The Cardio-VASCULAR System

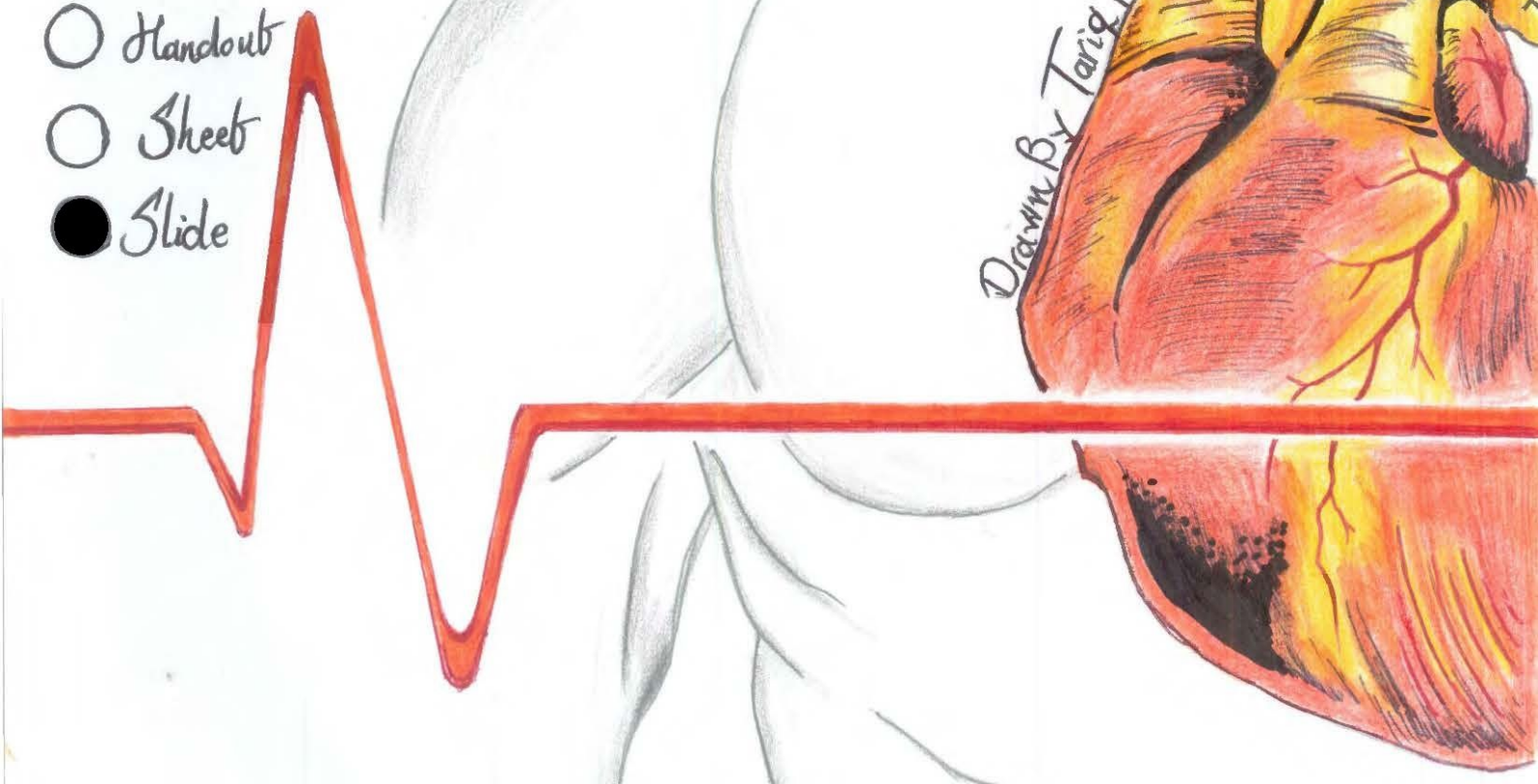
- ○ Anatomy
- ○ Histology
- ● Pathology
- ○ Pharmacology
- ○ Physiology
- ○ Microbiology

Lec #: 1

Dr. Name: Dr.Nisreen

Done By:

