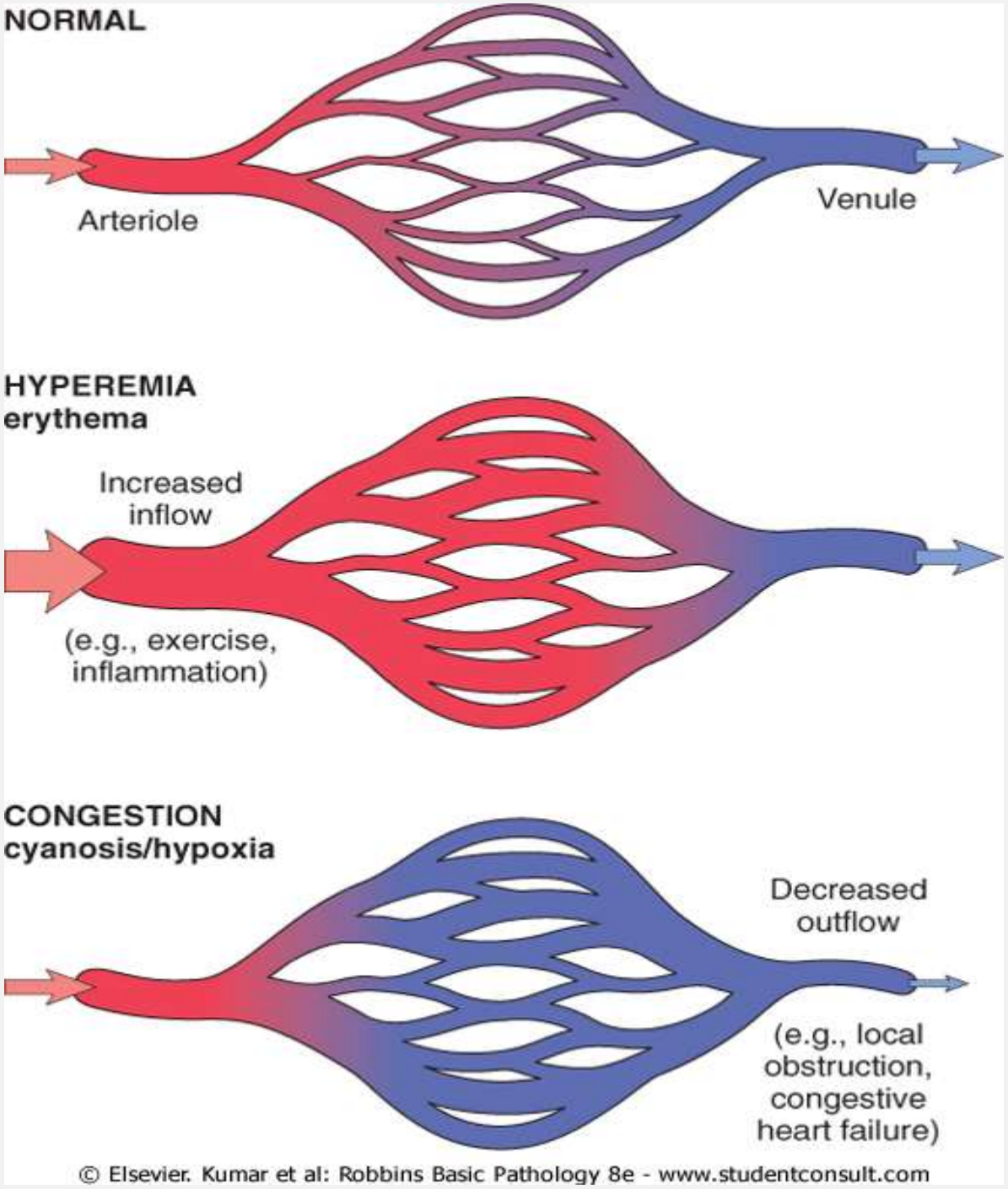
Clinical Correlation of Oedema

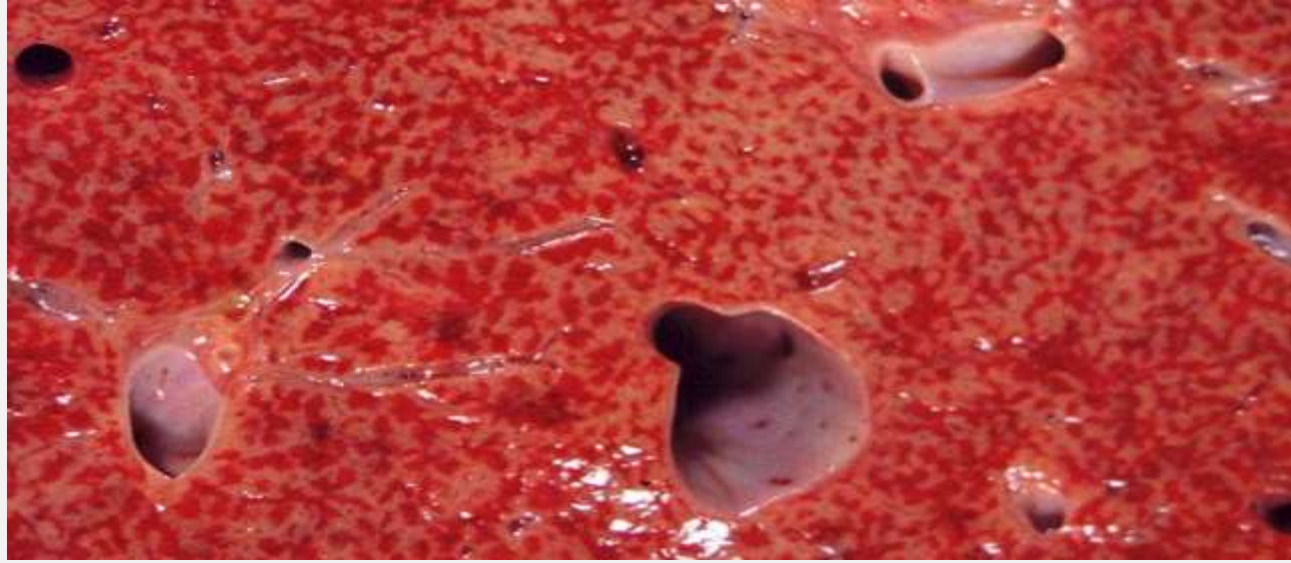
- **Local oedema** can impair wound healing or the clearance of infection.
- **Pulmonary oedema** can cause death by interfering with normal ventilatory function; Fluid in alveolar septa creates a favorable environment for bacterial infection.
- **Severe brain oedema** can cause brain herniation (extrusion of the brain) and brain stem compression
- **Subcutaneous oedema** signals underlying renal or RV cardiac disease

Hyperemia And Congestion

- These commonly occur together.
- Both indicate a local increased volume of blood in a particular tissue.
- Cut surfaces of hyperemic or congested tissues are haemorrhagic and wet.
- Hyperemia is an active process resulting from augmented blood flow due to arteriolar dilation (e.g., at sites of inflammation or in skeletal muscle during exercise).
- Congestion is a passive process resulting from impaired venous return out of a tissue.

- Hyperemic tissue is redder than normal because of engorgement with oxygenated blood.
- Congested tissues have a blue-red color as they are cyanosed
- Congestion may be peripheral, central or hypostatic
- In chronic passive congestion, the stasis of poorly oxygenated blood causes chronic hypoxia.





Acute Passive Congestion of the Liver. all those red "dots" are congested central veins!

Hyperemia

- Acute actively increased blood flow
- Bright red
- Warmer than usual
- Swollen
- Pulse may be felt readily
- Due to the elastic recoil of arterioles, hyperemia is dissipated after death in skin and mucous membranes and is usually not apparent post-mortem
- Microscopically capillaries and occasionally arterioles are dilated and engorged with blood

