PATHOLOGY

بسم الله الرحمن الرحيم

FINAL | Lecture 1

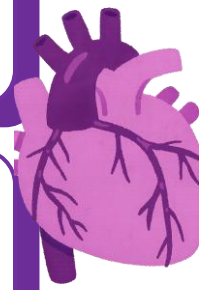
Pathology of Thrombosis

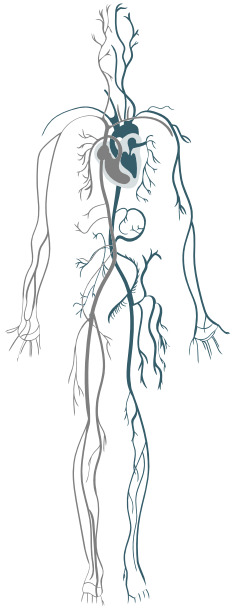
وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

اللهم إنّا نعوذ بك من شرور أنفسنا ومن سيئات أعمالنا

Written by: Mohammad Al-Asali

Reviewed by: Laith Joudeh





وَلِلَّهِ الْأَسْمَاءُ الْحُسْنَى فَادْعُوهُ بِهَا

المعنى: الخالق المالك المدَبّر، المربّي جميع خلقه بنِعَمه، ويُربيّ أولياءه بما يُصلح قلوبهم، ولا يجوز إطلاق اسم الرب على غير الله تعالى إلا مضافاً، كرب الأسرة.

الورود: ورد في القرآن (٩٠٠) مرة.

الشاهد: ﴿ ٱلْحَمْدُ لِلَّهِ رَبِّ ٱلْعَٰلَمِينَ ﴾ [الفاتحة:١].

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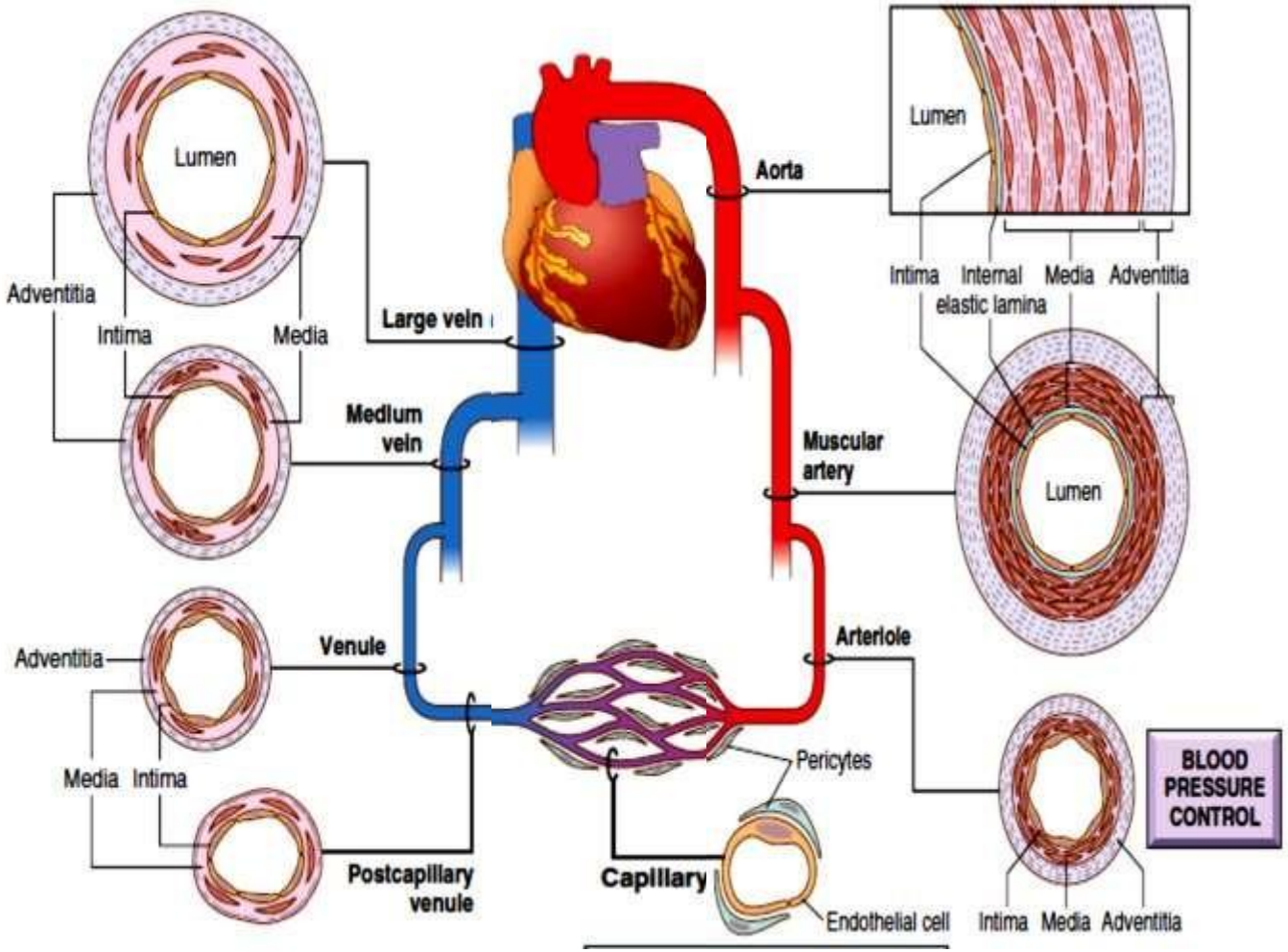
اضغط هنا لشرحٍ أكثر تفصيلًا

