CVS
PATHOLOGY

Modified NO: 1

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THROMBOSIS-PATHOLOGICAL ASPECTS

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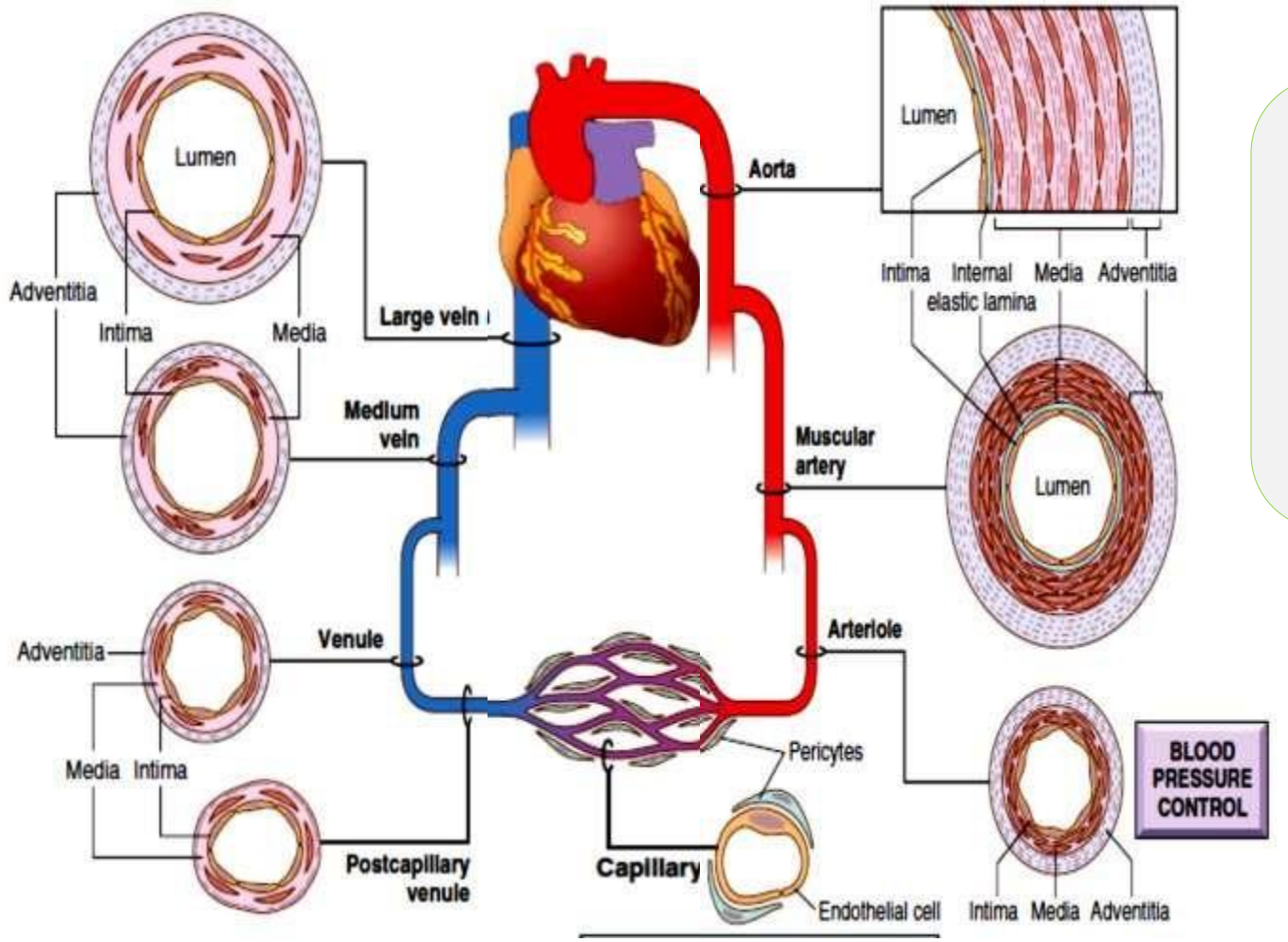
- In this lecture, we have an introduction to CVS pathology.
- We will discuss some concepts that will be repeated in the next lectures inshallah.
- We will talk about thrombosis ,specifically about its pathological aspects (the dark side of thrombosis)
- Thrombosis is a physiological process and a protective mechanism by which our body protects itself again blood loss and its effect in the body.
- The pathological thrombosis occurs when an unnecessary thrombosis be made.
- An example for a physiological thrombosis, a trauma causes cut ,injury or rupture. In this condition, we need a thrombosis to protect the body from bleeding.
- Another example, has an inherited mutation in factor V in the clotting system, this mutation lead to a higher tendency to form blood clot ,does this case cause a physiological or pathological thrombosis? It's a pathological thrombosis

CARDIOVASCULAR SYSTEM

Venous circulation

Arterial circulation



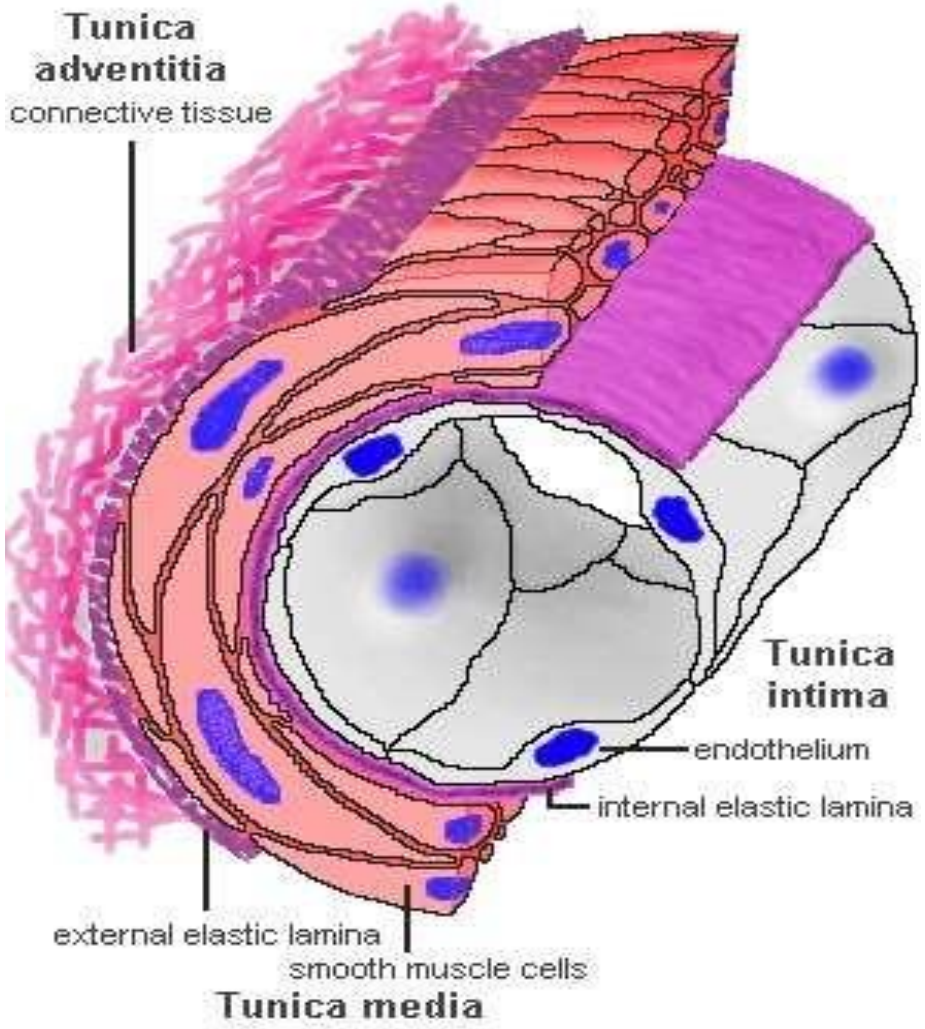
The venous and arterial circulation are connected to each other generally by two points:

1- The heart

2- Inside the tissue

We will talk about the details in the next lecture inshallah.