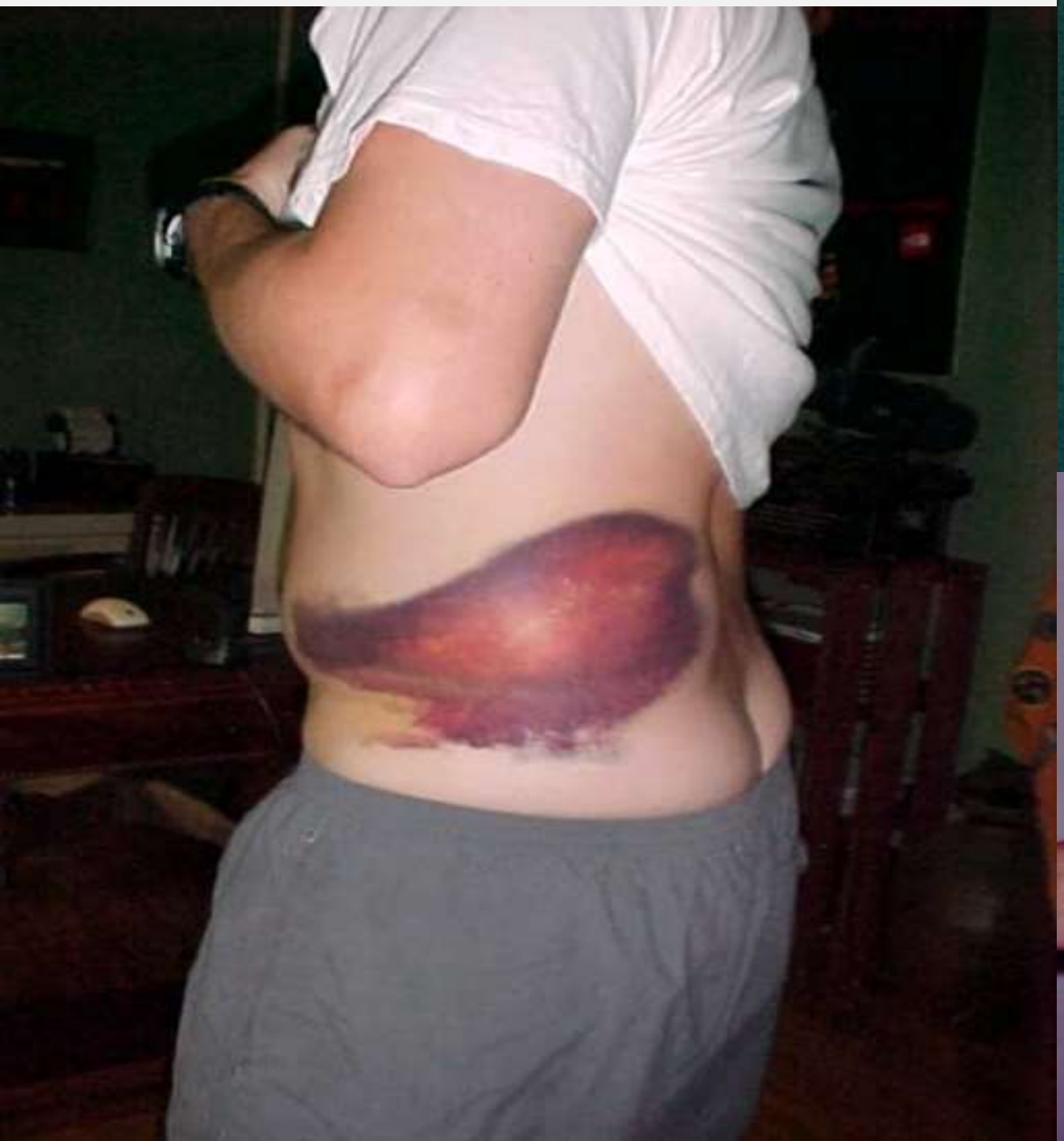
Congestion

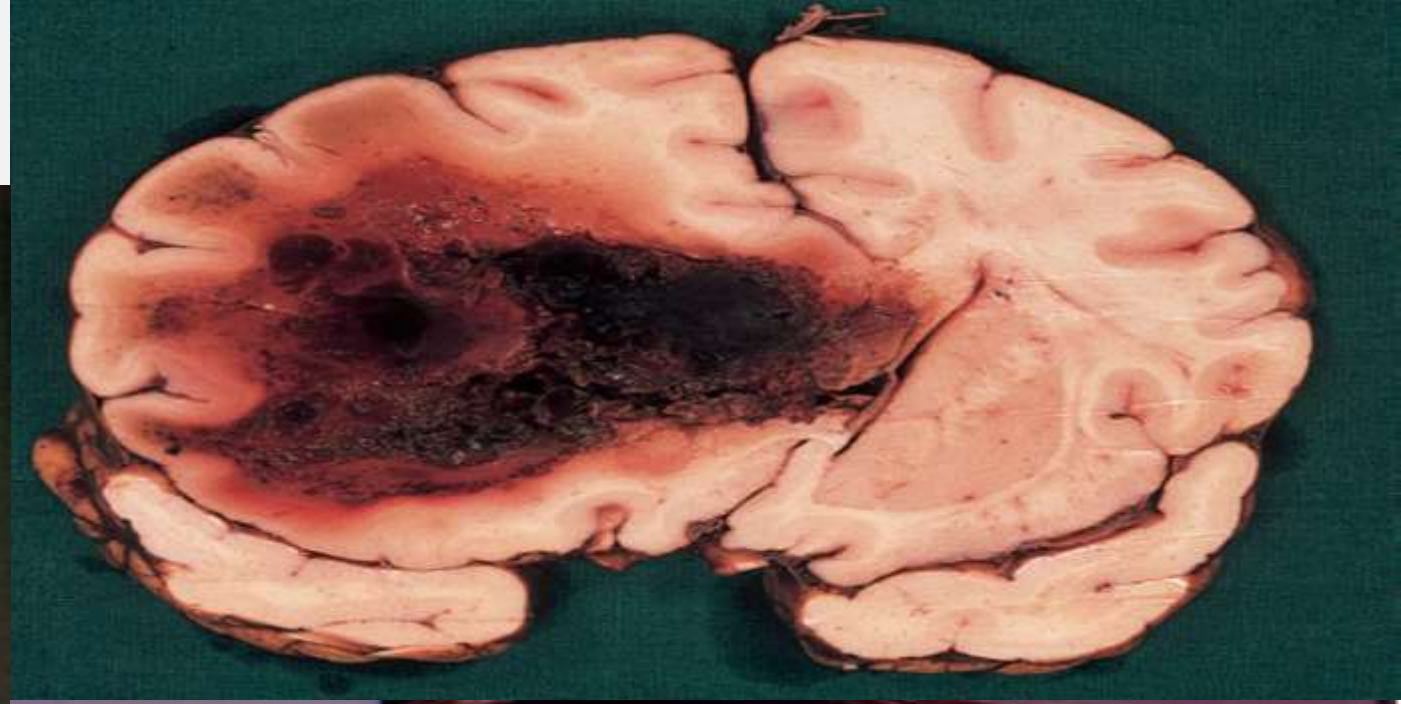
- Chronic passively reduced outflow
- Dark blue-red tinge
- Swollen
- Cooler than normal
- After death the color becomes even more dark blue and the cut surface of such tissues oozes blood freely
- if chronic, the tissue may have a brown color
- Microscopically capillaries and veins are engorged with blood and may see excessive hemosiderin in tissues (lungs)

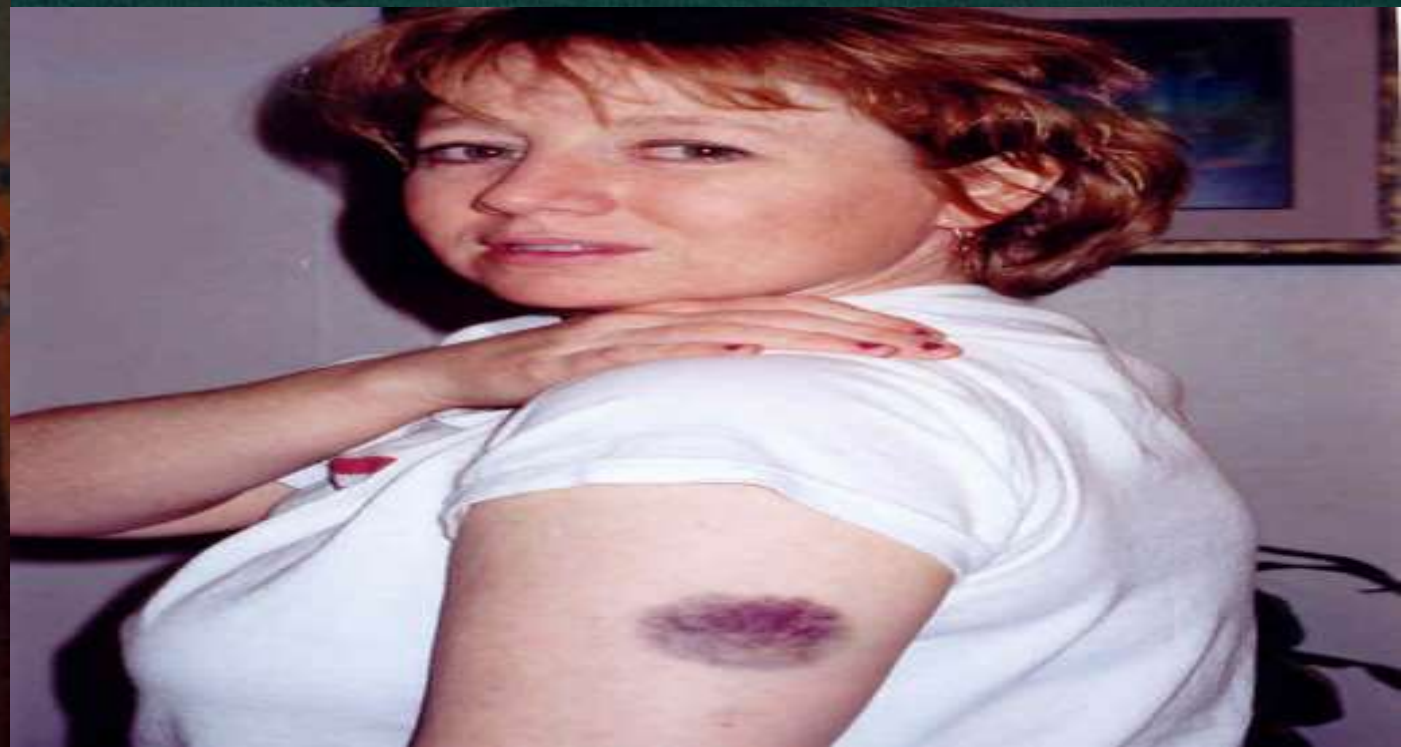
Haemorrhage

- ***Haemorrhage* is extravasation of blood from vessels into the extravascular space.**
- Hemorrhage can be external or can be confined within a tissue; any accumulation is referred to as a ***haematoma***.
- Greater losses of more than 1/3 of blood volume can cause haemorrhagic (hypovolemic) shock.
- Bleeding that would be trivial in the subcutaneous tissues may cause death if located in the brain.

Haemorrhage







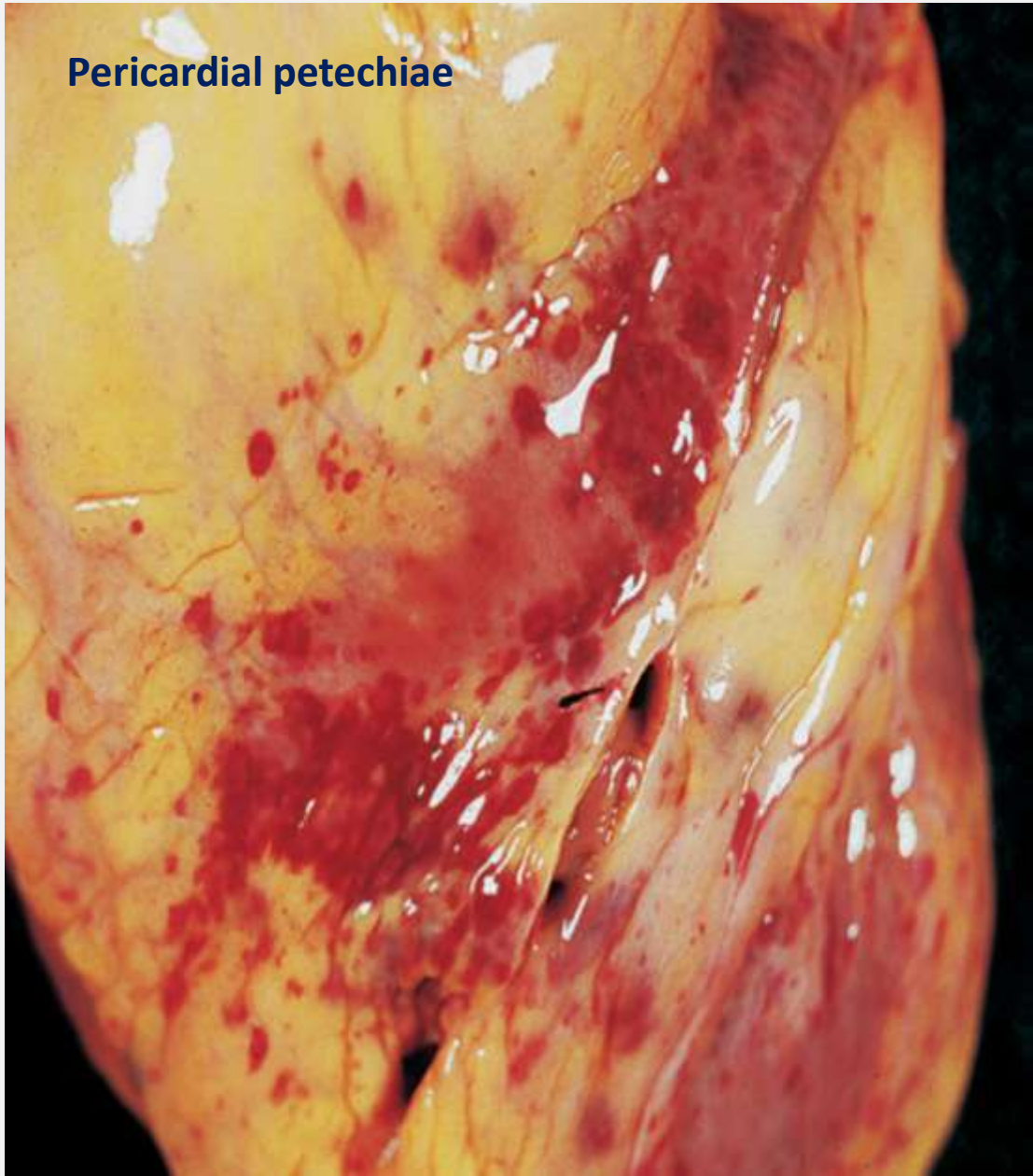
Classification of Hemorrhages

Petechiae

- 1- to 2-mm hemorrhages into skin, mucous membranes, or serosal surfaces

Typically associated with:

- Locally increased intravascular pressure
- thrombocytopenia,
- defective platelet function, or
- clotting factor deficiencies.

