Doctor.021

no.1

CVS PATHOLOGY

Writer: Rama Aldaqqa

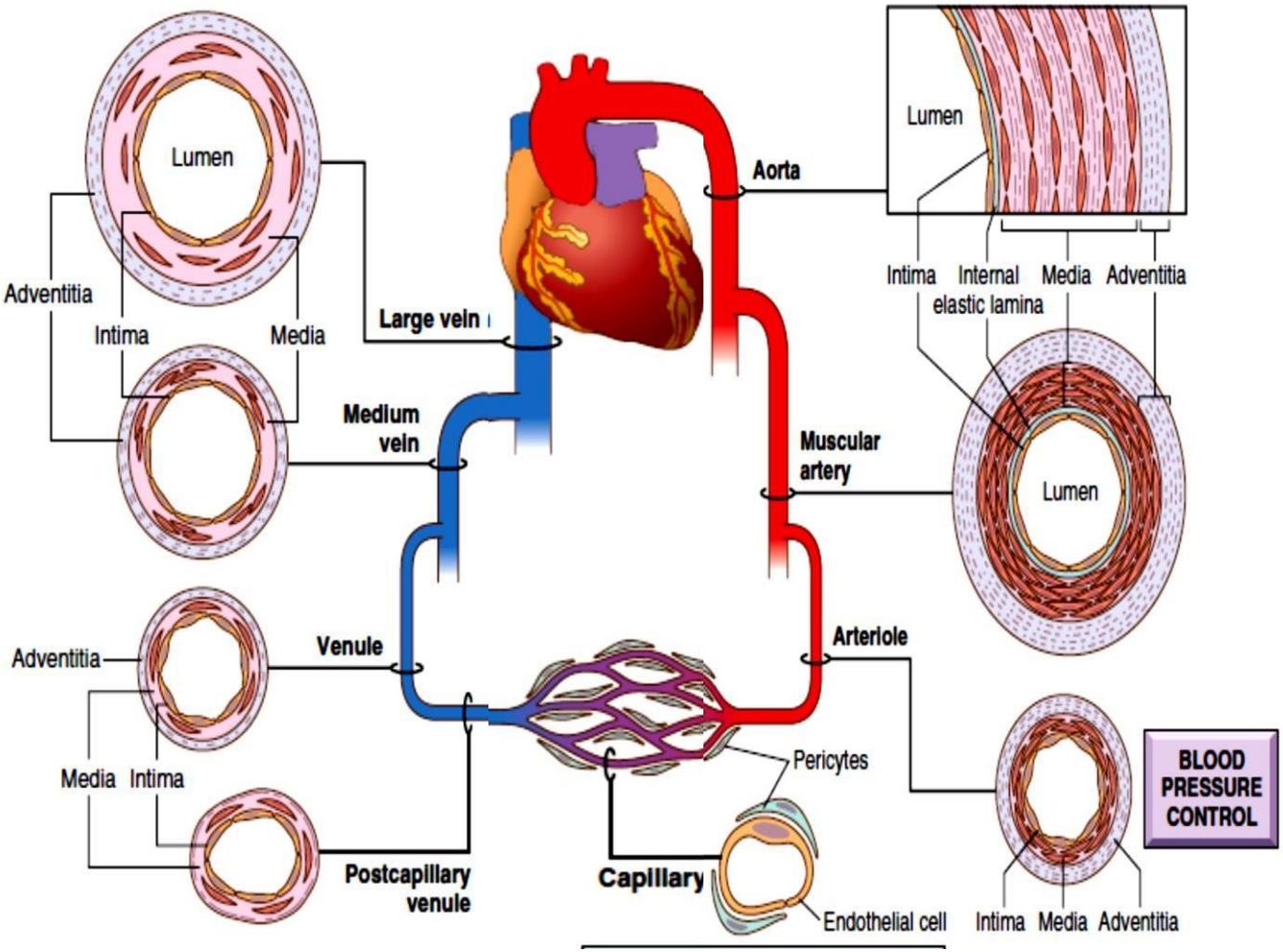
Corrector: Layan Lafi

Doctor: Nisreen Abu Shahin

CARDIOVASCULAR SYSTEM

Venous circulation

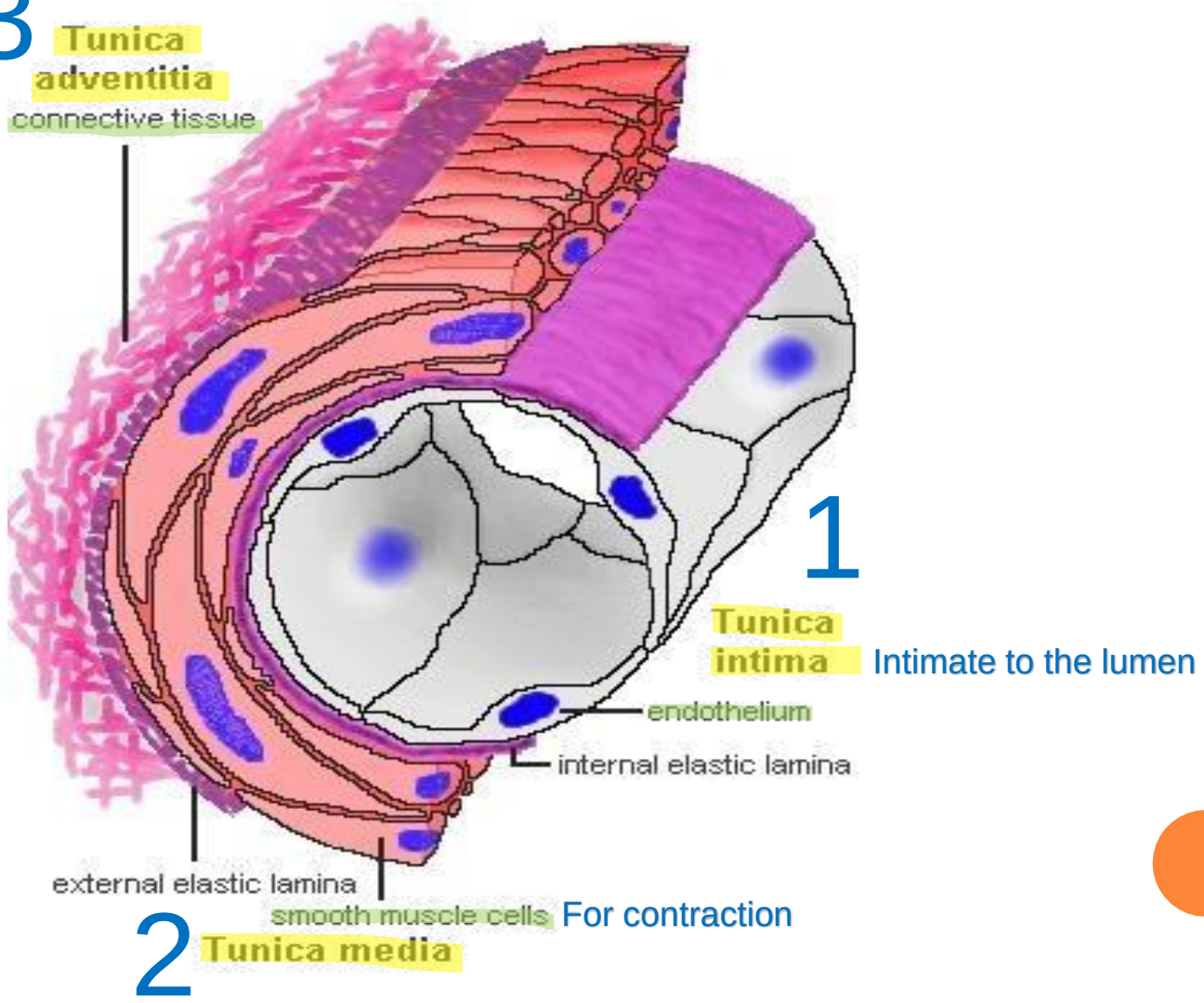
Arterial circulation



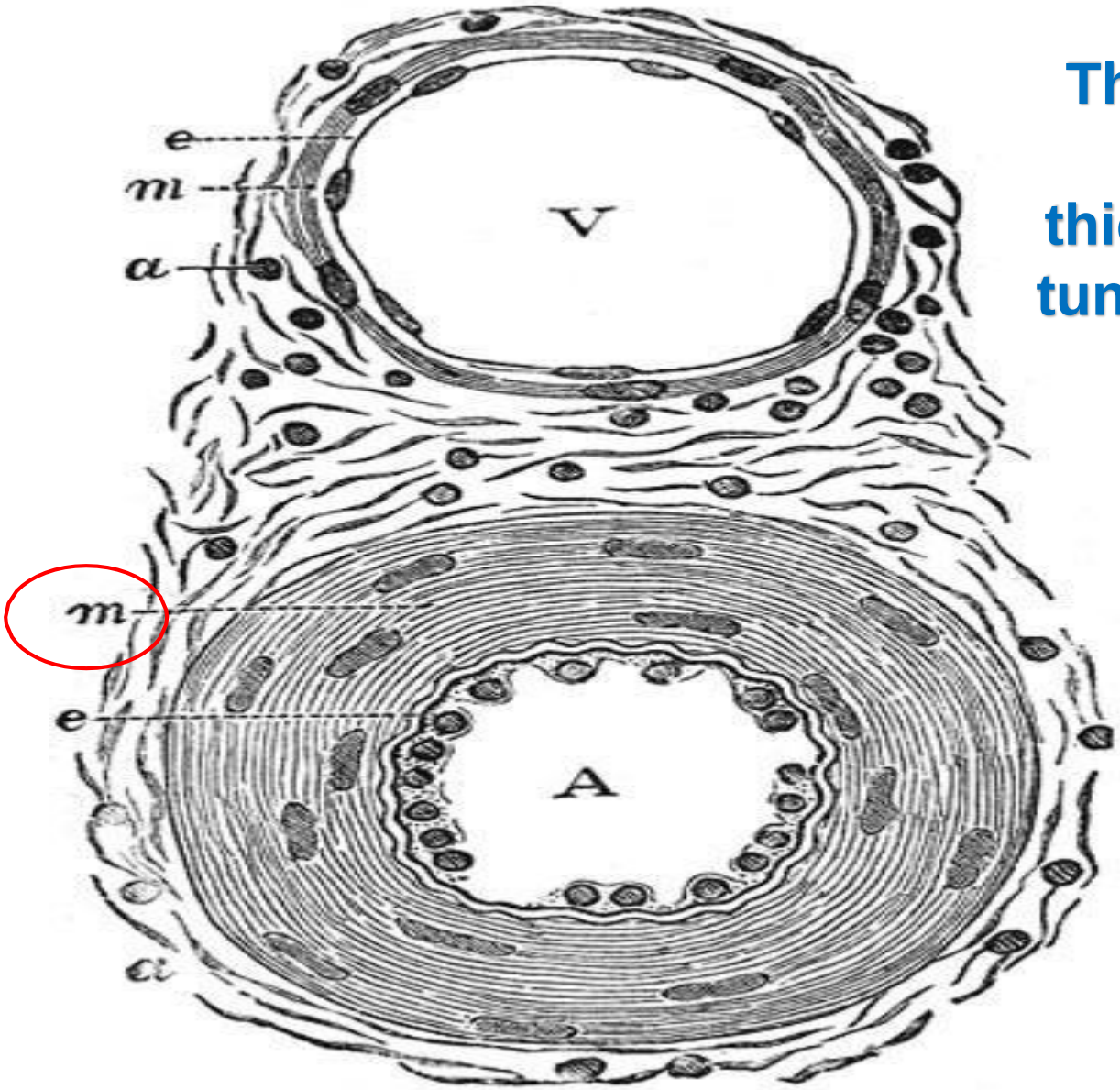
Normal blood vessel histology

For:
-support
-blood and nerve supply

We have 3 layers



ARTERY (A) VS VEIN (V)