NORMAL BLOOD VESSEL HISTOLOGY



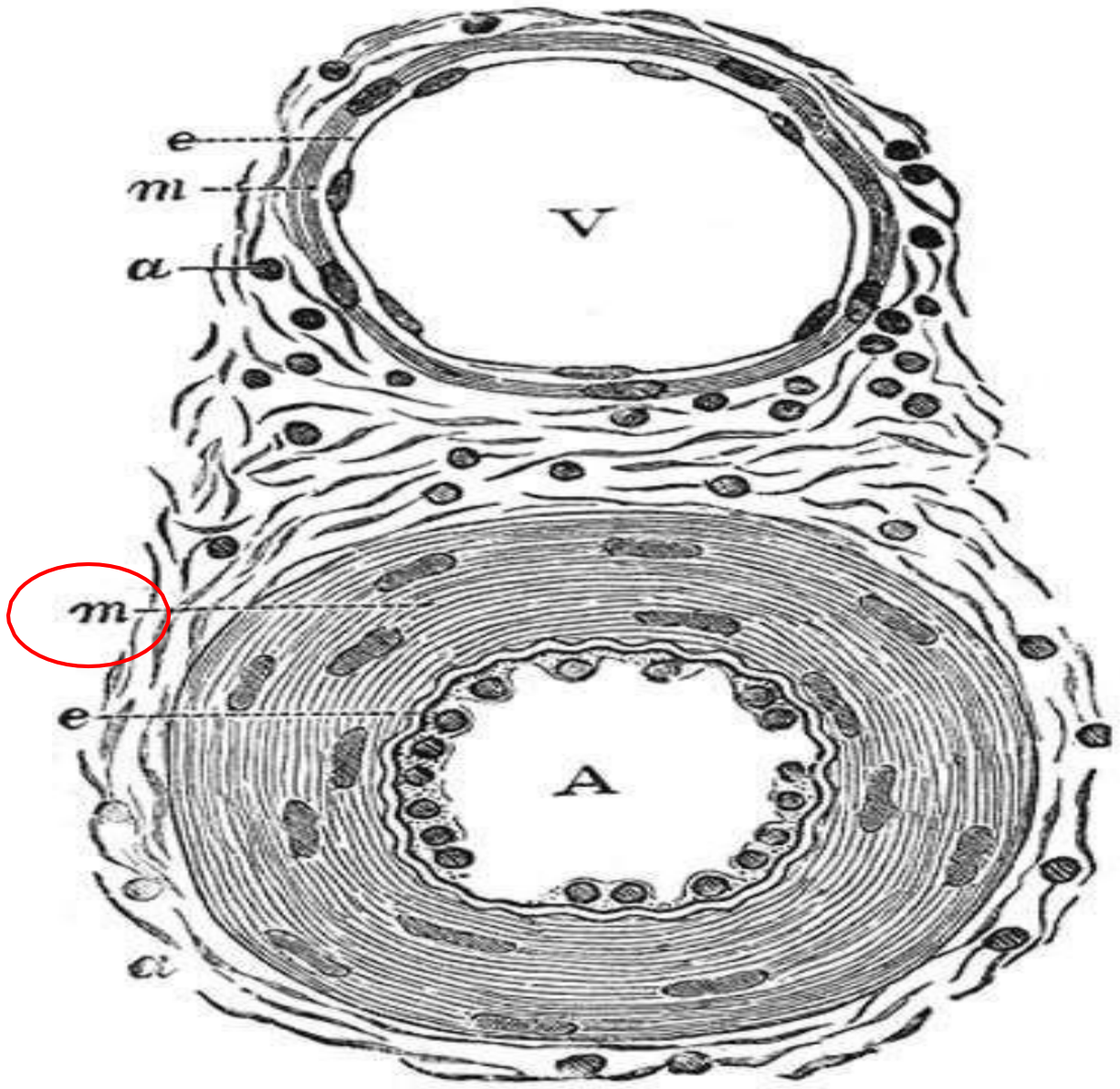
- We will talk a little bit about the histology of blood vessels and its compositions.
- In this cross section for an artery ,it shows a multiple layers:-

1- The inner most layer is called tunica intima, which is composed of a special type of cells called endothelial cells (It is also present in the endocardium).

2-The second layer is called tunica media which composed of a smooth muscle cells that helps in contraction.

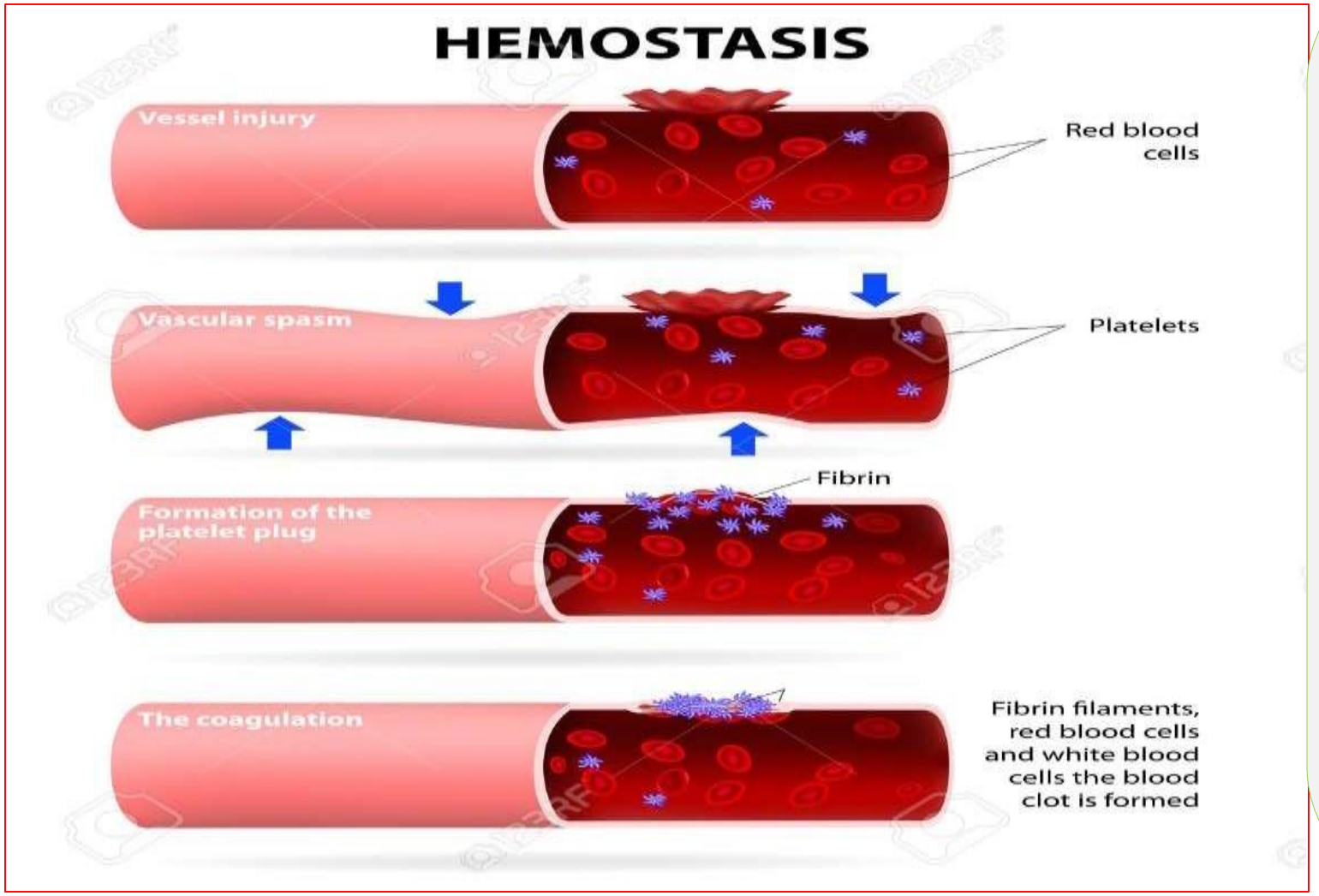
3- The outer layer is called tunica adventitia which composed of a connective tissue that give the support the wall.

ARTERY (A) VS VEIN (V)



- During our lectures, we will notice some diseases that affect the vein and another different diseases that affect the arteries and this is due to very important differences in the structure of veins or arteries, but it could be critical because in the previous slide I said that they have the same structure (tunica intima, media and adventitia), the difference between them is the thickness of the smooth muscles layer (arteries have more smooth muscle cells and probably other matrix proteins
- This difference will imply different functions ,different elasticity and difference in diseases that affect veins and arteries.