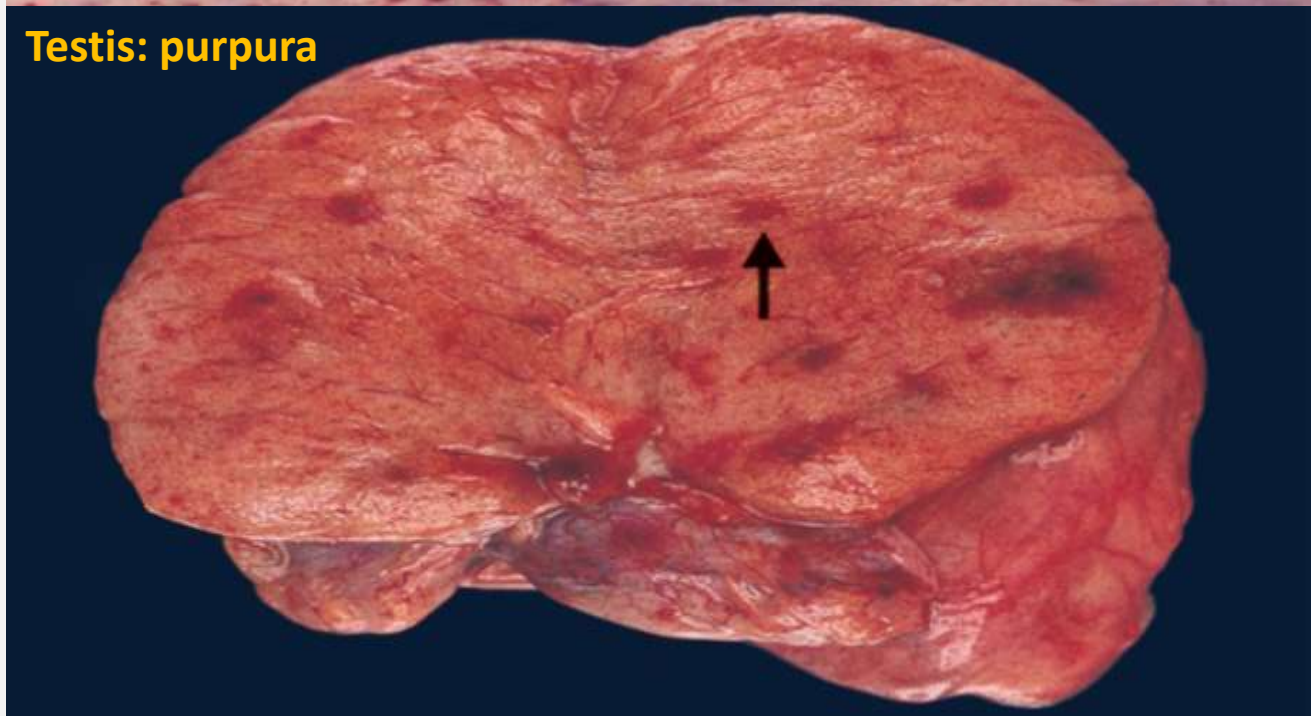


Purpura

- Are slightly larger (3- to 5-mm) hemorrhages

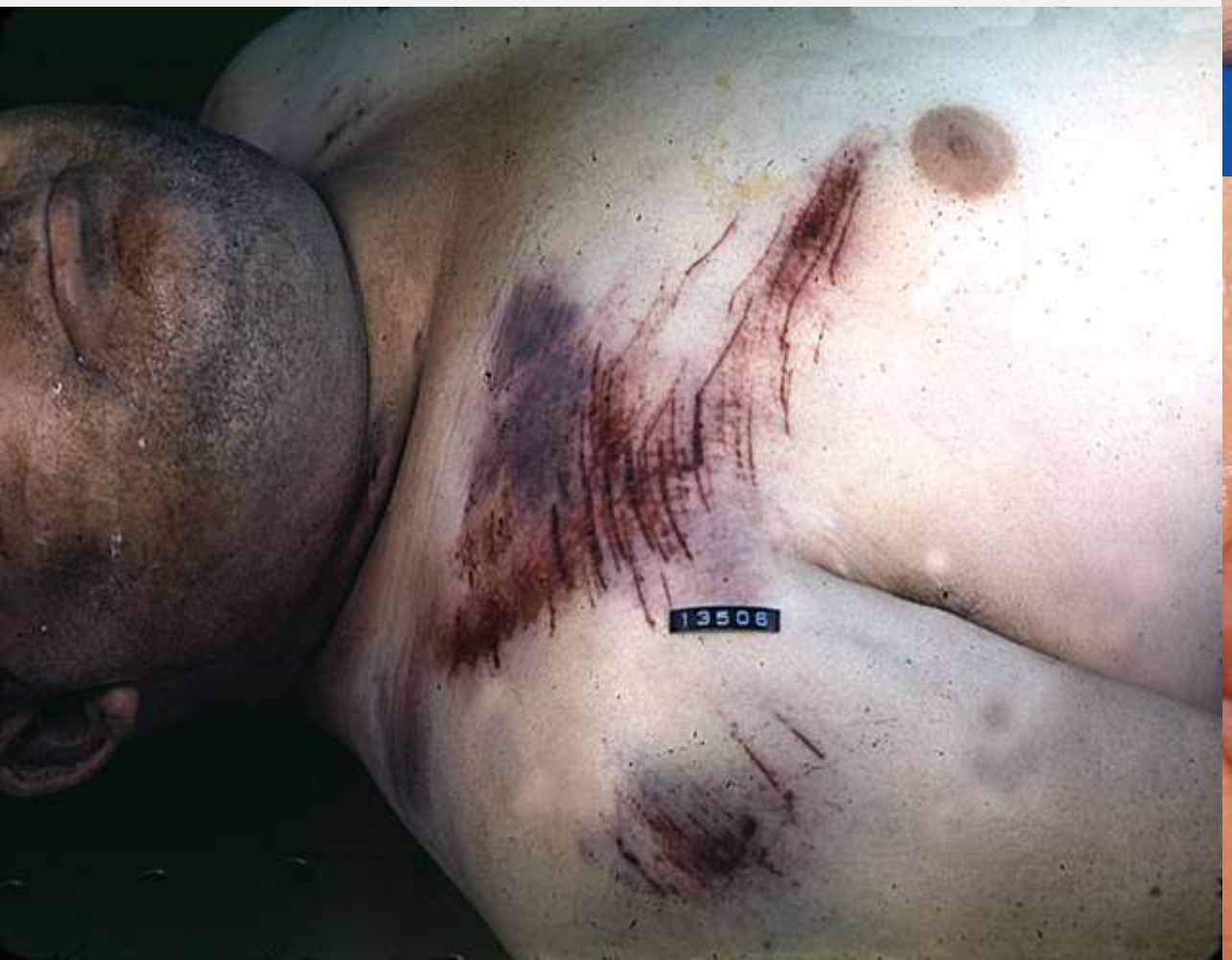
Can occur with

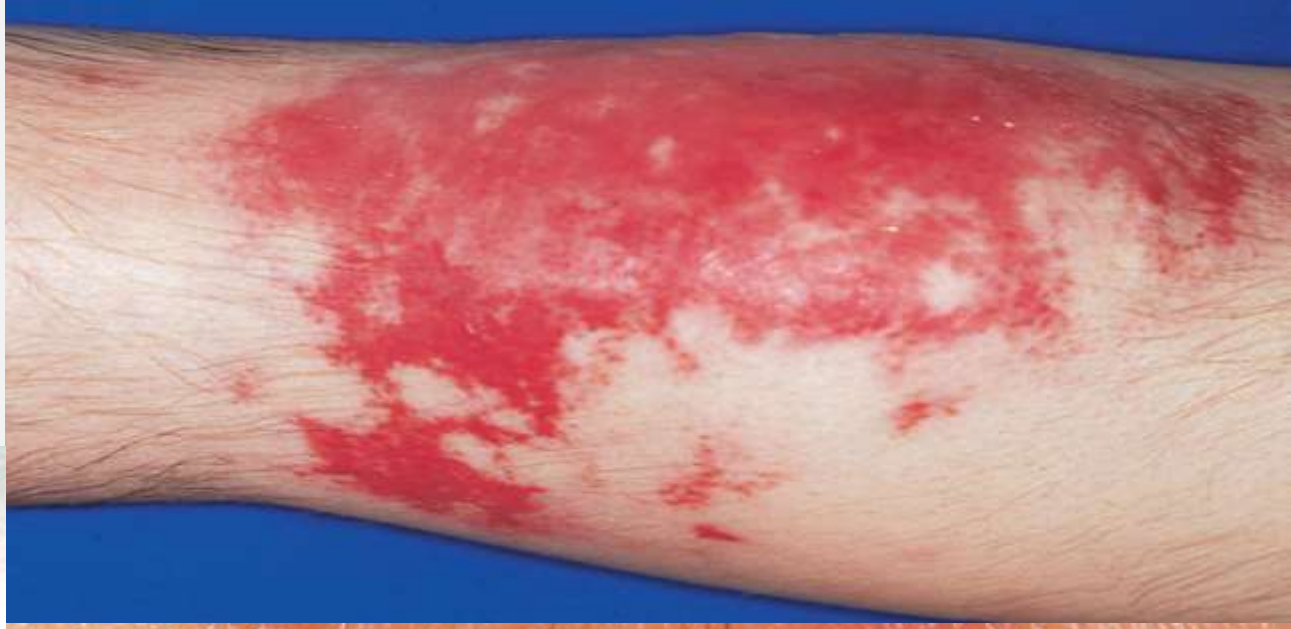
- trauma,
- vasculitis, or
- increased vascular fragility.
- Can be associated with many of the same disorders that cause petechiae

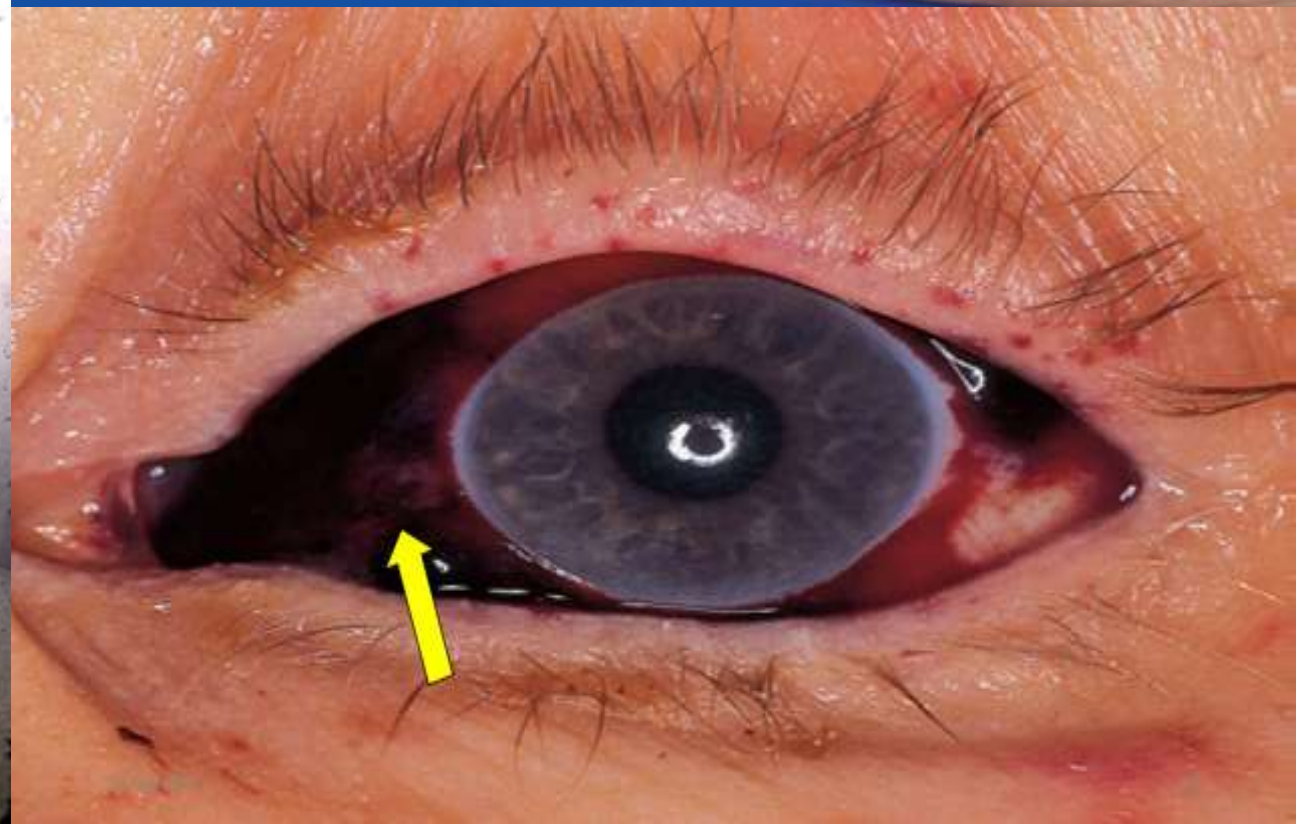


Ecchymoses

- are larger (1- to 2-cm) subcutaneous hematomas (bruises).