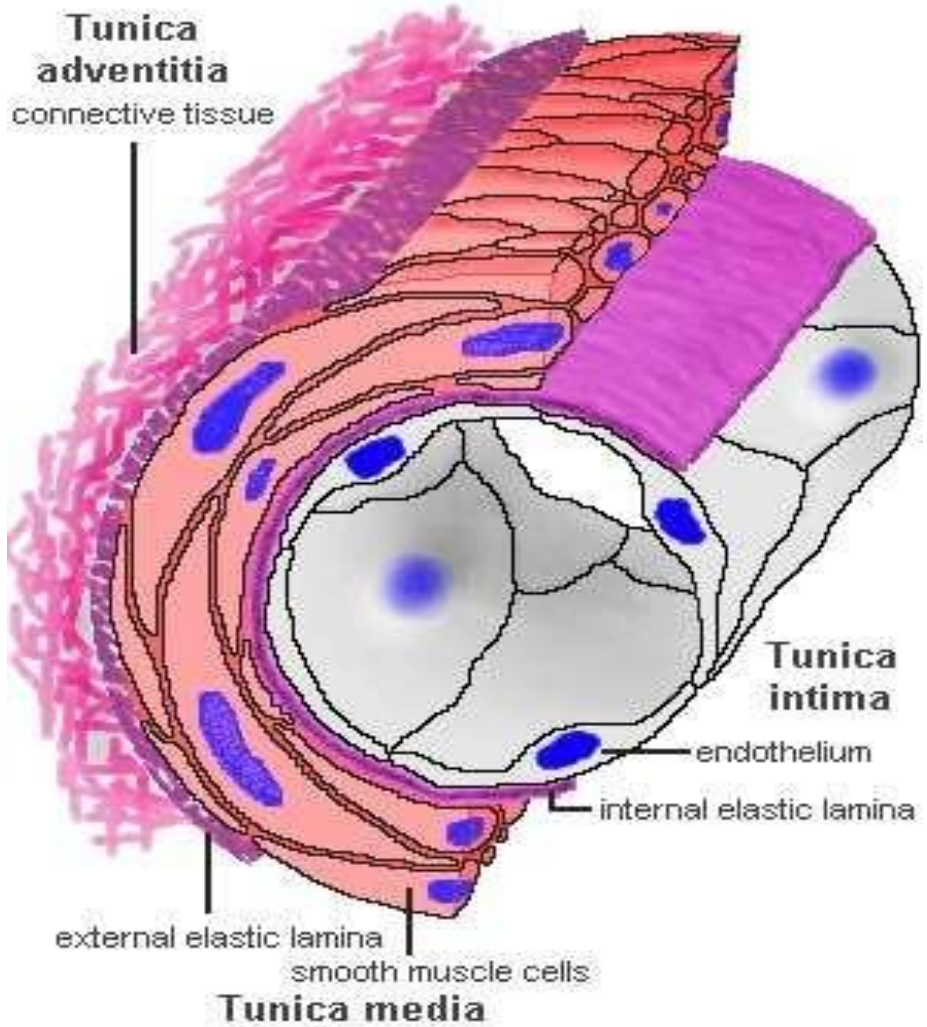
CARDIOVASCULAR SYSTEM

Venous circulation

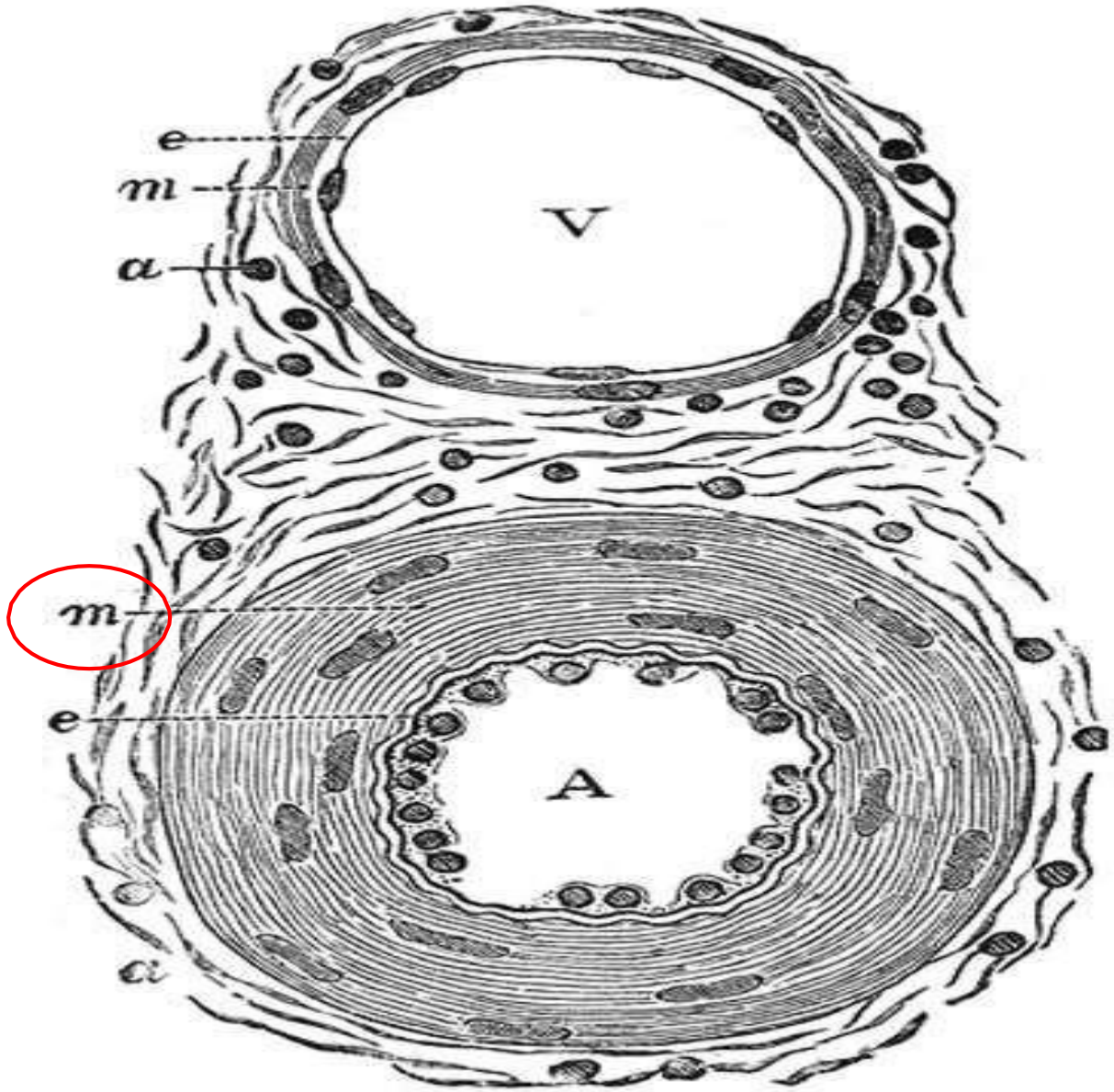
Arterial circulation



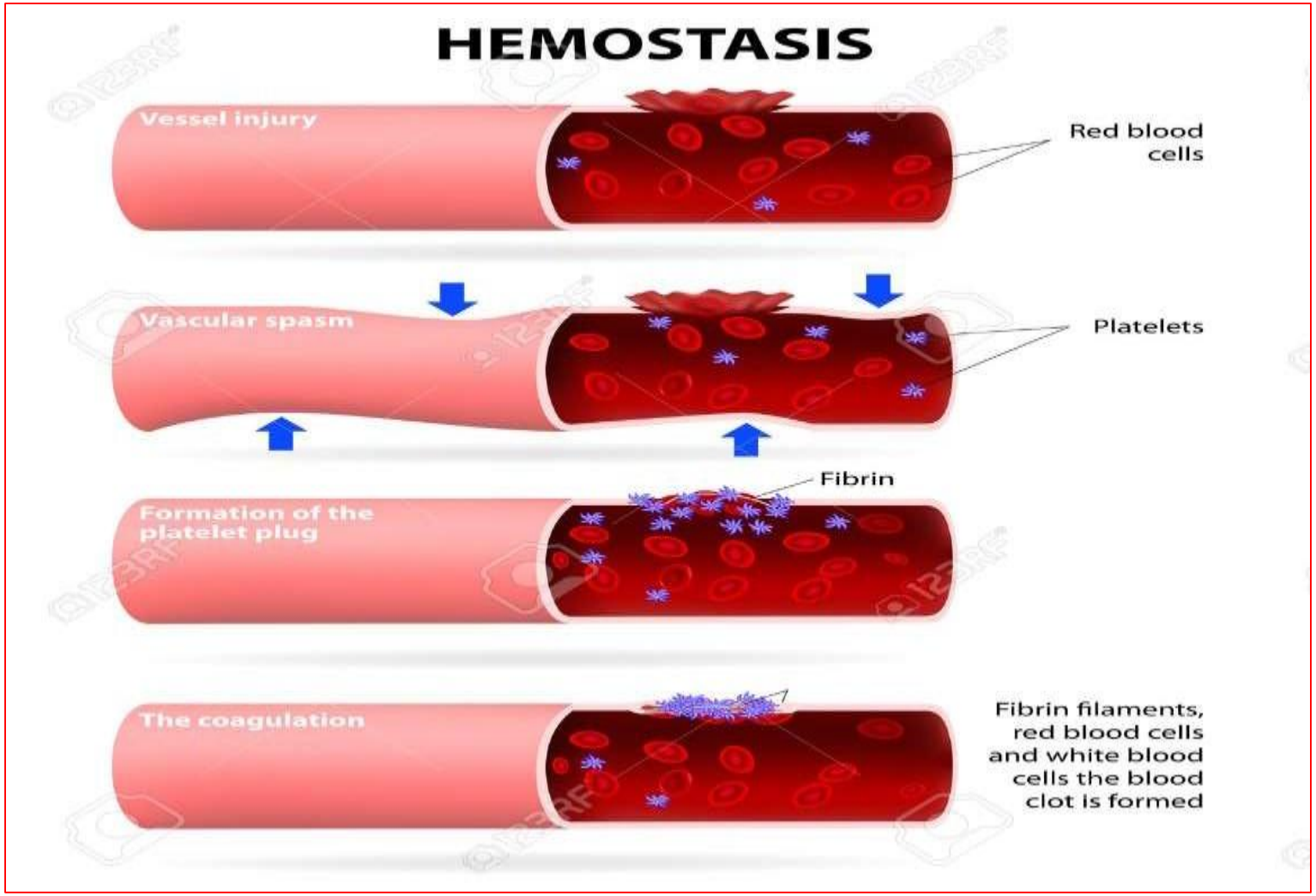
Normal blood vessel histology



ARTERY (A) VS VEIN (V)