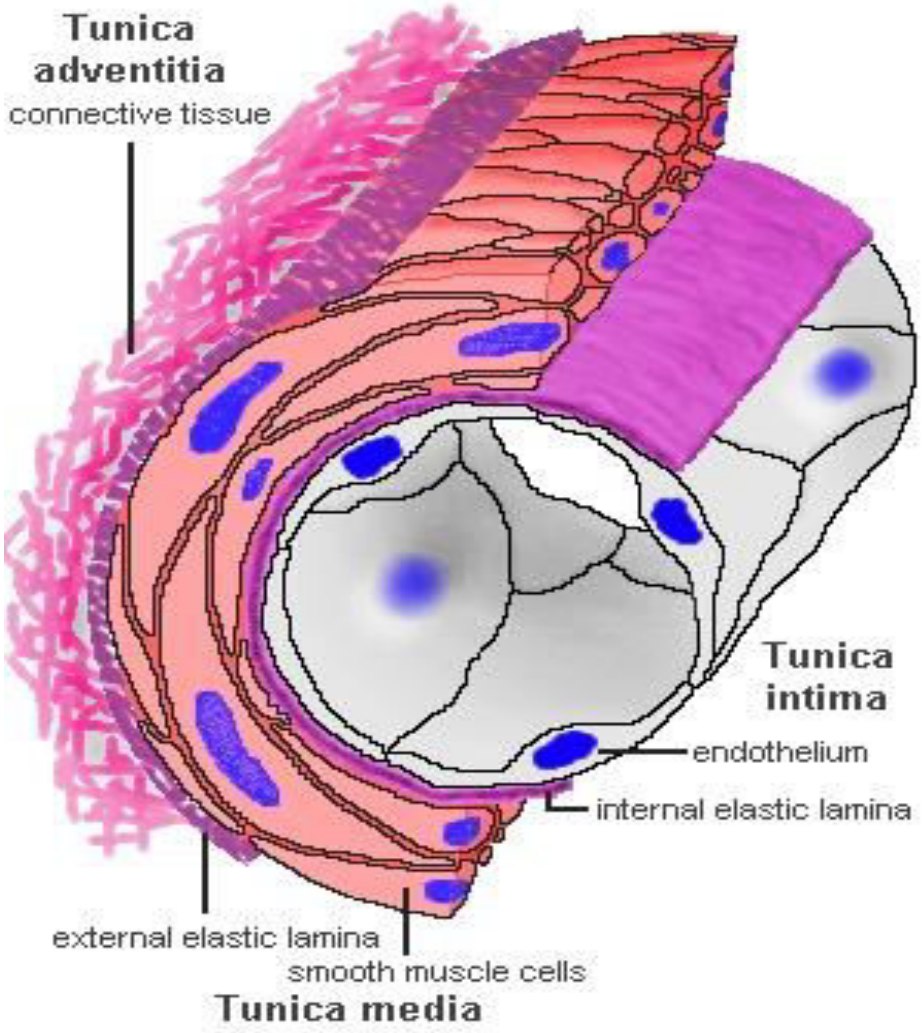
- ○ Handout
- ○ Sheet
- ● Slide



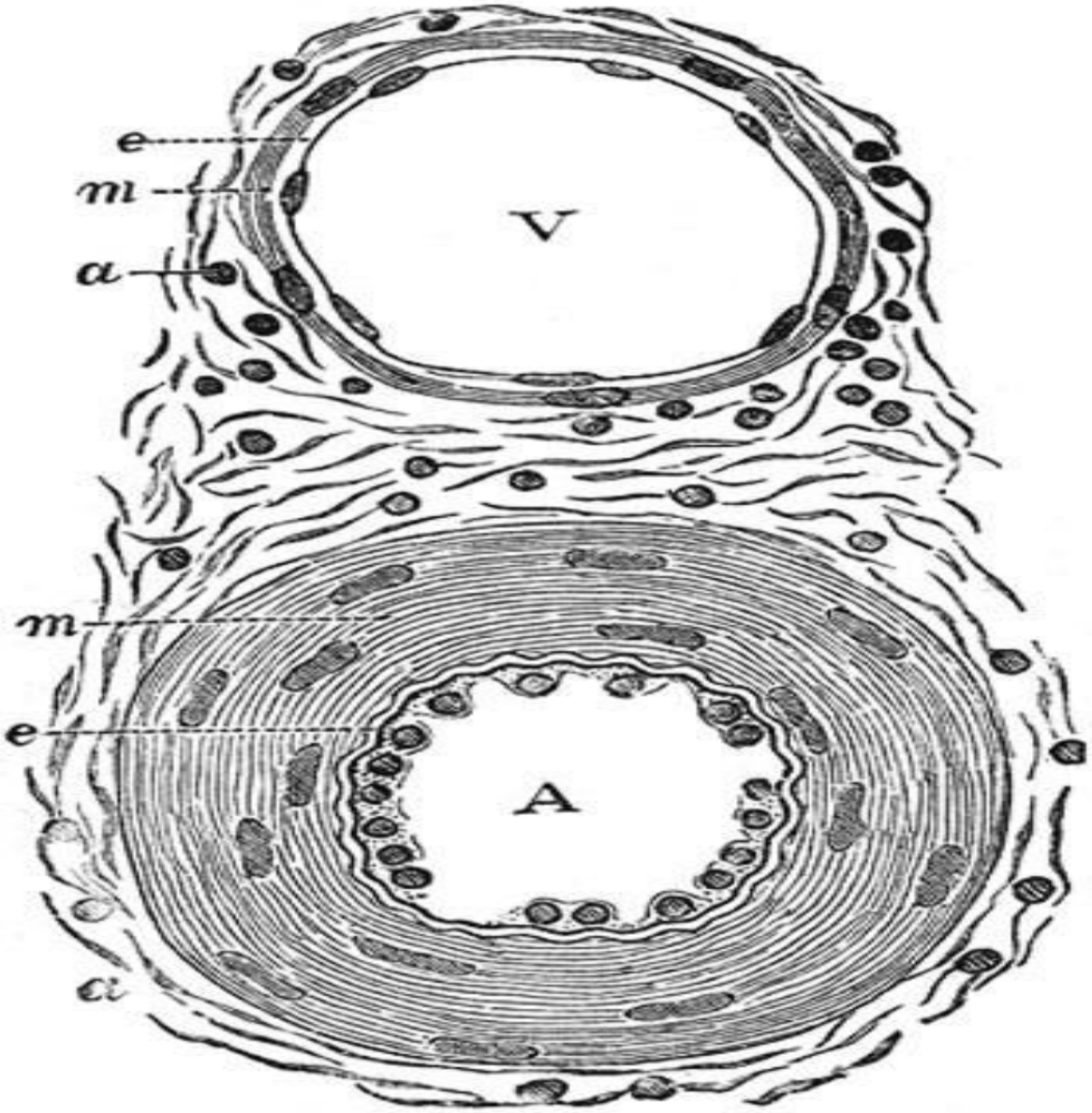
Thrombosis

Dr. Nisreen Abu Shahin
Assistant Professor of Pathology
Pathology Department
University of Jordan

Normal blood vessel histology



Artery (A) vs vien (V)

