Pathology

Subject : Hemodynamics lecture 5 Ischemia , thrombosis, arterial , venous

Lec no : lec-19_

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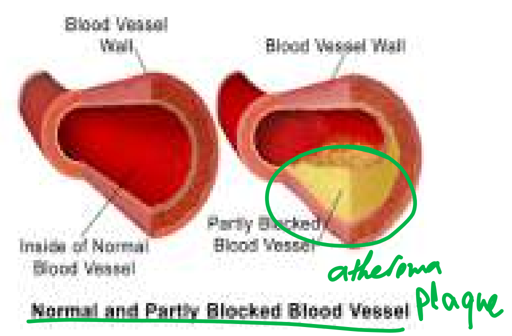
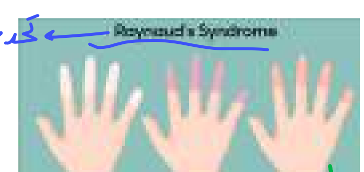
وَقُل رَّبِّ زِدْنِي عِلْمًا

Causes of ischemia

ischemia will couse hypoxia and reversible cell injury after that necrosis

- Ischemia is decrease blood supply to the tissue and organ due to complete or partial obstruction of blood vessels might be caused by many factors
- Sudden Complete obstruction cause by ;
- 1- thrombosis
- 2- embolisim
- 3-ligation (surgical)
- Partial Gradual obstruction caused by
- 1- inflammation as in endarteritis obliterance (syphilis) due to fibrosis of blood vessel and decrease the elasticity
- 2-degenerative disease (atherosclerosis)
- 3- Spasm (as in coronary arteries which lead to angina or myocardial infarction) or raynauds phenomena as in peripheral vessels of the hands and feet in cold weather
- pressure by tumour from outside blood vessels





Effect of Obstruction of blood supply

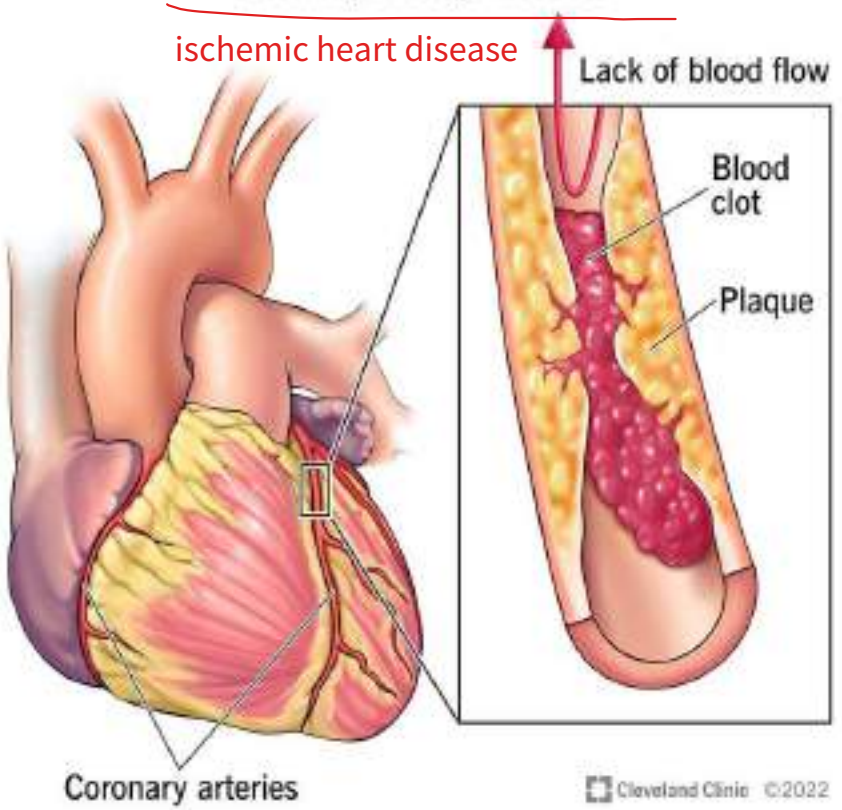
- If obstruction Sudden , Complete obstruction it will lead to infarction (dead of tissue) if there is NO EFFICENT COLLATERALS
- Or gangrene if associated with tissue putrefaction (by bacterial action of saprophyte bact))
- IF there is Collaterals (anastomosis)--- No effect (no tissue damage)
- If Obstruction Partial ,gradual without collaterals --- degenerative changes ,atrophy , fibrosis (no infarction)
- Partial with collateral No tissue damage

obstruction

- sudden
  - partial → mild ischemia
  - complete → sudden.necrosis (Infarction)
- gradual
  - complete → not affect
  - partial

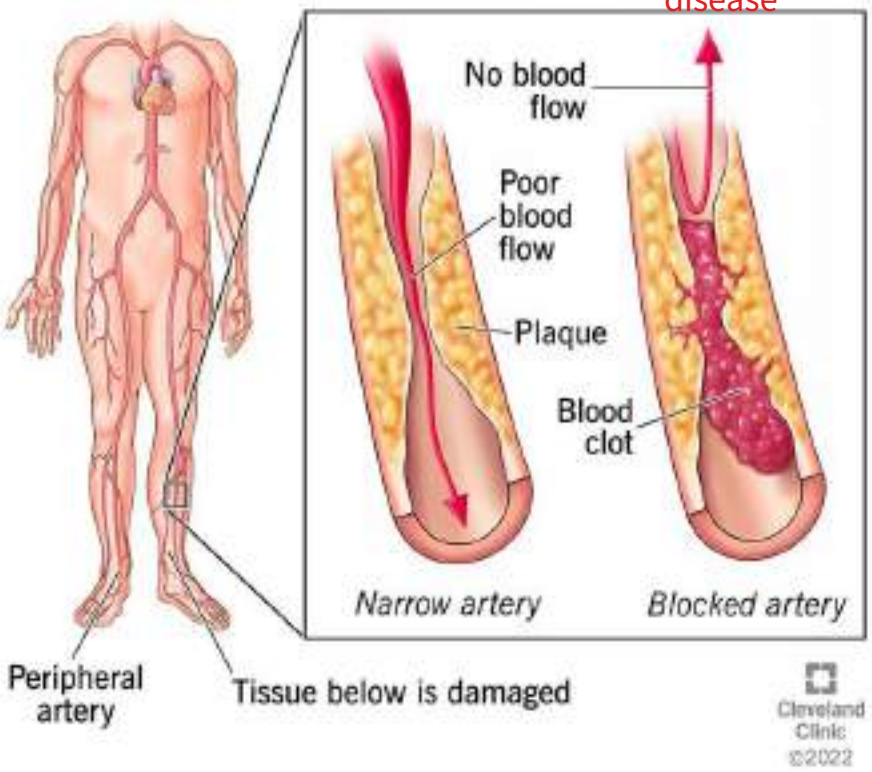
Coronary Artery Disease

ischemic heart disease



Peripheral Artery Disease

perepheral vascular disease



Thrombosis

Thrombosis is Formation of undissoved mass compsed of blood constituent formed during life inside the blood vessels.