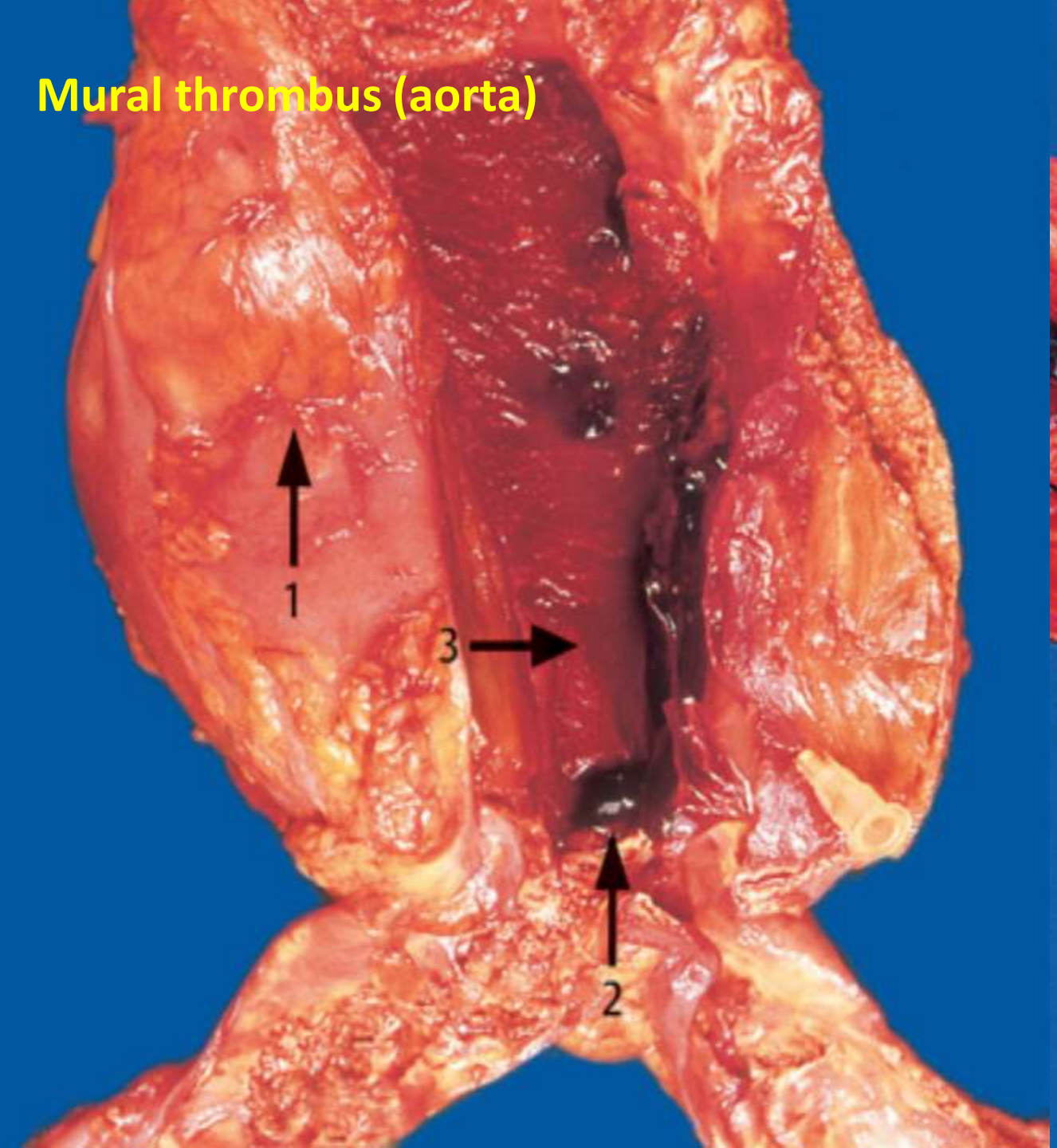


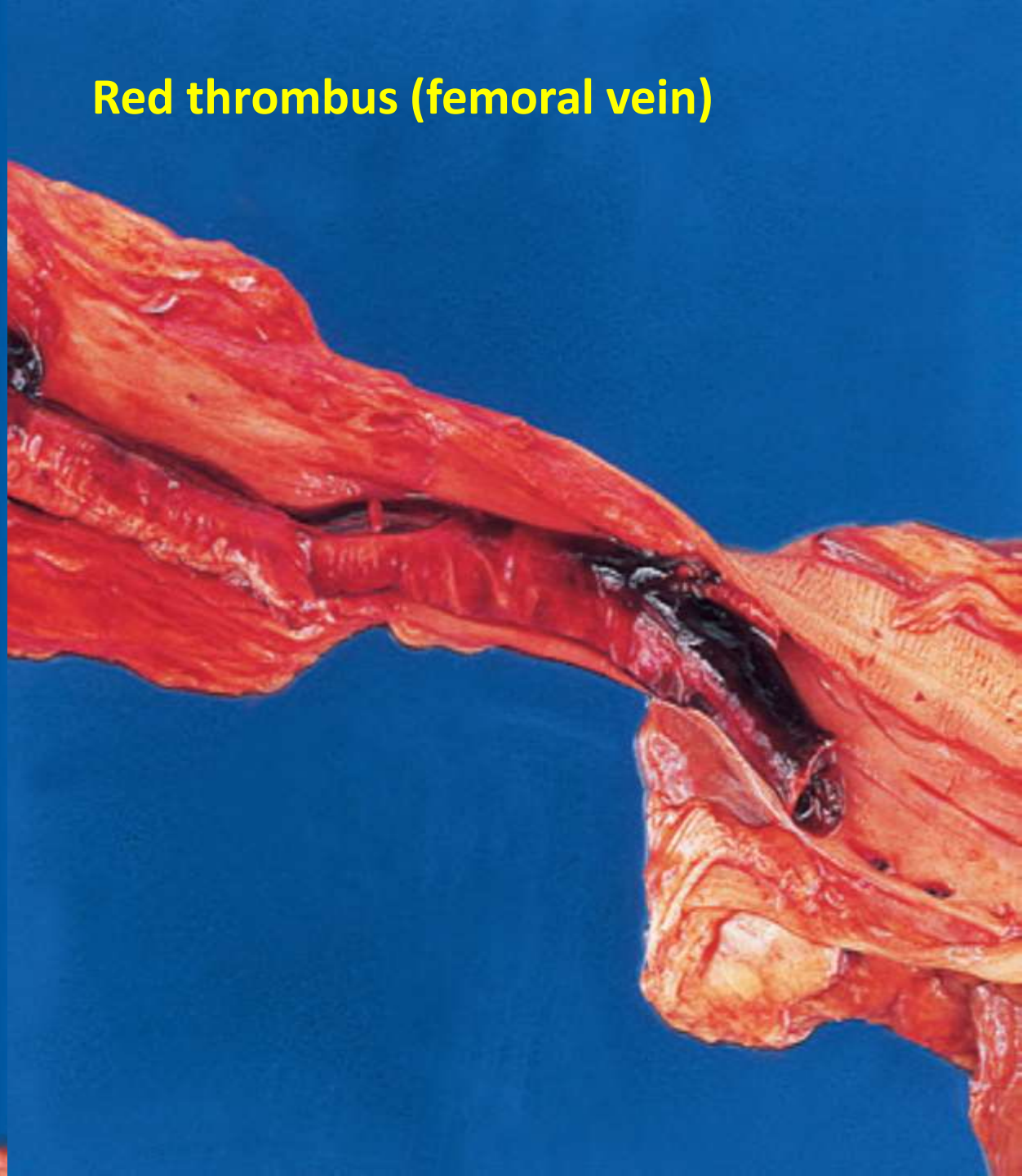


- **Haemorrhage according to location**
  - Epistaxis – blood from nares
  - Hematuria – blood in the urine
  - Haemarthrosis – blood in a joint
  - Haemothorax – blood in the thorax
  - Haemopericardium – blood in the pericardial sac
  - Haemoperitoneum – blood in the abdominal cavity
  - Haemosalpinx – blood in a tube, usually refers to oviduct
  - Hyphema – blood in the anterior chamber of the eye
  - Haemoptysis – coughing up blood
  - Haematemesis – vomiting blood
  - Haematochezia – presence of blood in the stool
  - Melena – presence of tarry blood in the stool

Thrombosis

- Normal ***hemostasis*** is a consequence of tightly regulated processes that maintain blood in a fluid, clot-free state in normal vessels while inducing the rapid formation of a localized hemostatic plug at the site of vascular injury.
- ***Thrombosis*** is the pathologic form of hemostasis
- it involves blood clot (***thrombus***) formation in uninjured vessels or thrombotic occlusion of a vessel after relatively minor injury.
- Thrombi are focally attached to the underlying vascular surface.
- The propagating portion of a thrombus tends to be poorly attached and therefore prone to fragmentation, generating an ***embolus***.


Mural thrombus (aorta)
1
3
2

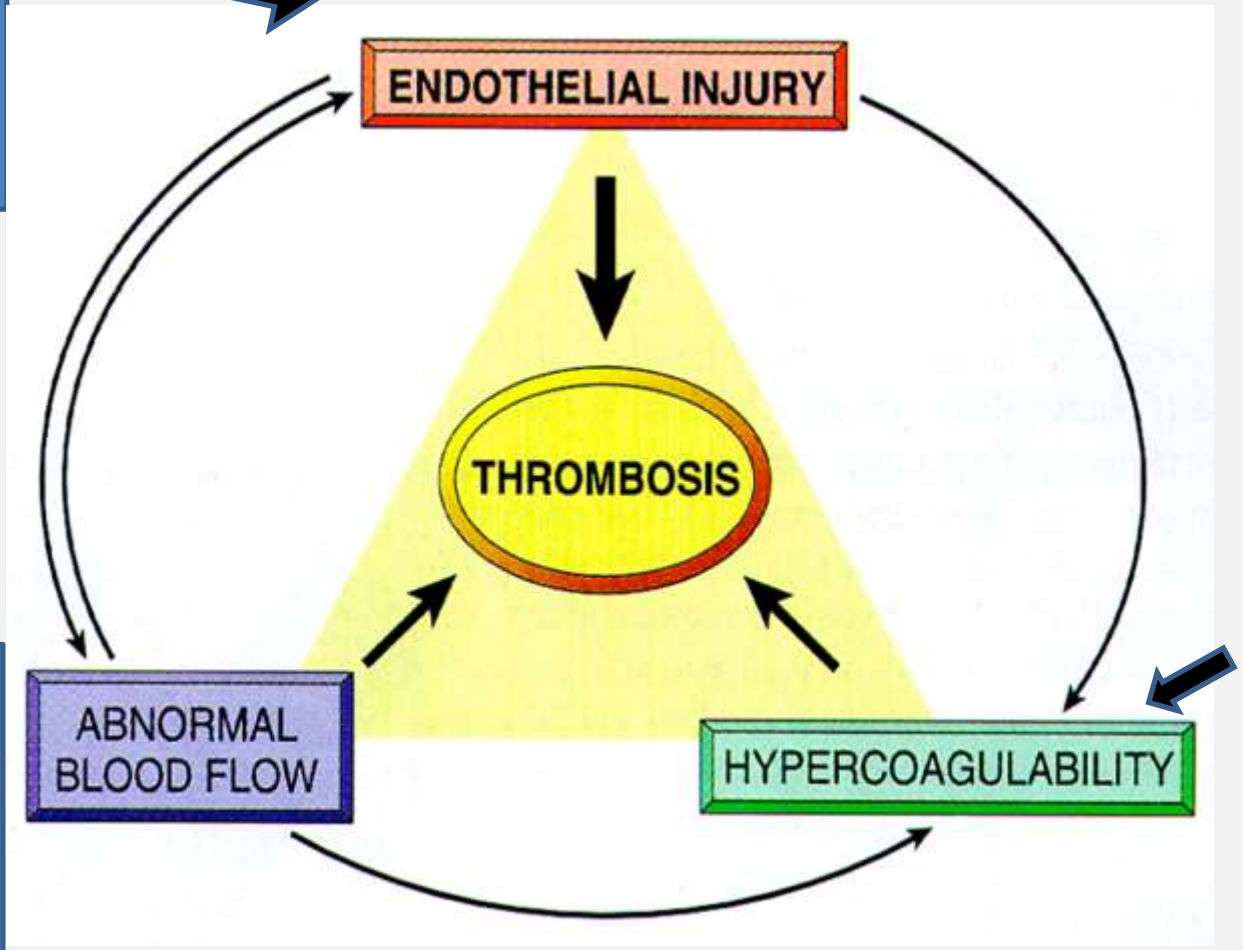

Red thrombus (femoral vein)

Pathogenesis of Thrombosis

- There are three primary influences on thrombus formation (called ***Virchow's triad***):
  - (1) endothelial injury,
  - (2) stasis or turbulence of blood flow, and
  - (3) blood hypercoagulability.