PHYSIOLOGY OF THROMBOSIS

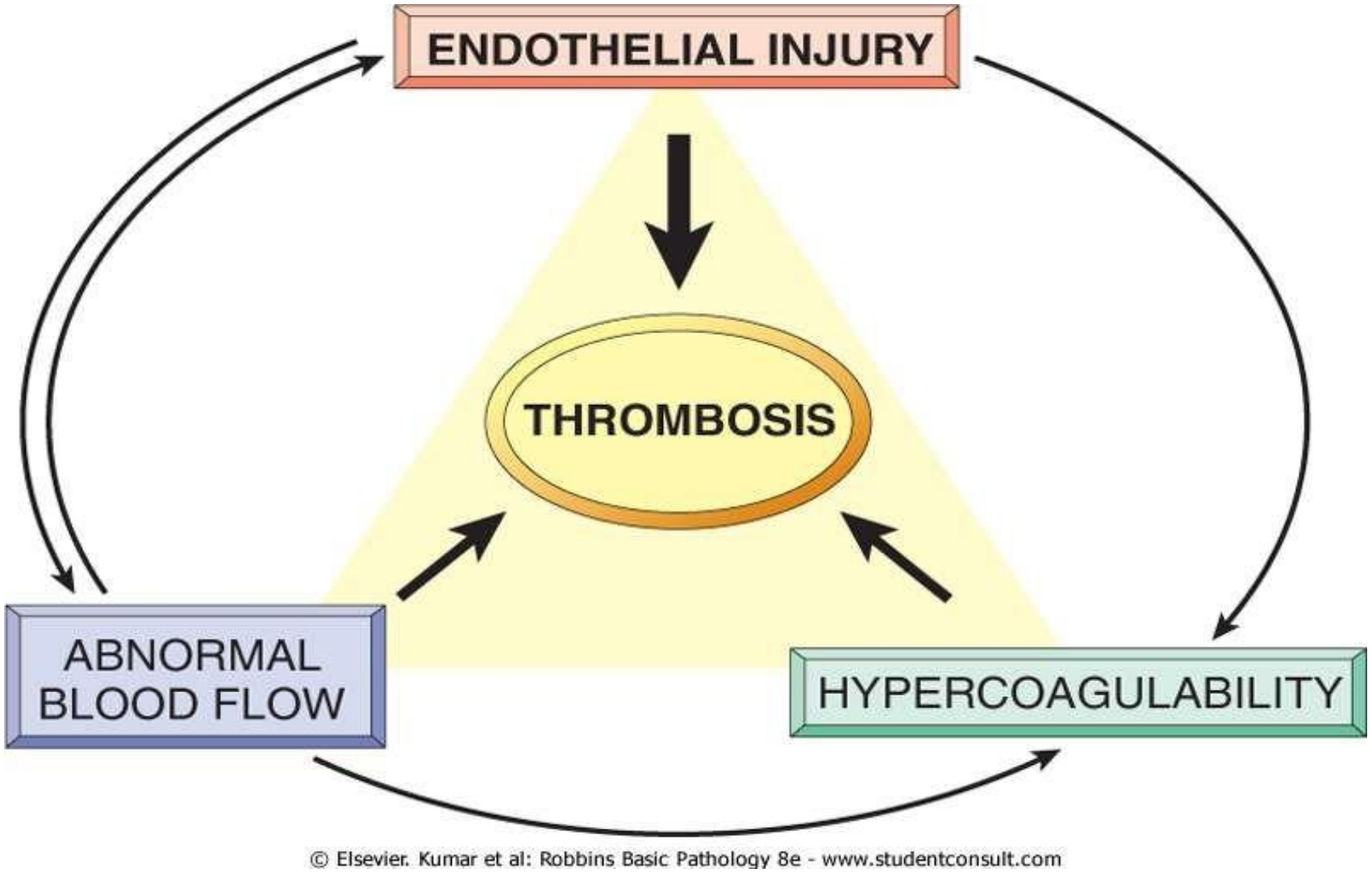


- The most important target of the physiology of thrombosis is to preserve haemostasis (prevention of blood loss that caused by rupture or wound in the wall of the blood vessel) by forming a blood clot.
- This blood clot will be produced by activation of clotting system inside the body and formation of fibrin and platelets colt and close the wound.
- But, when we can say that there is a pathological thrombosis, there is no wound ,but our body is forming a blood clot in an inappropriate place ,time or without any justification.

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



- We discussed previously that the injury is a physiologically thrombosis ,but here we don't have cut or wound in the wall of the blood vessel ,we have at "the stage of endothelial cells" changes in the microenvironment which make stimulation or injury in the endothelial cells.
- The presence of any of these factors at a certain time and place makes a pathological thrombosis.
- And it can cause by more than one factor or all of them or one factor can cause another factor to be occurred.

THROMBOSIS- PATHOLOGICAL ASPECTS

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

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

Remember: the endothelial cells present in the inner most layer (tunica intima).

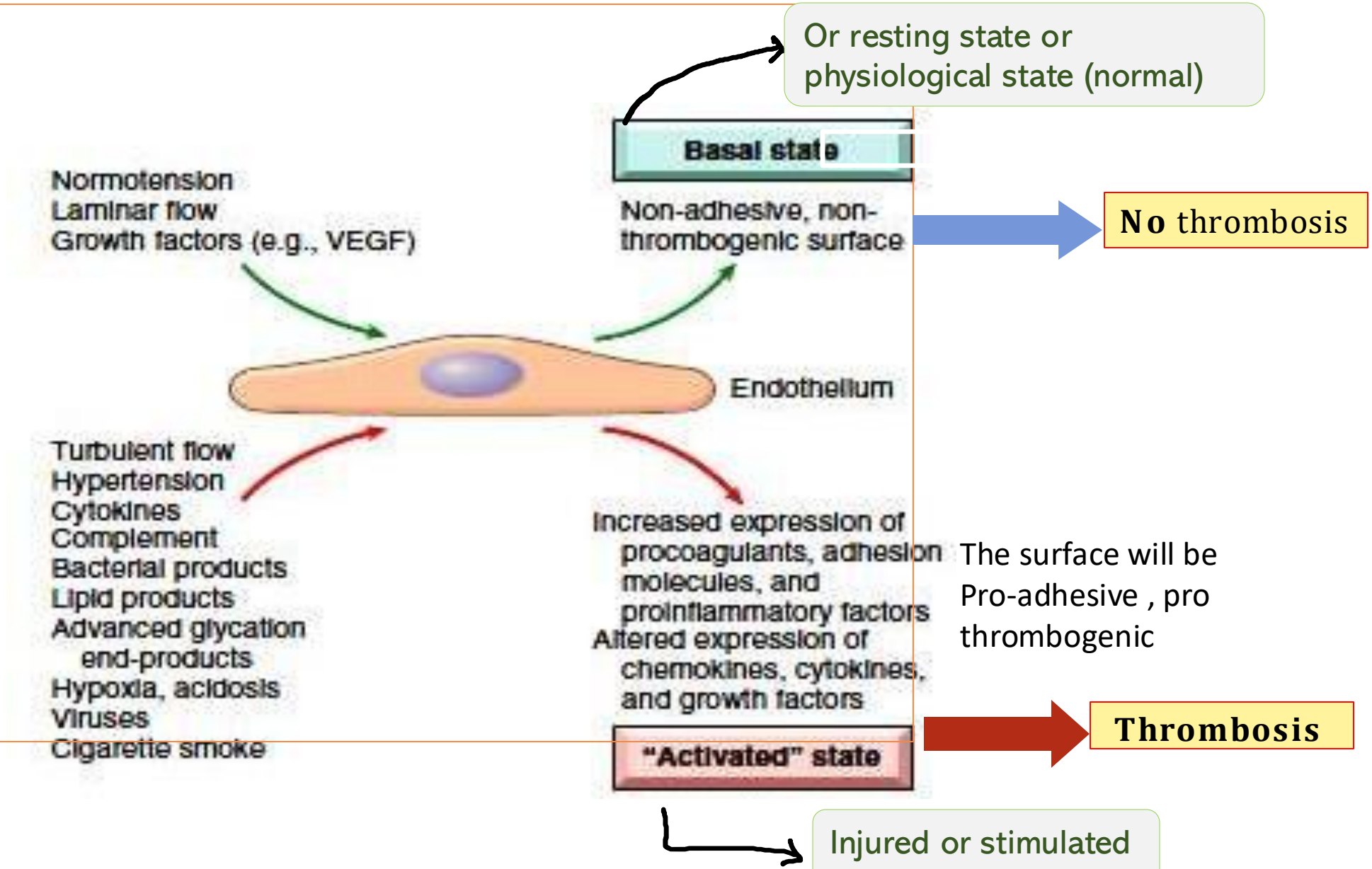
*** Endothelial cells are special type of cells that cover the inside surface of blood vessels and heart.**

The endothelial cells under physiological circumstances is said to be protective against pathological thrombosis (The endothelial cells by itself play a role in protection against pathological thrombosis. (non-adherent, non-thrombogenic surface)

Contribution of Endothelial Cells to Coagulation

The dr read everything

The injury caused by a change in the microenvironment of the cell like: Abnormal blood flow ,Inflammation, high cholesterol or abnormal substances like abnormal glycation which occurs in diabetes patients.