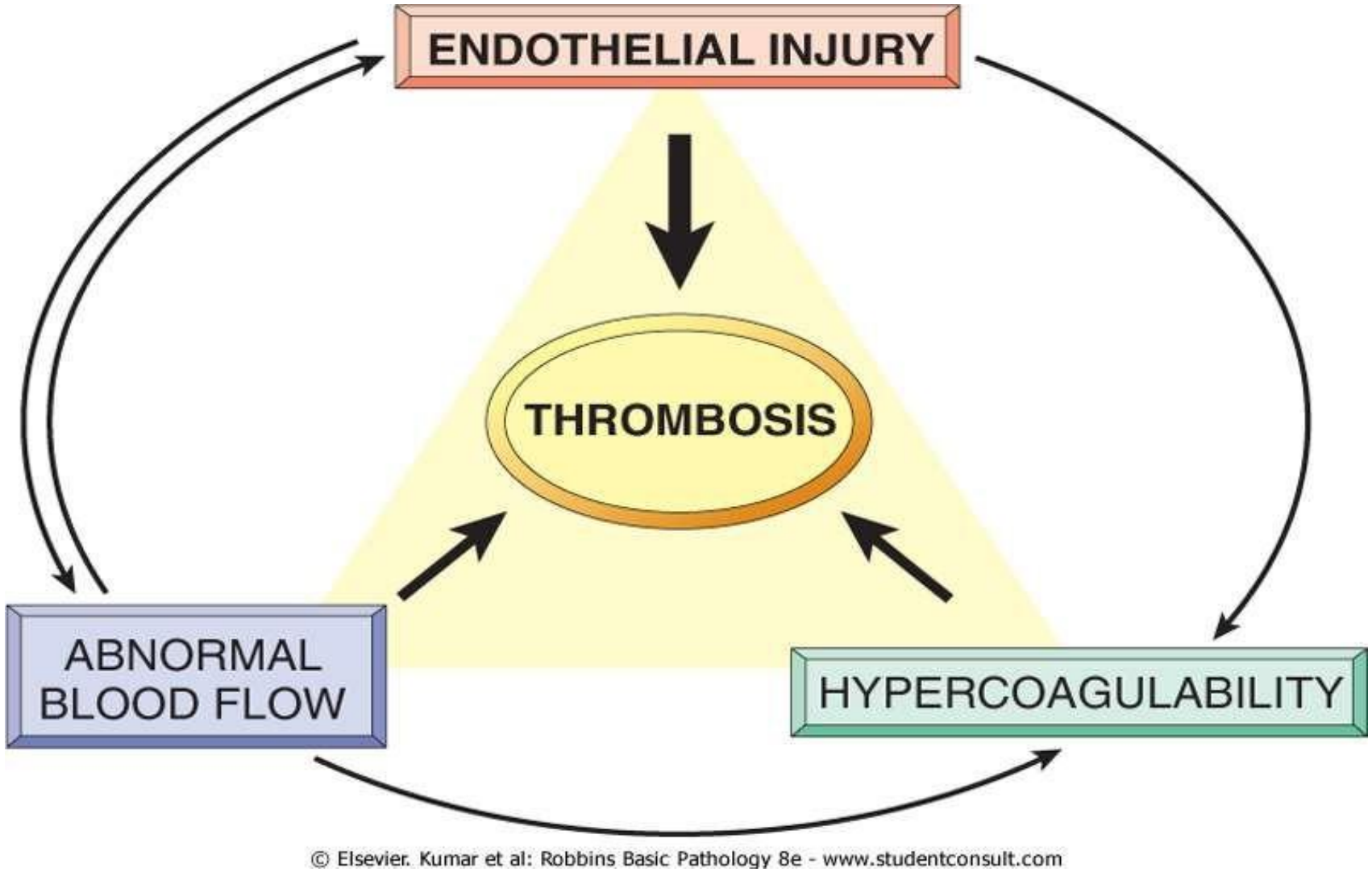
PHYSIOLOGY OF THROMBOSIS



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

Virchow's triad



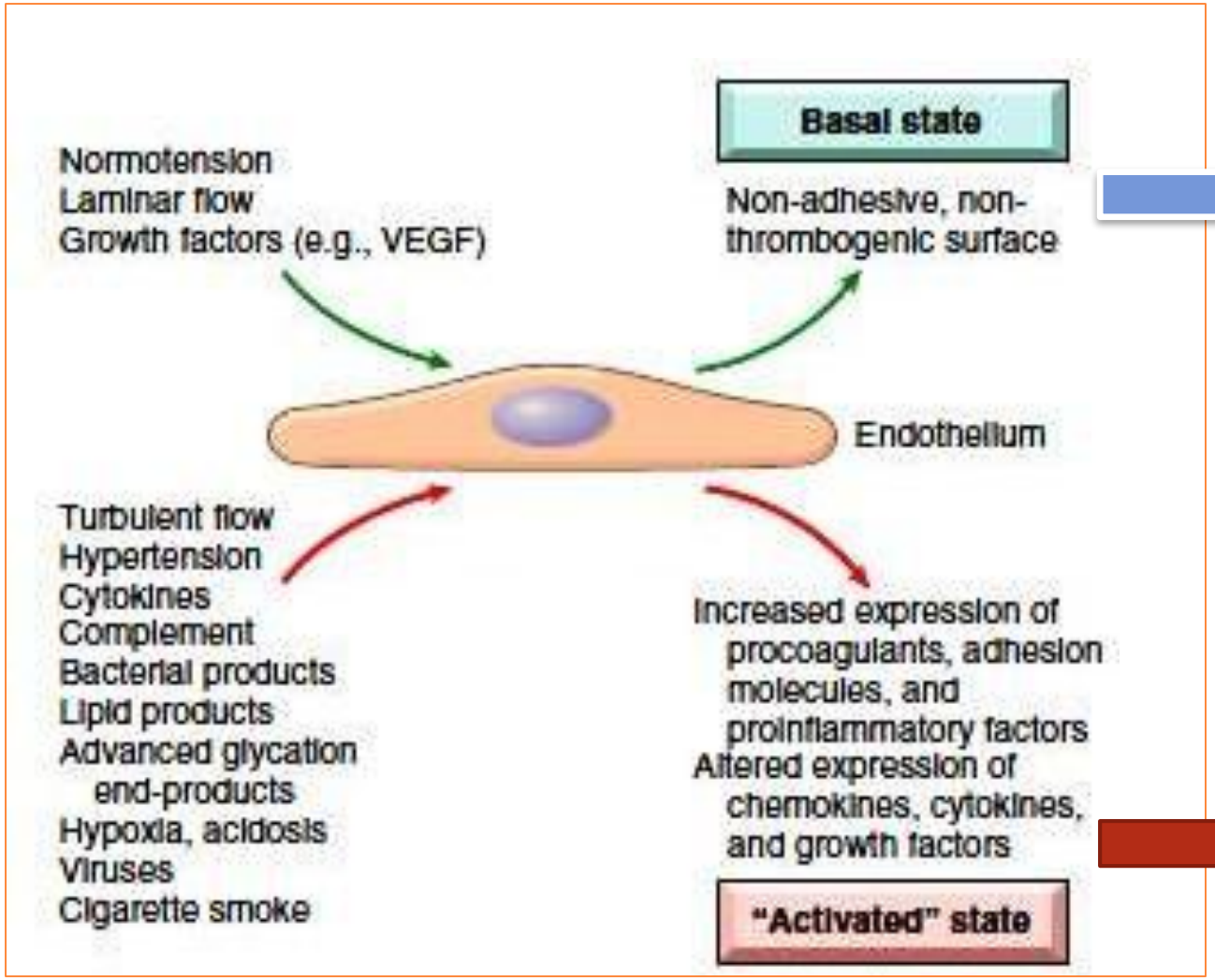
Thrombosis – Pathological Aspects

- Pathogenesis (called Virchow's triad):
- In cases of pathological thrombosis, a patient may exhibit **one, two, or all three** components of Virchow's triad, and these factors can **interact with one another**. The triad includes **(SHE)**:

1. **S**tasis/turbulence (abnormal blood flow)
2. Blood **H**ypercoagulability
3. **E**ndothelial* Injury (Heart, Arteries)

- **Any combination** of these components may contribute to clot formation.
- *Endothelial cells are special type of cells that cover the inside surface of blood vessels and heart.