Pathogenesis of Thrombosis

- **Physical loss of endothelium**
- **Significant endothelial dysfunction** due to hypertension, nicotine, radiation, lipids, etc

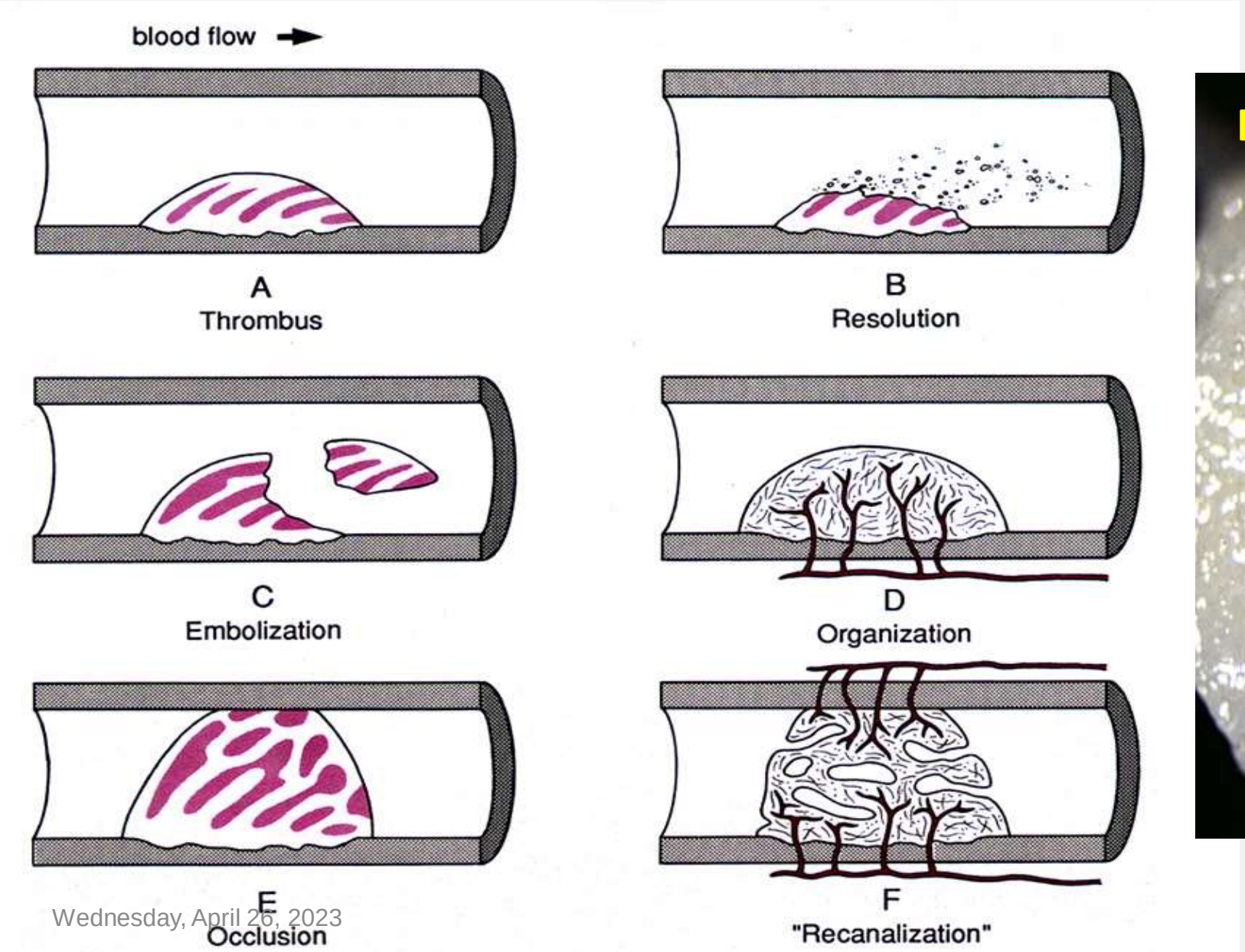


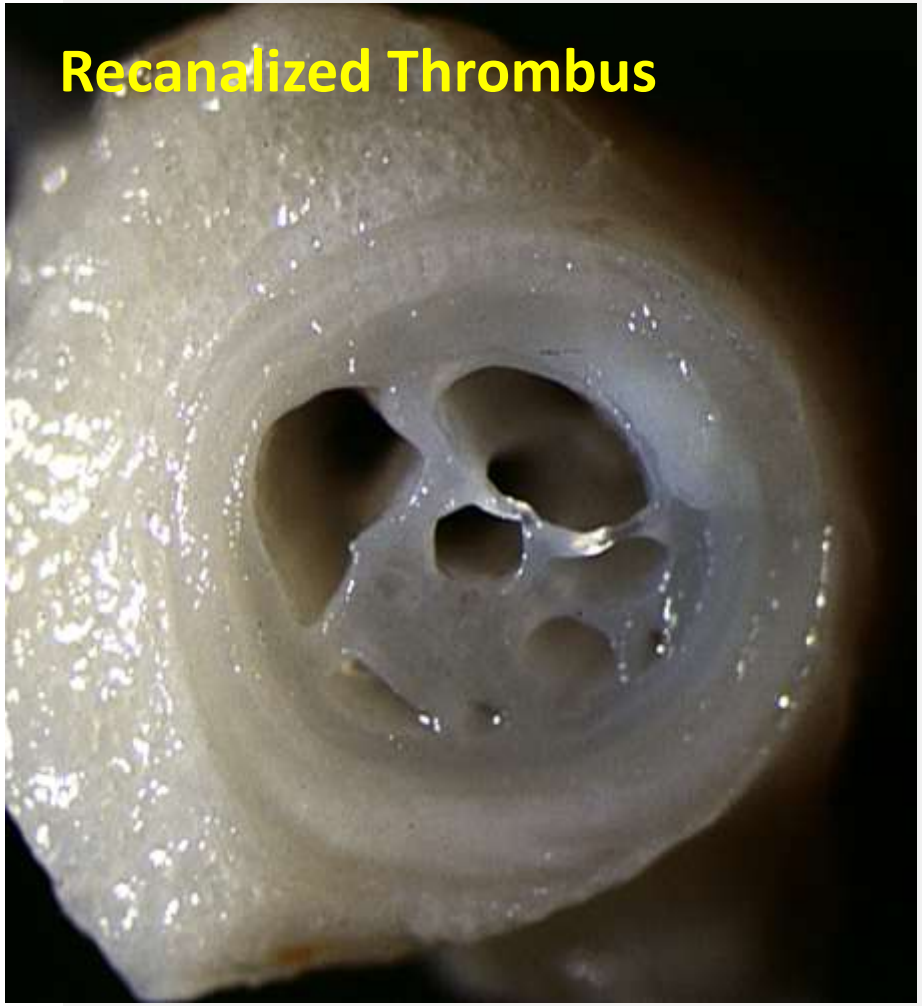
Stasis and turbulence Disrupt laminar flow and bring platelets into contact with the endothelium, Prevent dilution of activated clotting factors by fresh-flowing blood, Retard the inflow of clotting factor inhibitors and permit the buildup of thrombi, etc

Risk factors:

- **mutations in the factor V gene and the prothrombin**
- **oral contraceptive use**
- **pregnancy**
- **disseminated cancers**
- **advancing age**
- **Smoking**
- **obesity.**

Fate of the Thrombus





Clinical Correlations:

Venous versus Arterial Thrombosis

- Arterial thrombi tend to grow in a retrograde direction from the point of attachment, while venous thrombi extend in the direction of blood flow (thus both tend to propagate toward the heart).
- Venous thrombi can cause **congestion** and **oedema** in vascular beds distal to an obstruction, and have capacity to **embolize** to the lungs and cause **death**.
- Conversely, while arterial thrombi can embolize and even cause downstream tissue **infarction**, their role in **vascular obstruction** at critical sites (e.g., coronary and cerebral vessels) is much more significant clinically.

Thrombus - Morphology

Arterial

- Almost always arise from heart
- Grow in retrograde fashion (direction of flow)
- Forms at site of Endothelial injury (AS), turbulence (aneurysms)
- Pale/ white
- Lines of Zahn
- Firmly adherent to vessel wall
- From emboli → Cause infarctions (lower extremities – 75%, Brain, Kidney, spleen)

Venous

- Deep veins (popleteal → Femoral → Iliac),
- Antigrade (towards heart-direction of flow)
- At site of stasis (lower extremities)
- Red / dark
- No lines of Zahn
- Loosely attached (easily embolize)
- Emboli cause Pulmonary embolism (silent in 50% of pts.)

Antemortem Thrombi.

1. Gross- Dry,granular,firm,friable
2. Adherant to vessel wall.
3. Shape- May or may not fit their vascular contours.
4. Surface contains apparent lines of Zahn.

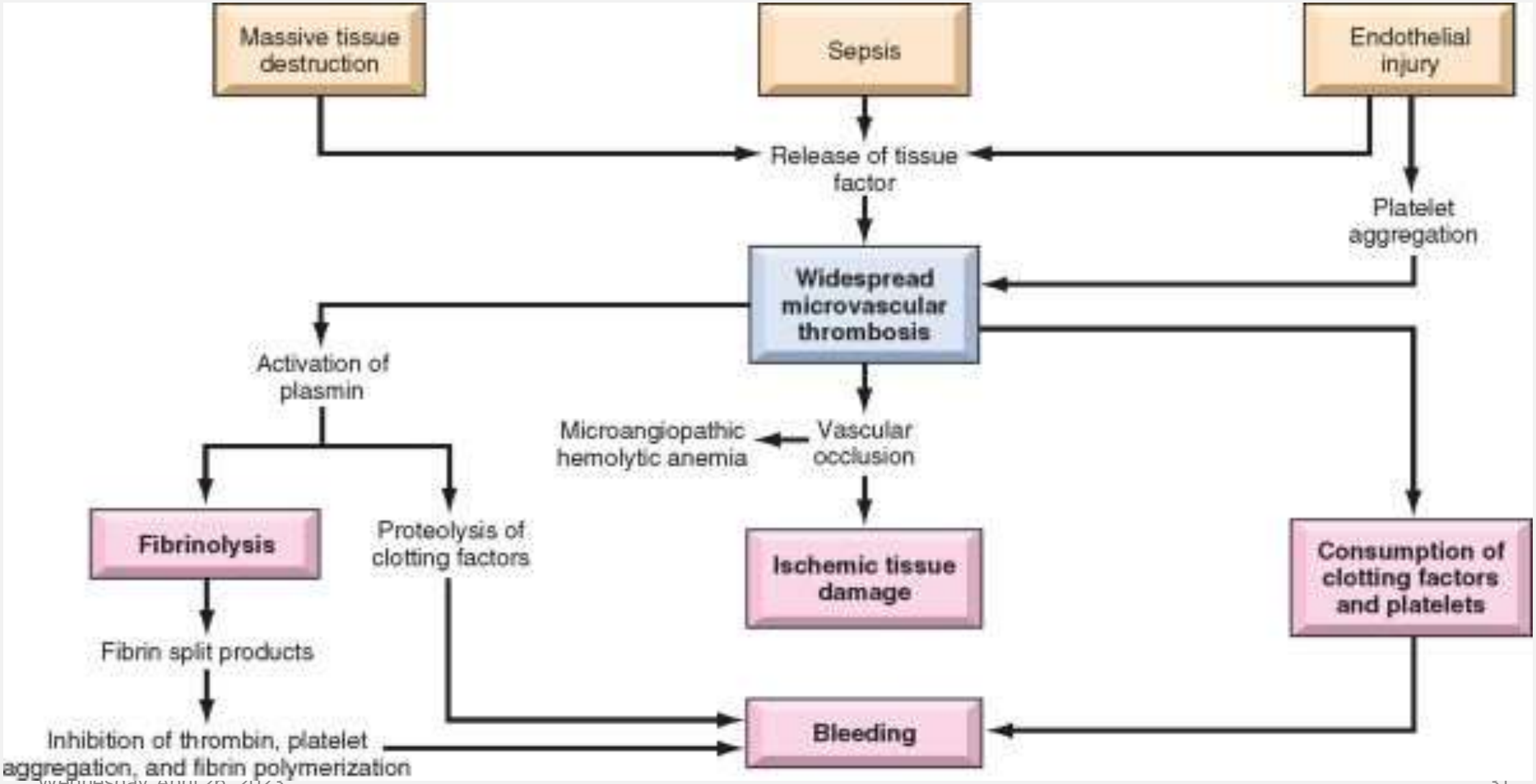
Postmortem clots.

1. Gross-Gelatinous, soft, rubbery.
2. Weakly attached.
3. Take the shape of vessel or its bifurcation.
4. The surface is chicken fat yellow covering the underlying red currant jelly.

Disseminated Intravascular Coagulation

- **Definition**: Thrombohemorrhagic disorder which occurs as a secondary complication in a variety of diseases.
- **Aetiology**: systemic activation of the coagulation pathways, leading to the formation of thrombi throughout the microcirculation.
- Can give rise to either tissue hypoxia and microinfarcts or to a bleeding disorder.