كتله غير قابله للذوبان مكونه من مكونات الدم خلال الحياة تتكون داخل الوعاء الدموي

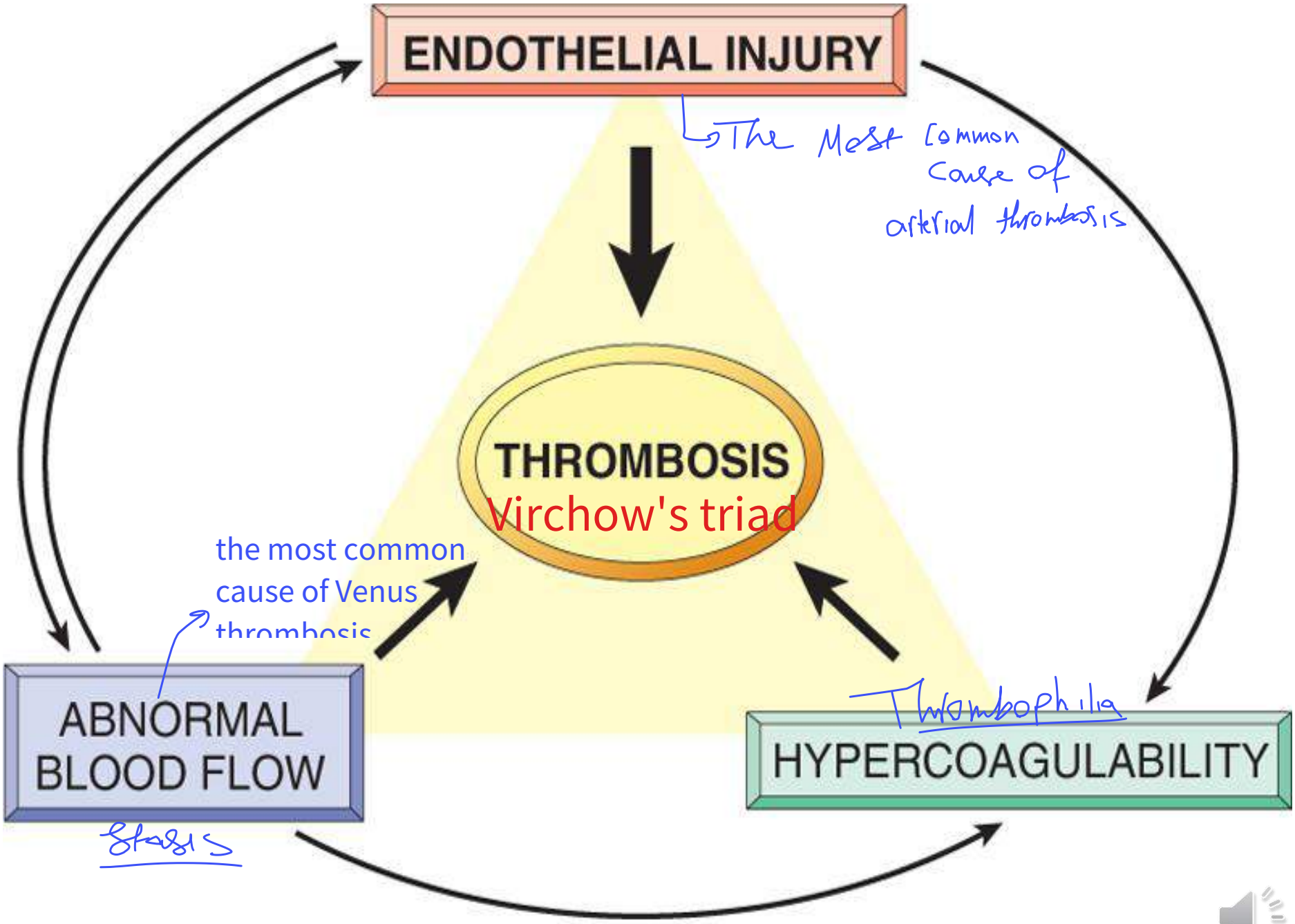
Causes of thrombosis

***Virchow's triad*:**

(1) Endothelial injury

(2) Stasis *or* turbulence of blood flow

(3) Blood hypercoagulability



Thrombosis

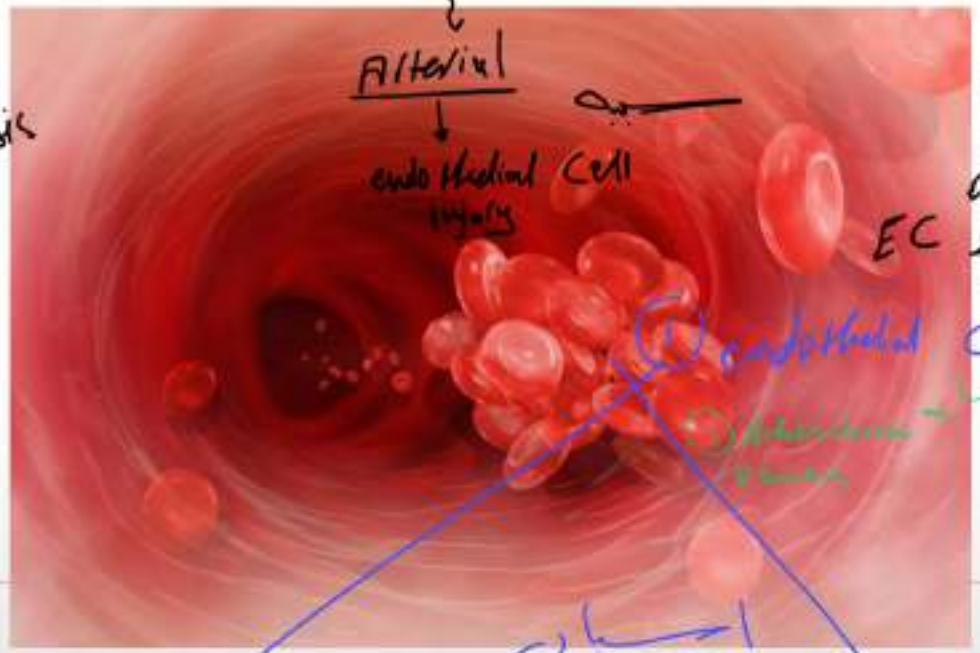
Venous

Hypercoagulability

Stasis

Arterial

endothelial cell injury



Intracardiac thrombosis

EC injury

Stasis

endothelial cell injury

Thrombosis

Virchow's triad

1. MI
2. Atrial fibrillation
3. Endocarditis

Stasis

Hypercoagulability (Thrombophilia)

1- Endothelial injury

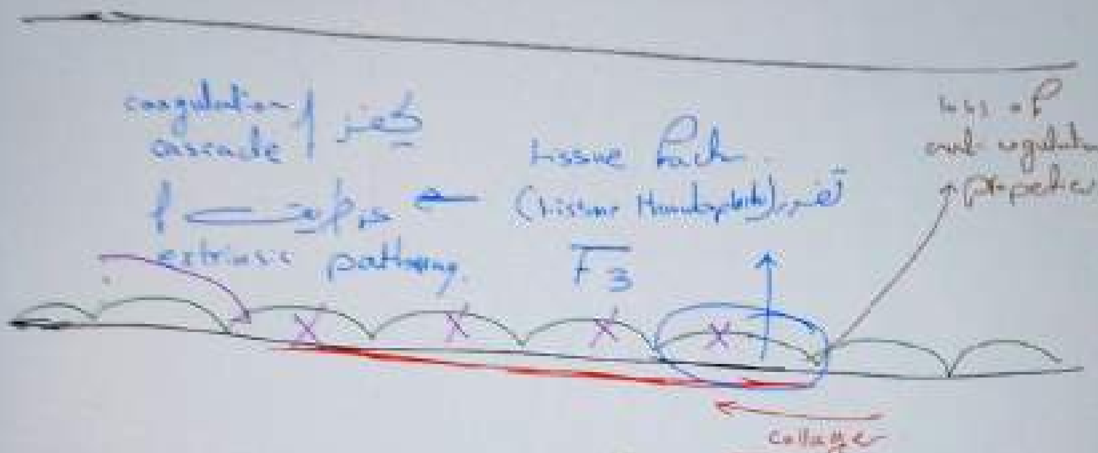
- The commonest cause of thrombus formation, **mainly in the heart and arterial circulation**.
- Loss of endothelium exposes subendothelial ECM, releases tissue factor, and reduces local production of PGI2 and plasminogen activators.
- **Any dynamic imbalance** of the prothrombotic and antithrombotic effects of endothelium can influence clotting locally.