Contribution of Endothelial Cells to Coagulation



No thrombosis

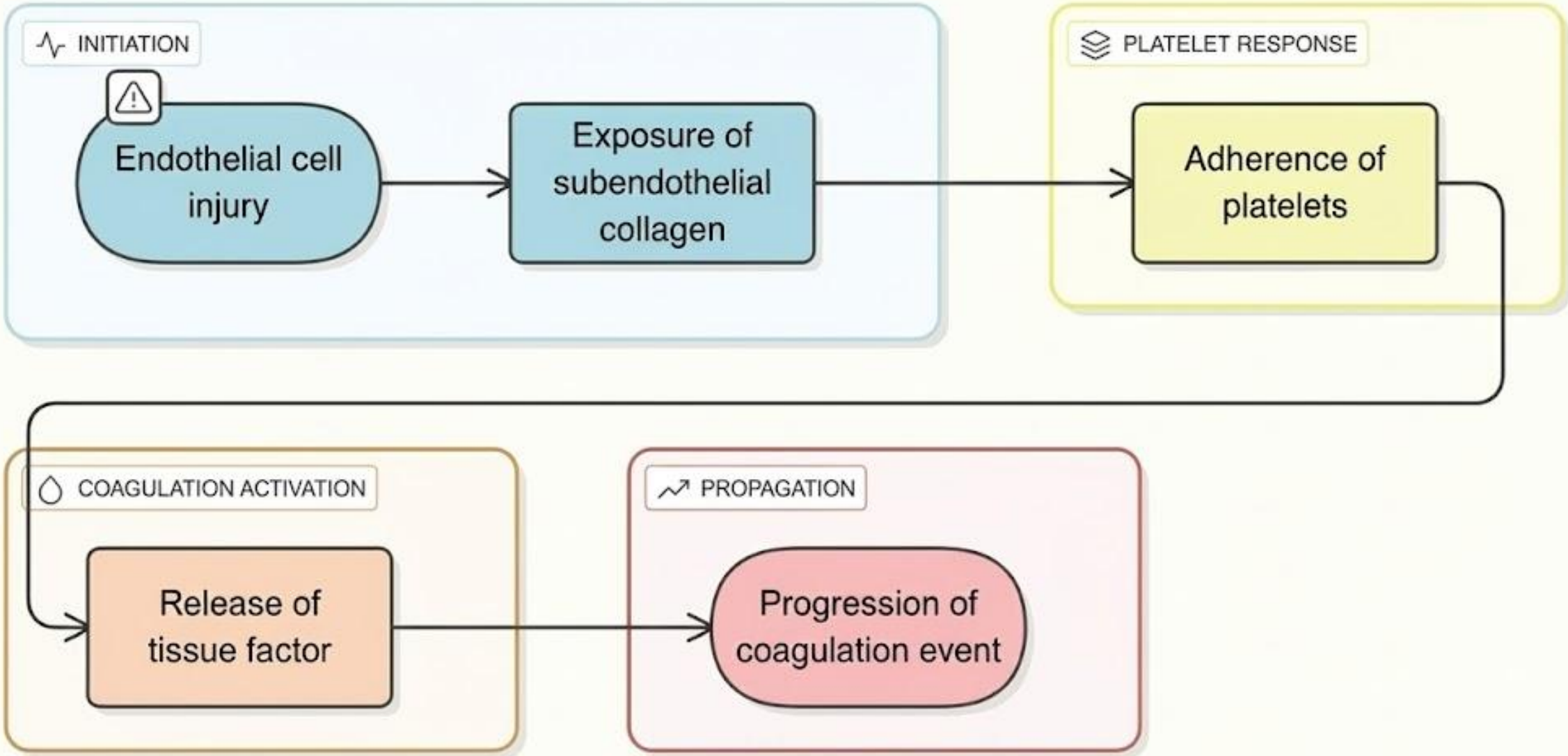
thrombosis

Contribution of Endothelial Cells to Coagulation

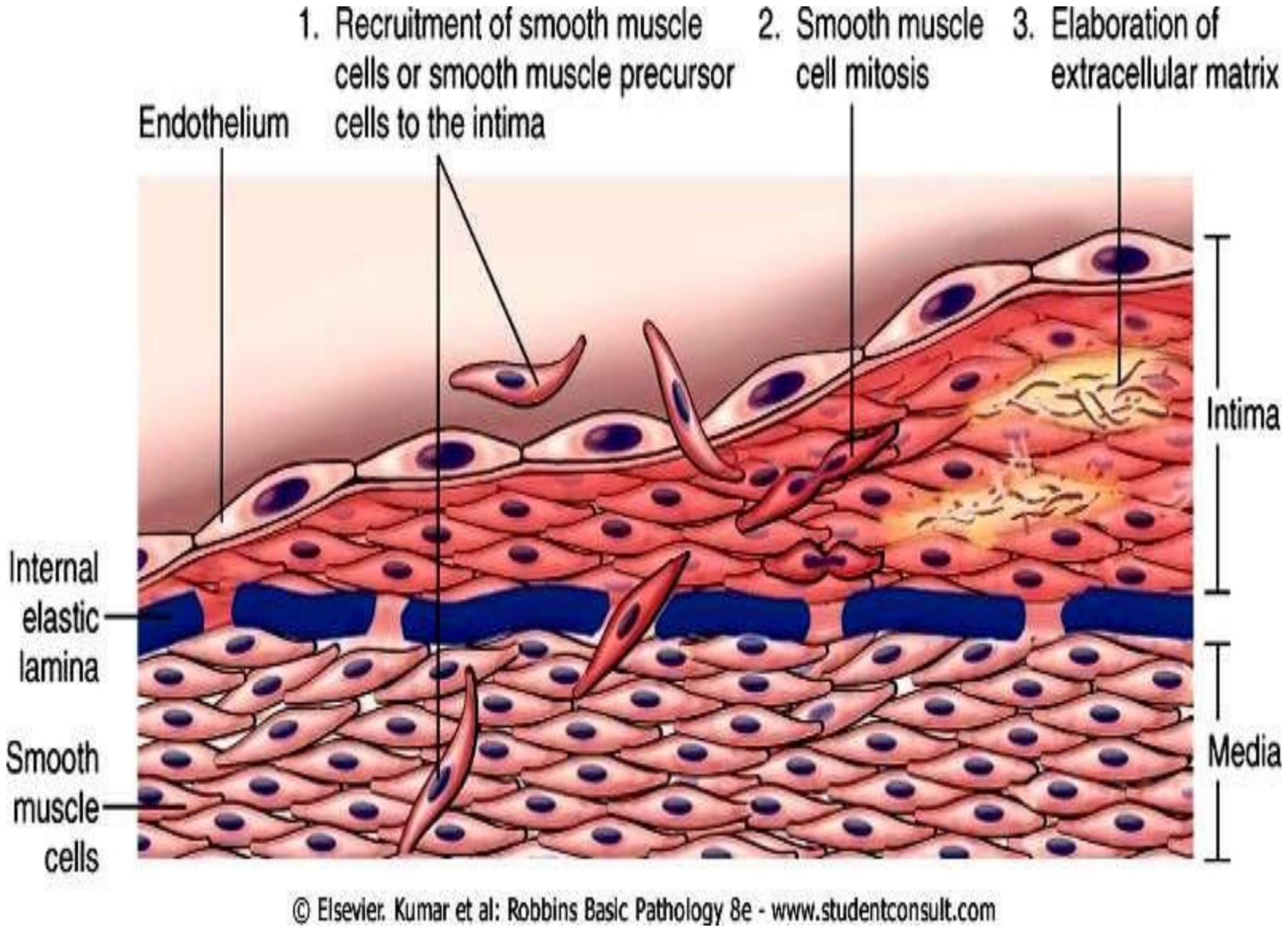
- Under normal (basal) conditions, endothelial cells provide a **non-adhesive, non-thrombogenic** surface that protects the body from unnecessary or pathological thrombosis.
- This basal state is maintained by a stable microenvironment, including:
  - **Normal blood pressure**
  - **Normal (laminar) blood flow**
  - **Growth factors that support endothelial integrity**
- In this state, thrombosis does not occur.

Contribution of Endothelial Cells to Coagulation

- In pathological thrombosis, endothelial cells may become **damaged or functionally activated**.
- **Endothelial injury → endothelial activation**
- Activation occurs when the microenvironment becomes **abnormal due to the previously mentioned factors**. Once activated, endothelial cells promote thrombosis by increasing the expression of:
  - **Pro-coagulant factors**
  - **Adhesion molecules**
  - **Pro-inflammatory factors**
  - **Chemokines, cytokines, and growth factors**
- This shift **favors pathological thrombosis**.


INITIATION
Endothelial cell injury
Exposure of subendothelial collagen
PLATELET RESPONSE
Adherence of platelets
COAGULATION ACTIVATION
Release of tissue factor
PROPAGATION
Progression of coagulation event