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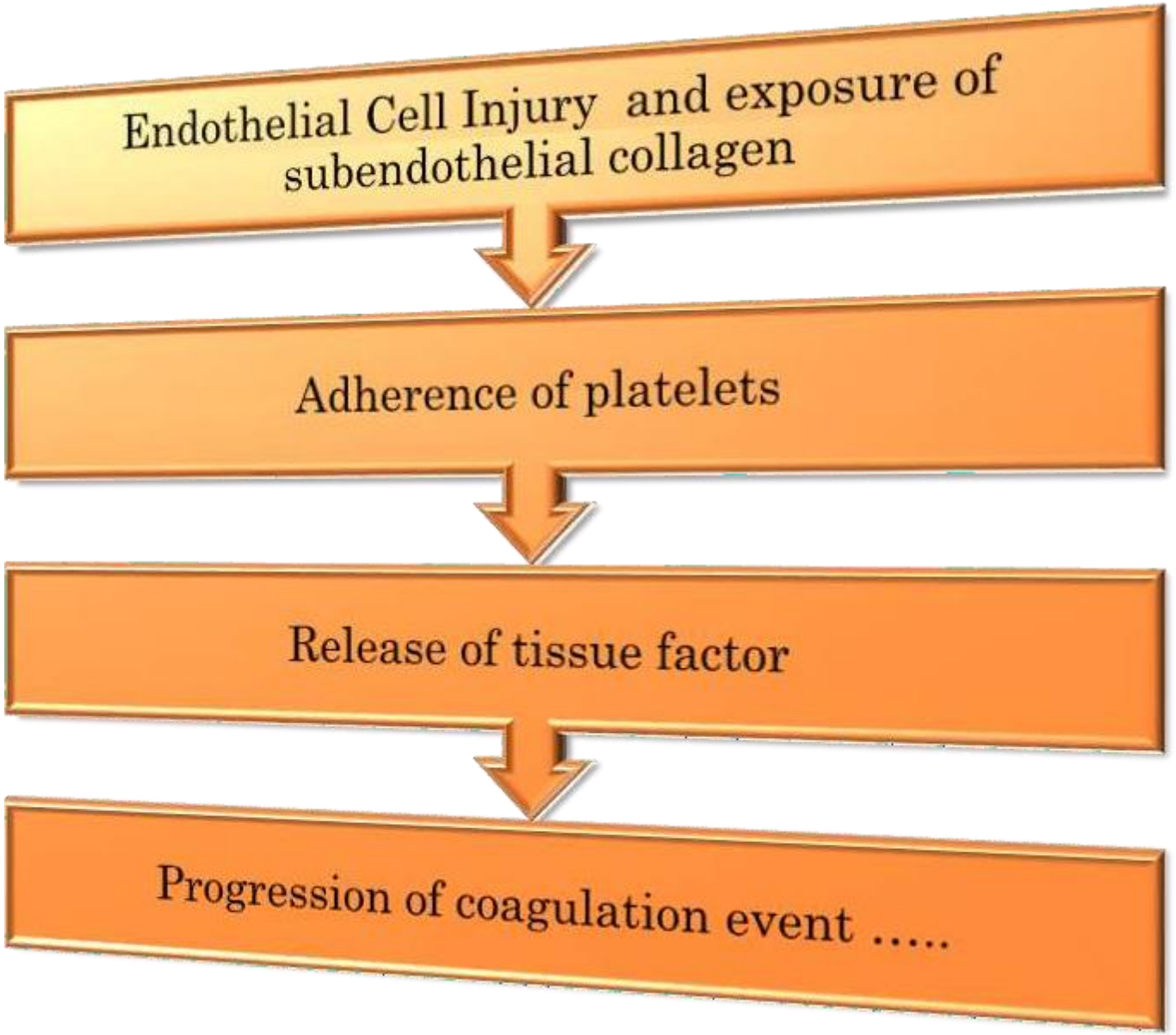
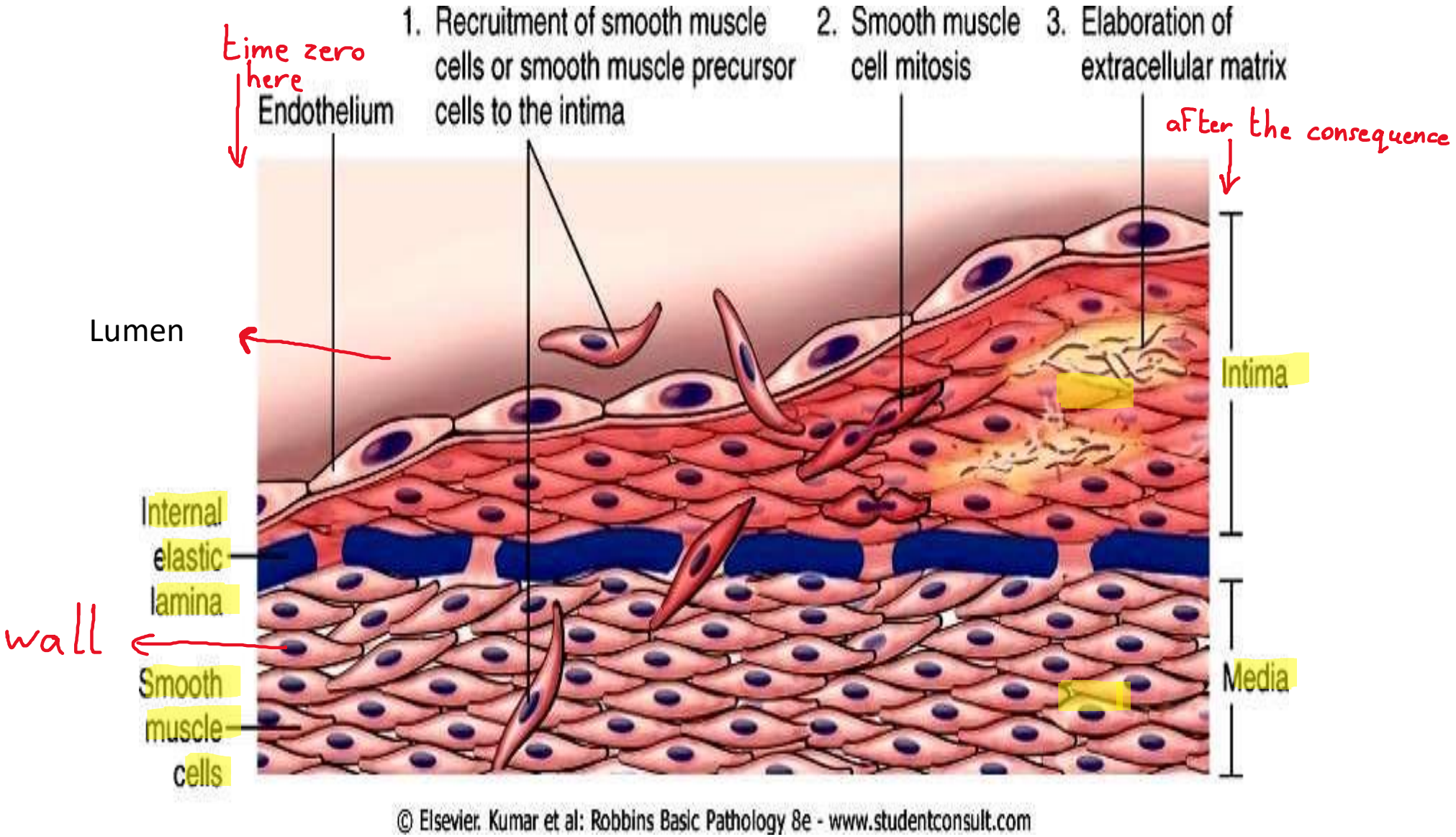


Response of Vascular Wall Cells to Injury



This picture will follow us in next lectures (just understand the concept here).
On the left side of the picture(onset of injury), this is a normal wall of blood vessel ,but in the right side of the picture (after the consequence of the injury), we have after the events.
Remember:
Intima—>endothelial cells.
Media—>smooth muscle cells.
The difference between time zero and after the consequences of the injury is increased the thickness of the intima which cause luminal stenosis which affect the lumen and the diameter of the blood vessel which they are a tubes and it affects the flow of the blood which affect the tissues supplied by this blood vessel (an artery for example).
In all next lecture, we will discuss this orientation that we will think about the consequence that result from a certain abnormality and the consequence on the patient.
This events that is occurred in response of the vascular wall injury include not only endothelial cells injury ,but it also includes recruitment of smooth muscles cells from the media to the intima and inside intima it can undergo cell division and mitosis , and it can elaborate extra cellular matrix proteins ,so it increases the thickness of the intima.
The most important consequence for this response is reduction of the luminal area and reduction of blood flow which will lead to tissue hypoxia and infraction.

Response of Vascular Wall Cells to Injury

- Injury results in a **healing response**

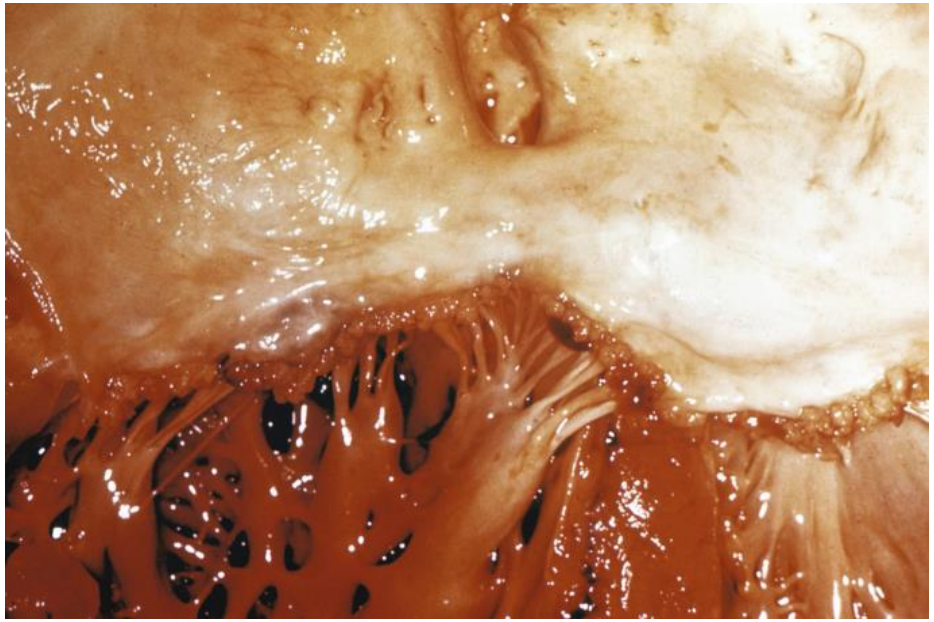
- **Pathologic effect of vascular healing:**

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

Causes of Endothelial injury

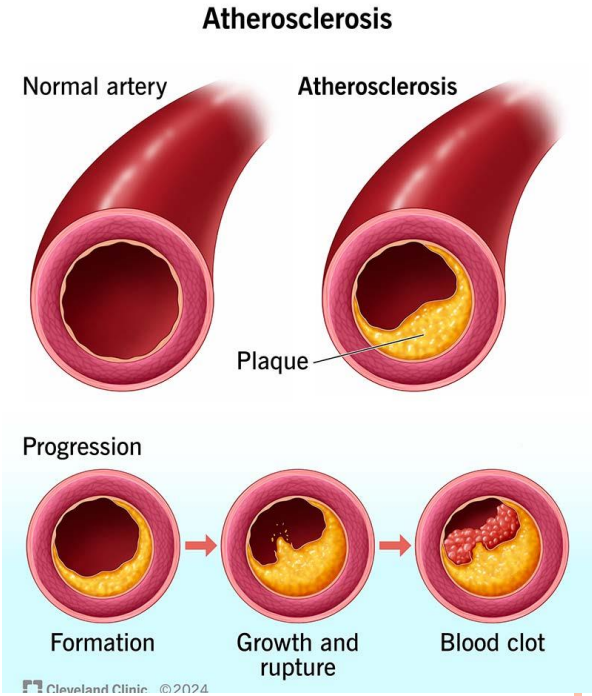
Note that these information in blue colour are extra , you can skip them

1. ***Valvulitis :*** Inflammation of a valve (especially of a cardiac valve as a consequence of rheumatic fever)
2. ***MI :*** A heart attack, technically called a myocardial infarction or MI, happens when there is a blockage that prevents the oxygen-rich blood from getting to the heart,
3. ***Atherosclerosis :*** The buildup of fats, cholesterol and other substances in and on the artery walls. This buildup is called plaque. The plaque can cause arteries to narrow, blocking blood flow. The plaque also can burst, leading to a blood clot