increase prothrombotic properties

decrease antirombotic properties

كيف تؤدي EC injury لحدوث

thrombosis

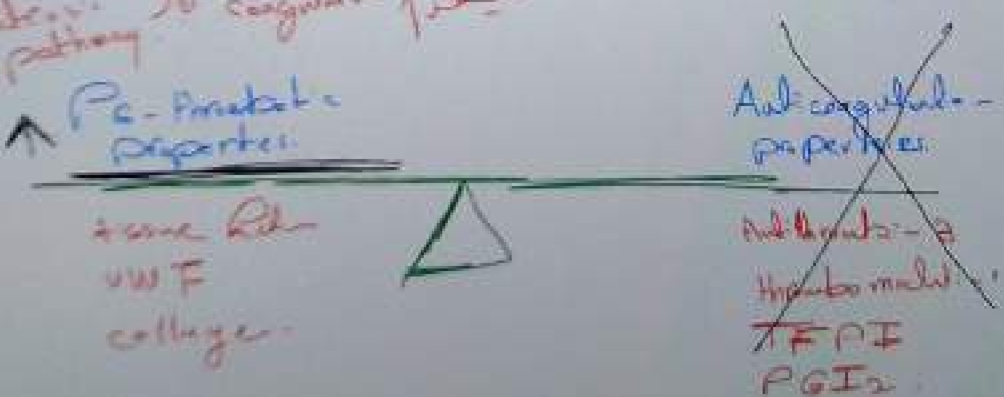


thrombosis ↑ ... تحفيز ← vWF

① platelet adhesion — ارتباط

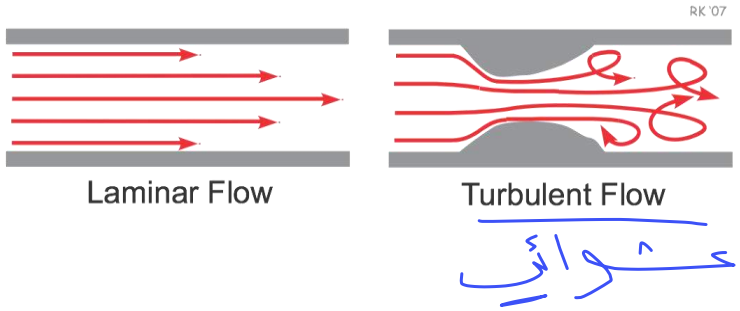
② Hageman factor تحفيز

intrinsic pathway الـ coagulation ↑ تحفيز



Chronic endothelial dysfunction can be induced by a variety of insults:

all of the following can cause endothelial cell injury

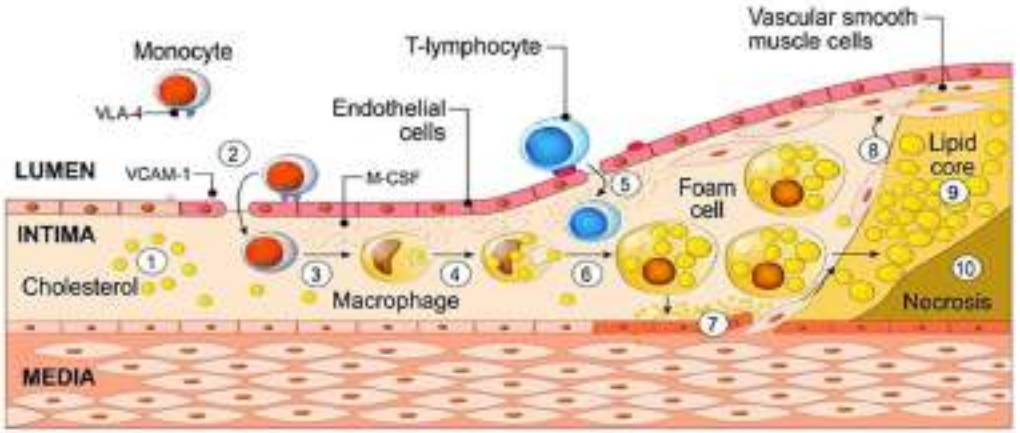


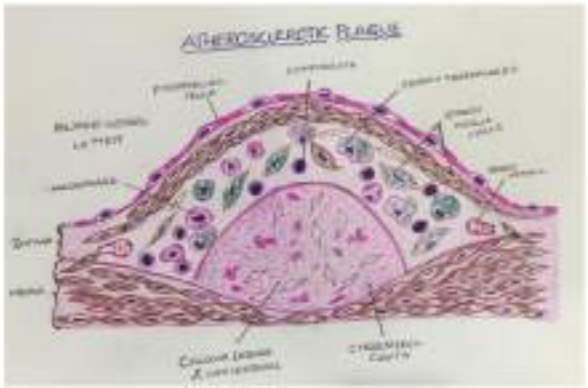
- ✓ Hypertension
- ✓ Turbulent blood flow
- ✓ Bacterial products
- ✓ Radiation injury
- ✓ Metabolic abnormalities such as hypercholesterolemia — increase cholesterol volume and it will cause atherosclerosis
- ✓ Toxins absorbed from cigarette smoke

Atherosclerosis is a result of chronic endothelial injury

- Atherosclerosis is a chronic inflammatory disease of the inner wall of large- and medium-sized arteries.
- Its basic pathogenic mechanisms are inflammation and oxidative stress involving interactions with multiple genetic, epigenetic and environmental factors.

Pathogenesis of atherosclerosis

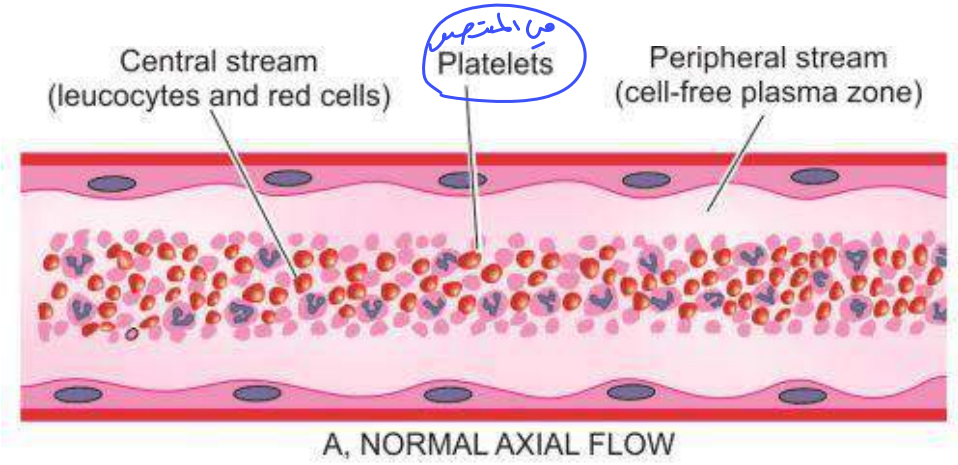




2- Alterations in Normal Blood Flow

stasis of the blood

- Normal laminar blood flow: platelets (and other blood cells) are found mainly in the center of the vessel lumen, separated from the endothelium by a slower-moving layer of plasma
- **Turbulence** contributes to **arterial and cardiac thrombosis** by causing endothelial injury or dysfunction.
- **Stasis** is a major contributor to the development of **venous thrombi.**



Stasis → اقتراب clotting factor
platelets & الـ
EC &
سهل يصير → زيادة الخثرات &
حدوث Thrombosis

Turbulence contributes to **arterial and cardiac thrombosis** by causing endothelial injury or dysfunction.