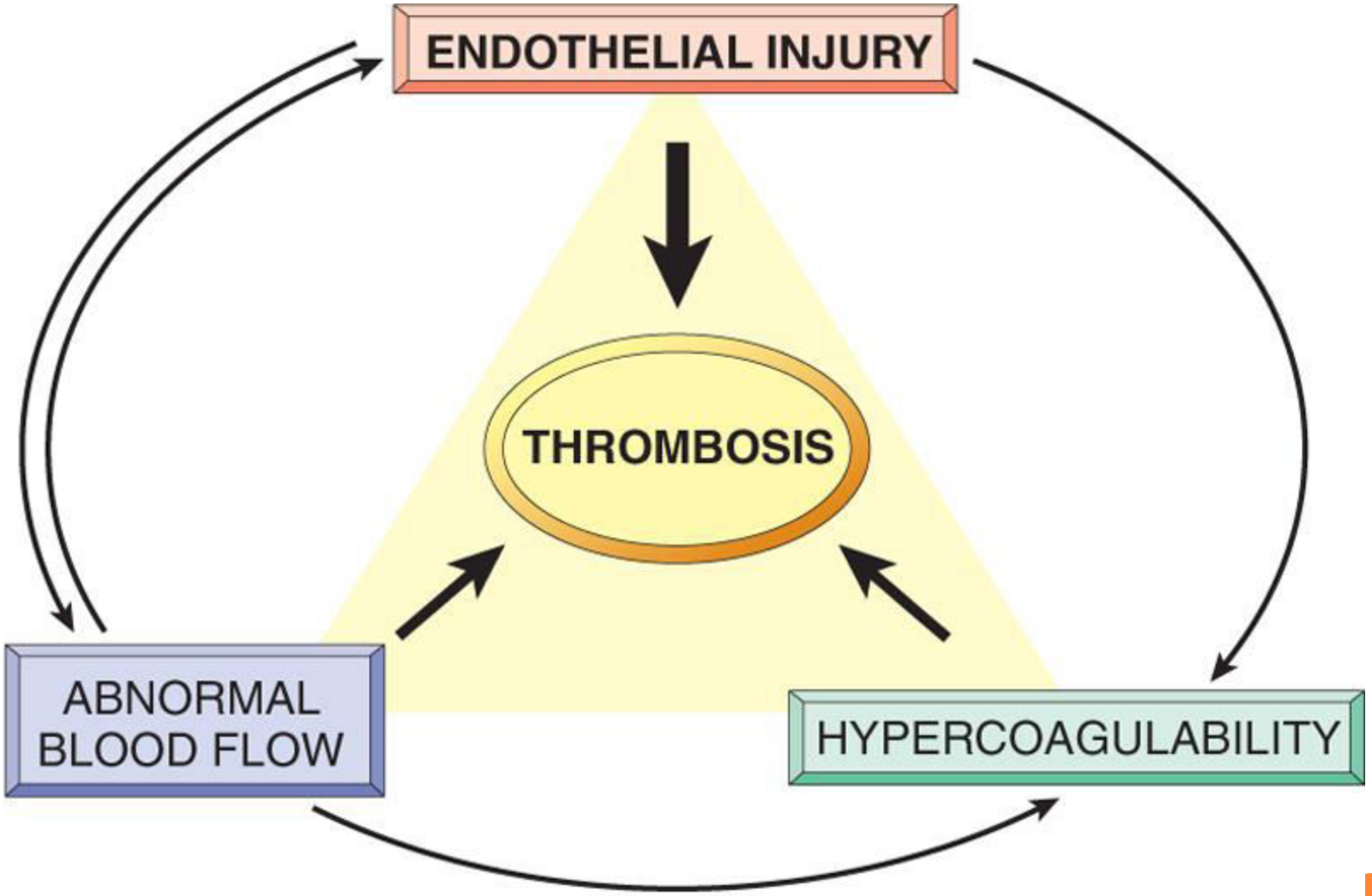


THROMBOSIS

- **Pathogenesis (called *Virchow's triad*):**

1. ***Endothelial* Injury (Heart, Arteries)***
2. ***Stasis (abnormal blood flow)***
3. ***Blood Hypercoagulability***

