Hemodynamic disorders

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Lec 2

Hemostasis:

Normal hemostasis is a consequence of regulated processes that maintain blood in a fluid state in normal vessels.

- **It also permit the rapid formation of a hemostatic clot at the site of a vascular injury.**
- **The pathologic counterpart of hemostasis is thrombosis which involves blood clot formation within intact vessels.**
- **Hemostasis involve three components:**

1- Normal endothelium

2- Normal platelets

3- Normal coagulation cascade

The endothelium has antithrombotic properties which are:

(a) Antiplatelets effect

(b) Anticoagulant properties

(c) Fibrinolytic properties

(d) Prothrombotic properties

Hemostasis: sequences of events after vascular injury:

1- Transient arteriolar vasoconstriction due to reflex ~~neurogenic mechanism & local secretion of endothelial~~ derived vasoconstrictors.

2- Platelets adhere to the exposed sub endothelial extra cellular matrix (ECM) &activated leading to additional platelets aggregation forming primary haemostatic plug.

3- Tissue factors release at site of injury & with platelets factors, there will be activation of coagulation cascade leading to fibrin deposition .

Thrombin activated in coagulation cascade causing further platelets recruitment &secondary hemostasis.

4- Polymerized fibrin & platelets aggregation form solid permanent plug to prevent any further hemorrhage.

THROMBOSIS:

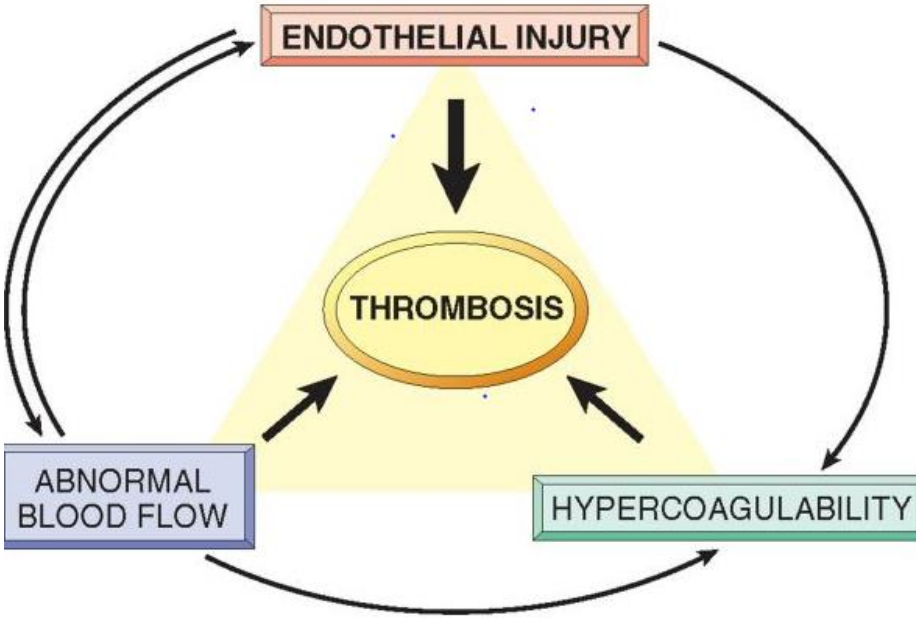
Formation of solid or semisolid mass from blood constituents within the cardiovascular system during life.

Pathogenesis: (virchows triad):

1- Endothelial injury

2- Alteration of blood flow

3- Hypercoagulability



1- Endothelial injury:

a- Myocardial infarction .

b- over atherosclerotic plaque.

c- Trauma or inflammatory vascular injury (myocarditis and vasculitis)

d- Hypertension.

e- Subacute bacterial endocarditis.

2- Alteration of blood flow: either

A- Turbulence: Important in arterial & cardiac thrombosis by causing endothelial injury & local pockets of stasis.

B- Stasis: Is major factors in venous thrombosis.

Both turbulence &stasis cause

1- Disruption of laminar blood flow & bring platelets in contact with endothelium.

2- Prevent dilution of clotting factors by fresh flowing blood.

3- Retard flow of clotting factor inhibitors & permit build up of thrombus.