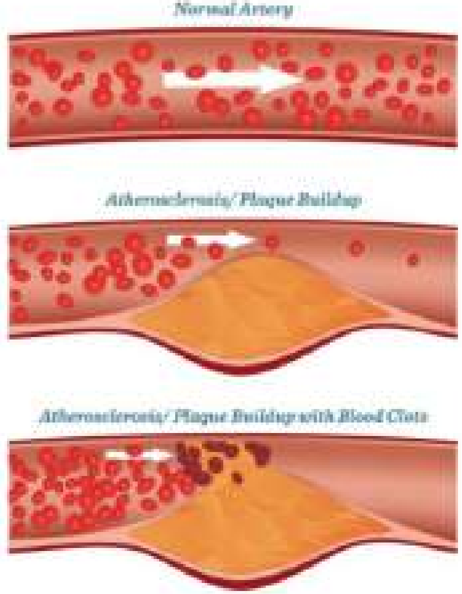


Figure 36 : Complicated atheromatous plaques, most show central ulceration, the **yellow fatty debris** is seen in the plaque at the top right. The brown color of the ulcerated plaques on the left is due to **mural thrombosis**, an important source of **thromboemboli.**

6.59 Atherosclerosis : aorta

Stasis and turbulent (chaotic) blood flow have the following effects:

- ✓ Both promote endothelial cell activation and enhanced procoagulant activity.
- ✓ Stasis allows platelets and leukocytes to come into contact with the endothelium when the flow is sluggish.
- ✓ Stasis slows the washout of activated clotting factors and impedes the inflow of clotting factor inhibitors.

decrease the removing of activated clotting Factor

Stasis

Can be seen in several clinical settings:

1- Ulcerated atherosclerotic plaques (**turbulent**)

2- Abnormal aortic and arterial dilations, called aneurysms (**stasis**)

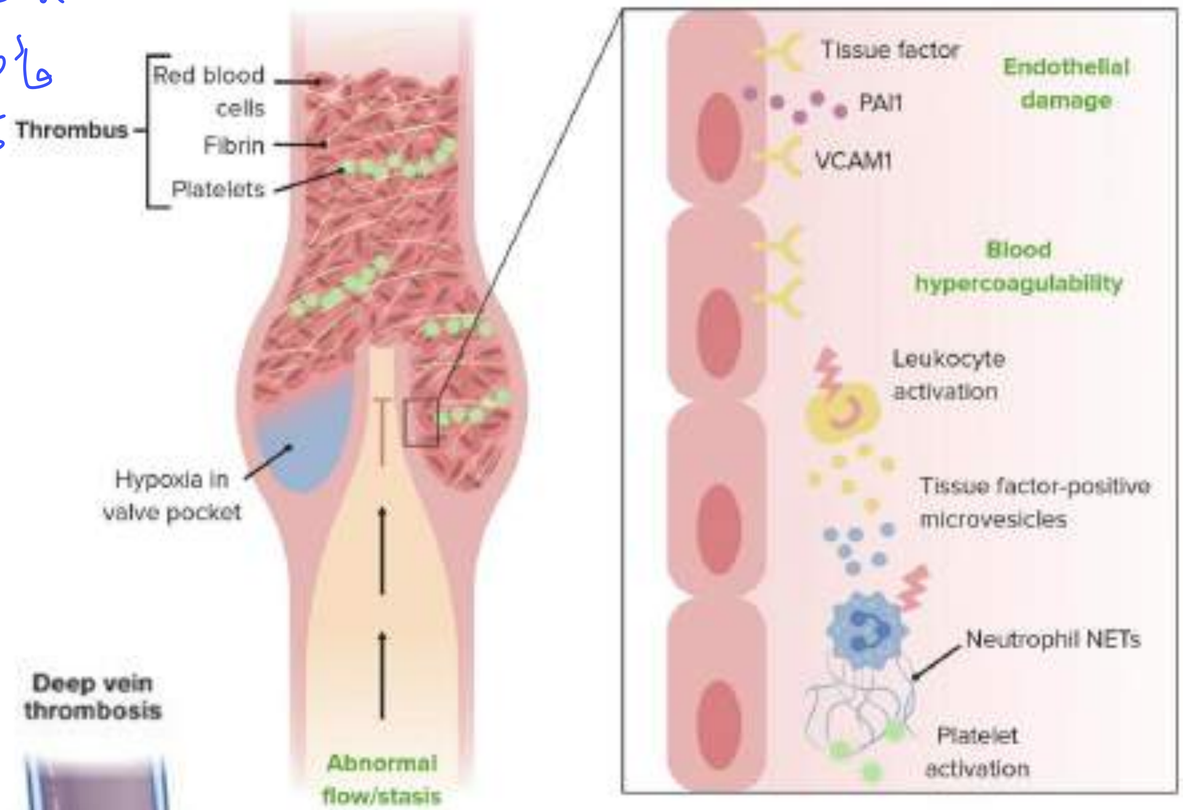
3- Hyperviscosity syndromes (such as polycythemia;) increase resistance to flow and cause small vessel **stasis**.

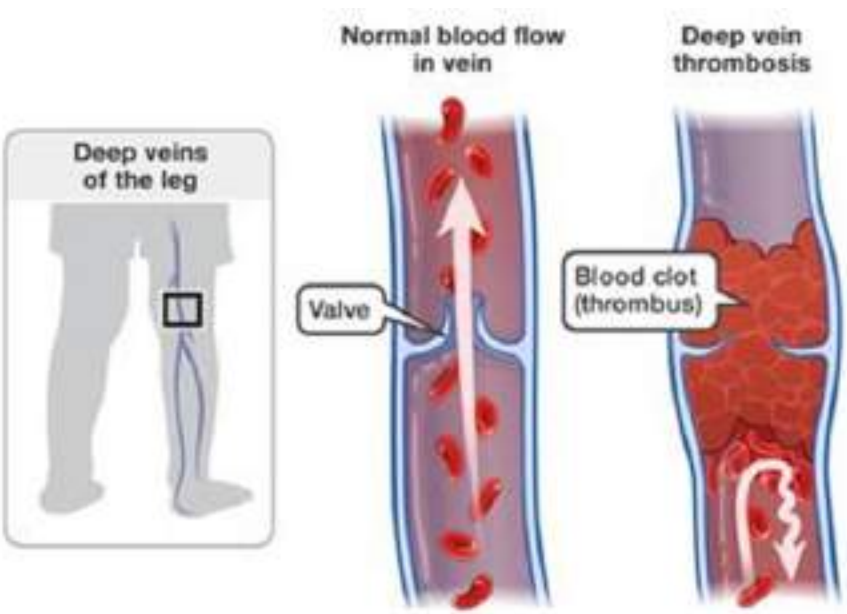
4- Deformed red cells in sickle cell anemia cause vascular occlusions, with the resultant **stasis**