*** Endothelial cells are special type of cells that cover the inside surface of blood vessels and heart.**

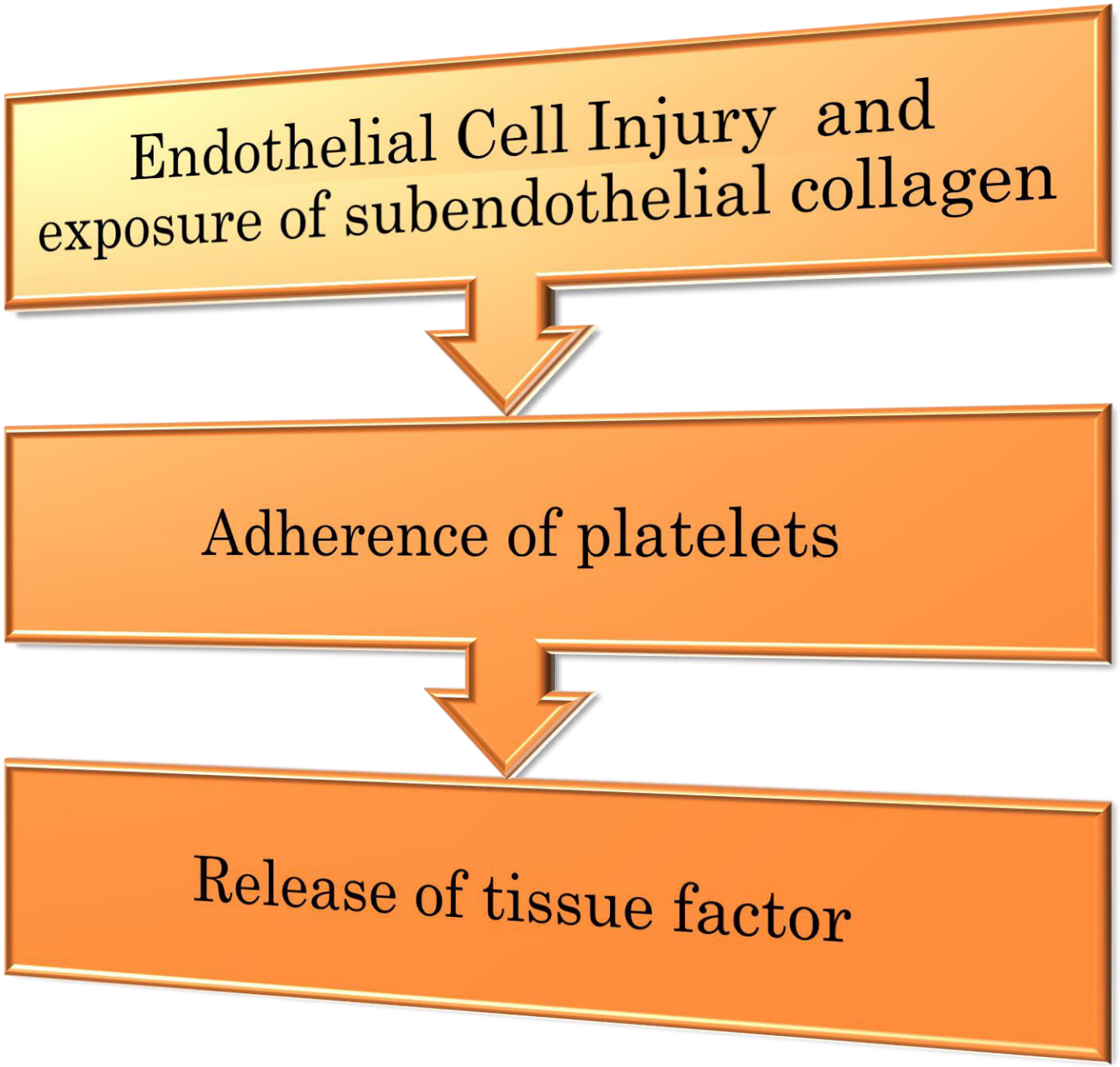


Contribution of Endothelial Cells to Coagulation

- **Intact endothelial cells maintain liquid blood flow by:** 1- inhibiting platelet adherence
  2- preventing coagulation factor activation
  3- lysing blood clots that may form.
- **Endothelial cells can be <u>stimulated</u> by direct injury or by various cytokines that are produced during inflammation.**
- **Endothelial injury results in:**

1- expression of **procoagulant proteins** (tissue factor and vWF)→local thrombus formation.

2- exposure of underlying vWF and basement membrane collagen→ platelet aggregation and thrombus formation.


Endothelial Cell Injury and exposure of subendothelial collagen
Adherence of platelets
Release of tissue factor

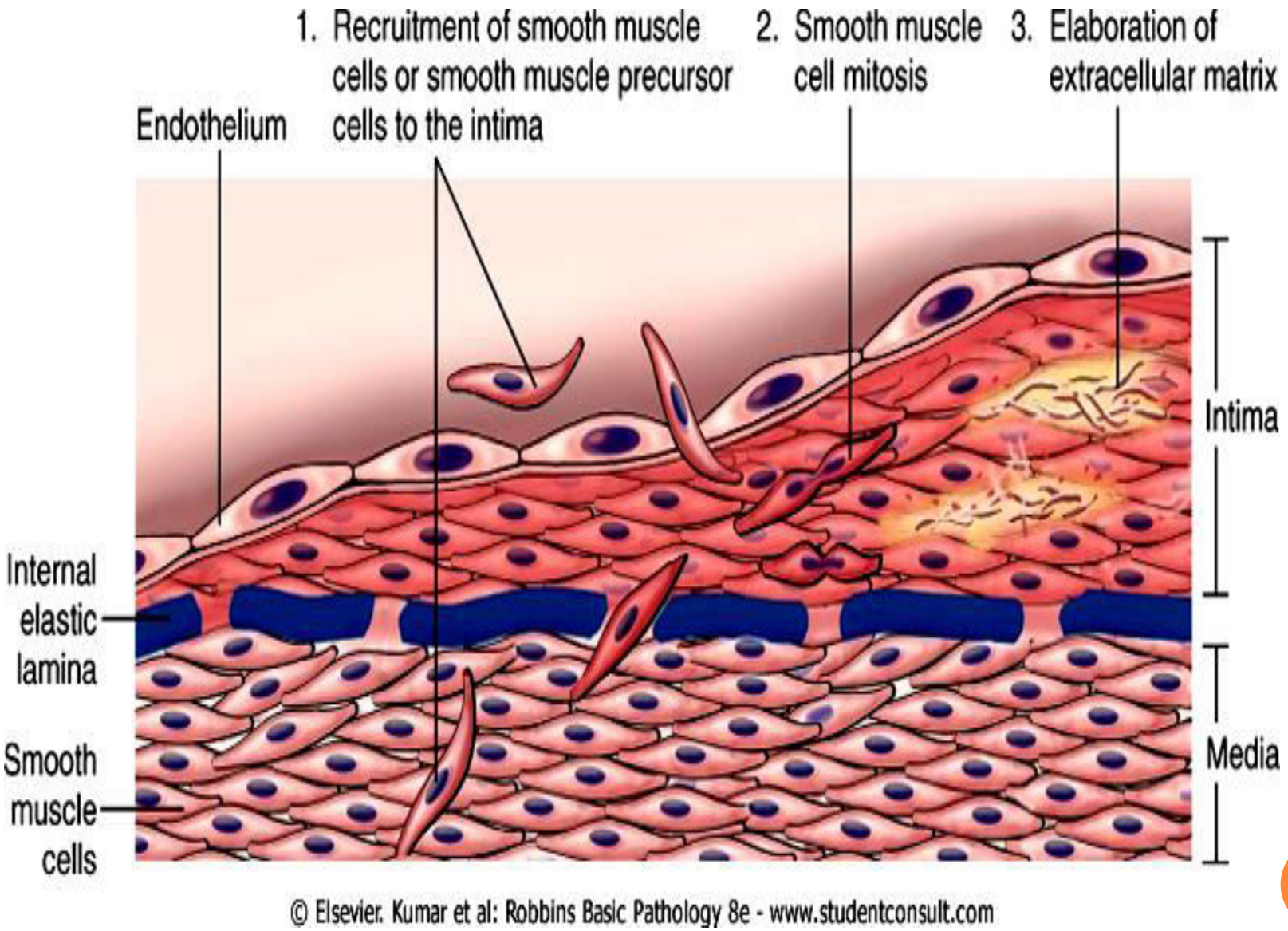
Response of Vascular Wall Cells to Injury

- **Injury to the vessel wall results in a healing response, involving:**

1- Intimal expansion by proliferating SMCs and newly synthesized ECM.