4- Promote endothelial activation leading to local thrombosis, adhesion of leukocytes

Turbulence & stasis cause thrombosis in:

1- Ulcerated atherosclerotic plaques

2- Aneurysm

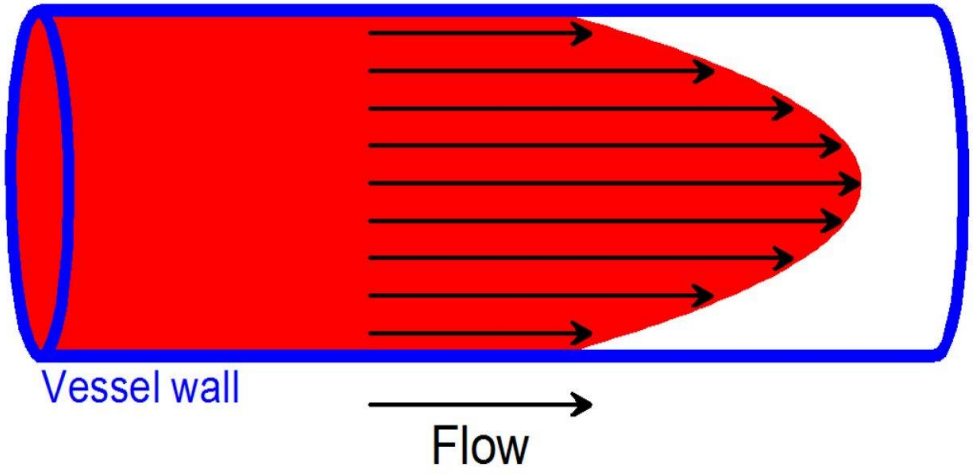
3- Myocardial infarction.

4- Mitral stenosis cause left atrial dilatation& atrial fibrillation leading to stasis & thrombosis

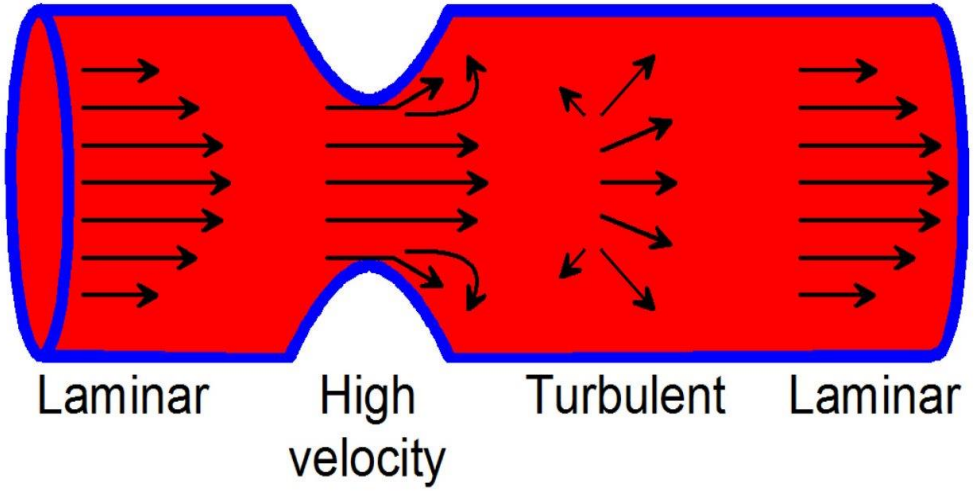
5- Hyperviscosity syndrome e.g polycythemia causing stasis in small vessels

6- Sickle cell anemia causing small vessels occlusion leading to stasis and thrombosis.

Laminar blood flow



Turbulent blood flow



3- Hypercoagulablity:

Divided into primary & secondary disorders.

Primary disorders

As in mutation in factor V and Inherited mutation of antithrombin III, protein C&S leading to venous thrombosis & recurrent thromboembolism in adolescent& early adult life.

Secondary disorders:

1- Heart failure or trauma causing vascular endothelial injury or stasis.

2- Oral contraceptive pills because of increase hepatic synthesis of coagulation factors& decrease synthesis of antithrombin III.

3- Dissemenated tumors because of release of procoagulant tumor products.

4- Advancing age because of increase platelets aggregation & decrease PGI2 by endothelium.

5- Smoking.

6- Obesity

7- Lupus anticoagulants which are antibodies directed against anionic phospholipids & high frequency of venous & arterial thrombosis .