Response of Vascular Wall Cells to Injury



Response of Vascular Wall Cells to Injury

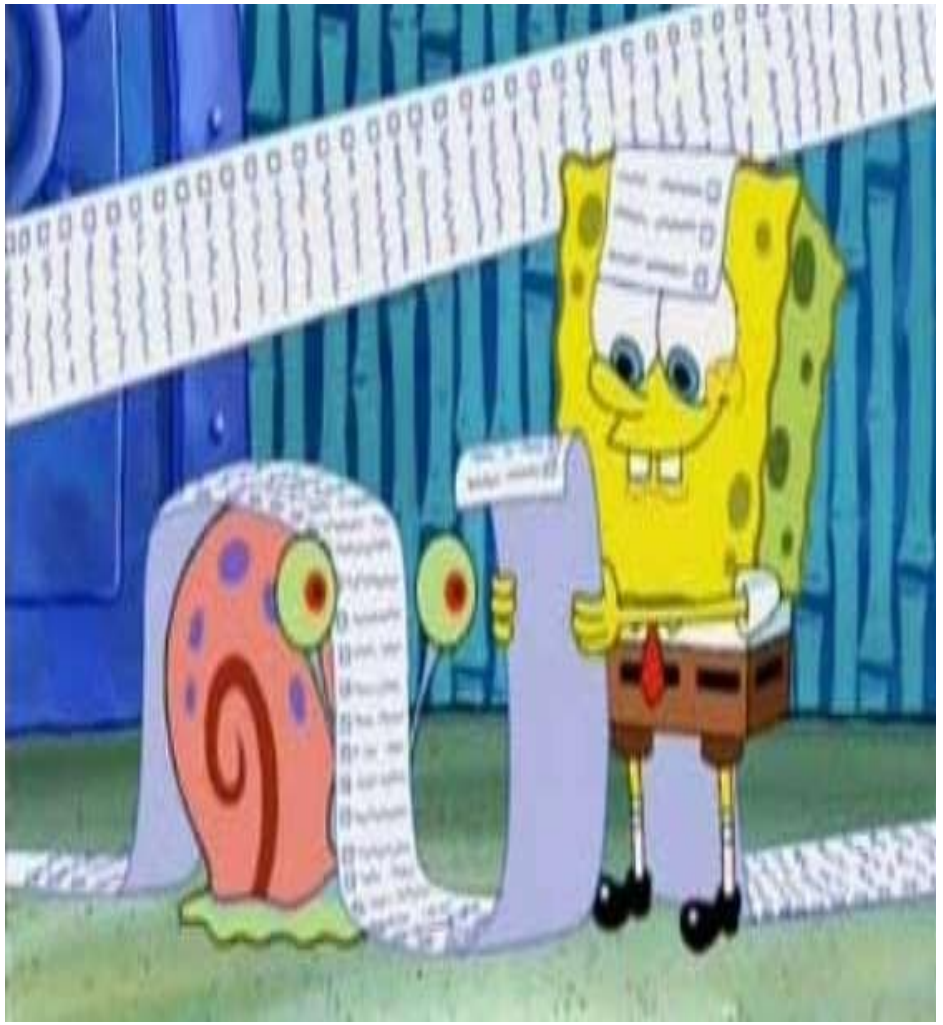
- When the vascular wall is injured, **both endothelial cells and smooth muscle cells** are affected. Smooth muscle cells respond by:
  - **Migrating from the tunica media into the tunica intima**
  - **Proliferating within the intima**
  - **Producing extracellular matrix proteins**
- These changes constitute the **vascular wall response to injury**.
- In the diagram, the left side shows the vessel **before injury**, while the right side shows the **post-injury response**. The intima becomes **thicker due to increased cells and extracellular matrix**, which **narrows the vessel lumen and reduces blood flow**.
- Consequences may include:
  - **Tissue ischemia**
  - **Tissue necrosis**
  - **Possible infarction**

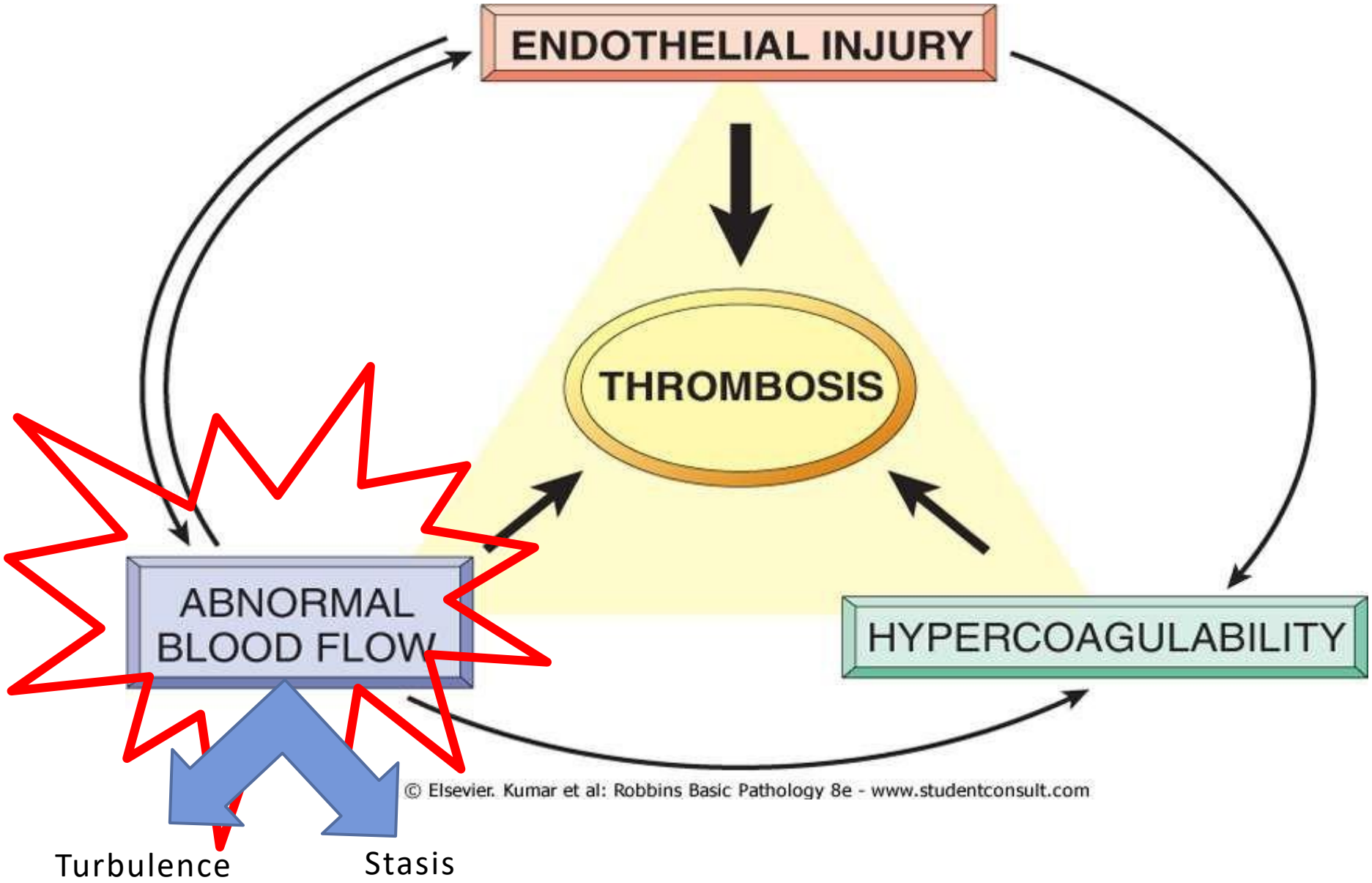
Response of Vascular Wall Cells to Injury

- Injury results in a healing response
- Pathologic effect of vascular healing:
- Excessive thickening of the intima → luminal stenosis & blockage of vascular flow

- Causes of Endothelial injury:

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




ENDOTHELIAL INJURY
THROMBOSIS
ABNORMAL BLOOD FLOW
HYPERCOAGULABILITY
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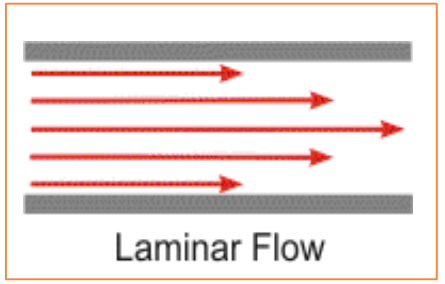
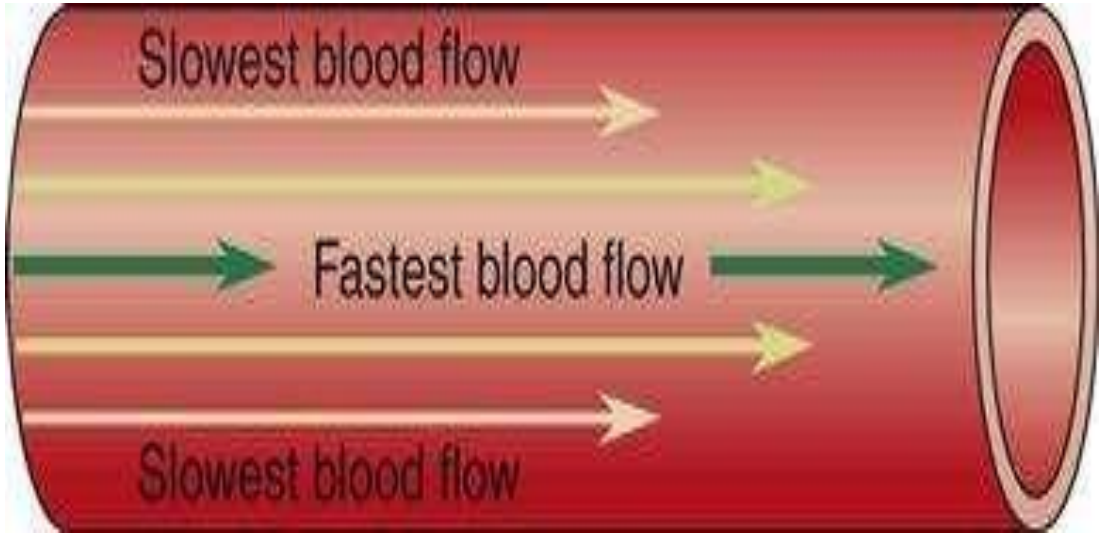
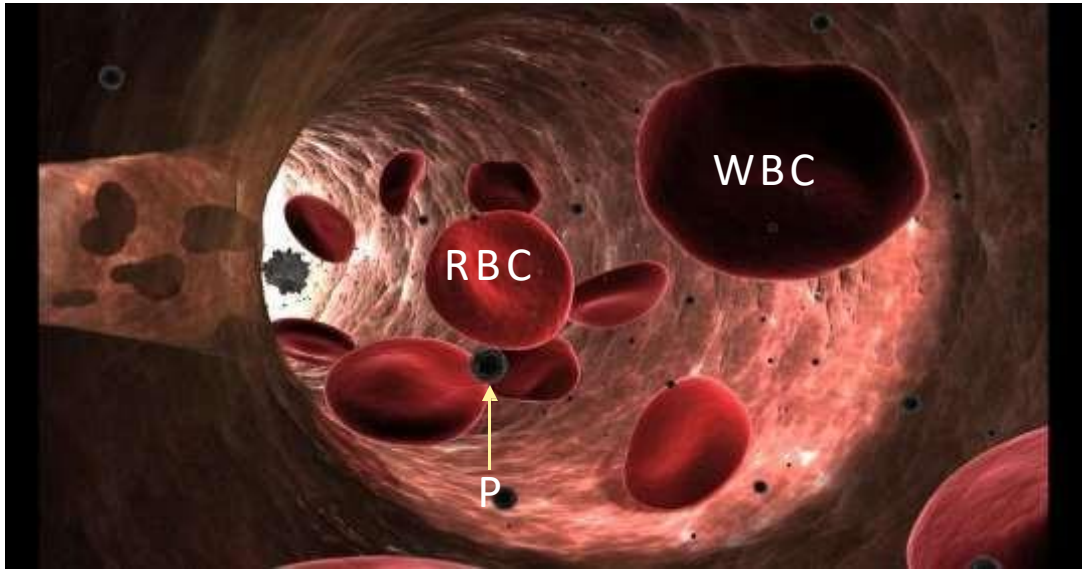
Turbulence
Stasis