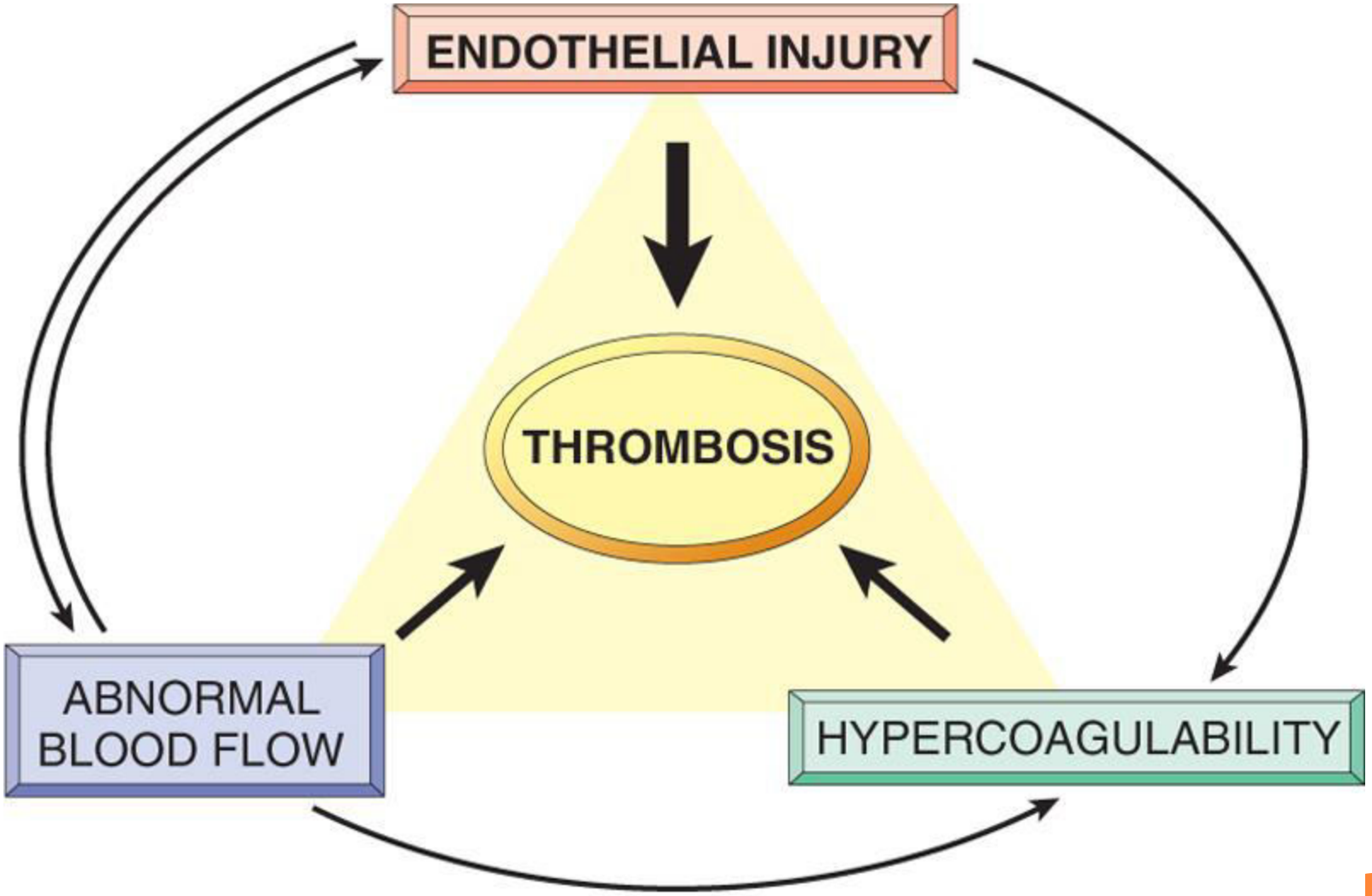
2- The recruitment and activation of the SMCs in which involves signals from cells (e.g., ECs, platelets, and macrophages), as well as mediators derived from coagulation and complement cascades.

- **Pathologic effect of vascular healing→ Excessive thickening of the intima → luminal stenosis & blockage of vascular flow**