Aetiology, Pathogenesis & Complication of DIC

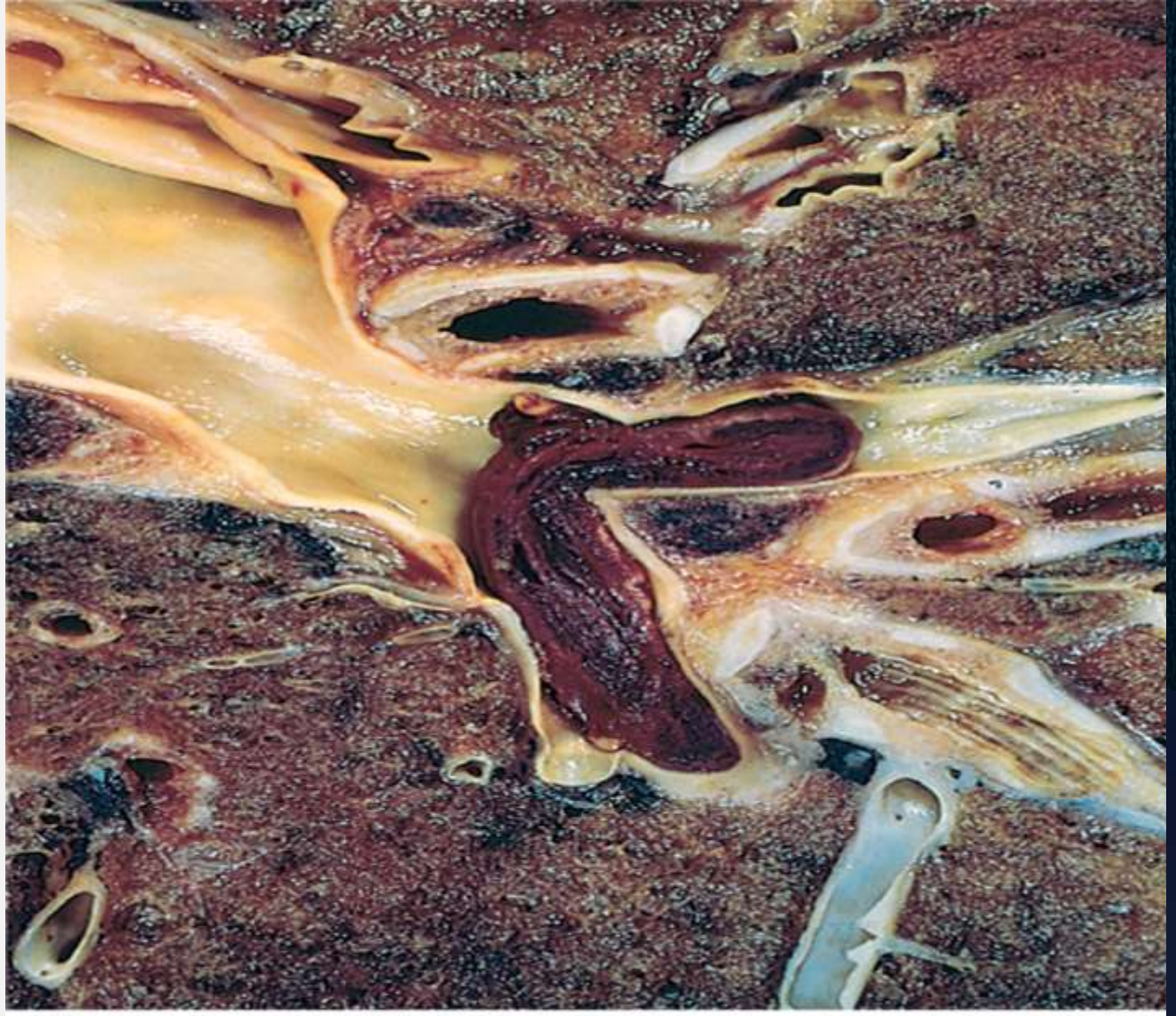


Clinical Course of DIC

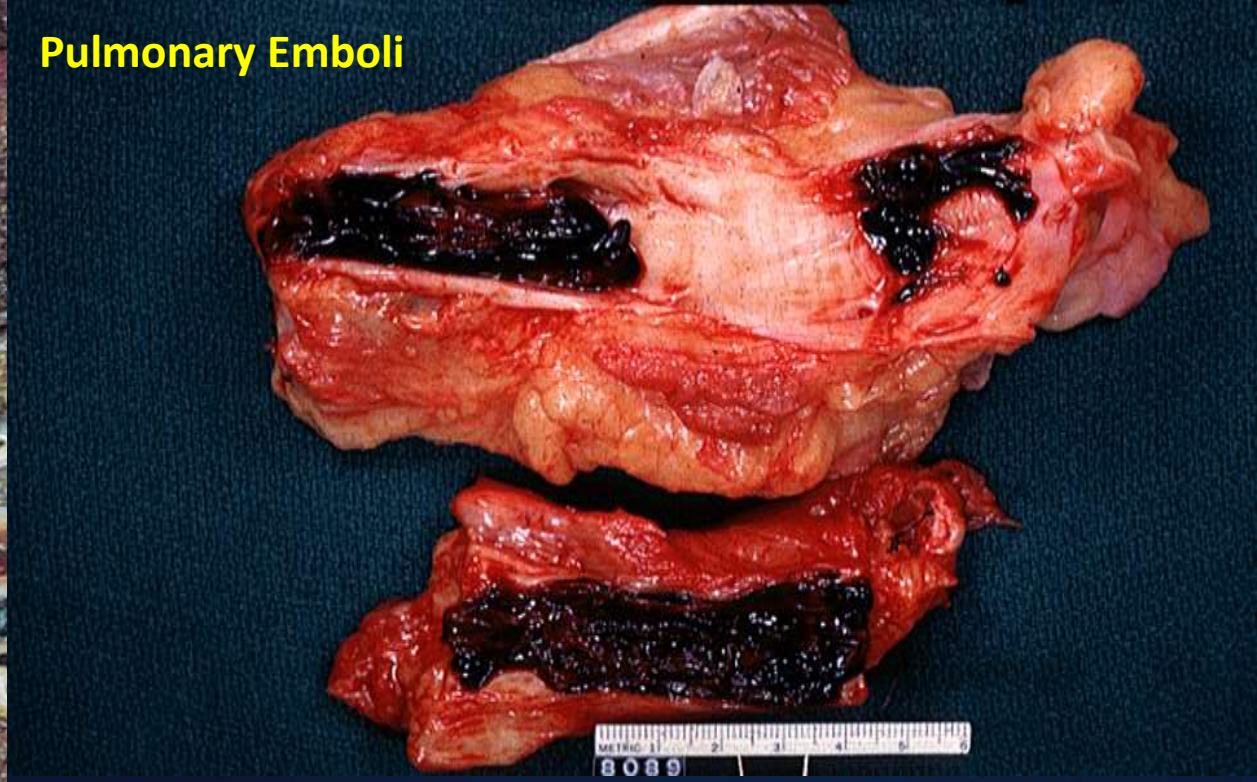
- In general, acute DIC is dominated by a bleeding diathesis, whereas chronic DIC tends to present with symptoms related to thrombosis.
- The manifestations may be minimal, or there may be shock, with acute renal failure, dyspnea, cyanosis, convulsions, and coma.
- There may be severe hemorrhage into the gut or urinary tract.
- Thrombocytopenia and prolongation of PT and PTT (resulting from depletion of platelets, clotting factors, and fibrinogen).
- Fibrin split products are increased in the plasma.

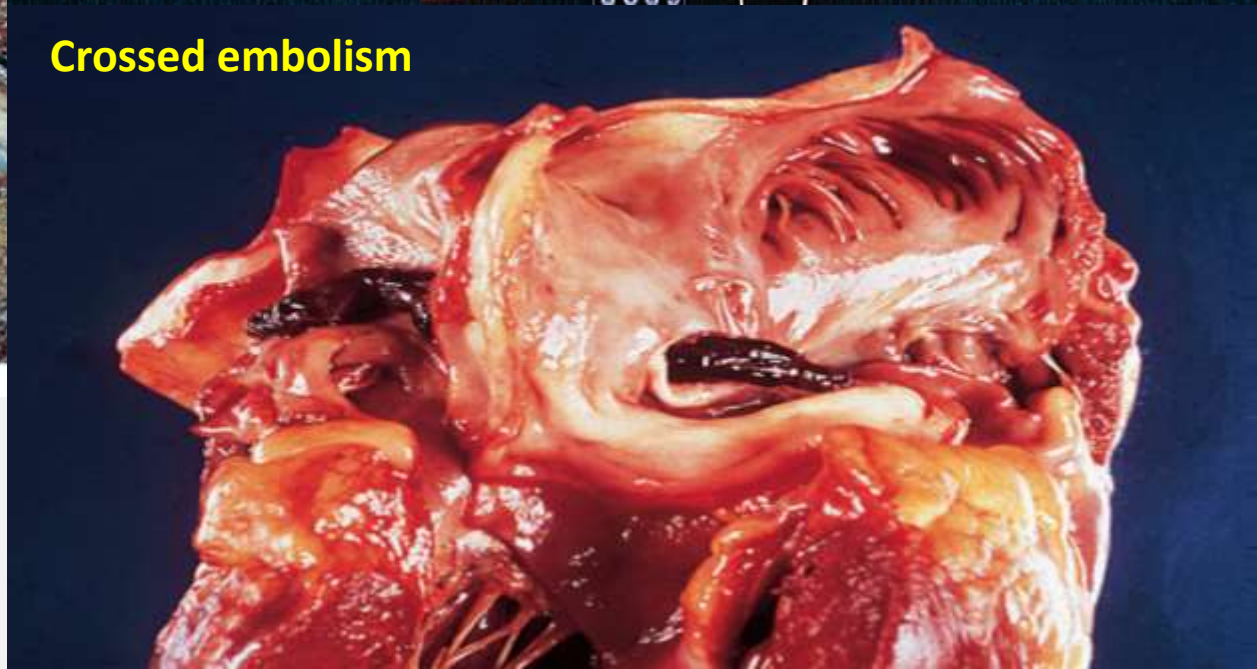
Embolism

- **An *embolus* is a detached intravascular solid, liquid, or gaseous mass that is carried by the blood to a site distant from its point of origin.**
- Virtually 99% of all emboli represent some part of a dislodged thrombus, hence the term ***thromboembolism***.
- Rare forms of emboli include fat droplets, bubbles of air, atherosclerotic debris (cholesterol emboli), tumor fragments, bits of bone marrow, or foreign bodies such as bullets.
- Inevitably, emboli lodge in vessels too small to permit further passage, resulting in partial or complete vascular occlusion.
- The consequences of thromboembolism include ischemic necrosis (infarction) of downstream tissue.



Saddle Embolus derived from a lower extremity deep venous thrombosis and now impacted in a pulmonary artery branch.





Pulmonary Vs Systemic Thromboembolism

- In more than 95% of cases of pulmonary thromboembolism, venous emboli originate from deep leg vein thrombi above the level of the knee.
- Systemic thromboembolism refers to emboli in the arterial circulation. Most (80%) arise from intracardiac mural thrombi.
- In contrast to venous emboli, which tend to lodge primarily in one vascular bed (the lung), arterial emboli can travel to a wide variety of sites.

Amniotic Embolism

- The underlying cause is entry of amniotic fluid (and its contents) into the maternal circulation via a tear in the placental membranes and rupture of uterine veins

Fat Embolism

- Microscopic fat globules can be found in the circulation after fractures of long bones (which contain fatty marrow) or after soft-tissue trauma.

Air Embolism

- Gas bubbles within the circulation can obstruct vascular flow (and cause distal ischemic injury).
- Air may enter the circulation during obstetric procedures or as a consequence of chest wall injury.
- When air is breathed at high pressure (e.g., during a deep-sea dive), increased amounts of gas (particularly nitrogen) become dissolved in the blood and tissues.
- If the diver then ascends (depressurizes) too rapidly, the nitrogen expands in the tissues and bubbles out of solution in the blood to form gas emboli.

Infarction

- **An infarct is an area of ischemic necrosis caused by occlusion of either the arterial supply or the venous drainage in a particular tissue.**
- Nearly 99% of all infarcts result from thrombotic or embolic events, and almost all result from arterial occlusion.
- infarction may also be caused by other mechanisms, such as local vasospasm, expansion of an atheroma secondary to intraplaque hemorrhage, or vascular compression, vessel twisting, or traumatic vessel rupture.
- Infarcts caused by venous thrombosis are more likely in organs with a single venous outflow channel (e.g., testis and ovary).

Morphology of Infarcts

- Infarcts are classified on the basis of their color (reflecting the amount of hemorrhage) and the presence or absence of microbial infection. Therefore, infarcts may be either red (hemorrhagic) or white (anemic) and may be either septic or bland.

Red infarcts occur with venous occlusions;

- in loose tissues (eg. lung) that allow blood to collect in the infarcted zone;
- in tissues with dual circulations eg. lung and small intestines;
- in tissues that were previously congested because of sluggish venous outflow;
- when flow is re-established to a site of previous arterial occlusion and necrosis.