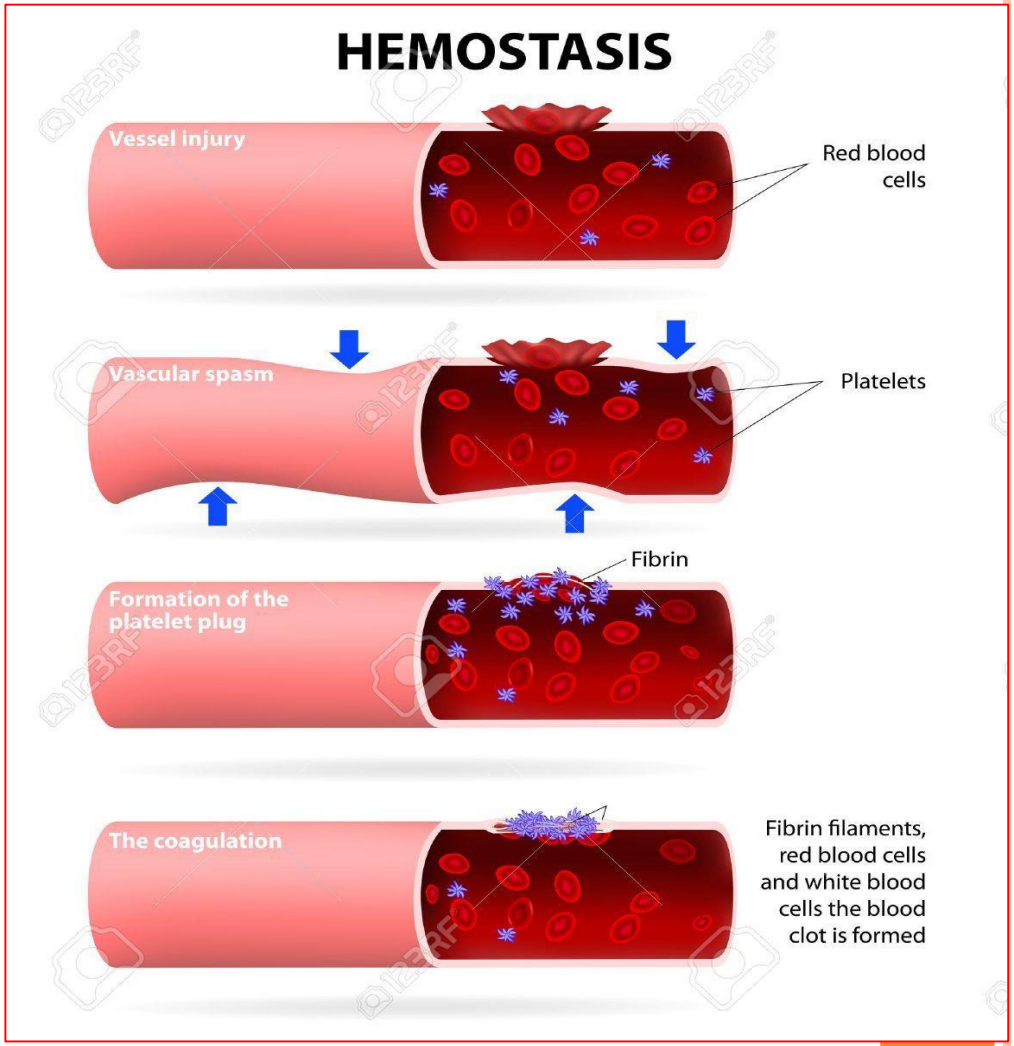


They differ in the thickness of tunica media

This structural difference leads to functional differences and pathological differences.
Based on this structural difference , veins will be exposed to more diseases than arteries.

Physiology of thrombosis

Hemostasis is a protective mechanism (physiological process) to prevent / reduce blood loss → by forming a Thrombus