* RBCs العشية تستطيع التعبير الحركي في شكلها عند العبور من small vessel
لكن عند فقدانها هذه الخاصية تصبح هي السبب في الـ stasis

*في هذه الصورة حدث thrombus
فأصبح لدي stasis + اقتران كل
مكونات التجلط مع بعض

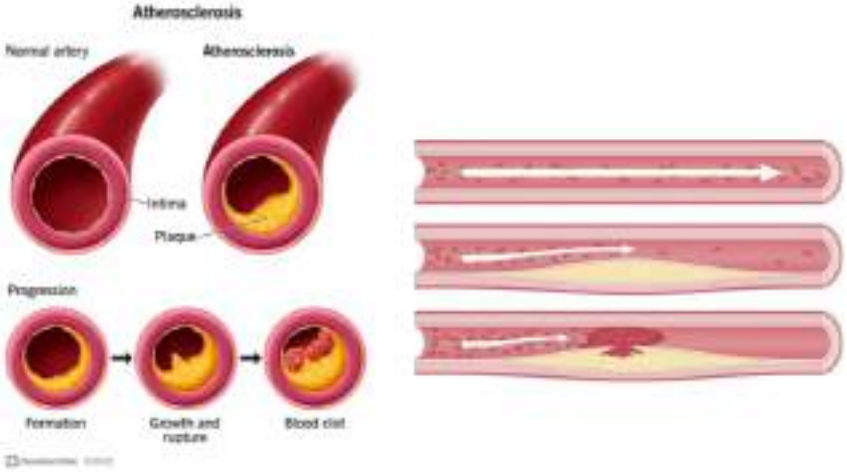
Stasis is a major contributor to the development of **venous thrombi**



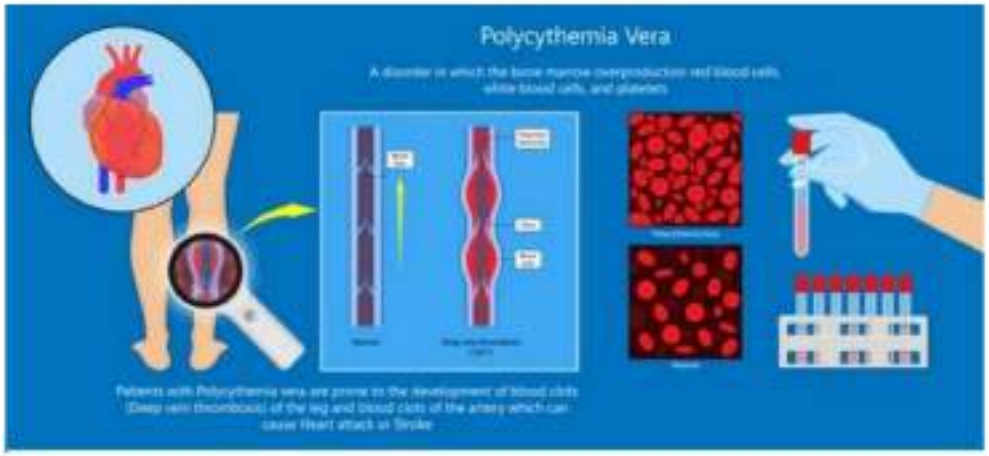


*ال(valve) يمنع الدم من العودة للوراء في (vein) ← وهذا
شكله حين تؤدي إلى deep venus valve

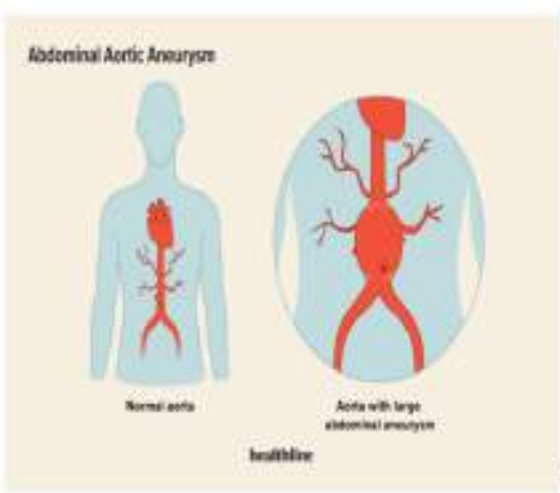
1- Ulcerated atherosclerotic plaques (turbulent)

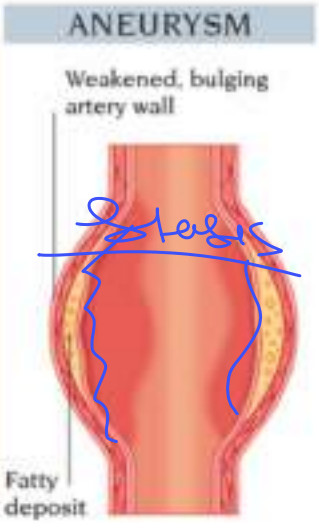


3-Hyperviscosity syndromes (such as **polycythemia**) increase resistance to flow and cause small vessel **stasis**

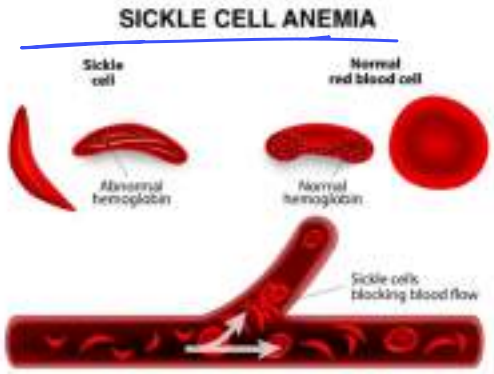


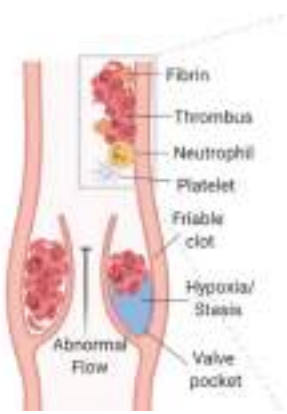
2- Abnormal aortic and arterial dilations, called aneurysms (stasis)





4- Deformed red cells in **sickle cell anemia** cause vascular occlusions, with the resultant **stasis**





3- Hypercoagulability

thrombophilia

- An important underlying risk factor for **venous thrombosis**
- Primary (genetic) and secondary (acquired) disorders .