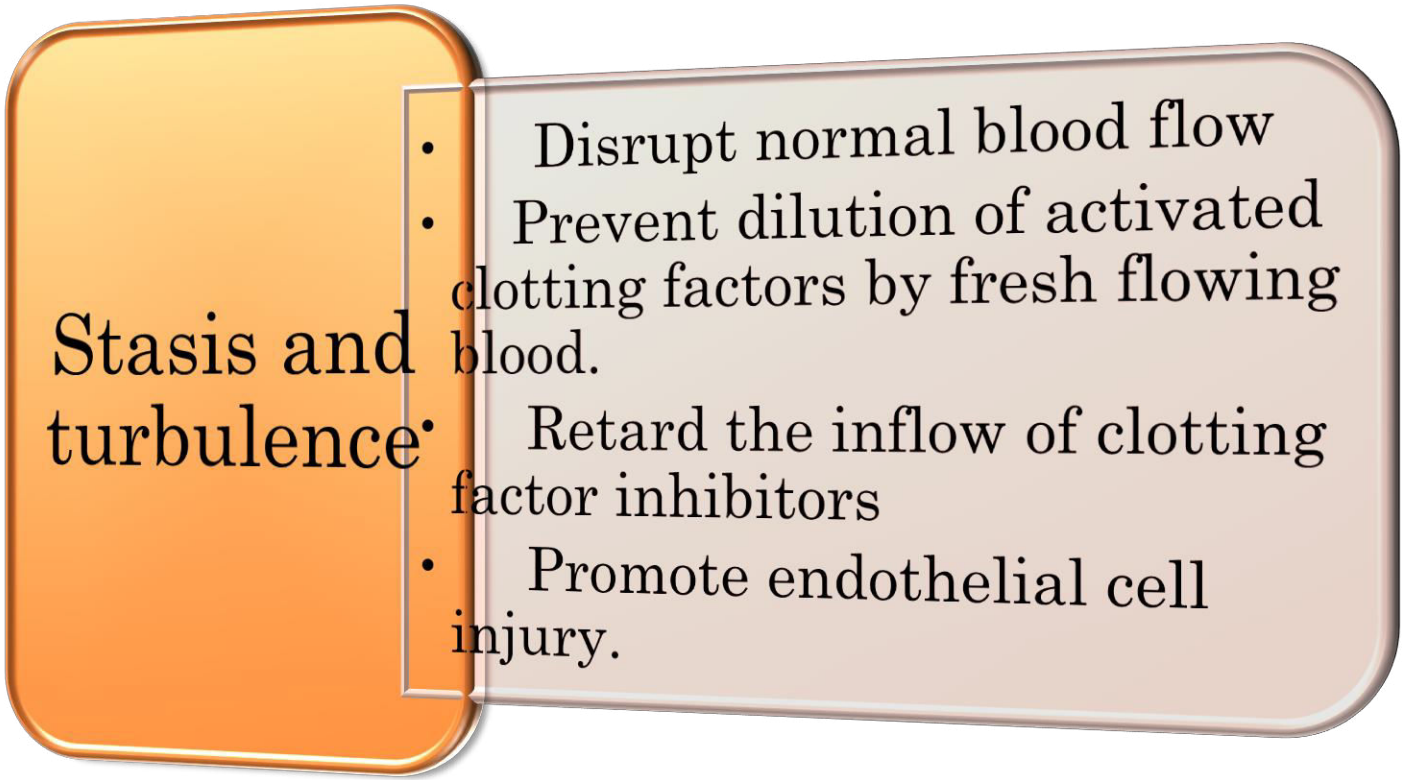
Causes of Endothelial injury

1. ***Valvulitis***
2. ***MI***
3. ***Atherosclerosis***
4. ***Traumatic or inflammatory conditions***
5. ***Increased Blood Pressure***
6. ***Endotoxins***
7. ***Hypercholesterolemia***
8. ***Radiation***
9. ***Smoking***



Stasis

- *Stasis is a major factor in **venous** thrombi*
- Normal blood flow is ***laminar (p***latelets flow centrally in the vessel lumen, separated from the endothelium by a slower moving clear zone of plasma)
- Stasis and turbulence cause the followings:



Causes of Stasis

1. ***Atherosclerosis***
2. ***Aneurysms***
3. ***Myocardial Infarction (Non-cotractile fibers)***
4. ***Mitral valve stenosis (atrial dilation)***
5. ***Hyper viscosity syndrome (PCV and Sickle Cell anemia)***

Hypercoagulability

A. Genetic (primary):

- mutations in the factor V gene and the prothrombin gene are the most common

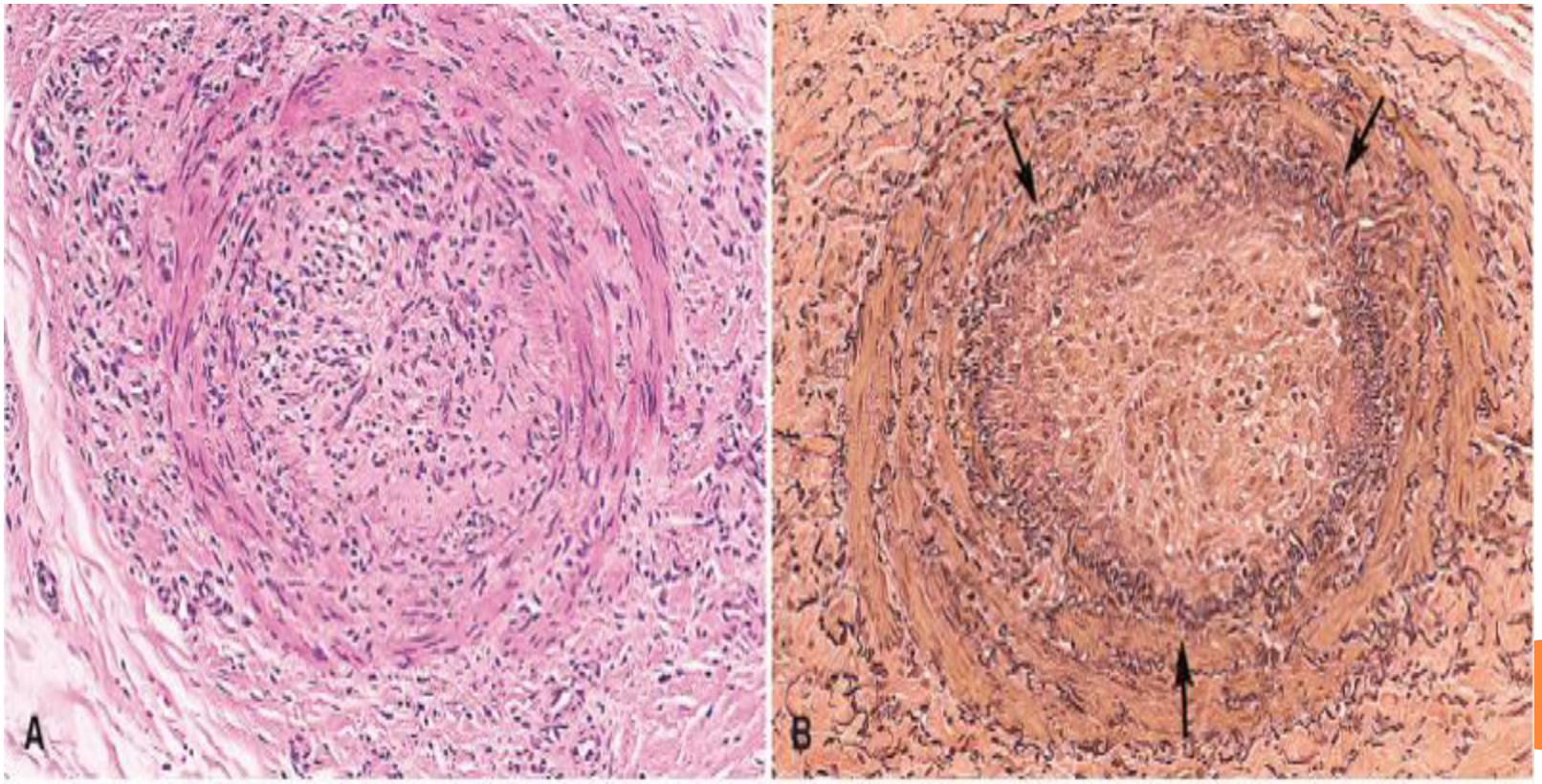
B. Acquired (secondary):