THROMBOSIS- PATHOLOGICAL ASPECTS

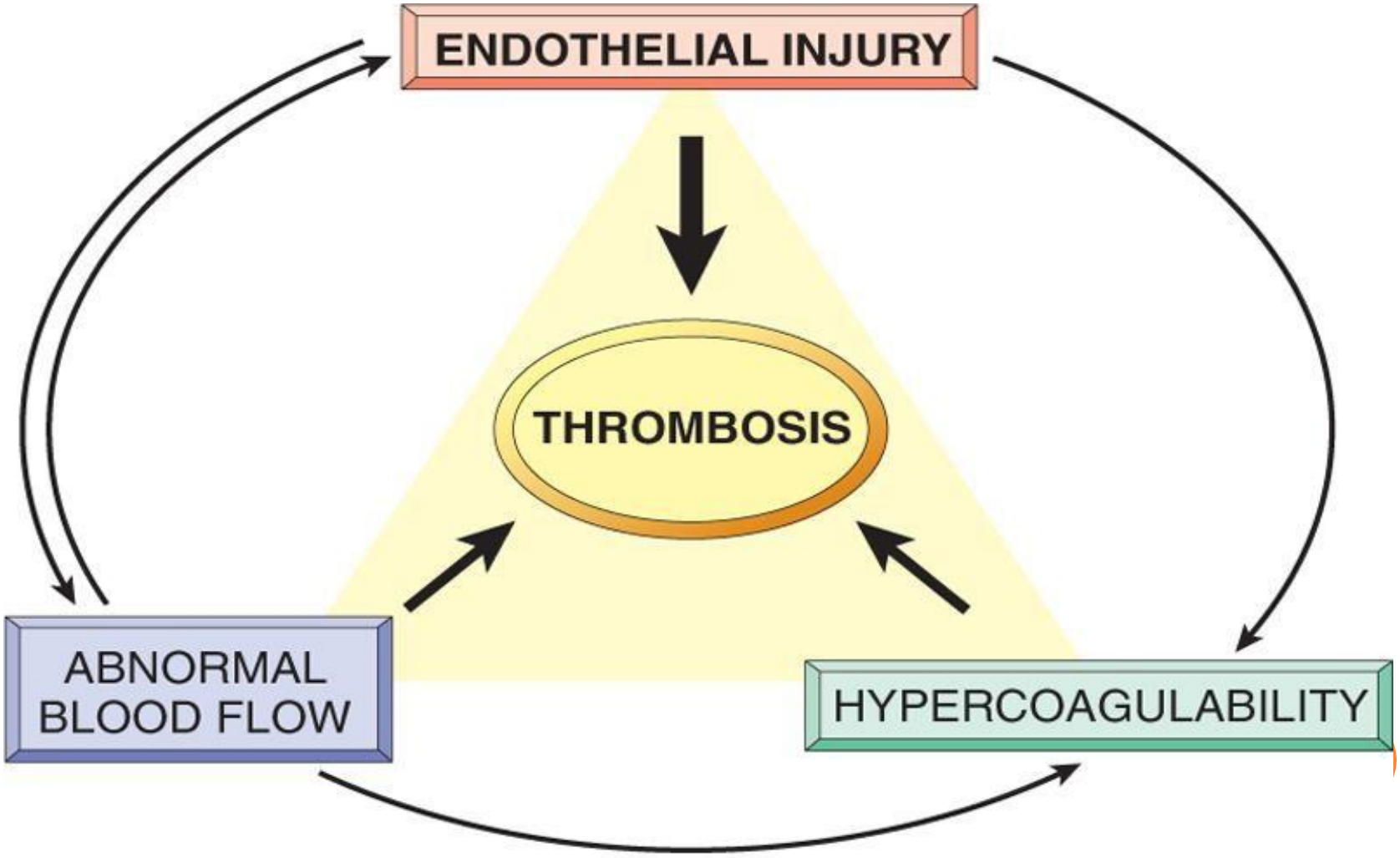
- Blood coagulation is a very important physiological event to protect our hemostasis, and life
- However, at certain points, this process can be pathological that may endorse injury and cause harm to our body
- This happens whenever unnecessary blood clotting is activated

When there is no trauma , (no need for hemostasis activation)

- **The "pathological" thrombosis is caused by the presence of at least one of 3 factors (together called Virchow's triad):**

Virchow's triad

Endothelial cells present in intima layer of blood vessel , they are important cells in maintaining of blood vessel function , maintaining blood flow inside blood vessel and under normal physiological circumstances they also prevent unnecessary coagulation.



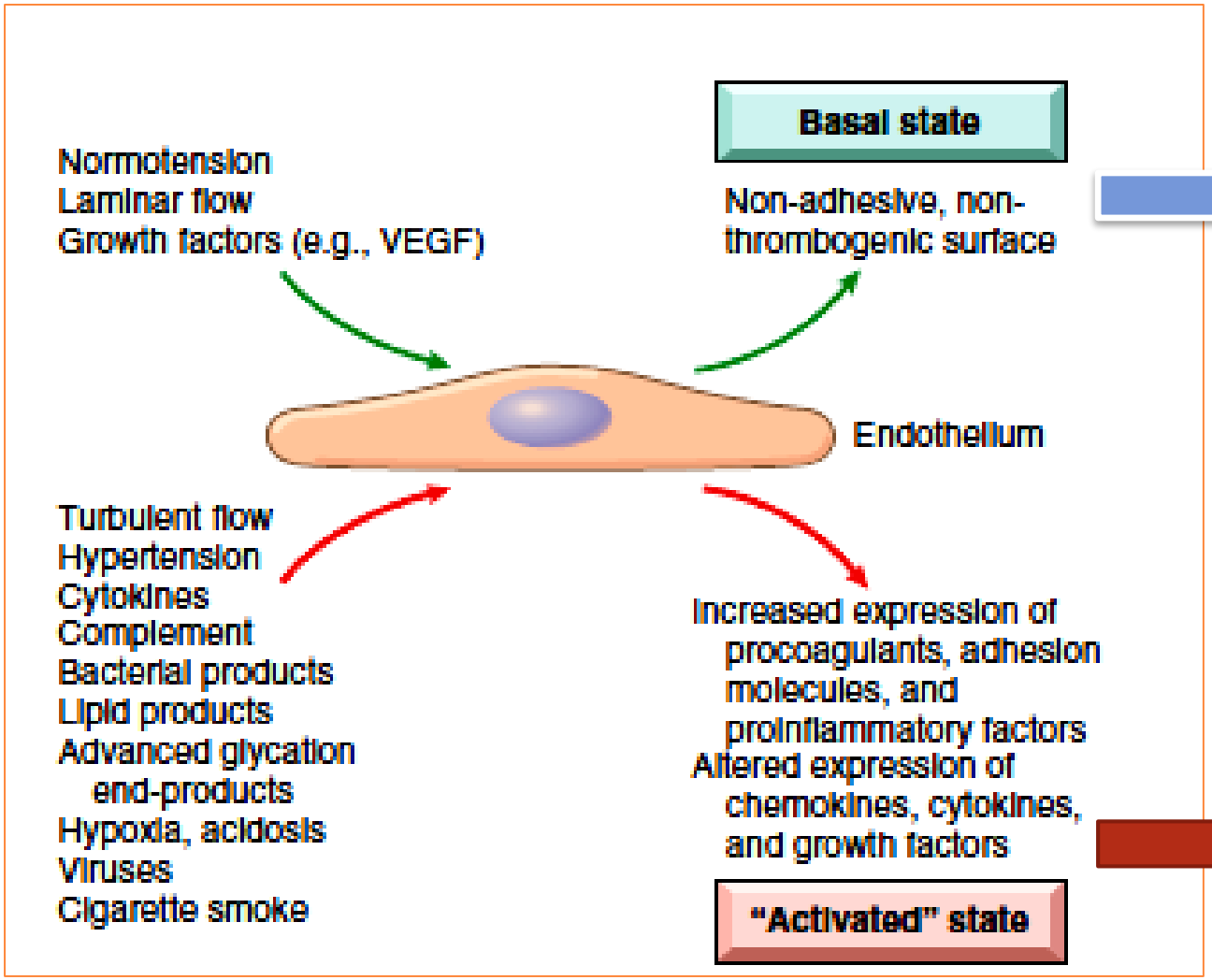
THROMBOSIS - PATHOLOGICAL ASPECTS

- **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.** Their name inside the heart "Endocardial cells"

Contribution of Endothelial Cells to Coagulation



When microenvironment is normal → resting state

Circumstances for being endothelial cells in resting state

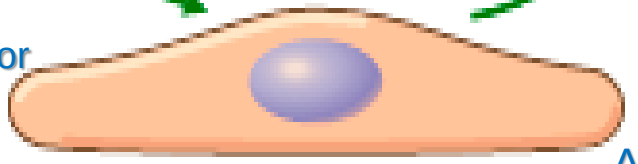
- Normotension
- Laminar flow
- Growth factors (e.g., VEGF)

Basal state

Non-adhesive, non-thrombogenic surface

No thrombosis

The endothelial cells will prevent unnecessary thrombosis by having non adhesive , non thrombogenic surface



Endothelium

Activated or injured endothelial cells

Circumstances for activating endothelial cells

- Turbulent flow
- Hypertension
- Cytokines
- Complement
- Bacterial products
- Lipid products
- Advanced glycation end-products
- Hypoxia, acidosis
- Viruses
- Cigarette smoke