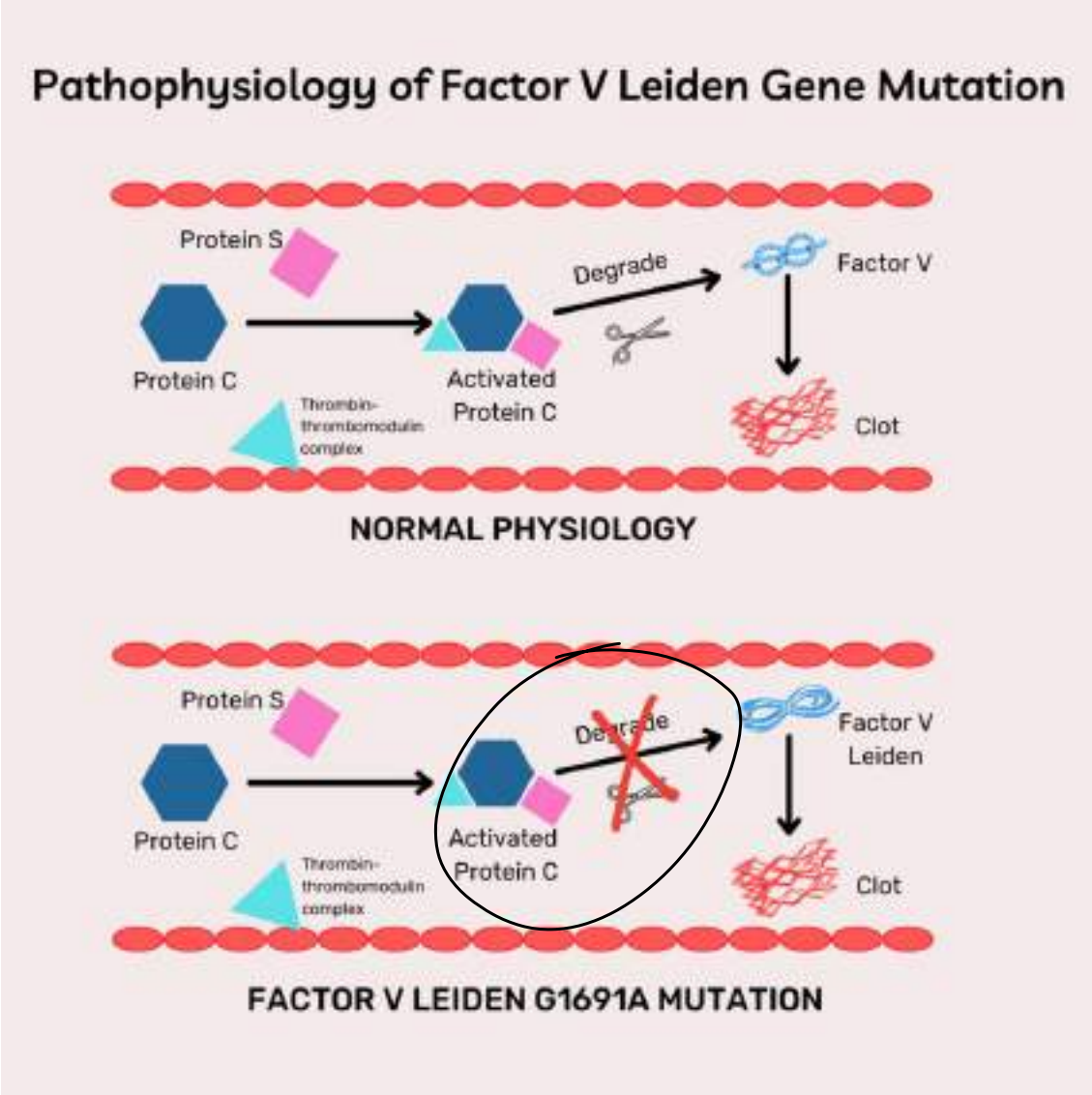
A- Inherited causes of hypercoagulability:

- Mutations in the **factor V gene** and the **prothrombin gene** are the most common.

- Approximately 2% to 15% of whites carry a specific factor V mutation (called the Leiden mutation). The mutation alters an amino acid residue in factor V and renders it resistant to protein C.

- Deficiencies of anticoagulants such as **protein C or protein S (rare) and antithrombin III**

Factor v Leiden mutation

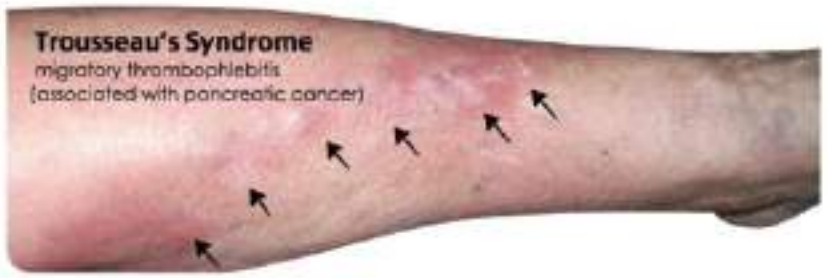


B. Acquired hypercoagulability

1. Oral contraceptive use and hyperestrogenic state of pregnancy may be related to increased hepatic synthesis of coagulation factors and reduced synthesis of antithrombin III .
2. Prolonged bed rest or immobilization
3. Disseminated cancers, release of mucin in adenocarcinoma predisposes to thrombus formation (migratory thrombophlebitis or Trousseau's syndrome).
4. Advancing age: due to increased platelet aggregation and reduced release of PGI2 from endothelium

Migratory thrombophlebitis or Trousseau's syndrome

Trousseau syndrome is an acquired blood clotting disorder that results in migratory thrombophlebitis (inflammation of a vein due to a blood clot) in association with an often-undiagnosed malignancy. Most associated with **pancreatic cancer.**



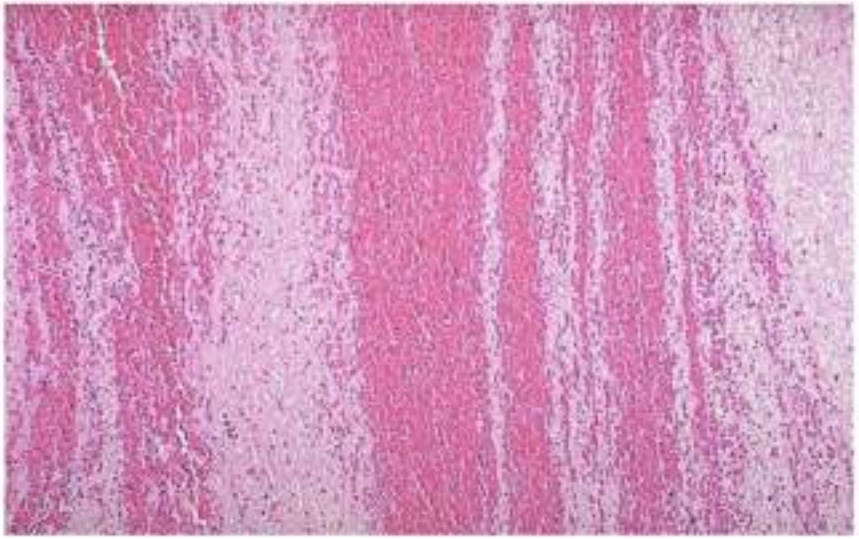
Thrombi

- Thrombi can have grossly (and microscopically) apparent laminations called **lines of Zahn**:
- **Lines of Zahn are characteristic of thrombus formed at the site of rapid arterial blood flow, with laminations produced by successive deposition of platelets and fibrin (pale layers) alternating with red blood cells (dark layers).**

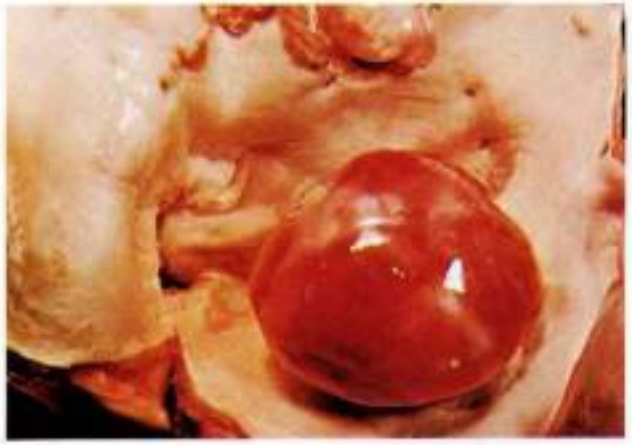
- Only found in thrombi that form in flowing blood

- Can distinguish antemortem thrombosis from the **bland nonlaminated** clots that form in the **postmortem state**.
- Thrombi occurring in heart chambers or in the aortic lumen are designated as **mural thrombi**.