Valvulitis – an extra picture

Atherosclerosis – an extra picture



Note that these information in blue colour are extra , you can skip them

4. Traumatic or inflammatory conditions

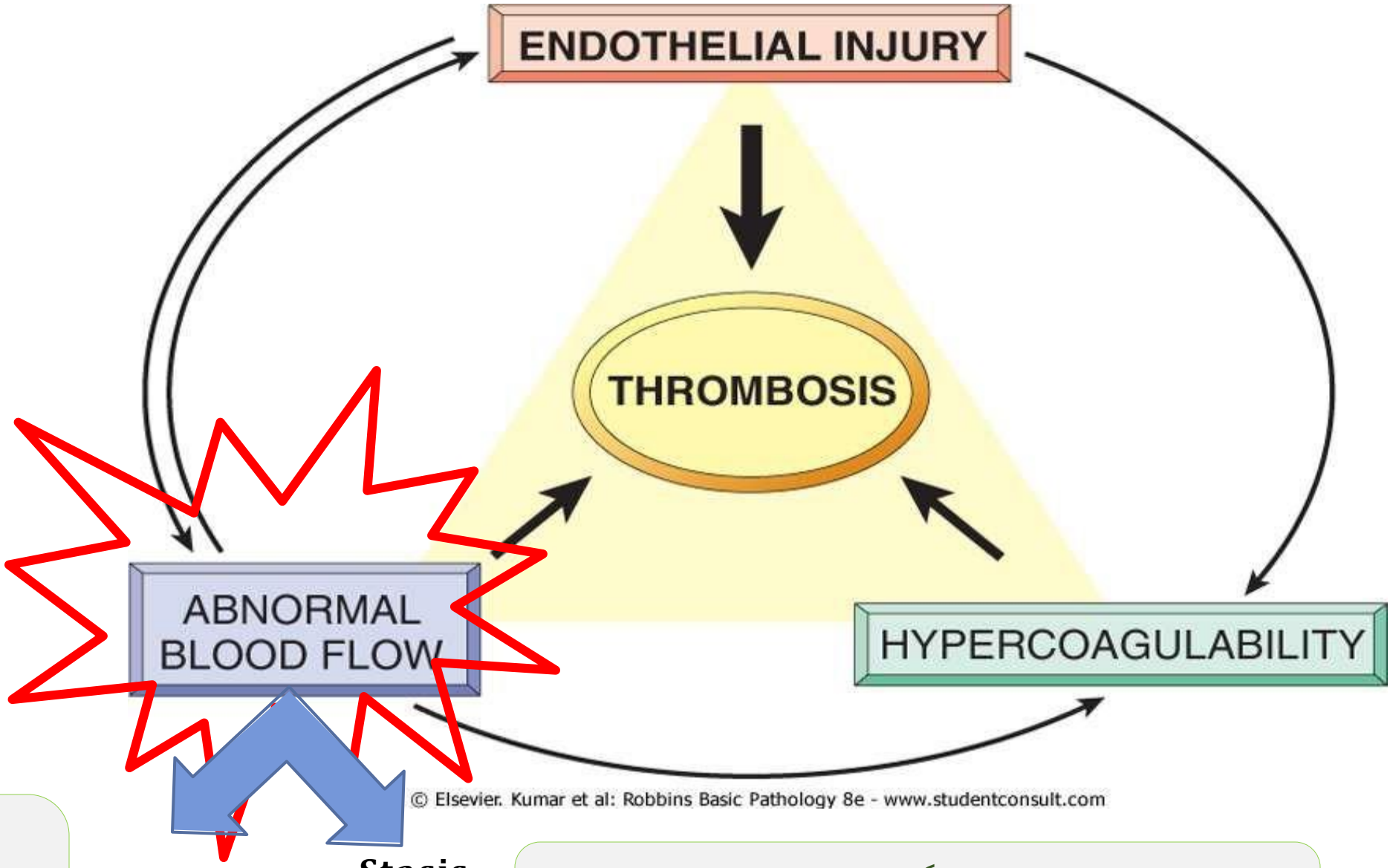
5. Hypertension

6. Endotoxins a lipopoly-saccharide found in the cell wall of Gram-negative bacteria, is a pyrogen which induces inflammation and fever as an immune response in higher organisms.

7. Hypercholesterolemia anion destroying nitric oxide, promoting oxidation of LDL and lipid accumulation within the vessel wall

8. Radiation Ionizing radiation directly activates and damages the endothelium via increased adhesion molecule expression, leukocyte-EC interactions, mitochondrial damage, barrier permeability, and apoptosis.

9. Smoking Nicotine causes your blood vessels to constrict or narrow, which limits the amount of blood that flows to your organs. Over time, the constant constriction results in blood vessels that are stiff and less elastic. Constricted blood vessels decrease the amount of oxygen and nutrients your cells receive.



Turbulence

فوضی ,اضطراب

- Chaotic and random fluctuations in flow

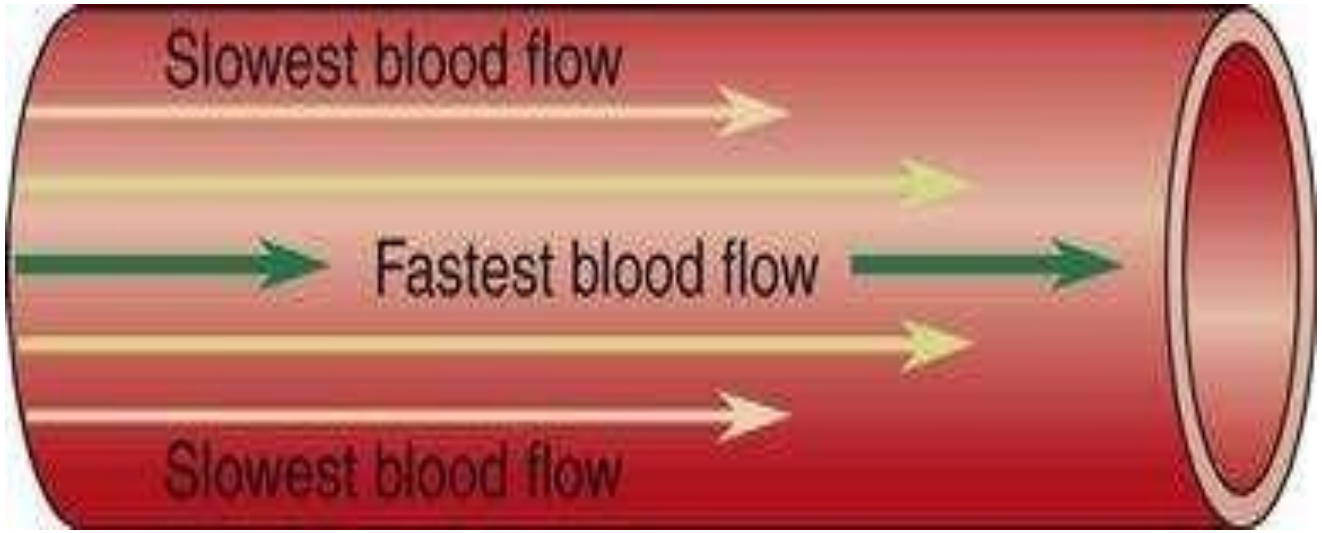
Stasis

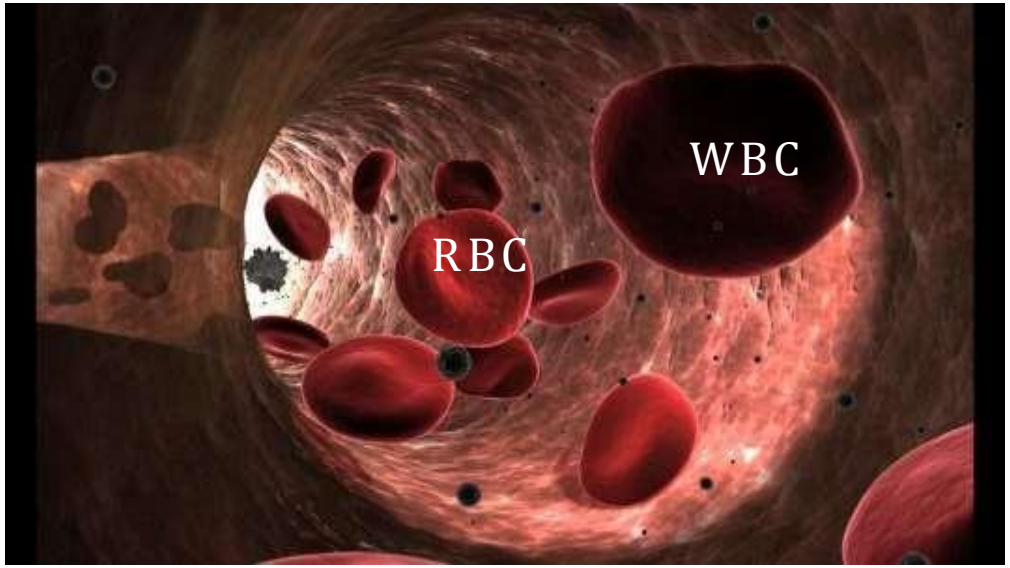
رکود

- The situation where blood is not able to flow properly through the tissues.

LAMINAR BLOOD FLOW (NORMAL)

UNIDIRECTIONAL , relatively straight





- Notice here , that the normal blood flow is said to be laminar (layered)

1- Blood moves in one direction (in a straight line).