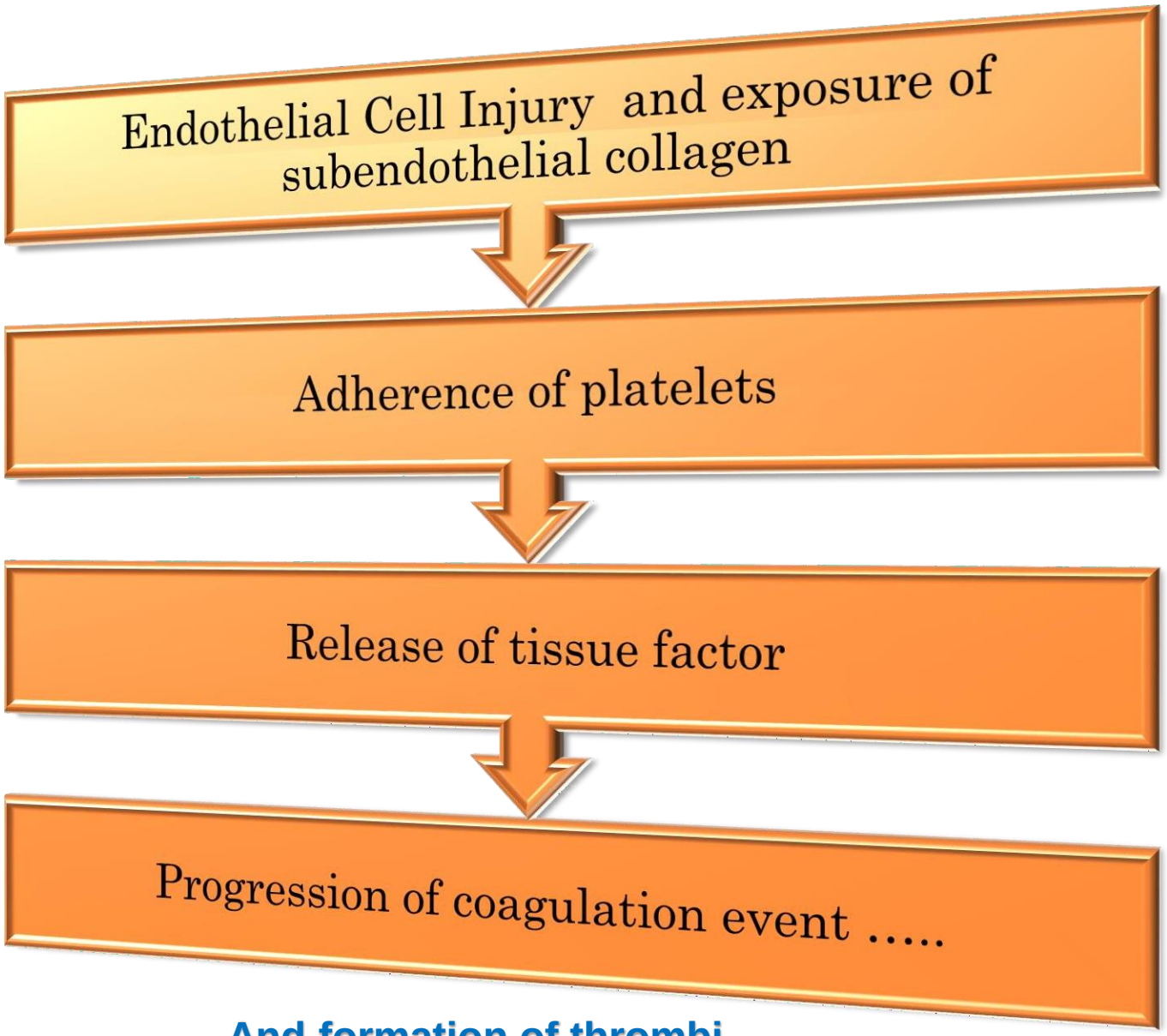
Increased expression of procoagulants, adhesion molecules, and proinflammatory factors

Altered expression of chemokines, cytokines, and growth factors

"Activated" state

thrombosis

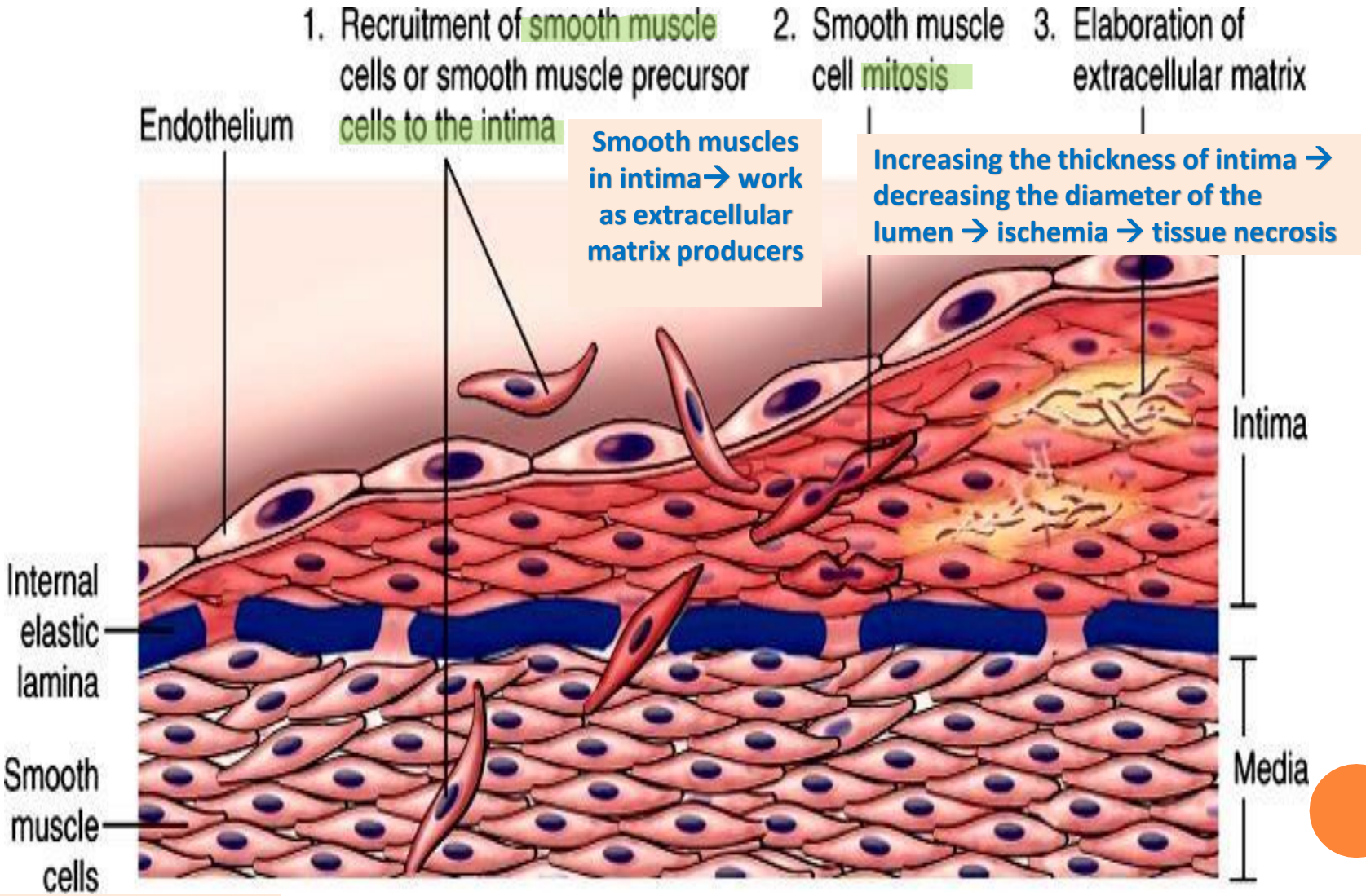
When microenvironment is abnormal → pathological state



And formation of thrombi

Response of Vascular Wall Cells to Injury

REMEMBER:
Cell injury → inflammation → healing



Smooth muscles in intima→ work as extracellular matrix producers

Increasing the thickness of intima → decreasing the diameter of the lumen → ischemia → tissue necrosis