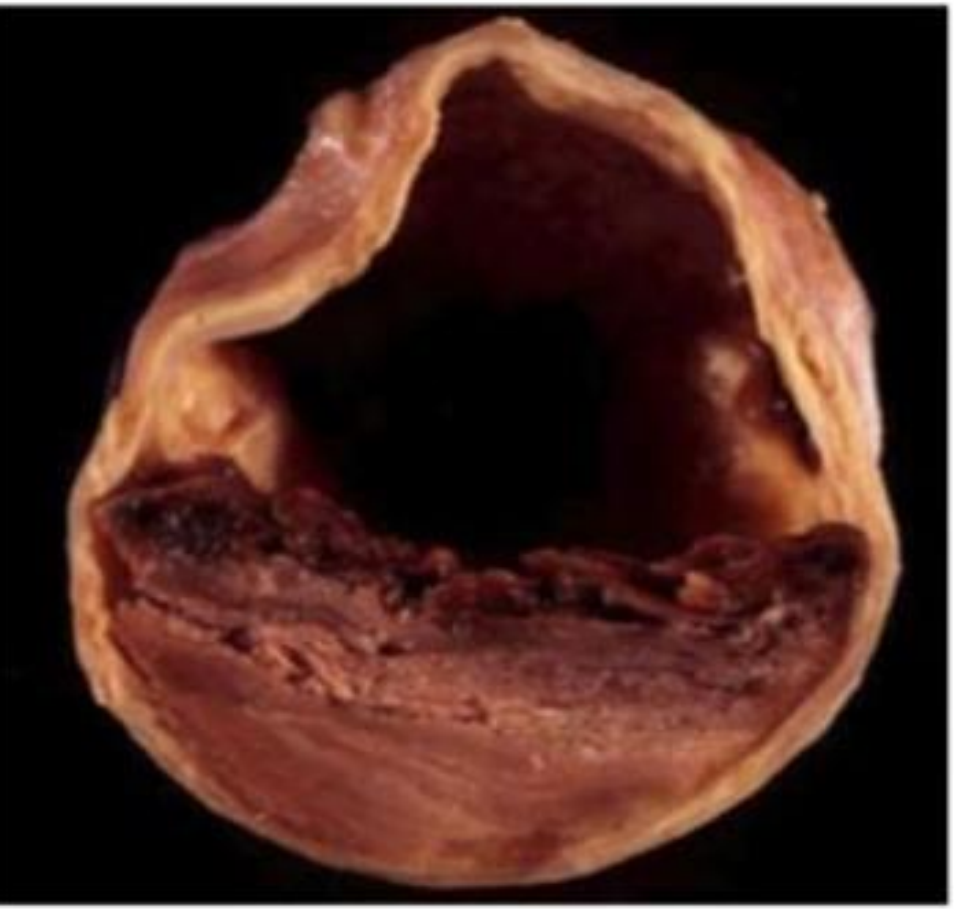
Those patients may have SLE or thrombosis is the only clinical manifestation.

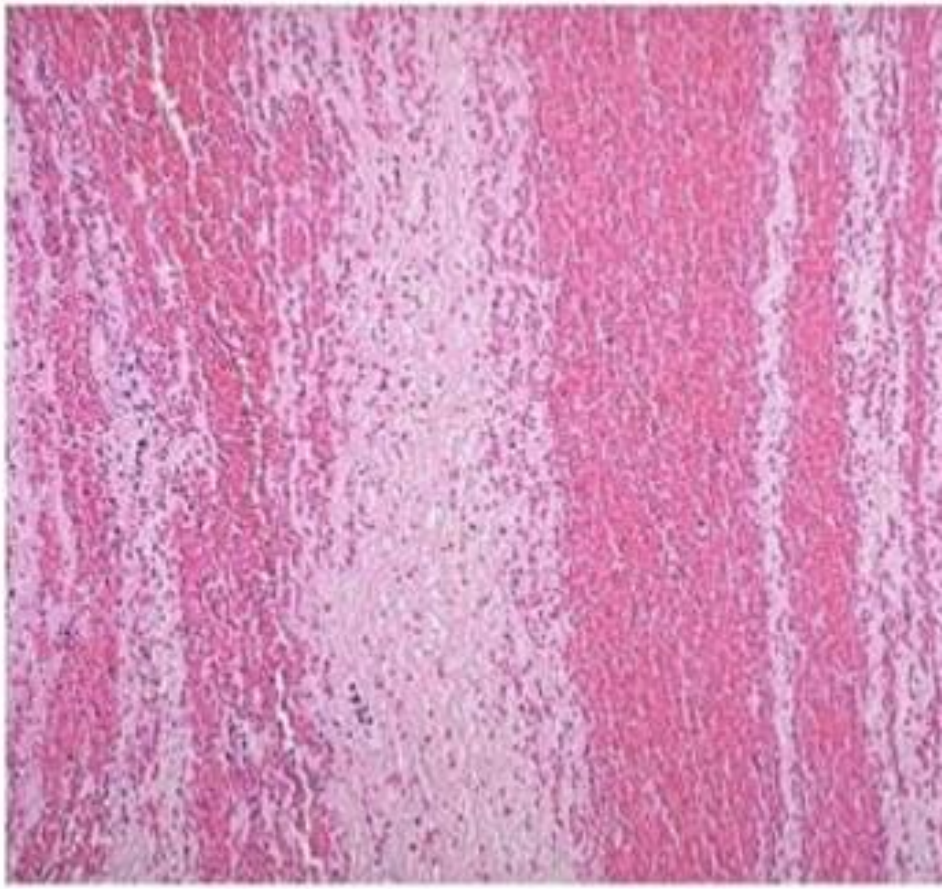
Morphology of thrombi:

- Thrombi can develop anywhere in the cardiovascular system (in cardiac chambers, on valves, or in arteries, veins, or capillaries).
- **Arterial or cardiac thrombi usually begin at sites of turbulence or endothelial injury; venous thrombi characteristically occur at sites of stasis.**
- Thrombi are focally attached to the underlying vascular surface; **arterial thrombi tend to grow retrograde from the point of attachment, while venous thrombi extend in the direction of blood flow** (thus both propagate toward the heart).
- The propagating portion of a thrombus is often poorly attached and therefore prone to fragmentation and **embolization.**

- **Grossly and microscopically**, thrombi often have laminated appearance called **lines of Zahn**; these represent pale platelet and fibrin deposits alternating with darker red cell–rich layers.
- Such laminations signify that a thrombus has formed in flowing blood; their presence can therefore distinguish **antemortem** thrombosis from the bland non laminated clots that occur **postmortem.**

Lines of zahn





- Thrombi occurring in heart chambers or in the aortic lumen are designated **mural thrombi**.
- Causes of mural cardiac thrombi :

Abnormal myocardial contraction (arrhythmias,myocardial infarction) or endomyocardial injury (myocarditis or catheter trauma)

- Thrombi on heart valves are called **vegetations**. Blood-borne bacteria or fungi can adhere to previously damaged valves (e.g., due to rheumatic heart disease) or can directly cause valve damage; in both cases, endothelial injury and disturbed blood flow can induce the formation of large thrombotic masses (**infective endocarditis**).
- Sterile vegetations can also develop on no infected valves in persons with hypercoagulable states, so-called **nonbacterial thrombotic endocarditis**.
- Less commonly, sterile, verrucous endocarditis (**Libman-Sacks endocarditis**) can occur in the setting of systemic lupus erythematosus.
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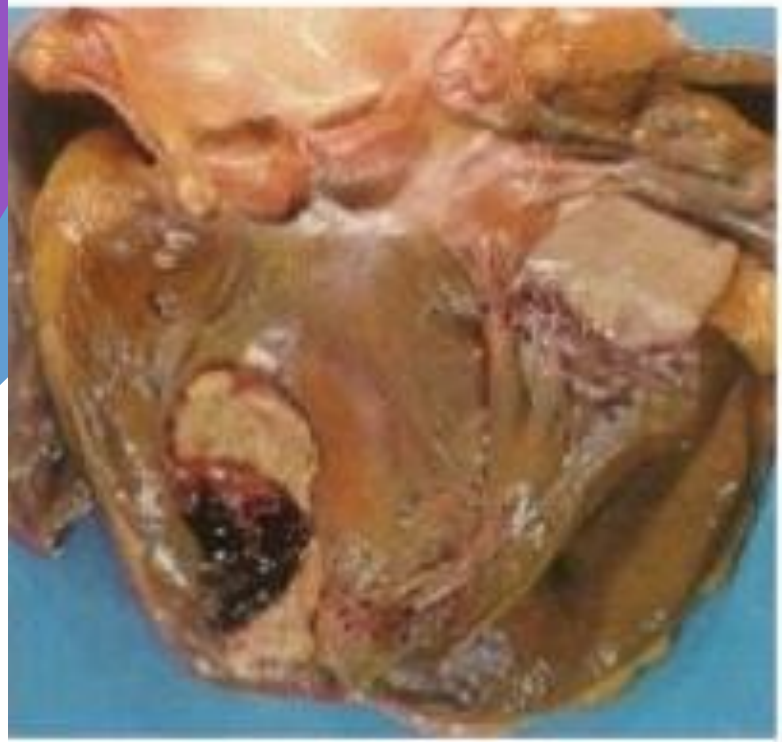
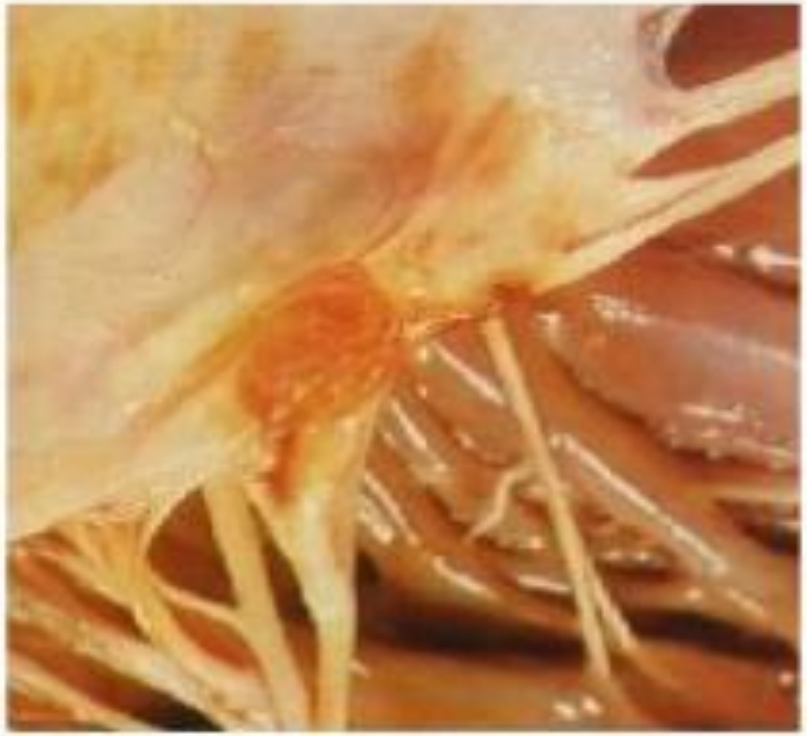
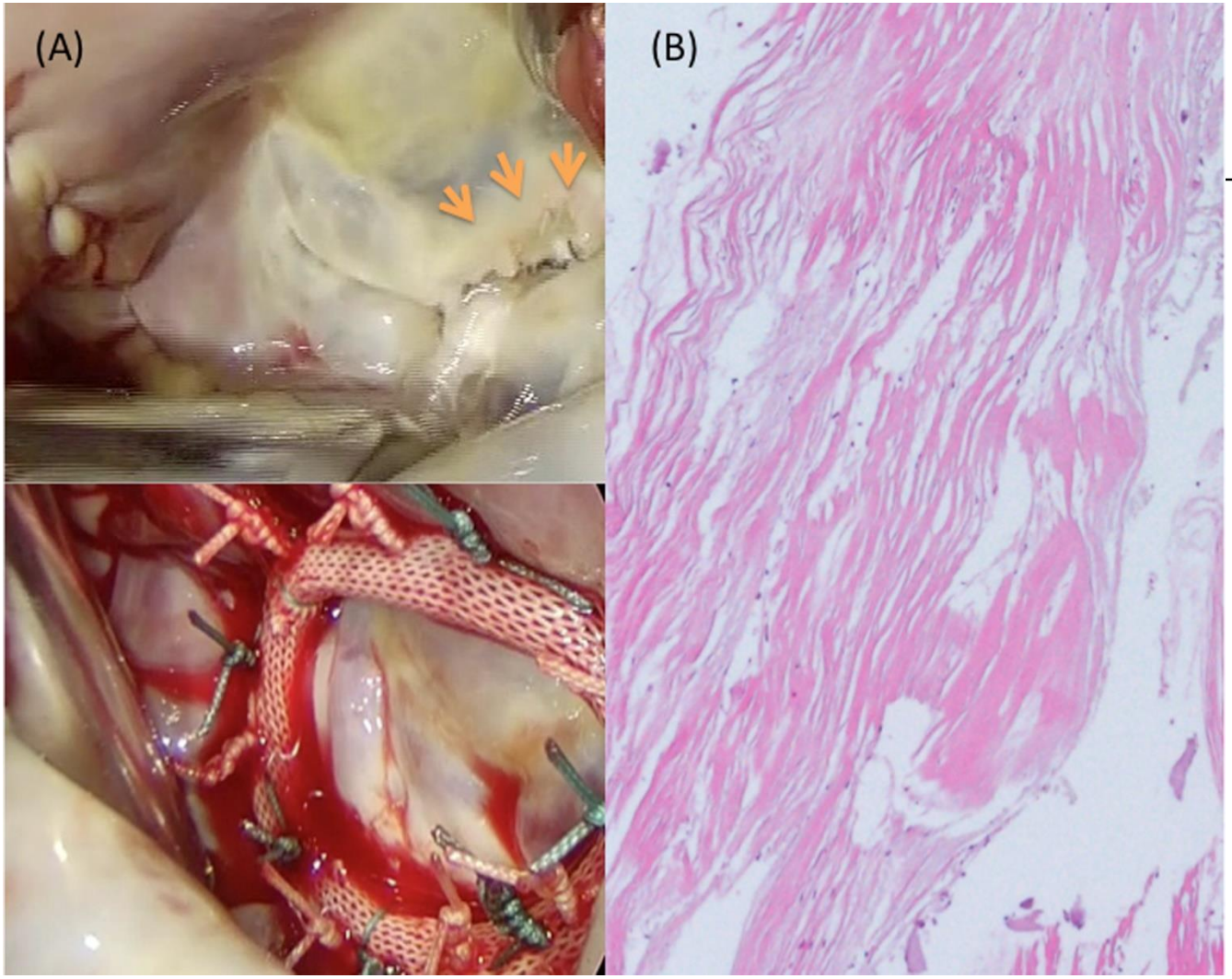