2- We have a difference in blood flow rates

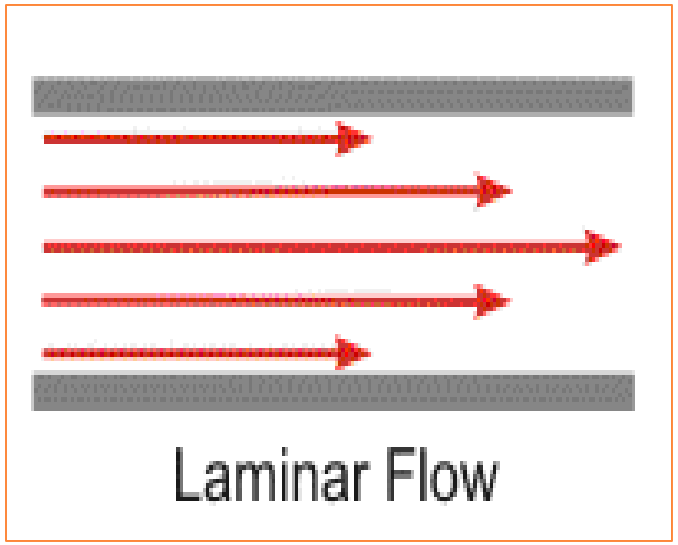
The fastest blood flow will be at the centre (for the smallest blood component like : RBCs , platelets) , and the slowest blood flow will be at the periphery (for the largest blood component like WBCs).

- Remember that blood is composed from : packed red blood corpuscles, plasma , white blood cells and platelets .

This characteristic (**LAMINAR BLOOD FLOW)** will prevent or minimize the chances to have unwanted thrombosis , How ?

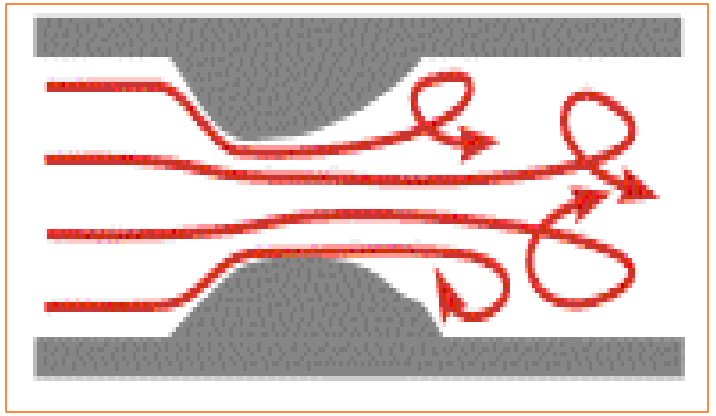
By keeping a distance between platelets and endothelial cells .

LAMINAR VS TURBULENT BLOOD FLOW



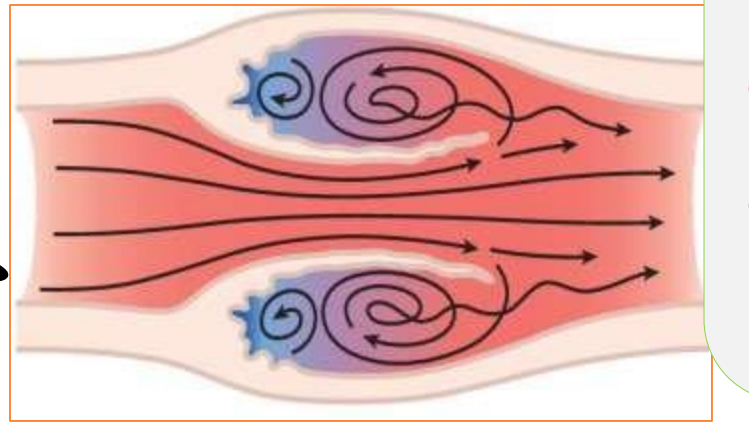
UNIDIRECTIONAL blood direction in different rates

Artery



- **Excessive thickness of blood vessel wall** due to atherosclerosis, embolus , thrombus ...etc.
- **Turbulence blood flow** --> so platelets can bind to the surface endothelium .
- Low blood velocity causes stasis .

Turbulent Flow

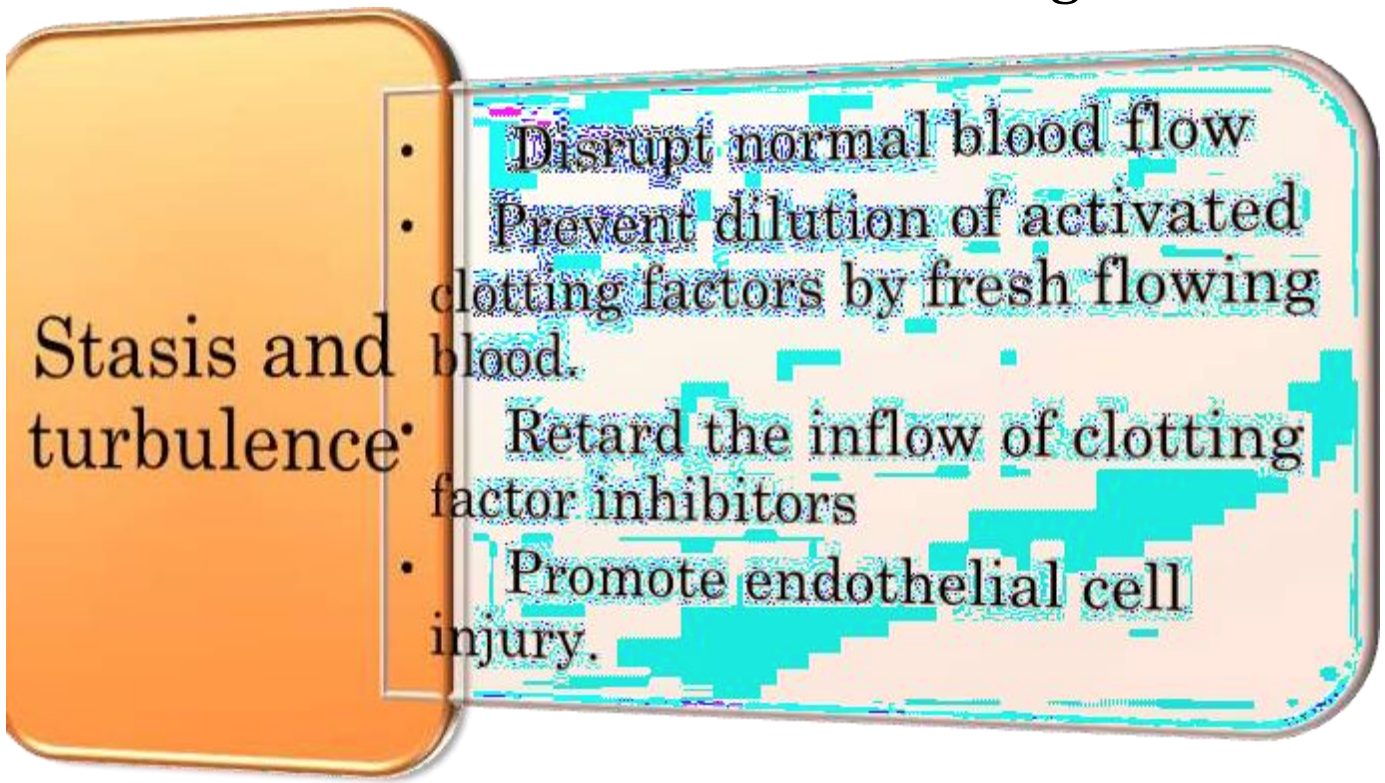


Vain with valve

- Abnormal dilation because of Aneurysms , varices … etc.
- **Turbulence blood flow near the wall of the blood vessel .**
- Slower blood flow rates which **increases the risk of thrombosis.**