Normally in media

Response of Vascular Wall Cells to Injury

- **Injury results in a healing response**

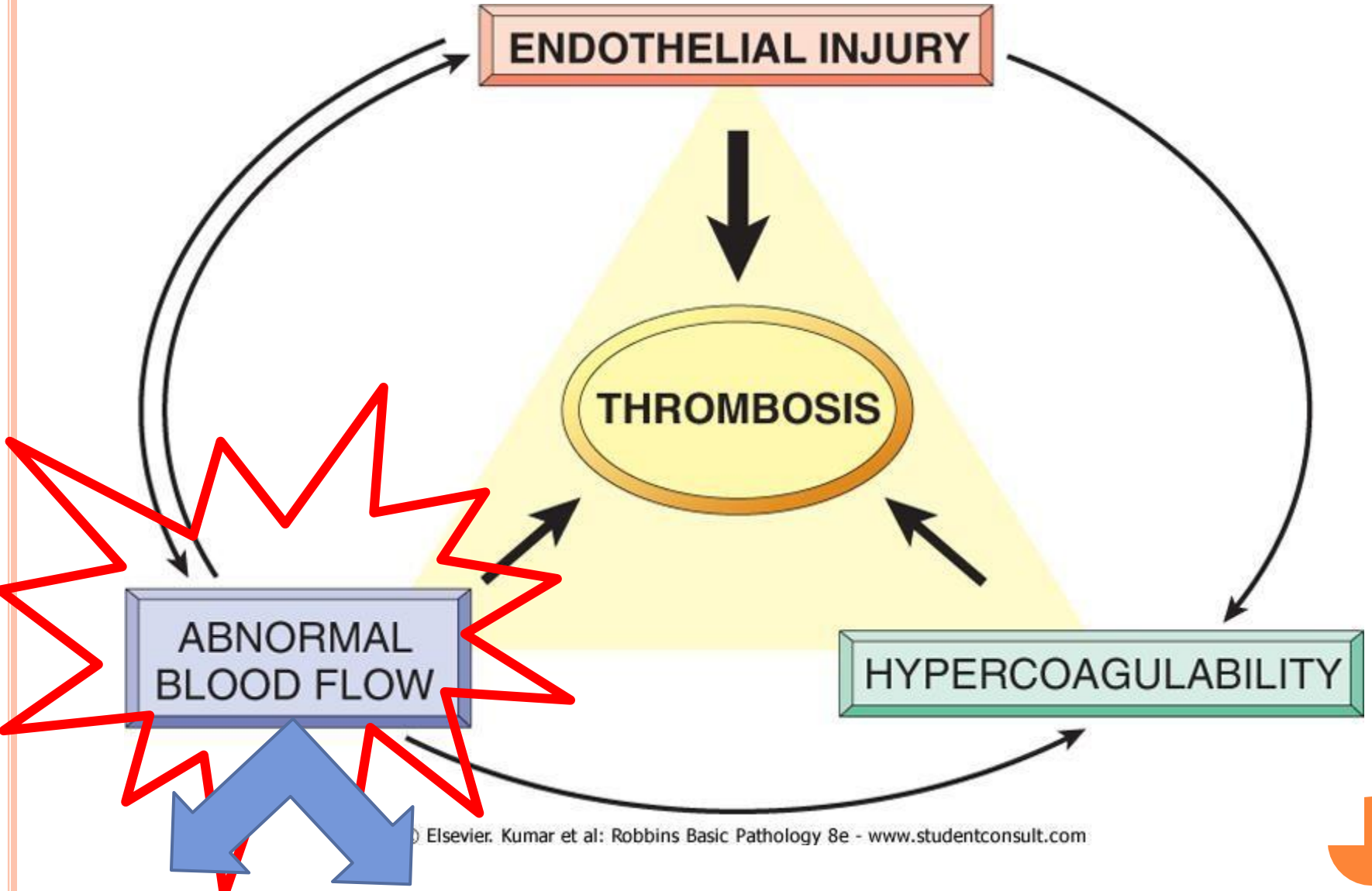
- **Pathologic effect of vascular healing:**

Excessive thickening of the intima →→
luminal stenosis & blockage of vascular flow
Lead to ischemia

Causes of Endothelial injury

*not for memorizing , just understand the concept to conclude the causes by yourself ☺

1. *Valvulitis*
2. *MI*
3. *Atherosclerosis*
4. *Traumatic or inflammatory conditions*
5. *Hypertension*
6. *Endotoxins*
7. *Hypercholesterolemia*
8. *Radiation*
9. *Smoking*
10. *……..etc.*



Turbulence
اضطراب

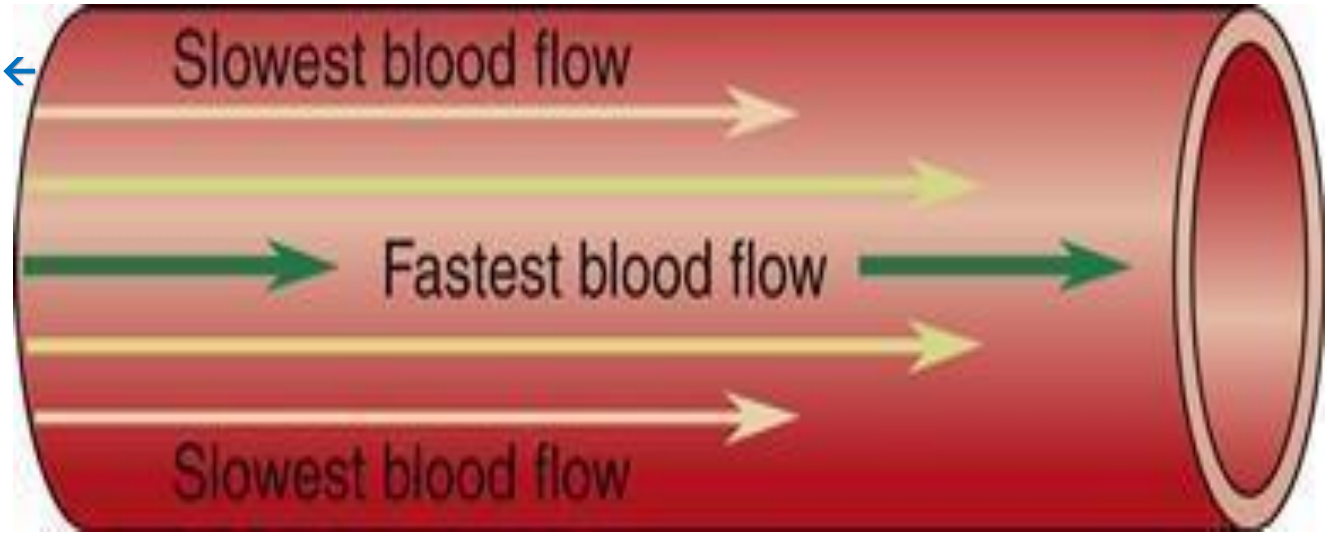
Stasis
ركود

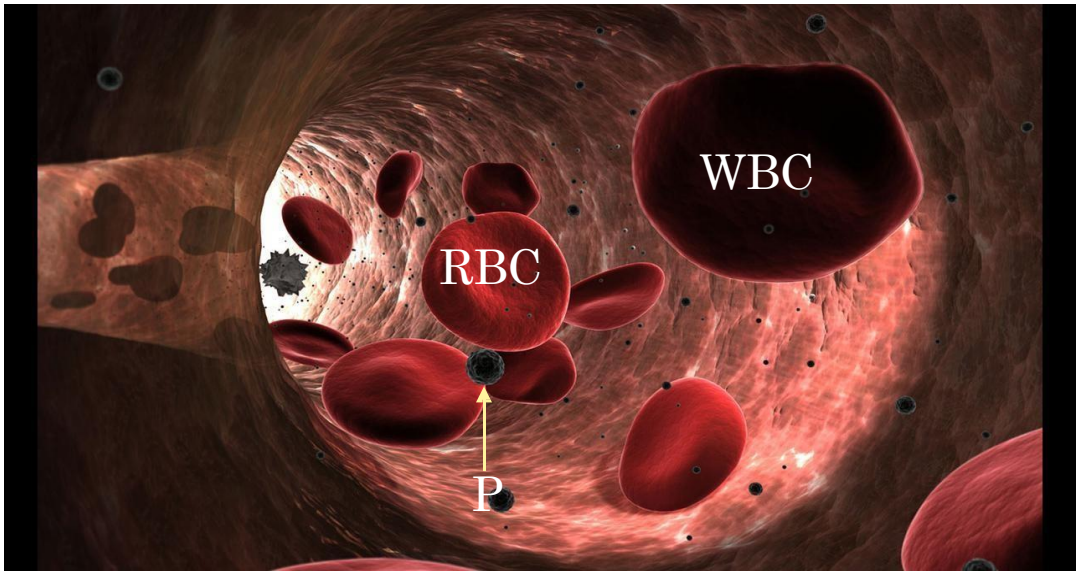
Normal

LAMINAR BLOOD FLOW

UNIDIRECTIONAL , relatively straight

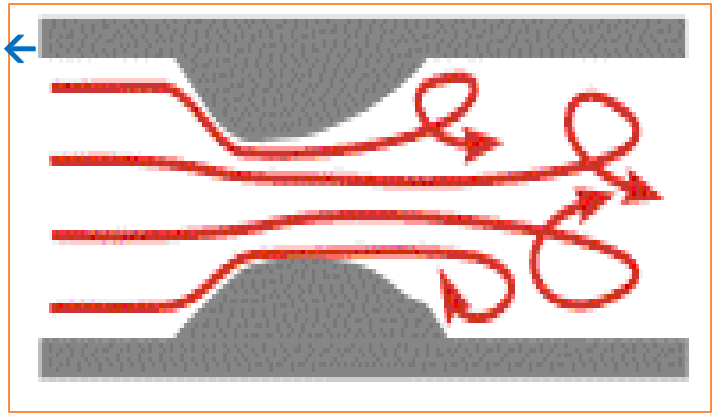
Prevents thrombosis by making the platelets flow in the center not in the periphery beside intima .