Mural thrombus



Vegetation



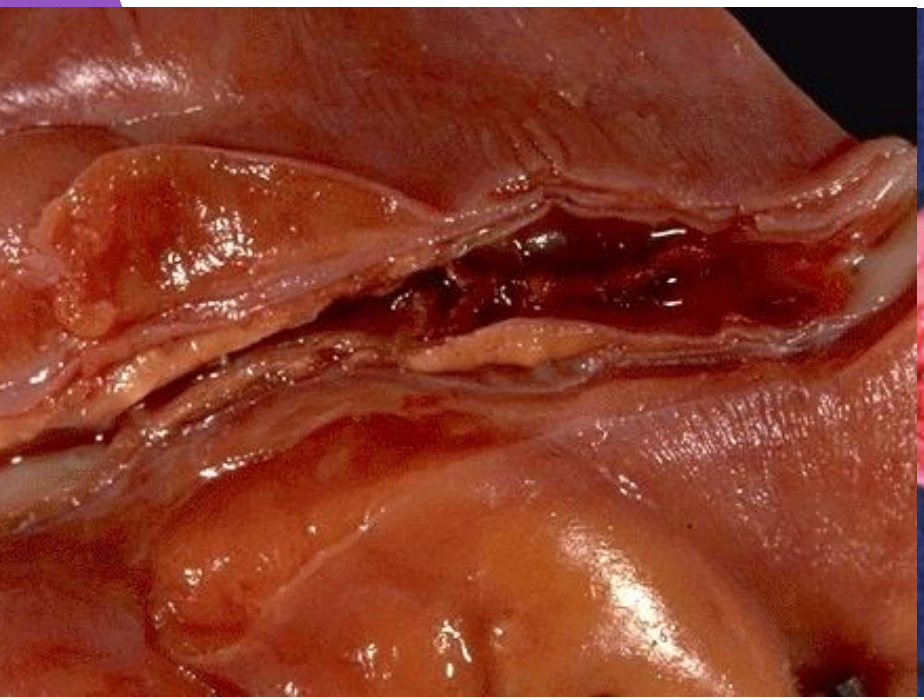
Libman-Sacks endocarditis

Arterial thrombi: (white thrombi)