Laminar Blood Flow **(Normal)**



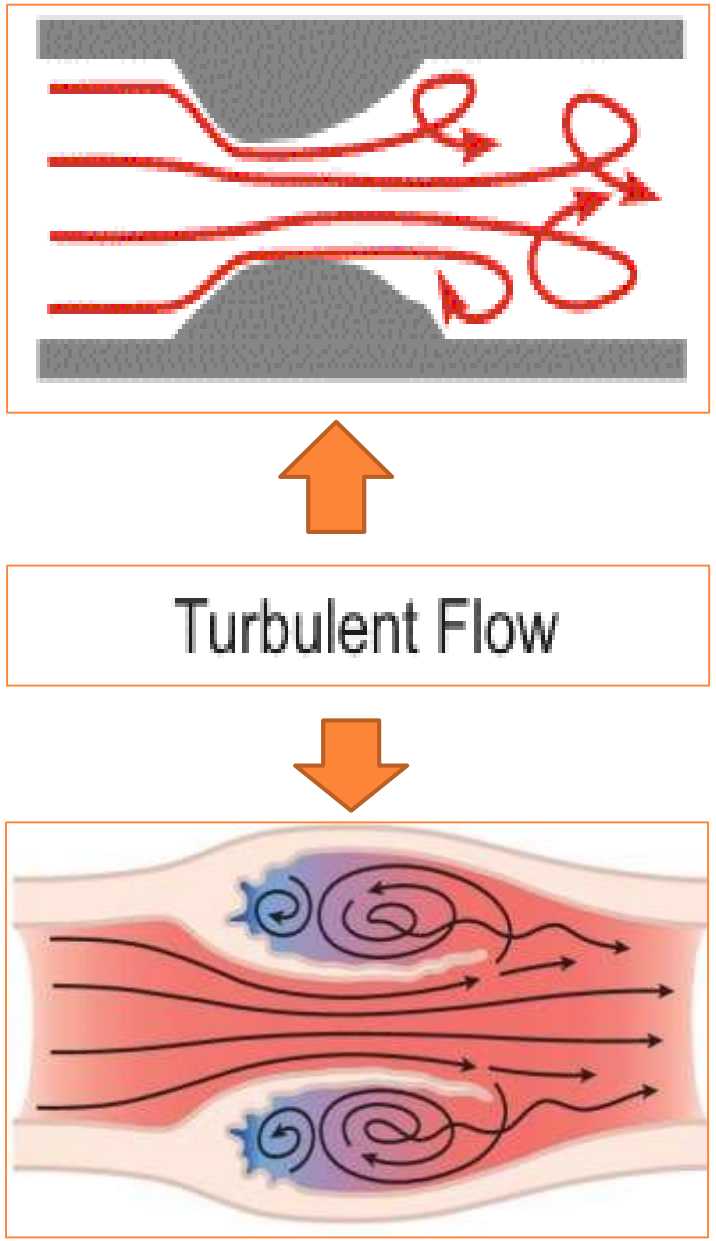
- Normal blood flow is laminar, meaning it moves in **parallel layers** with different velocities:
  - The **fastest flow occurs in the vessel center**
  - The **slowest flow occurs near the vessel wall**
- Laminar flow helps **prevent** thrombosis by keeping platelets **within the central stream and away from the endothelial surface**.





Laminar vs Turbulent Blood Flow

1. Turbulence due to a **narrowed vessel**
   - The vessel wall is **thickened**, narrowing the lumen.
   - Blood flow becomes **chaotic, with irregular direction and velocity**.
   - This **increases the risk of thrombosis**.
   - **Atherosclerosis is a classic example**.
2. Turbulent (Disturbed) flow in a **dilated vessel (aneurysm)**
   - The vessel wall is **abnormally dilated**.
   - Blood flow becomes **irregular and sluggish**, leading to **disturbed flow rather than true turbulence**.
   - This **turbulence** (disturbance) **promotes thrombosis**.

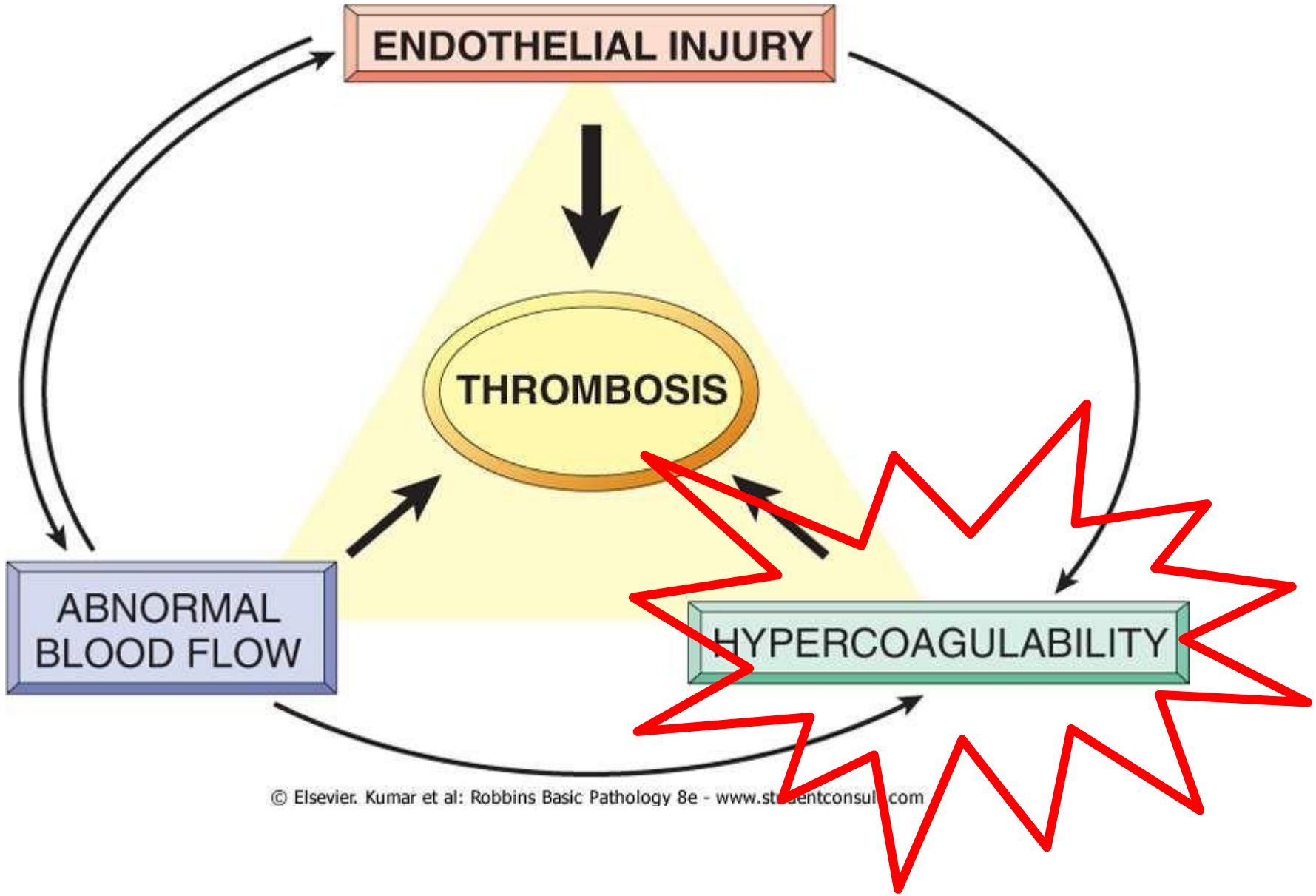


Stasis

- Stasis means slower-than-normal blood flow.
- Like turbulence (Disordered flow), it increases the risk of pathological thrombosis.
- Stasis is a major factor in venous thrombi
- Normal blood flow is laminar (platelets flow centrally in the vessel lumen, separated from the endothelium by a slower moving clear zone of plasma)
- In areas of stasis, blood moves more slowly than normal. As a result:
  - The delivery of anti-clotting factors to the area is reduced.
  - Thrombosis becomes stronger and more stable.
  - Fibrinolysis becomes weaker.
- Both stasis and turbulence can increase or decrease velocity in an abnormal and chaotic manner.