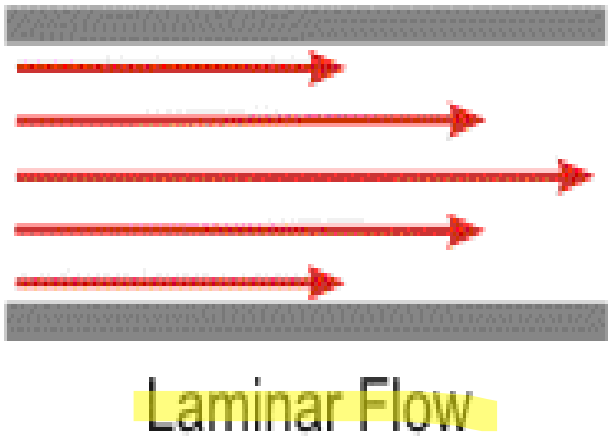
Laminar vs turbulent blood flow

Excessive thickness ← because of atherosclerosis, embolus , thrombus ...etc.



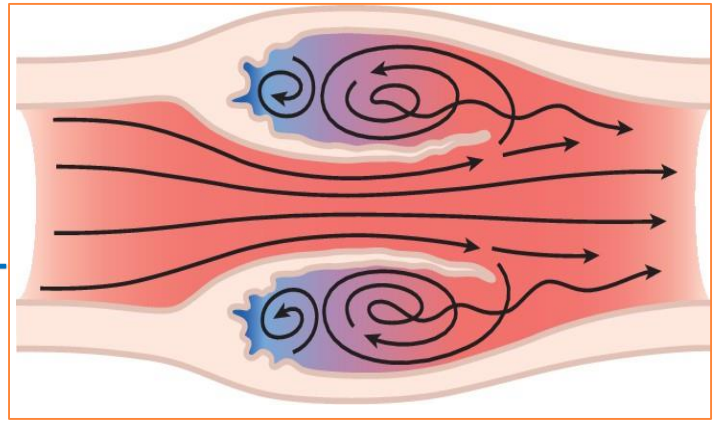
MULTIDIRECTIONAL

Turbulent Flow



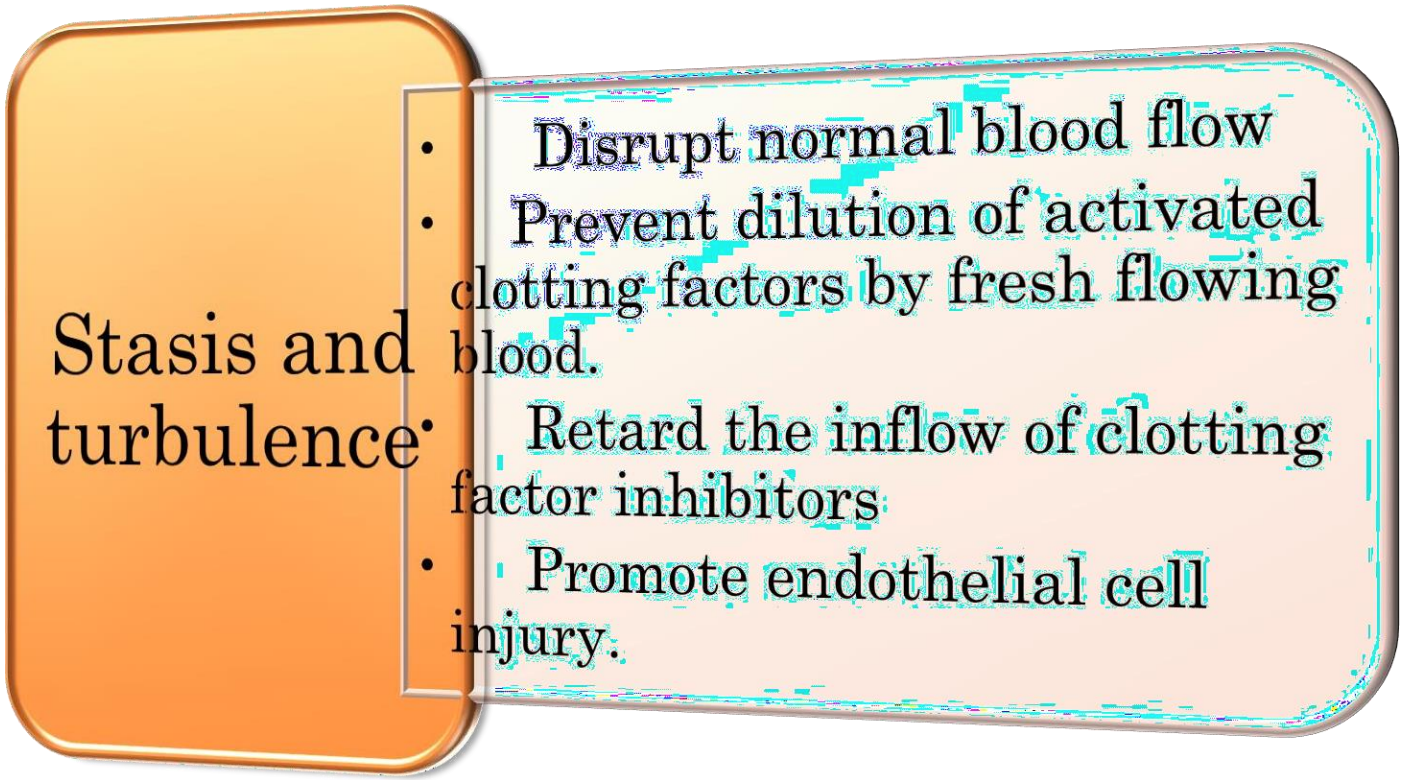
UNIDIRECTIONAL

Abnormal dilation ← because of Aneurysms , varices ...etc.



Stasis

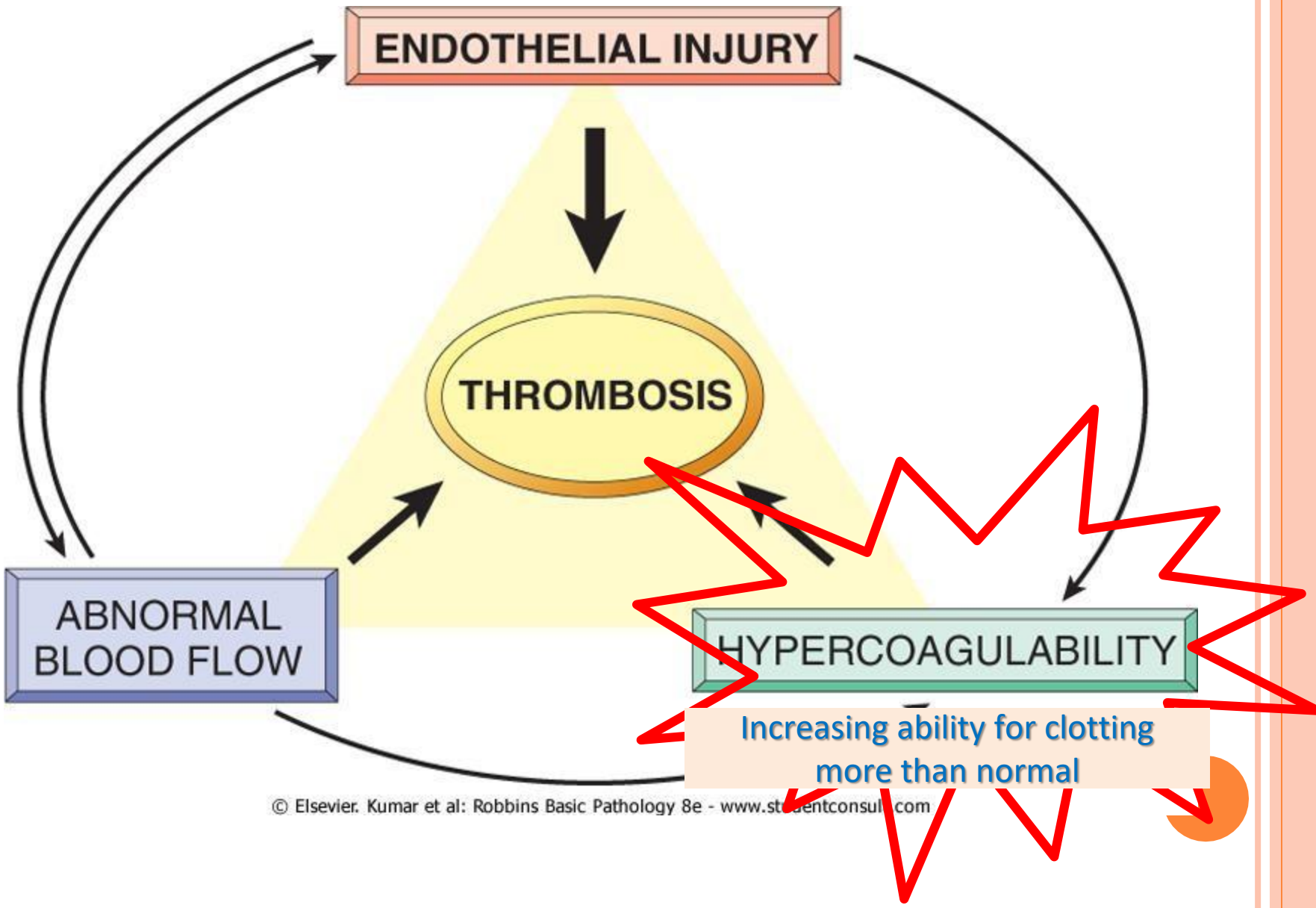
- *Stasis is a major factor in **venous** thrombi*
- Normal blood flow is ***laminar (p***latelets flow centrally in the vessel lumen, separated from the endothelium by a slower moving clear zone of plasma)
- Stasis and turbulence cause the followings:



Causes of Stasis

Not for memorization

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)***
6. ***……..***


ENDOTHELIAL INJURY
THROMBOSIS
ABNORMAL BLOOD FLOW
HYPERCOAGULABILITY
Increasing ability for clotting more than normal
© Elsevier. Kumar et al: Robbins Basic Pathology 8e - www.studentconsult.com

Hypercoagulability

A. Genetic (primary):

- most common of the genetic causes >> mutations in factor V gene and prothrombin gene Or mutation in the clotting factors inhibitors.