- multifactorial and is therefore more complicated
- causes include: Immobilization, MI, AF, surgery, fractures, burns, Cancer, Prosthetic cardiac valves …etc

MORPHOLOGY OF THROMBI

- **Can develop anywhere in the CVS (e.g., in cardiac chambers, valves, arteries, veins, or capillaries).**
- ***Arterial or cardiac* thrombi→ begin at sites of *endothelial injury* or turbulence; and are usually superimposed on an *atherosclerotic plaque***
- **Venous thrombi → occur at sites of stasis. Most commonly the veins of the lower extremities (90%)**
- **Thrombi are focally attached to the underlying vascular surface.**
- **The propagating portion of a thrombus is poorly attached →fragmentation and embolus formation**

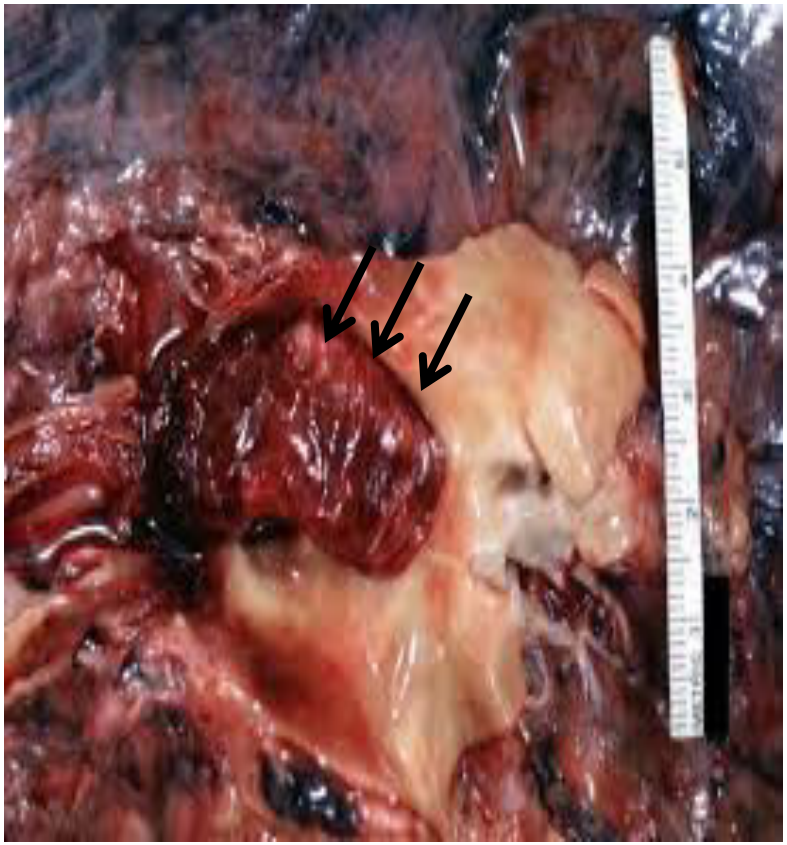
ARTERY WITH AN OLD THROMBUS. A, H&E-STAIN. B, STAIN FOR ELASTIC TISSUE.
THE ORIGINAL LUMEN IS DELINEATED BY THE INTERNAL ELASTIC LAMINA (*ARROWS*) AND IS TOTALLY FILLED WITH ORGANIZED THROMBUS, NOW PUNCTUATED BY A NUMBER OF RECANALIZED CHANNELS (WHITE SPACES).

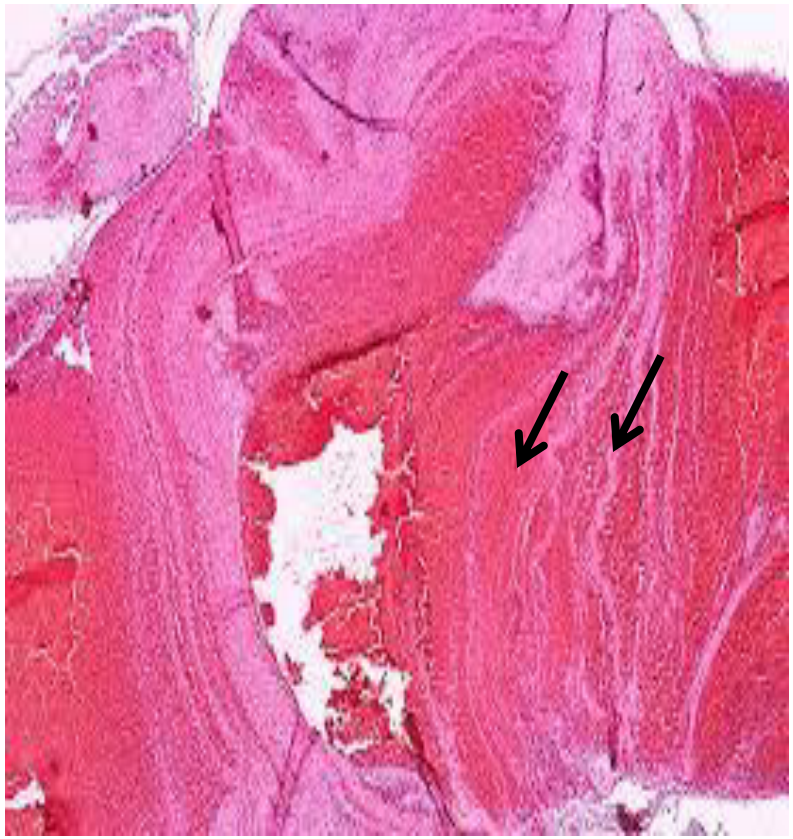


LINES OF ZAHN

- Thrombi can have grossly (and microscopically) apparent laminations called **lines of Zahn**; these represent pale platelet and fibrin layers alternating with darker erythrocyte-rich layers.
- Such lines are significant in that they represent thrombosis of **flowing** blood (can potentially distinguish antemortem thrombosis from postmortem clots)
- postmortem blood clots are bland non-laminated clots *(no lines of Zahn)*