Causes of Stasis

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



Hypercoagulability

- Definition: an **increased tendency to form blood clots** compared to the normal population. This tendency can be **inherited or acquired in an individual patient**.

A. Genetic (primary):
   - Inherited mutations in clotting factors or anti-clotting factors
   - mutations in **factor V** gene and **prothrombin** gene are the most common causes of primary

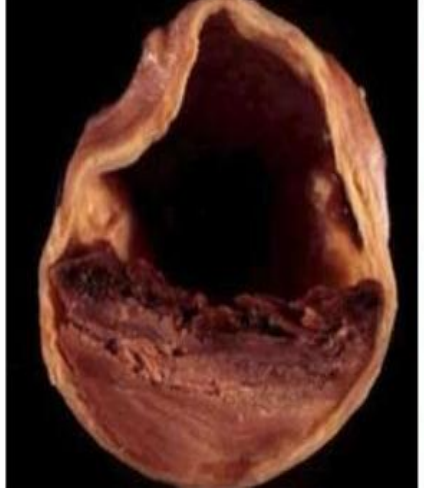
B. Acquired (secondary):
   - **Much more frequent** than primary causes
   - **Multifactorial** & **more complicated**
   - Causes include: Immobilization, MI, AF, arrhythmia, surgery, fractures, burns, Cancer, Prosthetic cardiac valves, etc.

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.
  - 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

Terms to Remember...

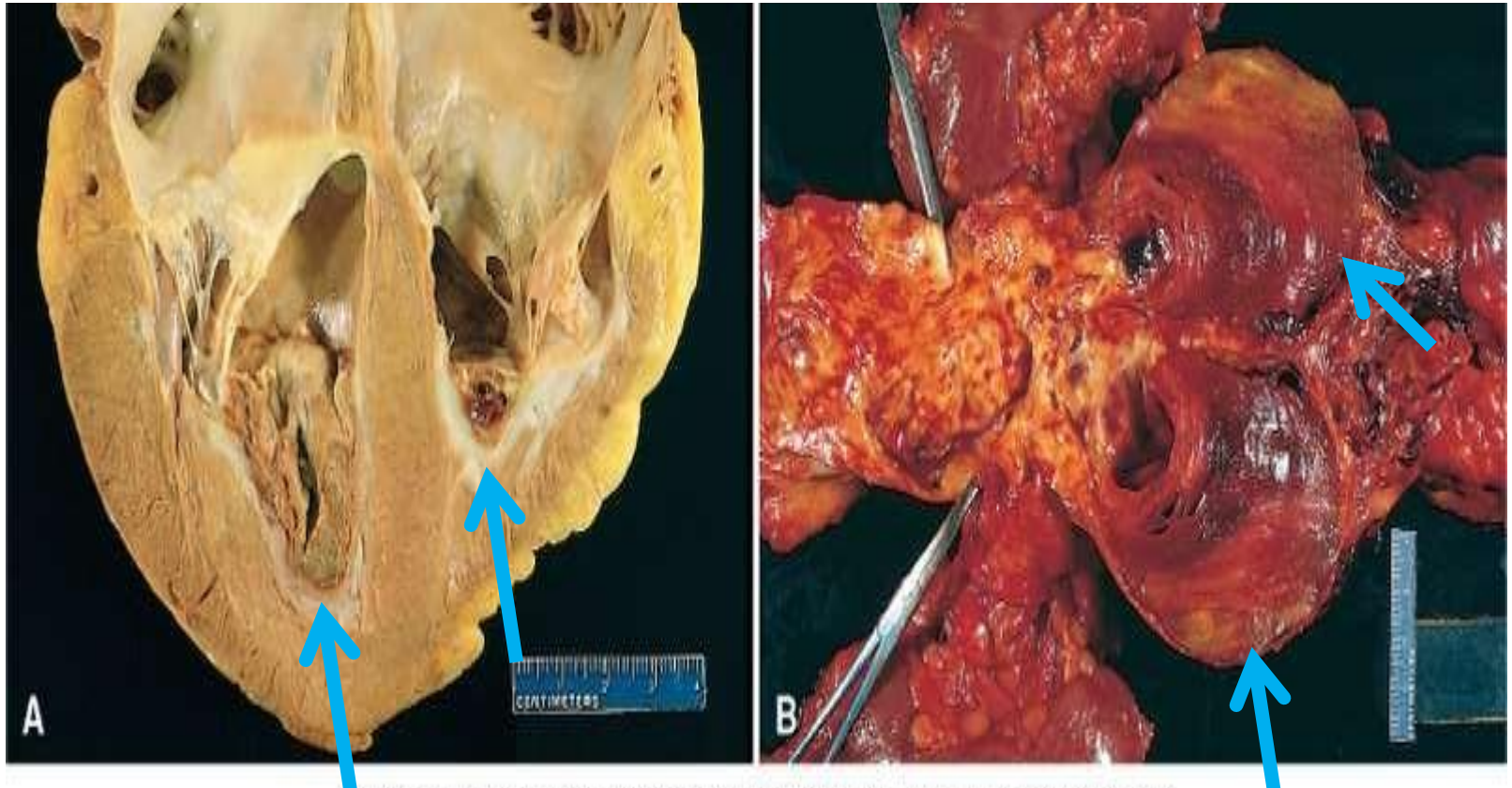
Lines of Zahn



- Gross and microscopically apparent laminations
- Represent alternating layers of pale platelet and fibrin layers alternating with Darker erythrocyte-rich layers found within a thrombus
- **They may be visible to the naked eye or under the microscope.**
- Significance? distinguish antemortem thrombosis from postmortem clots. They are especially important in **forensic** pathology.
- postmortem blood clots are non-laminated clots (no lines of Zahn)

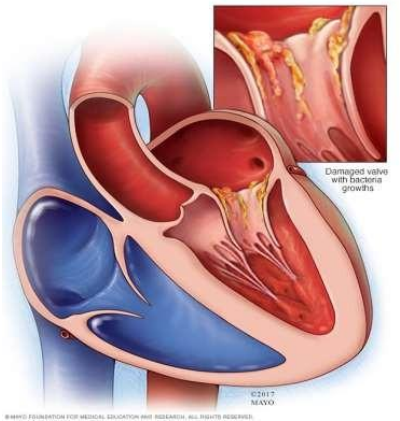
MURAL THROMBI = IN HEART CHAMBERS OR IN AORTIC LUMEN.

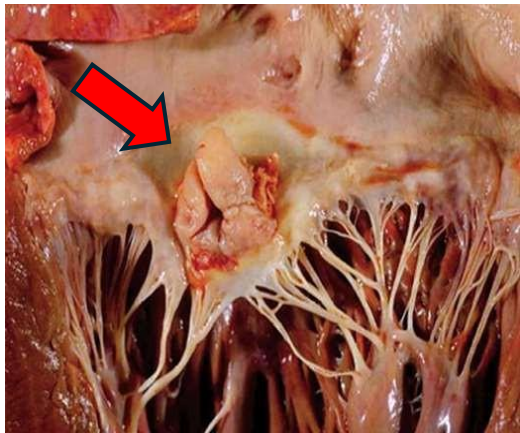
A mural thrombus is a thrombus **attached to the wall** of a **cardiac chamber or blood vessel**.