B. Acquired (secondary): →more common

- multifactorial & 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 free side of the thrombus)

- **The propagating portion of a thrombus is poorly attached →fragmentation and embolus formation**

Terms to remember ….

LINES OF ZAHN

- gross and microscopically apparent laminations
- represent pale platelet and fibrin layers alternating with darker erythrocyte-rich layers
- Significance? distinguish **antemortem** thrombosis from postmortem clots

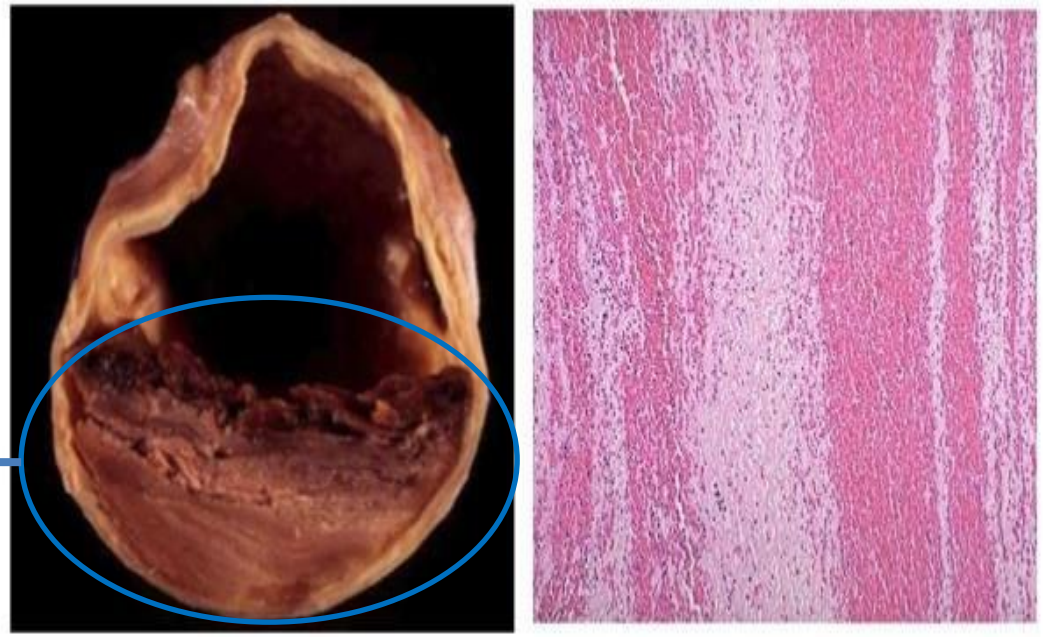
Pure forensic issue

After death

Before death→ so we can know if the thrombosis were the cause of death or formed after death.