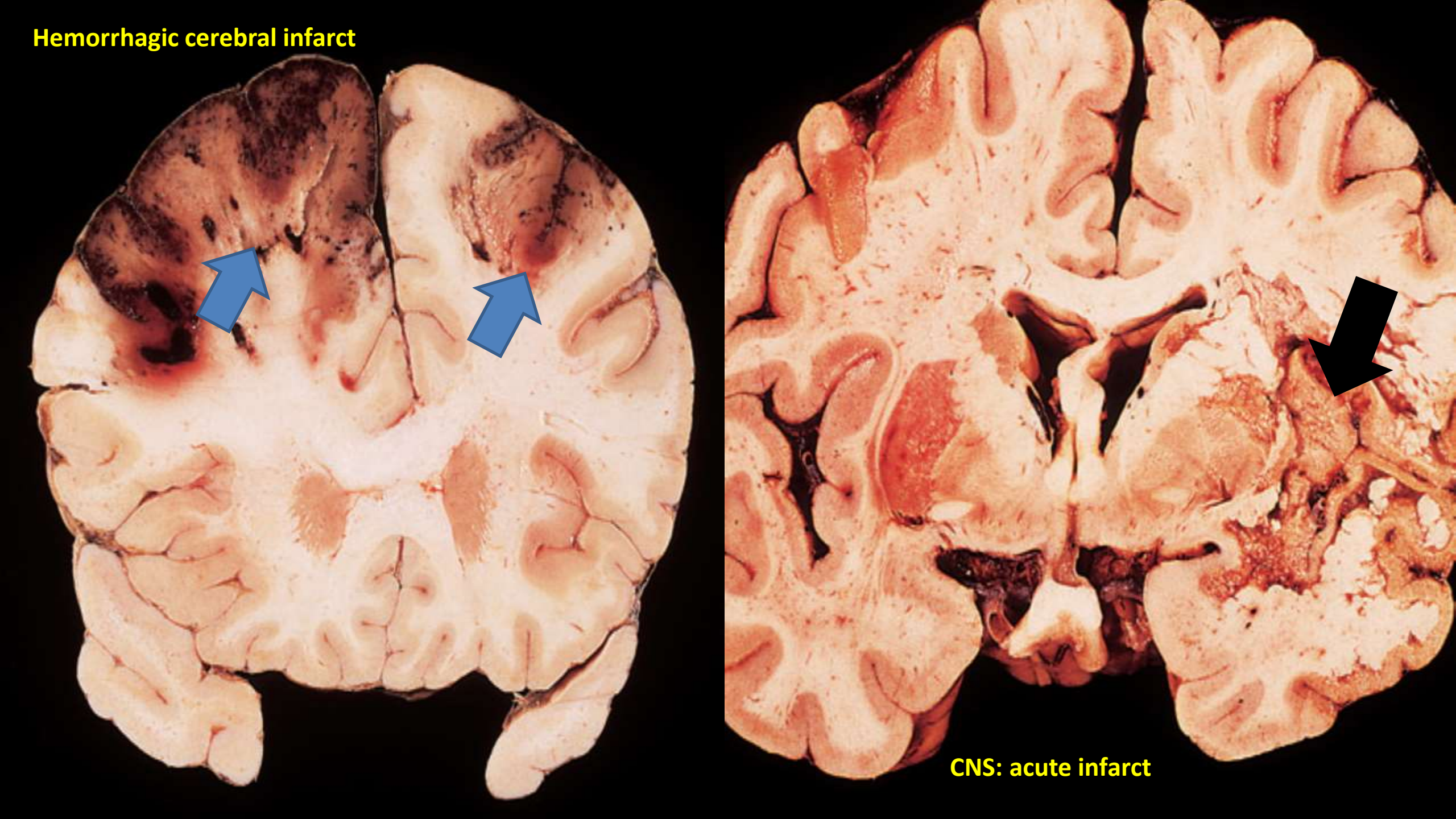
White infarcts

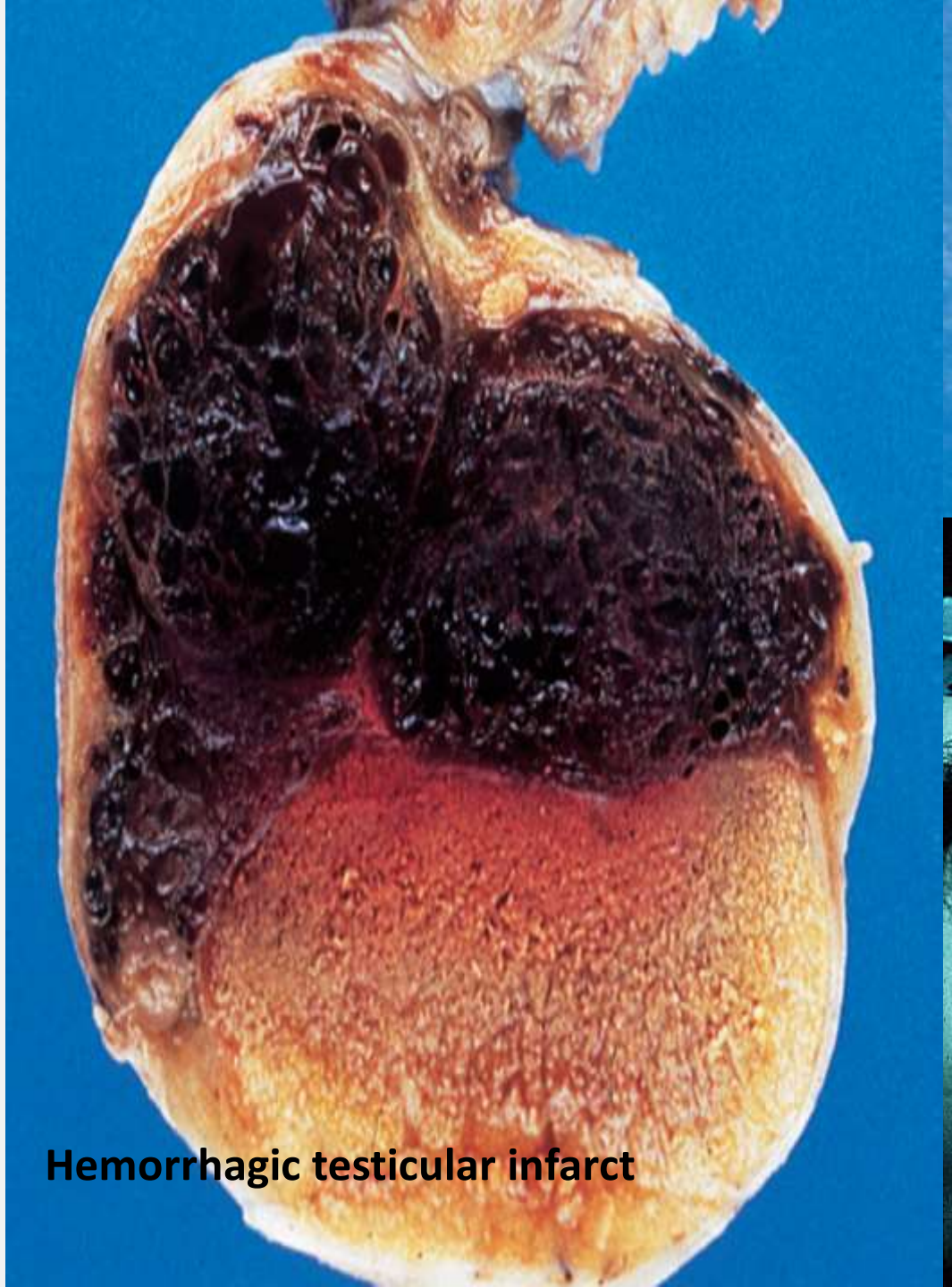
- occur with arterial occlusions or in solid organs, where the solidity of the tissue limits the amount of hemorrhage that can seep into the area of ischemic necrosis from adjoining capillary beds.
- In solid organs, the relatively few extravasated red cells are lysed, with the released hemoglobin remaining in the form of hemosiderin.
- Thus, infarcts resulting from arterial occlusions typically become progressively more pale and sharply defined with time.

- In spongy organs, by comparison, the hemorrhage is too extensive to permit the lesion ever to become pale.

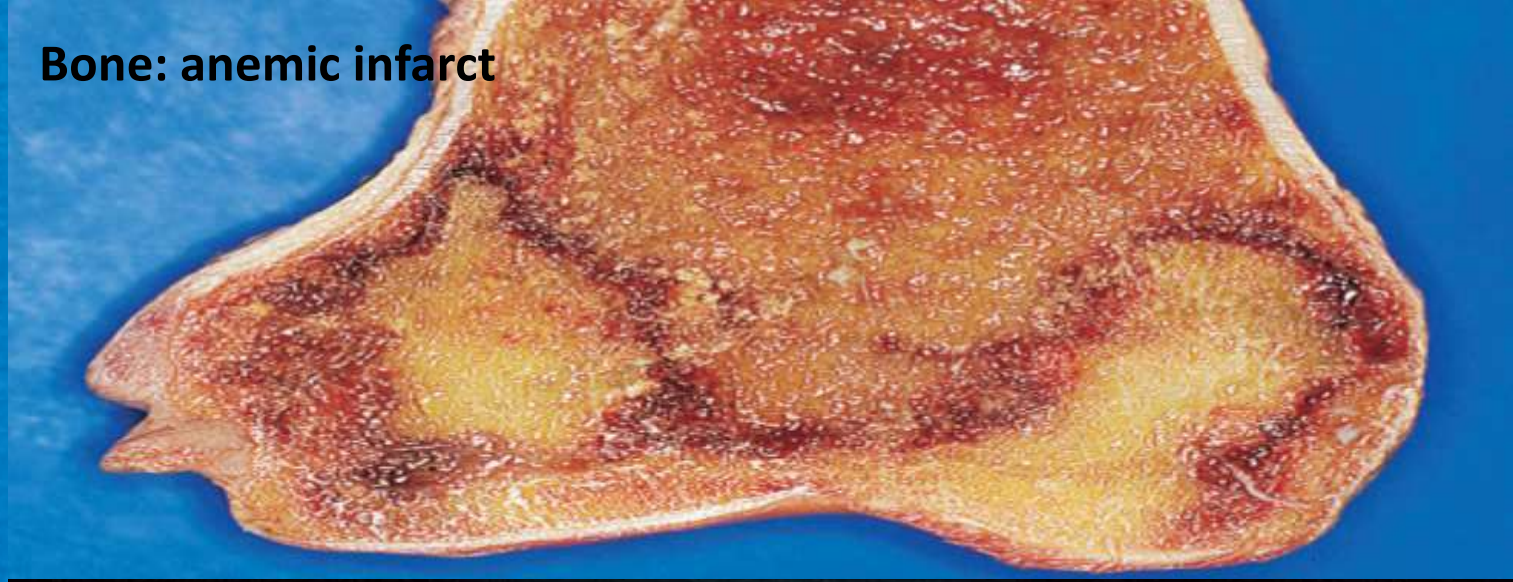
Septic infarctions

- occur when bacterial vegetations from a heart valve embolize or when microbes seed an area of necrotic tissue.
- In these cases the infarct is converted into an abscess, with a correspondingly greater inflammatory response.

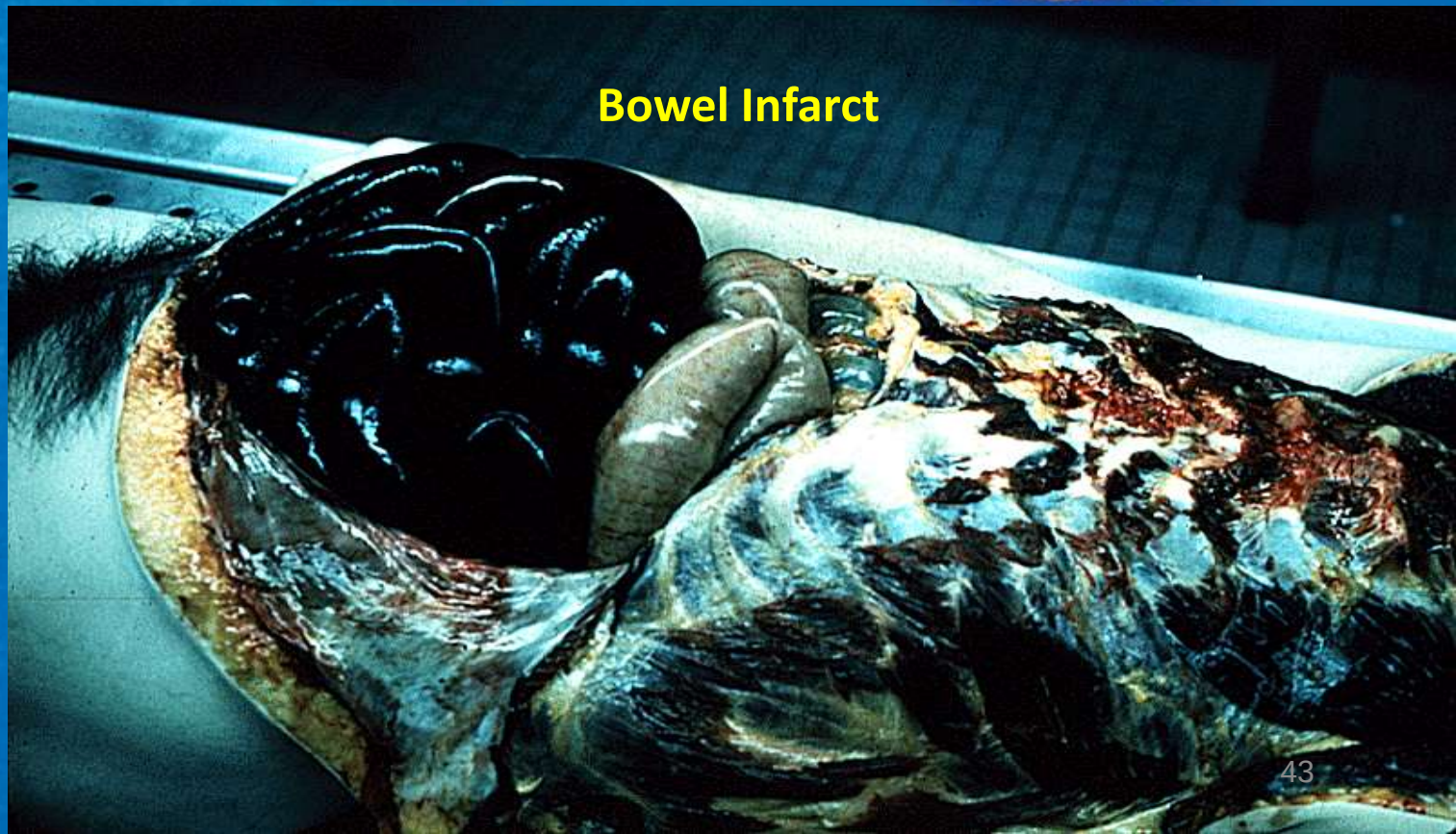

Hemorrhagic cerebral infarct
CNS: acute infarct



Hemorrhagic testicular infarct



Bone: anemic infarct



Bowel Infarct

Factors That Influence Development of an Infarct

1. The availability of an alternative blood supply

- This is the most important determinant of whether occlusion of a vessel will cause damage.
- The lungs, liver, the hand and forearm, with their dual arterial supply, are all relatively resistant to infarction.
- In contrast, renal and splenic circulations are end-arterial, and obstruction of such vessels generally causes infarction.