These are "lines of Zahn" which are the alternating pale pink bands of platelets with fibrin and red bands of RBC's forming a true thrombus.



Ball thrombus (mural thrombus): left atrium. The dilated, thick-walled left atrium is viewed from above, showing stenosed mitral valve . A globular red thrombus ball thrombus) lies free within the atrial lumen, & obstructing the mitral valve orifice intermittently.



6.45 Ball thrombus: left atrium

Arterial vs. venous thrombi

- **Arterial thrombi: relatively rich in platelets,** as the processes underlying their development (e.g., endothelial injury) lead to platelet activation.
- **Venous thrombi (phlebothrombosis):** tend to contain more enmeshed red cells because these thrombi form in the sluggish venous circulation, leading to the **red** color.

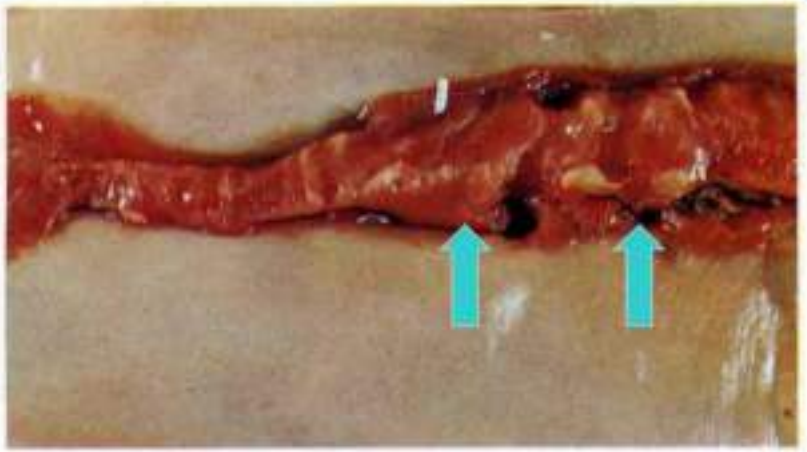
	Arterial thrombi	Venous thrombi
Etiology	Endothelial damage or turbulence	Stasis and hyperco-agulable states
Lines of Zahn	Prominent	Less prominent
Color	Gray	Red
Occlusive	Yes	Yes
Location	Heart; coronary, cerebral, aorta	Lower limb veins

6.65 Aneurysm: iliac arteries

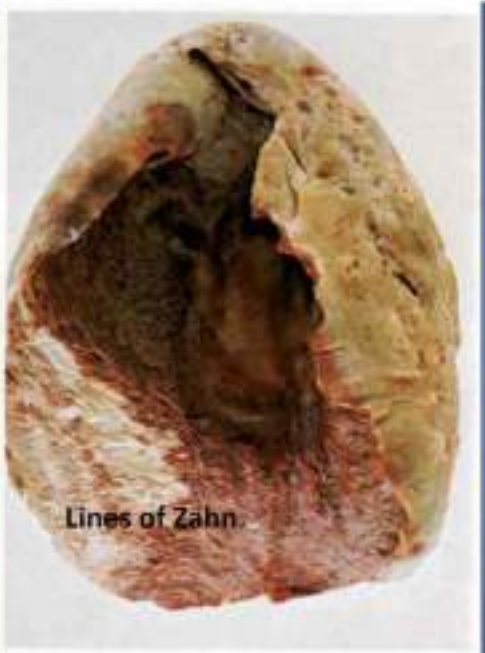
Fig. 37 : Saccular aneurysm of the iliac artery.

The lumen is filled with arterial thrombus, which is reddish-brown & shows greyish-white **lines of Zhan.**

F 39 : Venous Thrombosis. The **inferior vena cava contains** a long pale tapering thrombus .Thrombus is mural & firmly attached to the vein wall.



6.30 Thrombosis: inferior vena cava



6.66 Thrombus from aneurysm

Fig. 38 : Large thrombus, (measuring **20X12X12** cm) removed from an atheromatous abdominal aortic aneurysm (AAAA). The laminated structure **(lines of Zahn)** of the thrombus is clearly evident (lower left).

Fate of the Thrombus

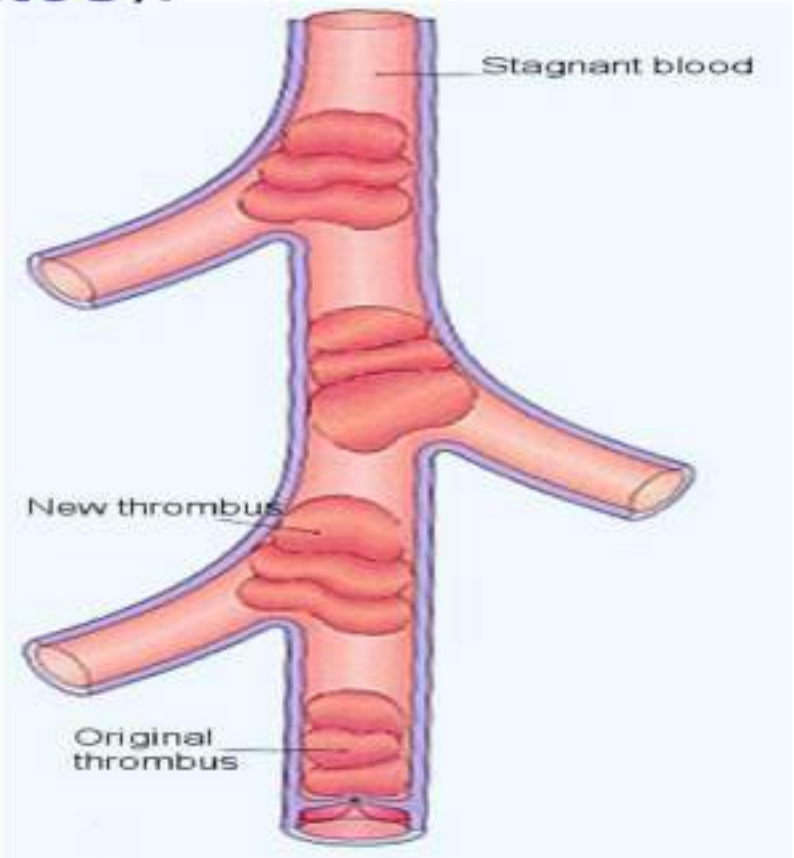
1. **Propagation:** Thrombus enlargement by accumulation of additional platelets and fibrin.

Propagation of a thrombus occurs towards the direction of the heart and involves the accumulation of additional platelets and fibrin. This means that it is anterograde in veins or retrograde in arteries.

2. **Embolization:** Fragment of thrombus is transported elsewhere in the vasculature.
3. **Dissolution**: In newly formed thrombus, activation of fibrinolysis may lead to its rapid shrinkage and complete dissolution.