LINES OF ZAHN





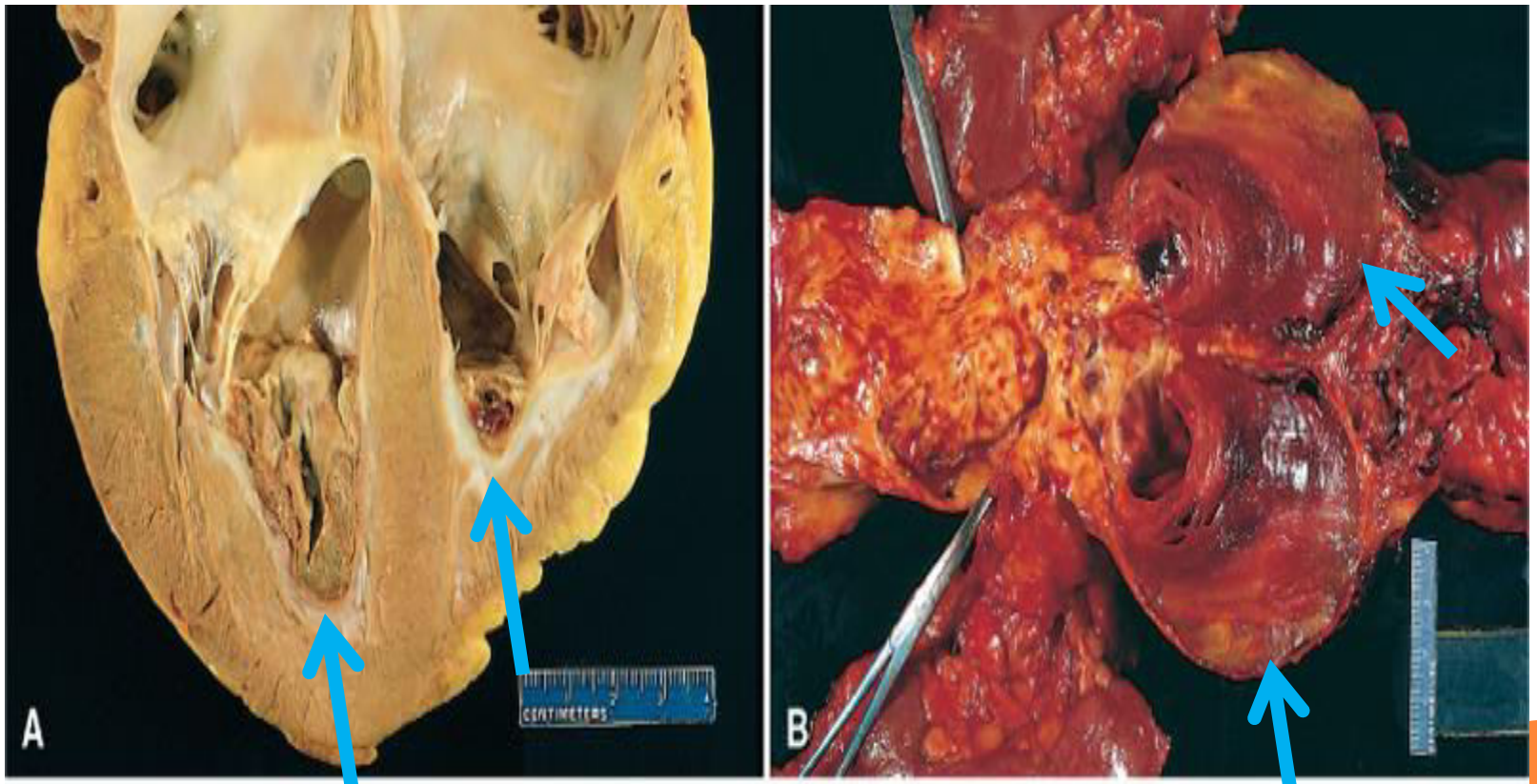
- **Mural thrombi**
- Thrombi occurring in heart chambers or in the aortic lumen.
- Causes include: Abnormal myocardial contraction (e.g. arrhythmias, dilated cardiomyopathy, or MI) or endomyocardial injury (caused by myocarditis, catheter trauma)
- **Vegetations**
- Thrombi on heart valves are called **vegetations:**

Types:

1- infectious (Bacterial or fungal blood-borne infections)→(e.g. infective endocarditis,).

2-Non-bacterial thrombotic endocarditis occur on sterile valves**.**

Mural thrombi



Fate of thrombi

1. ***Propagation*** → accumulate additional platelets and fibrin, eventually causing **vessel obstruction**
2. ***Embolization*** → Thrombi dislodge or fragment and are transported elsewhere in the vasculature
3. ***Dissolution*** → Thrombi are removed by fibrinolytic activity (only in ***recent*** *thrombi)*
4. ***Organization* and recanalization*** → Thrombi induce inflammation and fibrosis. These can *recanalize* (re-establishing some degree of flow), or they can be incorporated into a thickened vessel wall

**Organization refers to the ingrowth of endothelial cells, smooth cells and fibroblasts into the fibrin rich thrombus.*

5. ***Superimposed infection (Mycotic aneurysm)***

- **<u>Venous thrombi</u>**
- (veins of the legs) are most common

a. ***Superficial****: e.g. Saphenous veins.*

   - can cause local congestion, swelling, pain, and tenderness along the course of the involved vein, but they rarely embolize

a. ***Deep****: e.g. Popliteal, Femoral and iliac vein.*

- more serious because they may embolize
- can occur with stasis or in a variety of hypercoagulable states