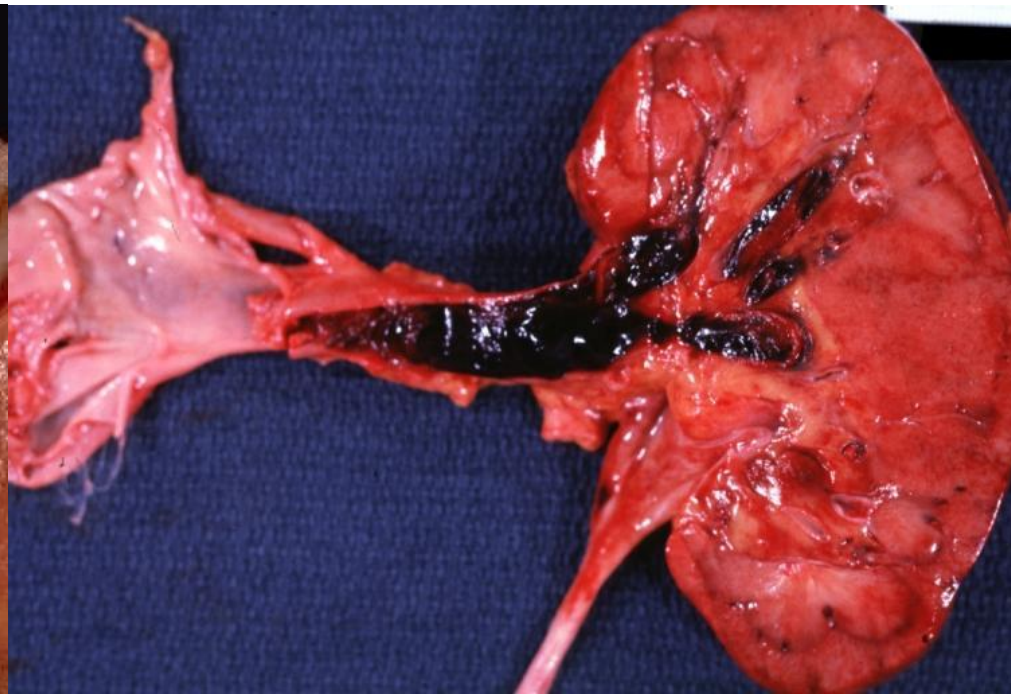
- Are usually occlusive.
- Most common sites are coronary, cerebral &femoral arteries, superimposed on atherosclerotic plaques.
- Firmly adheres to arterial wall.
- Grayish white &composed of platelets, fibrin, RBCs &degenerated WBCs(lines of Zhan).
- These are usually superimposed on a ruptured atherosclerotic plaque.

Venous thrombi: (red thrombi)

- ~~Almost occlusive because they form~~ in slowly moving blood.
- They contain more RBCs, known as red or stasis thrombi.
- Soft, gelatinous.
- 90% affect veins of lower limbs.



Thrombus is apparent in the lumen of the coronary. (White thrombus)



Renal_vein_thrombosis (red thrombus)

POST MORTEM THROMBUS:

- Confused with venous (red) thrombus.
- They are gelatinous with dark red dependent portion where RBCs settled by gravity with yellow fat “chicken fat” supernatant.
- Not attached to arterial wall.
- While red thrombi are: more firm, almost always have point of attachment & transaction reveals vague strands of pale gray fibrin.
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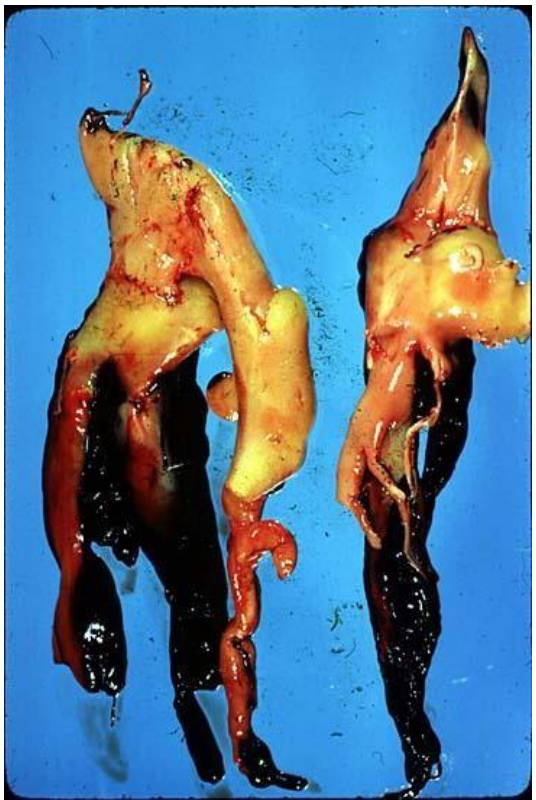

Fate of thrombus:

1- **Dissolution:** Activation of fibrinolytic pathway will lead to shrinkage & total lysis of recent ~~thrombus while older ones undergo fibrin~~ polymerization & become more resistant to proteolysis.