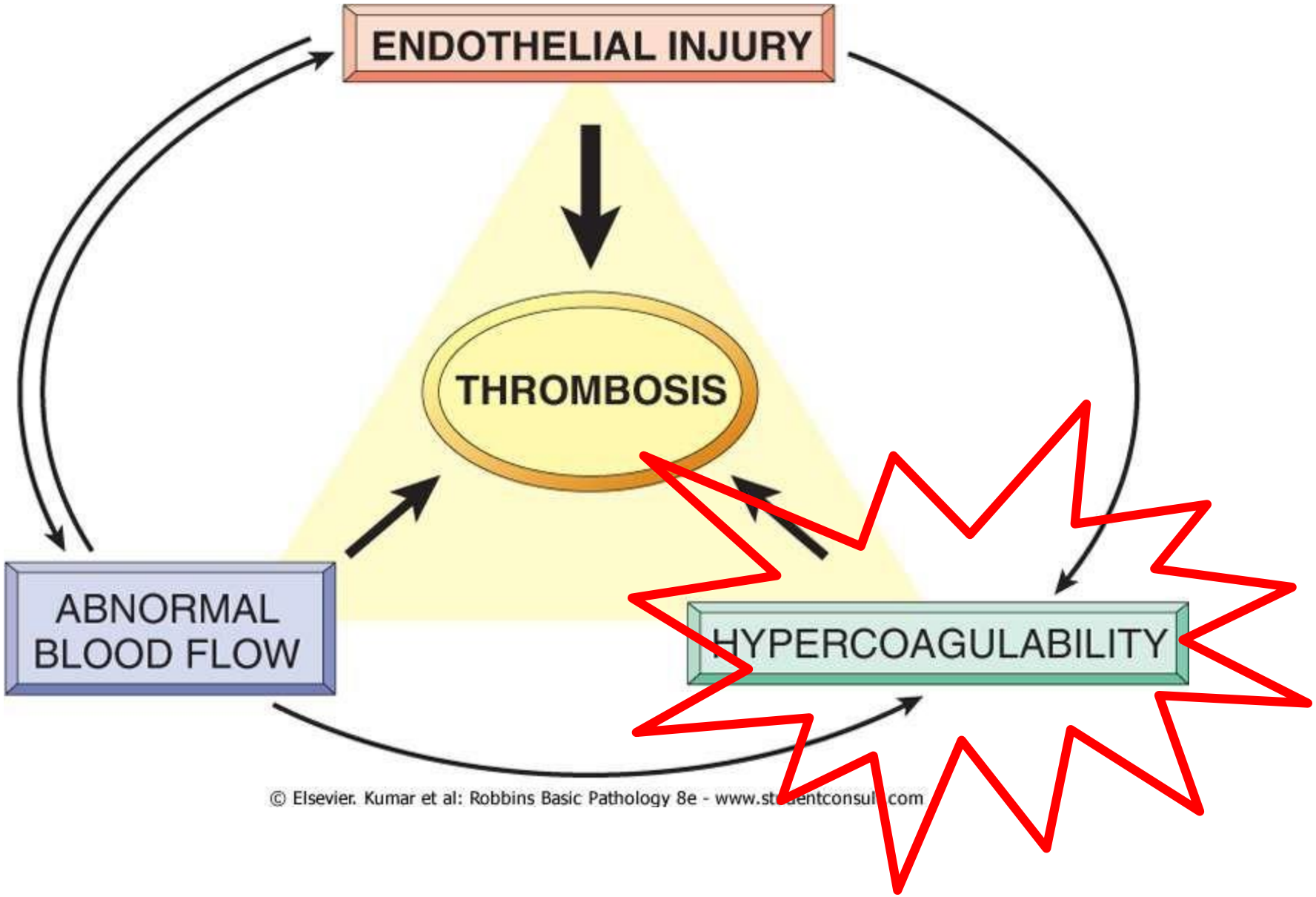
Stasis

- *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-contractile fibers)***
4. ***Mitral valve stenosis (atrial dilation)***
5. ***Hyper viscosity syndrome (PCV and Sickle Cell anemia)***


ENDOTHELIAL INJURY
THROMBOSIS
ABNORMAL BLOOD FLOW
HYPERCOAGULABILITY
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- **Hypercoagulability: higher ability to have a blood clot than the normal**

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 **Or mutation in the clotting factors inhibitors.**

B. Acquired (secondary):

- Much more frequent than primary causes
- multifactorial & more complicated
- causes include: Immobilization, MI(Myocardial infarction), AF (Atrial fibrillation), surgery, fractures, burns, Cancer, Prosthetic cardiac valves …etc

MORPHOLOGY OF THROMBI

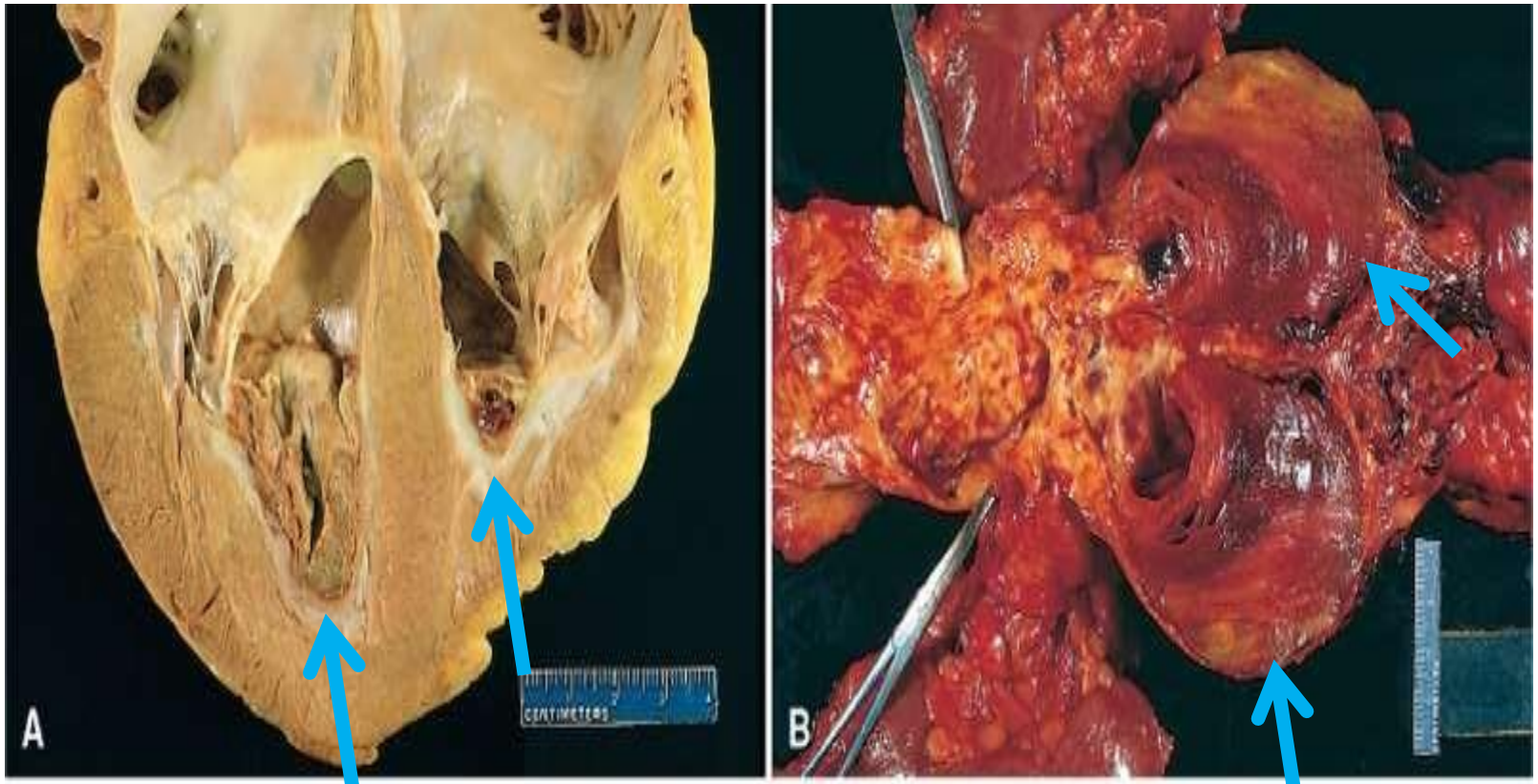
- Can develop anywhere in the CVS (e.g., in cardiac chambers, valves, arteries, veins, or capillaries).
- ***Arterial or cardiac*** thrombi→ begin at sites of ***endothelial injury*** or turbulence; and are usually superimposed on an ***atherosclerotic plaque***
- Venous thrombi → occur at sites of stasis.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

Terms to remember ….