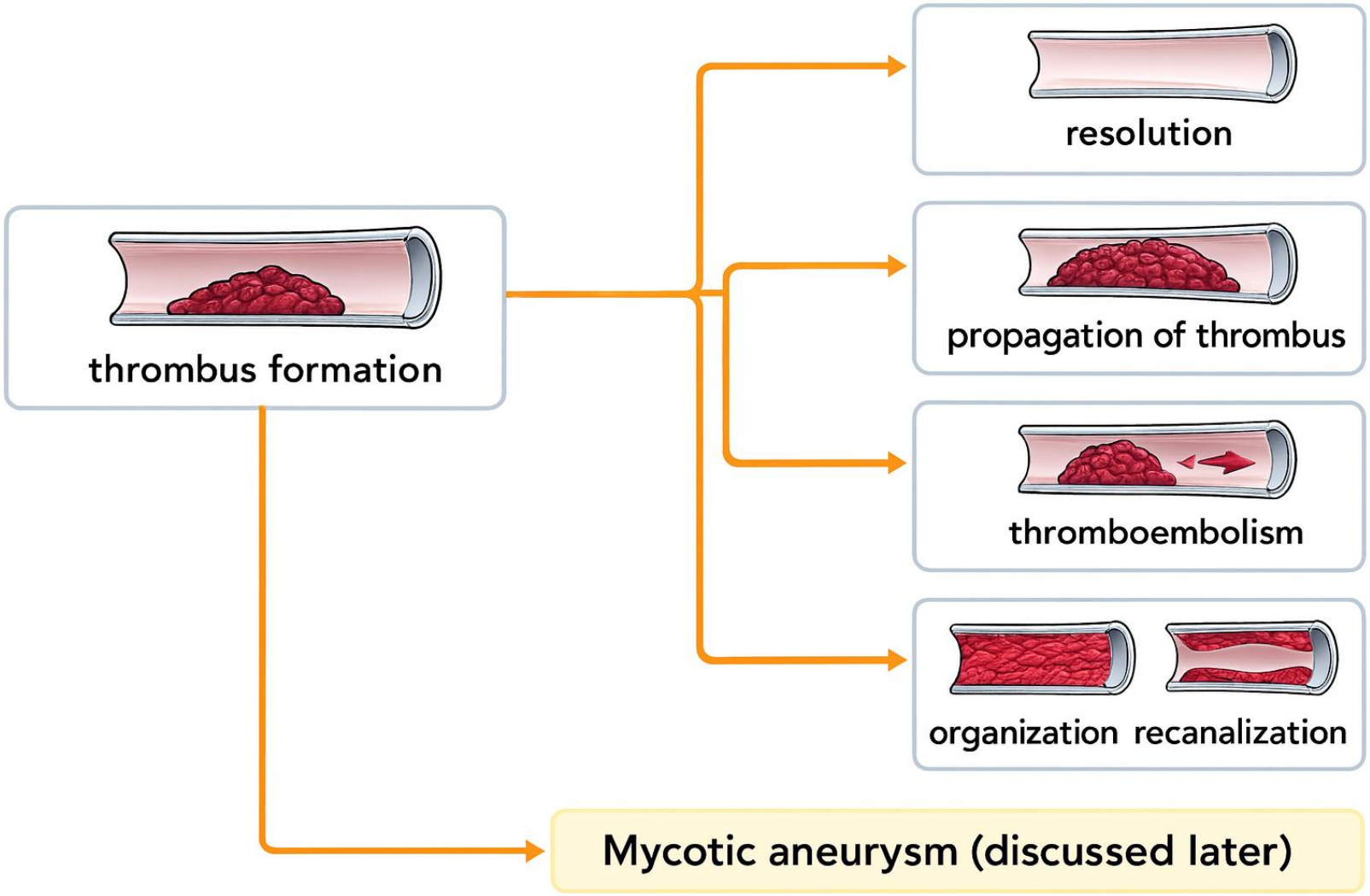
Cardiac Vegetations

- Definition: Thrombi on heart valves
  - Composed of: fibrin, platelets, inflammatory cells ± microorganisms (in infectious types)
- Types:
  1. Infectious (Bacterial or fungal blood-borne infections) e.g. infective endocarditis
     - Large, friable, destructive
  2. Non-infectious: e.g. rheumatic; **N**on-**B**acterial **T**hrombotic **E**ndocarditis (NBTE)
     - Small, bland, and non-destructive



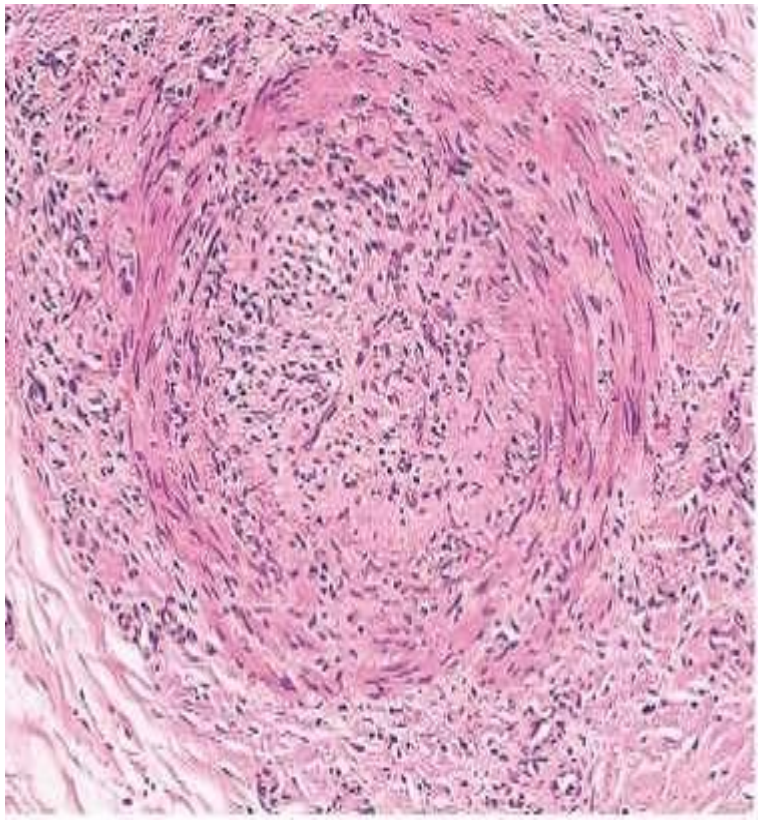


Fates of a thrombus

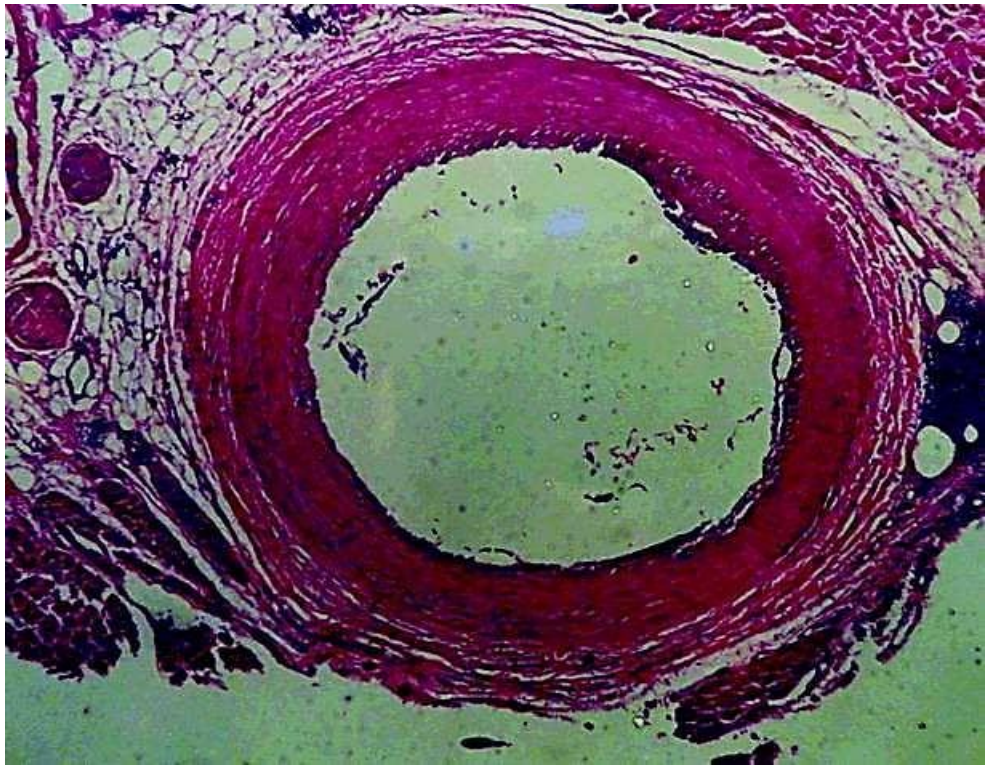


- Organization results in a **permanent structural change** within the vessel.
- A **mycotic aneurysm** is an **infectious aneurysm**:
  - **"Mycotic" means infection-related (not necessarily fungal)**
  - **"Aneurysm" refers to abnormal dilation of a blood vessel**

ORGANIZED ARTERIAL THROMBUS



A normal artery cross section for comparison



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

- *Organization refers to the ingrowth of new permanent tissue consisting of: collagen, ECM proteins, new endothelial cells, smooth cells and fibroblasts into the fibrin rich thrombus.

PATHOLOGY QUIZ

LECTURE 1

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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			