2- **Organization & recanalization:** Ingrowth of endothelial cells, smooth muscle cells & fibroblasts into fibrin rich thrombus will create conduits from one end of thrombus to other & re-establish continuity of original lumen.

3- **Propagation:** Thrombus accumulates more platelets & fibrin &lead to obstruction.

4- **Embolization:** Thrombus dislodges & transported to other sites.

Fate of Thrombus

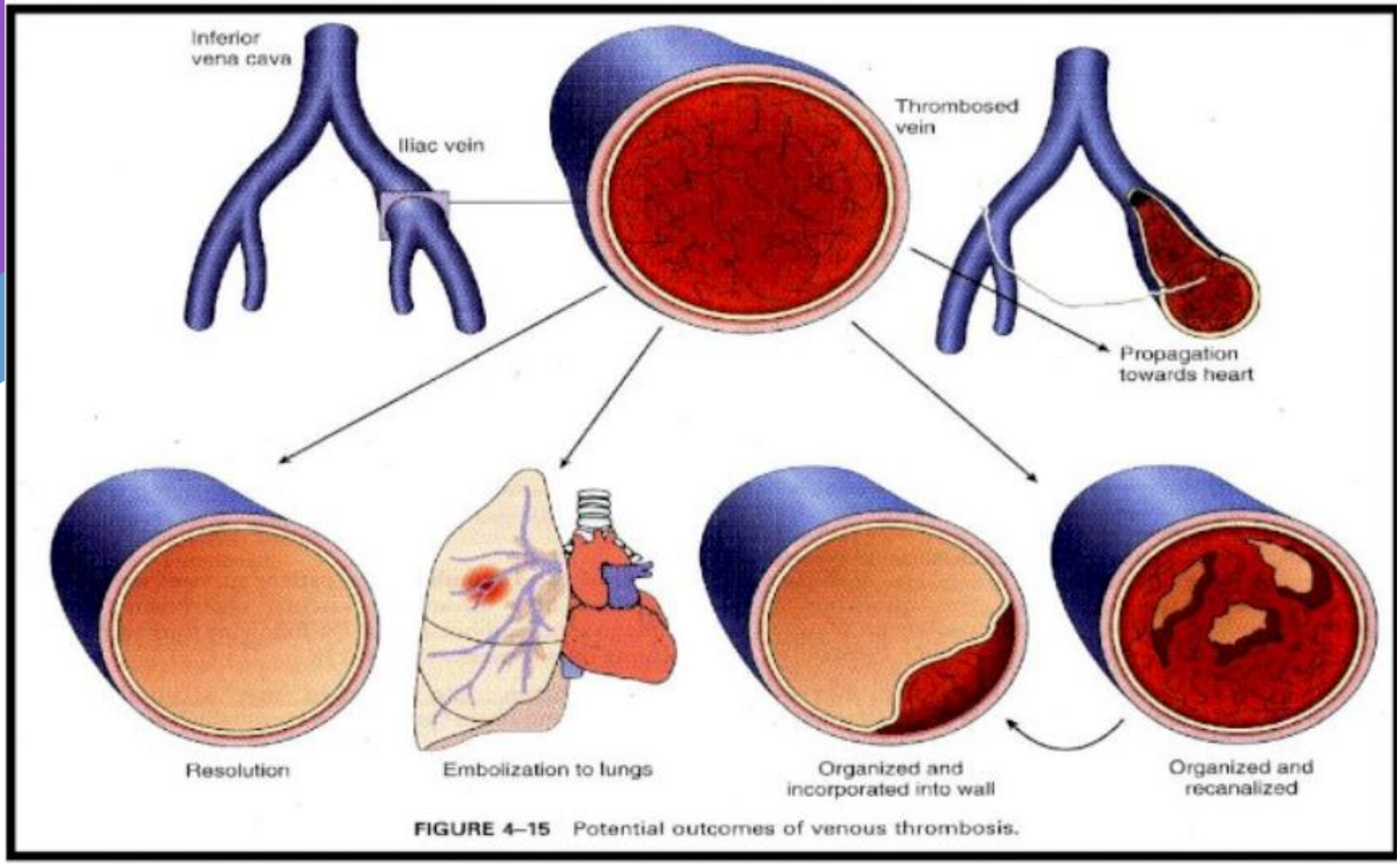

FIGURE 4–15 Potential outcomes of venous thrombosis.

Thank You !