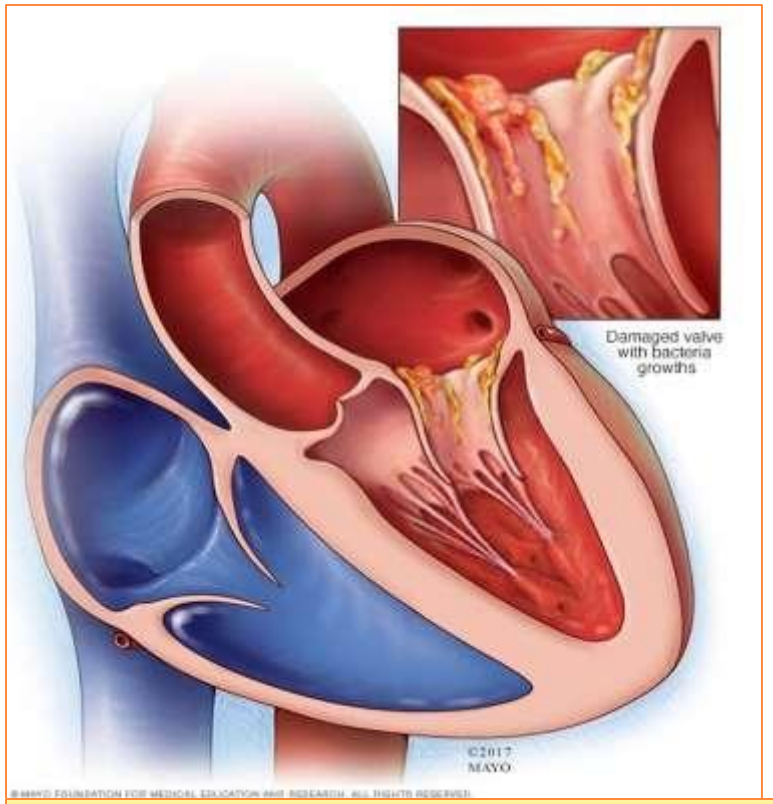
LINES OF ZAHN

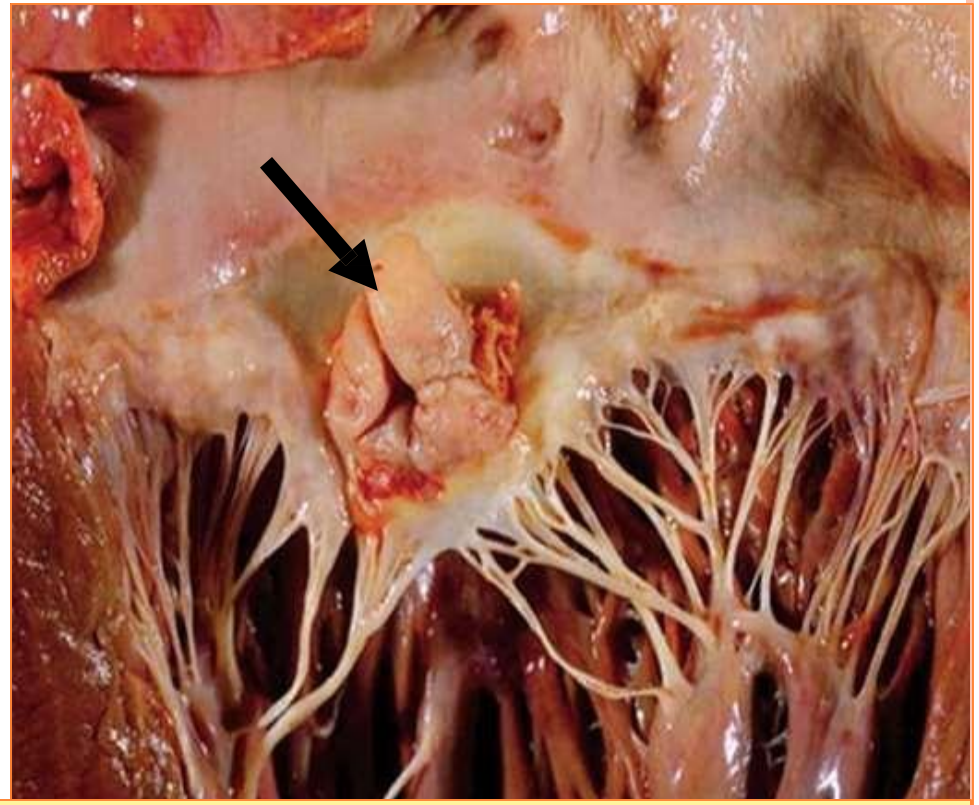
- gross and microscopically apparent laminations
- represent pale platelet and fibrin layers alternating with darker erythrocyte-rich layers
- Significance? distinguish **antemortem** Before death→so we can know if the thrombosis were the cause of death or formed after death.thrombosis from postmortem clots
- postmortem blood clots are non-laminated clots *(no lines of Zahn)*

MURAL THROMBI= - IN HEART CHAMBERS OR IN AORTIC LUMEN



CARDIAC VEGETATIONS





= Thrombi on heart valves , **specific on the heart valve**

Types:

1- infectious (Bacterial or fungal blood-borne infections)

e.g. infective endocarditis

2-non- infectious:

e.g. rheumatic; non-bacterial thrombotic endocarditis

1

- Resolution = Lysis or thrombus removal , this removal can happen by, endogenous anticoagulant's system , exogenously by medications (to lysis the blood).

1-

2

- No thrombus removal = thrombus propagation .
- No thrombus removal neither endogenously nor by a treatment .
- → Progression → It may block the blood vessel Bad fate.
- The consequence is an ischemia in the tissue that is supplied by this artery .

2-

3-

3

A thrombus fragmentations .

- They may close other tinny – small vessels (narrower lumen) --> construct ---> ischemia and tissue necrosis in completely different place .

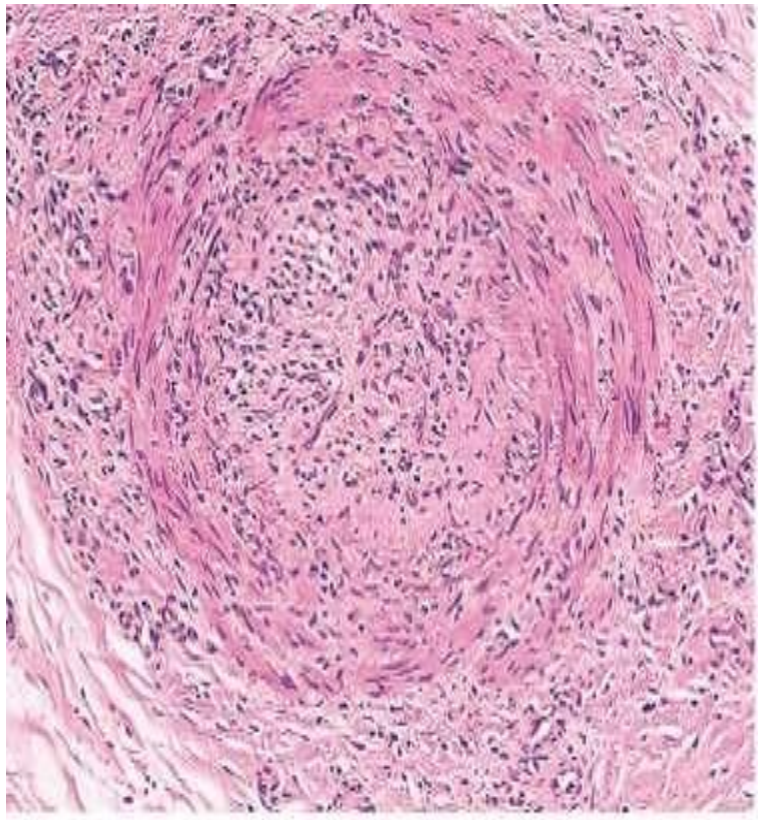
4-

4

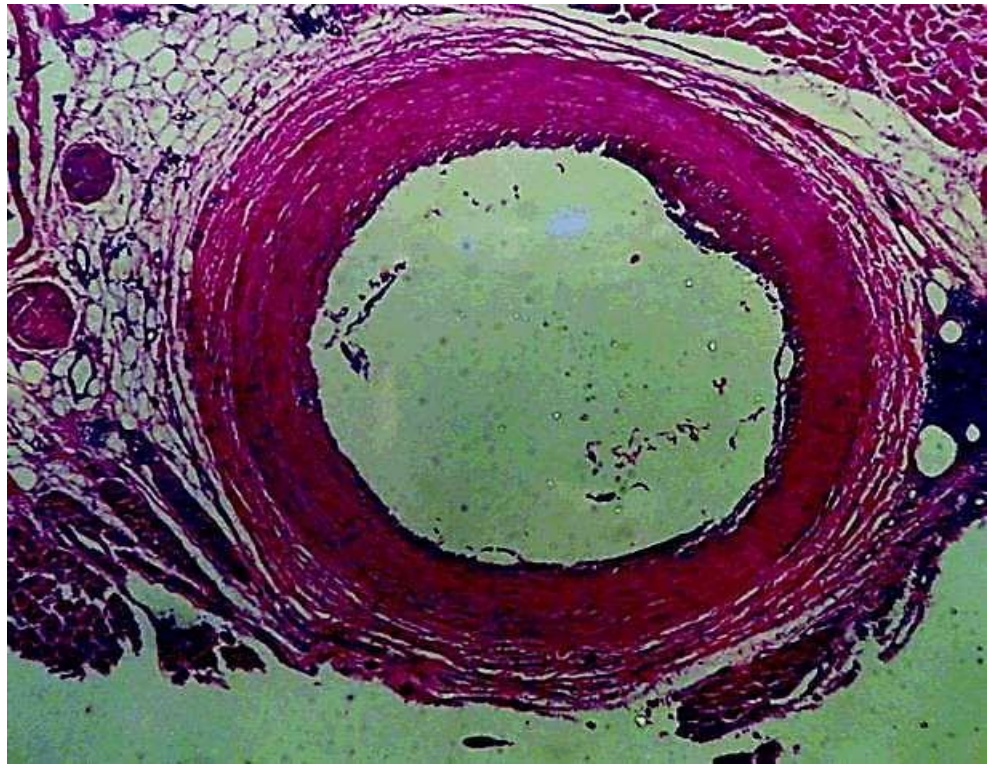
- Organization : tissue is replaced by another tissue (collagen & CT) but it stays in the same place .
- → Depends on the location .
- → Recanalization : open channel inside the thrombus .

Mycotic aneurysm (discussed later)

Organized arterial thrombus



A normal artery cross section for comparison



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 (<u>only in **recent** *thrombi*</u>)
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)***

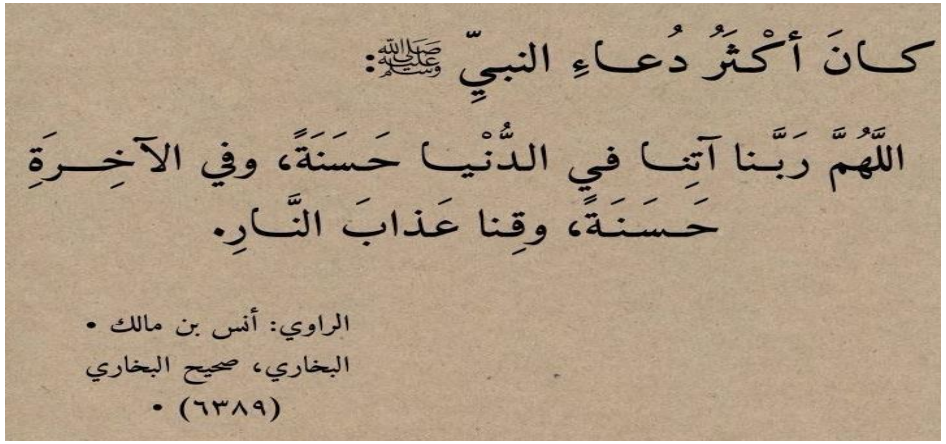
Past paper Questions

- All of the following matches regarding thrombosis are correct EXCEPT:
- A. Endothelial cell Injury: arterial thrombi.
- B. Stasis: venous thrombi.
- C. The propagating part: the adherent part of the thrombus.
- D. Hypercoagulability: immobilization (bed-rest).
- E. Recanalization: can establish some degree of blood flow.
- Answer: c

- Resolution is the fate that may occur in ONE of the following:
- A. Stable atheroma.
- B. Old thrombus.
- C. Recent thrombus.
- D. Old infarct.
- E. Vulnerable atheroma.
- Answer: c

- Organization means:
- A. Accumulation of additional platelets and fibrin that obstruct the vessel.
- B. Removing thrombi using fibrolytic mechanisms.
- C. Ingrowth of endothelial cells, smooth muscle cells and fibroblasts into fibrin rich thrombus.
- D. Fragmentation of thrombi and transport elsewhere in the vasculature.
- E. none of the above.
- Answer: c

Additional sources



VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2			
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا!!