2. Slowly developing occlusions

- Are less likely to cause infarction because they provide time for the development of alternative perfusion pathways.

3. The susceptibility of a tissue to hypoxia

- This influences the likelihood of infarction.
- Neurons undergo irreversible damage when deprived of their blood supply for only 3 to 4 minutes.
- Myocardial cells die after only 20 to 30 minutes of ischemia.
- In contrast, fibroblasts within myocardium remain viable after many hours of ischemia.

4. The partial pressure of oxygen in blood.

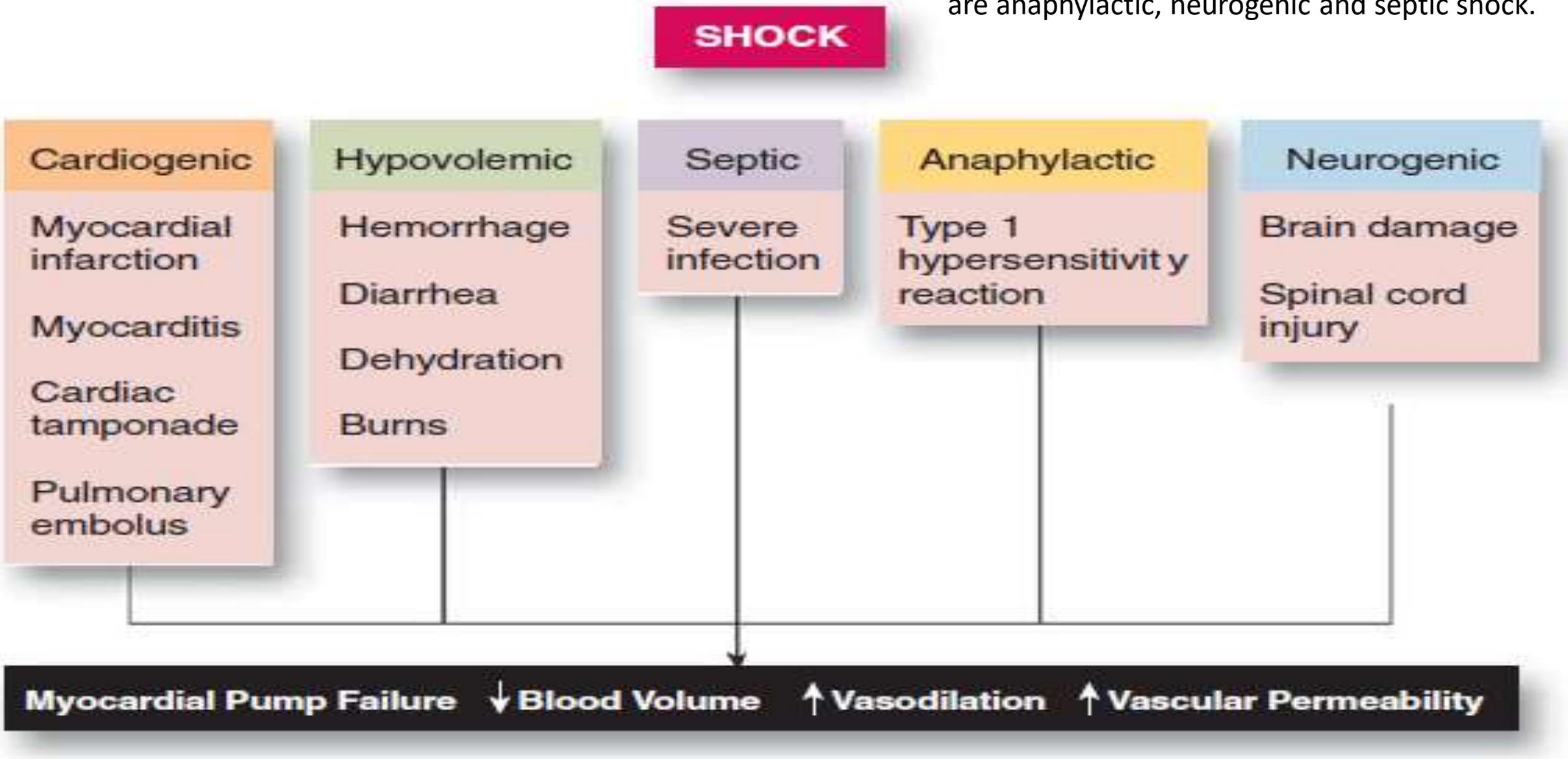
- Partial flow obstruction of a small vessel in an anemic or cyanotic patient might lead to tissue infarction, whereas it would be without effect under conditions of normal oxygen tension.
- In this way congestive heart failure, with compromised flow and ventilation, could cause infarction in the setting of an otherwise inconsequential blockage.

Shock

- **Shock is the final common pathway for a number of potentially lethal clinical events, including severe hemorrhage, extensive trauma or burns, large myocardial infarction, massive pulmonary embolism, and microbial sepsis.**
- Shock gives rise to systemic hypoperfusion; it can be caused either by reduced cardiac output or by reduced effective circulating blood volume.
- The end results are hypotension, impaired tissue perfusion, and cellular hypoxia.

Types Of Shock

Distributive Shock is a condition where the flow of blood is not evenly distributed. It is an umbrella for three other forms of shock which are anaphylactic, neurogenic and septic shock.



Pathophysiology of Shock

- The first stage is called the **initial phase**. Here the cardiac output tends to decrease, causing an impairment of tissue perfusion.
- Shock may progress to the second phase called **compensatory stage** if the cell has not been supplied with oxygen.
- The compensatory phase is the stage where the body alters its hemodynamic function to compensate for the poor tissue perfusion.
- The heart rate increase, the blood vessels begin constriction and the body begin to retain sodium and water.

- As the stage progresses, the blood glucose levels rises and the pulmonary respiratory rate increases (hyperventilation) in an attempt to blow off the effects of lactic acidosis produced in the first phase where the body switched over from aerobic to anaerobic metabolism.
- These changes set the stage for the progressive phase.
- The **progressive phase** is characterized by the beginning of the failure of the compensatory phase to bring back the body back to equilibrium.

- In this phase the cells are functioning on aerobic metabolism which does not produce enough energy to sustain cellular life and cells begin to die.
- Those cells that survive begins to see a failure of their sodium-potassium pumps which causes cell swelling.
- If left unchecked the progressive phase can cycle into the **refractory phase** which is characterized by multi-organ failure which may lead to death.

Clinical Course of Shock

- The clinical manifestations of shock depend on the precipitating insult.
- In hypovolemic and cardiogenic shock, the patient presents with hypotension; a weak, rapid pulse; tachypnea; and cool, clammy, cyanotic skin.
- In septic shock, however, the skin may be warm and flushed as a result of peripheral vasodilation.

- The cardiac, cerebral, and pulmonary changes that occur secondary to the shock state materially worsen the problem.
- If patients survive the initial complications, they enter a second phase, dominated by renal insufficiency and marked by a progressive fall in urine output as well as acidosis, and severe fluid and electrolyte imbalances.

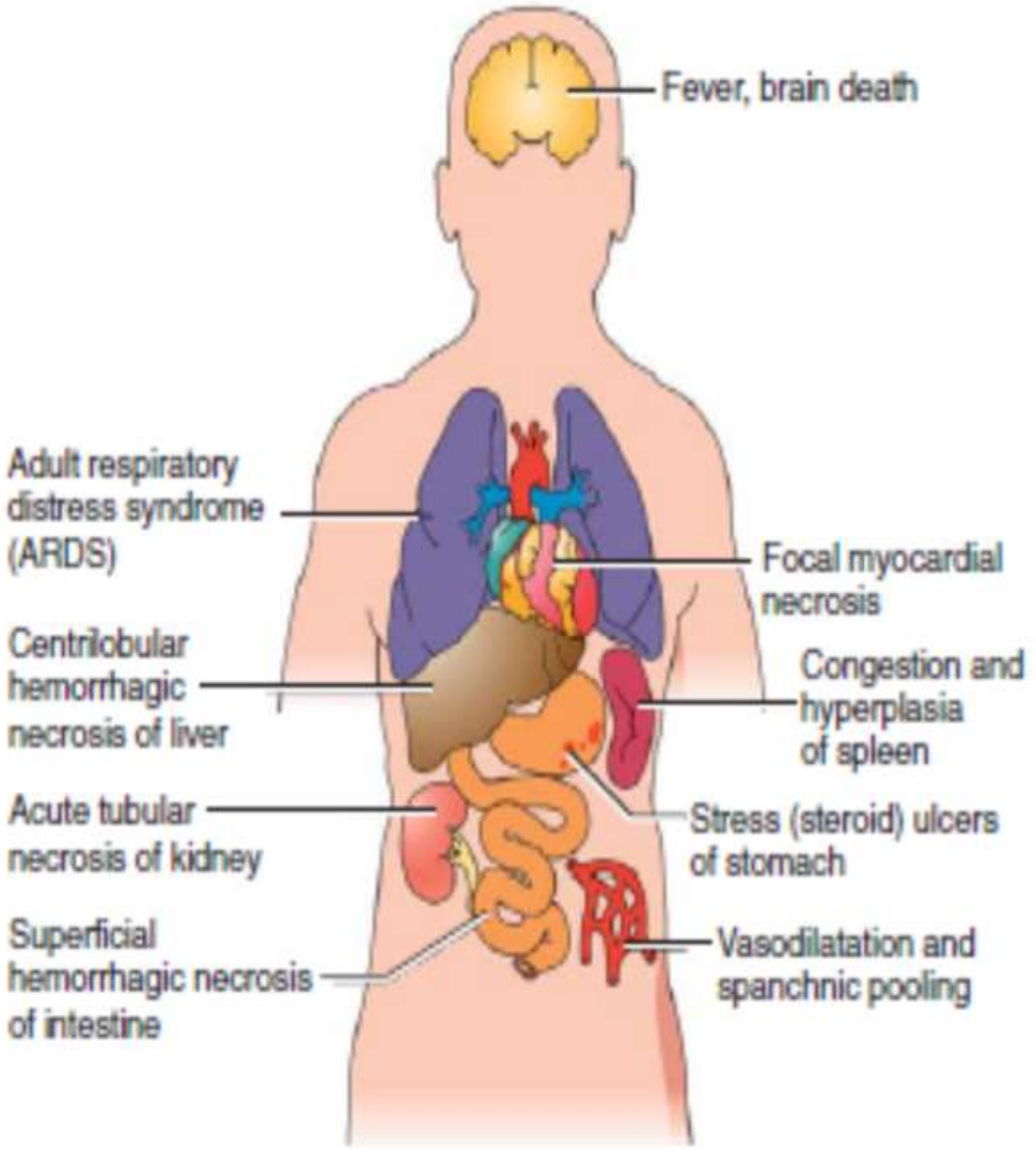


FIGURE 7-33. Complications of shock.

References & Credits

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End Of Lecture

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