- postmortem blood clots are non-laminated clots *(no lines of Zahn)*

- Lines of Zahn present in antemortem thrombus

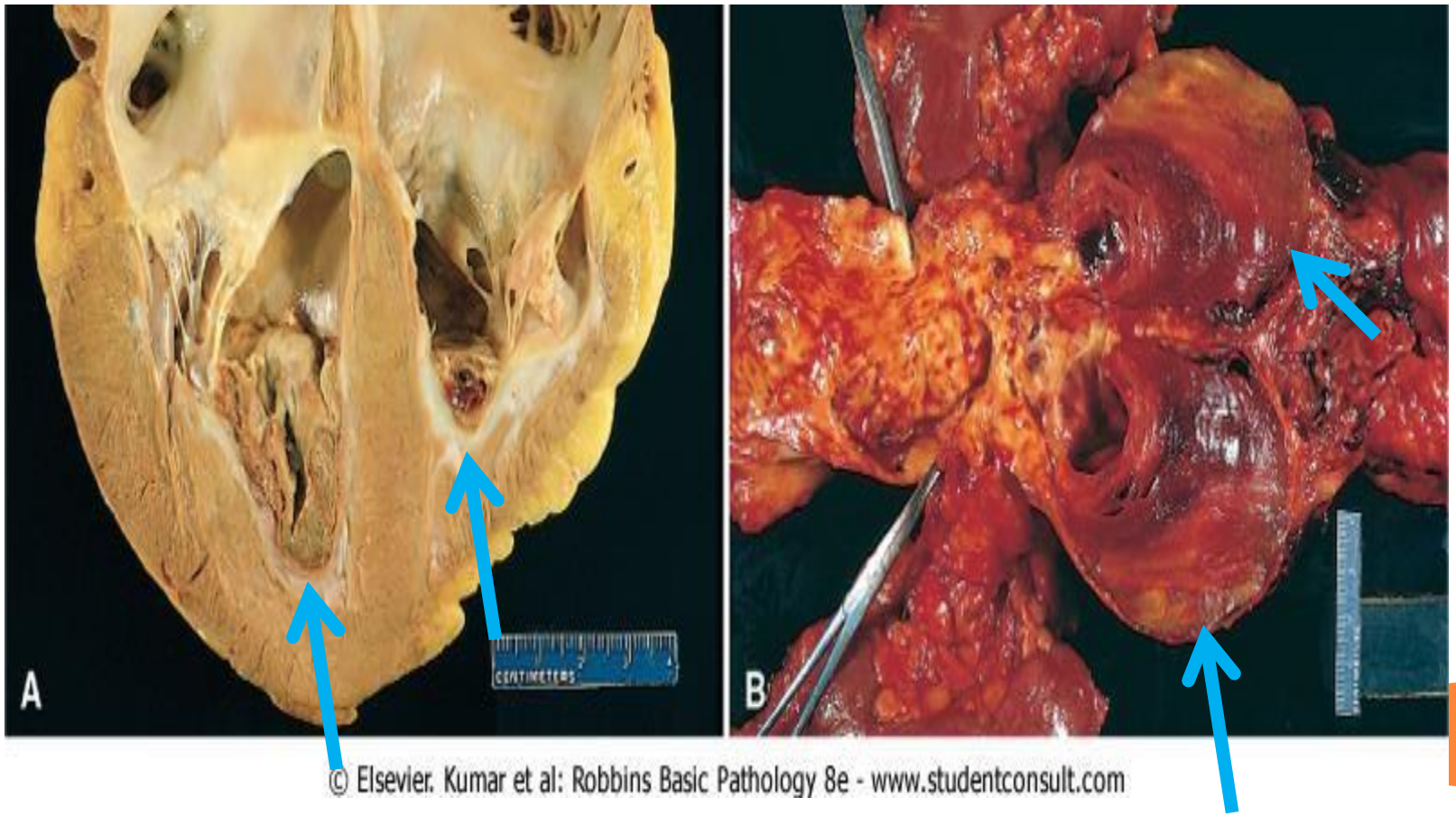


Thrombus

Different layers + colors grossly and microscopically

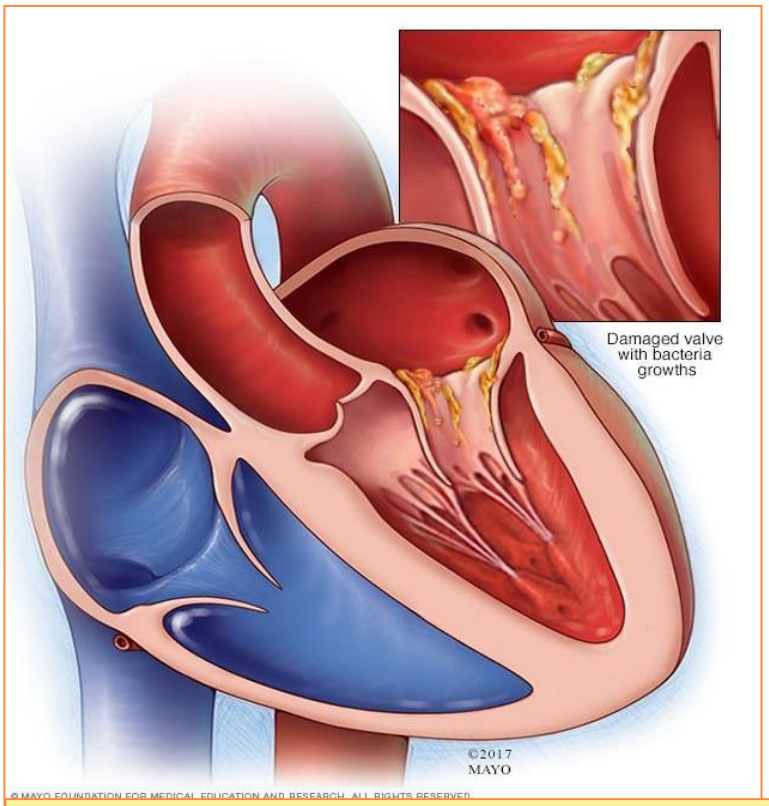
Wall of cavity

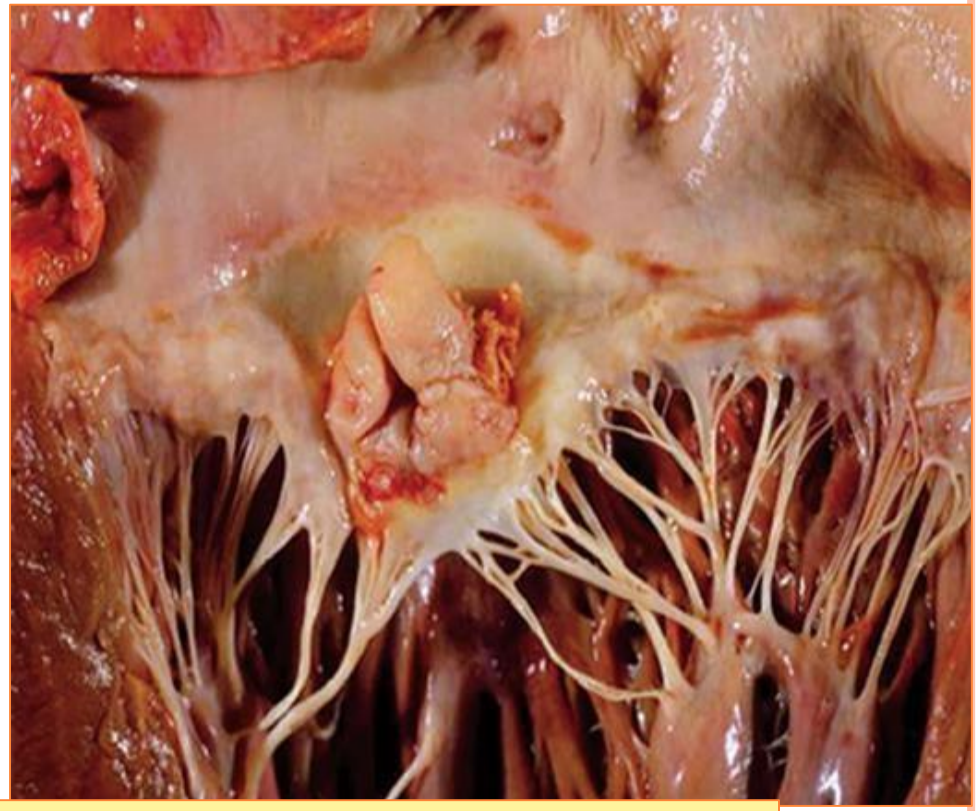
MURAL THROMBI= - IN HEART CHAMBERS OR IN AORTIC LUMEN



In cardiac valves

Cardiac Vegetations





= Thrombi on heart valves

Types:

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

2-non- infectious:
e.g. non-bacterial thrombotic endocarditis

Fates of a thrombus

→ Fibrinolytic system just in small + recent thrombi , the lysis can be in hours , caused :
- endogenous
- exogenous (by treatment)

→ this is the perfect fate.

resolusion
or dissolution

→ Progression
→ It may block the blood vessel
→ Bad fate.

→ Embolus formation
→very bad fate (potential killer) because this embolus sticks on the wall of the blood vessel and blocks it

→Organization : tissue is replaced by another tissue (collagen & CT) but it stays in the same place (prominent tissue)
→Depends on the location , it is very bad
→Recanalization : open channel inside the thrombus

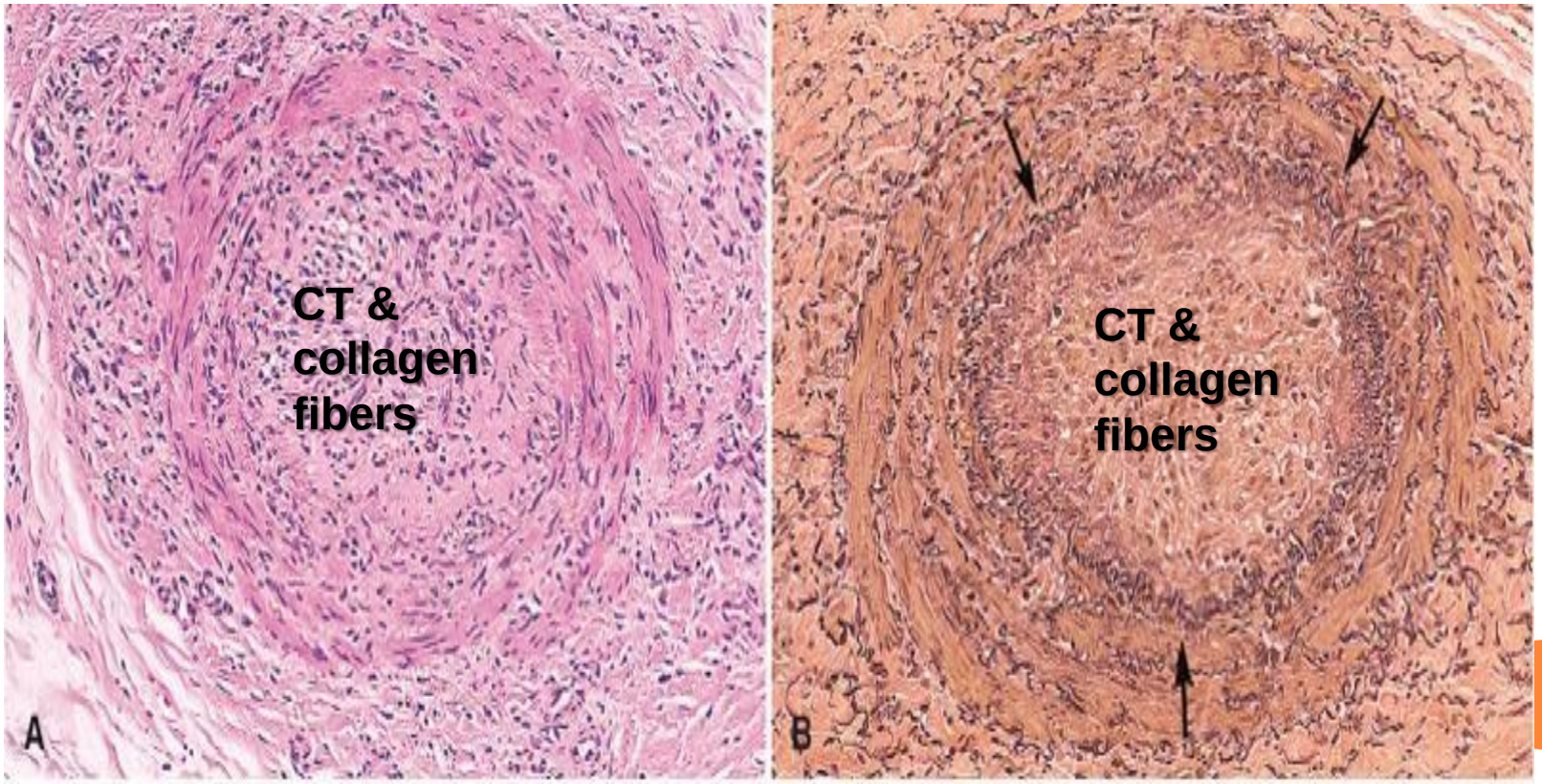
Mycotic aneurysm (discussed later)

Replaced by prominent tissue

ORGANIZED ARTERIAL THROMBUS

This pics isn't for memorizing

There is no lumen in this histological sections , which indicates tissue replacement.



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)***