Outcomes of thrombosis (Fates):

- **Propagation**
  - progressive spread of thrombosis
  - distally in arteries
  - proximally in veins



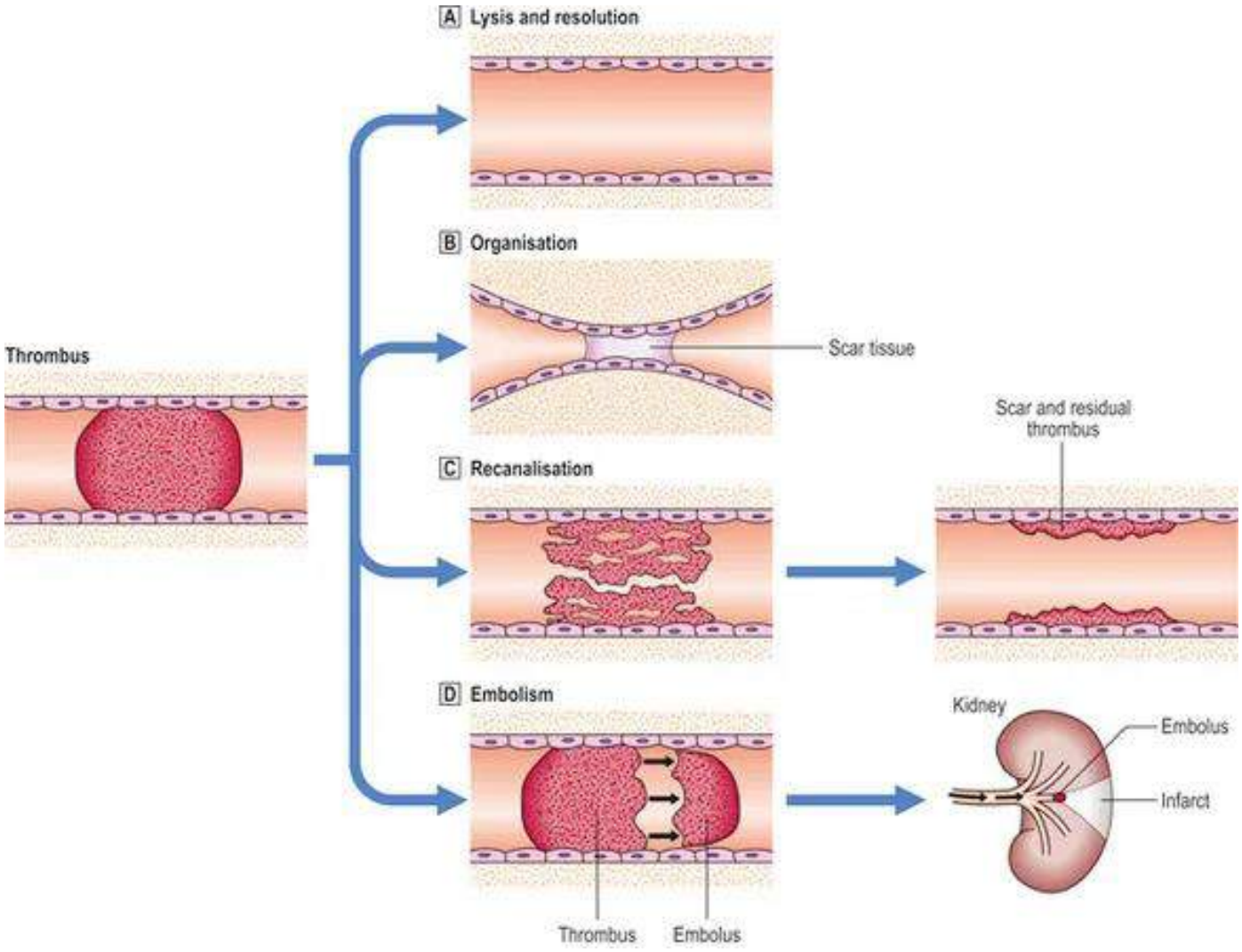
Fate of the Thrombus

4. Organisation and recanalization:

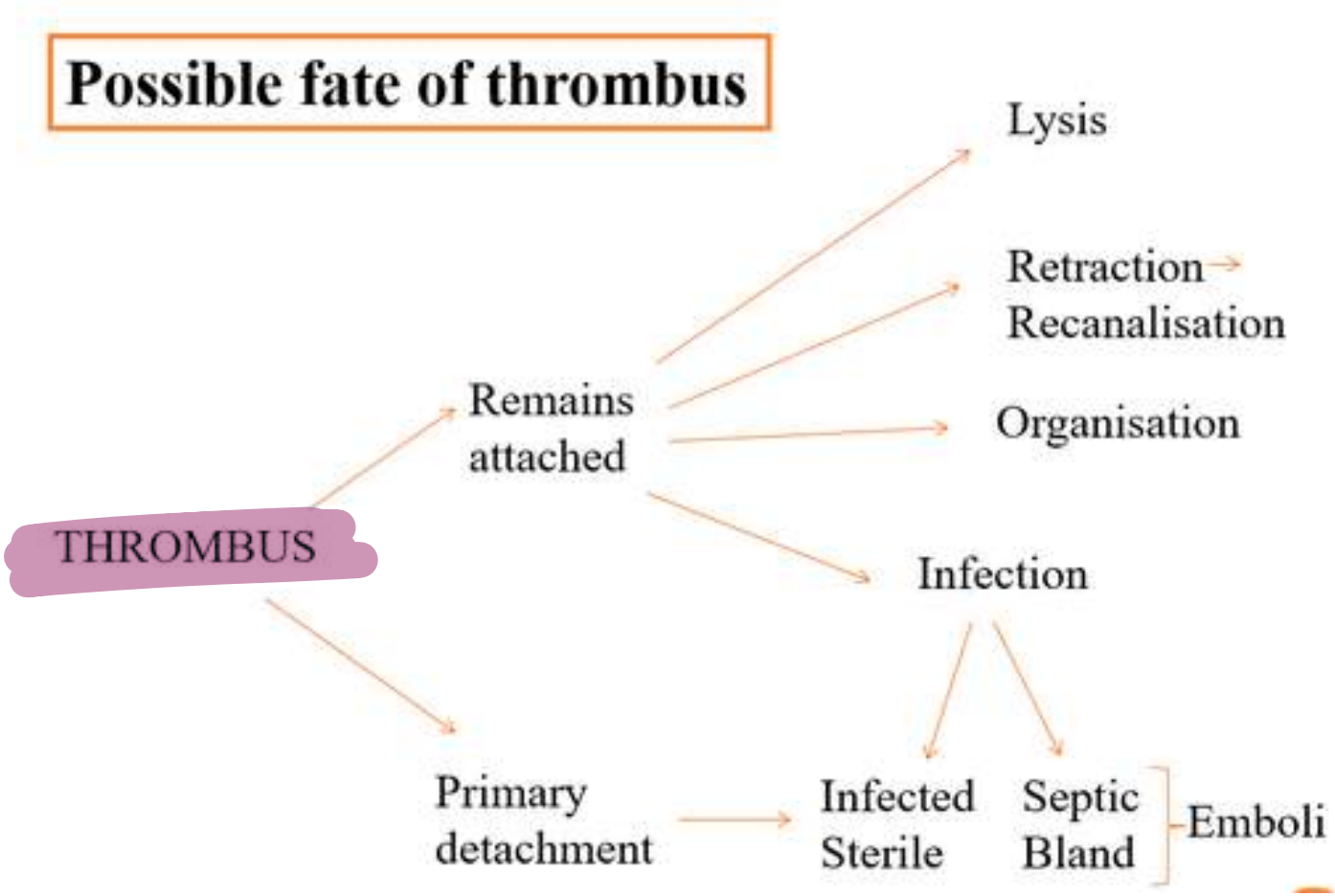
- Older thrombi become organized by the ingrowth of endothelial cells, smooth muscle cells, and fibroblasts into the fibrin-rich thrombus
- In time, capillary channels are formed and create conduits along the length of the thrombus, thereby reestablishing the continuity of the original lumen.

5. Bacterial seeding of thrombus: serve as a culture medium, and the resulting infection may weaken the vessel wall, leading to formation of a **mycotic aneurysm**.

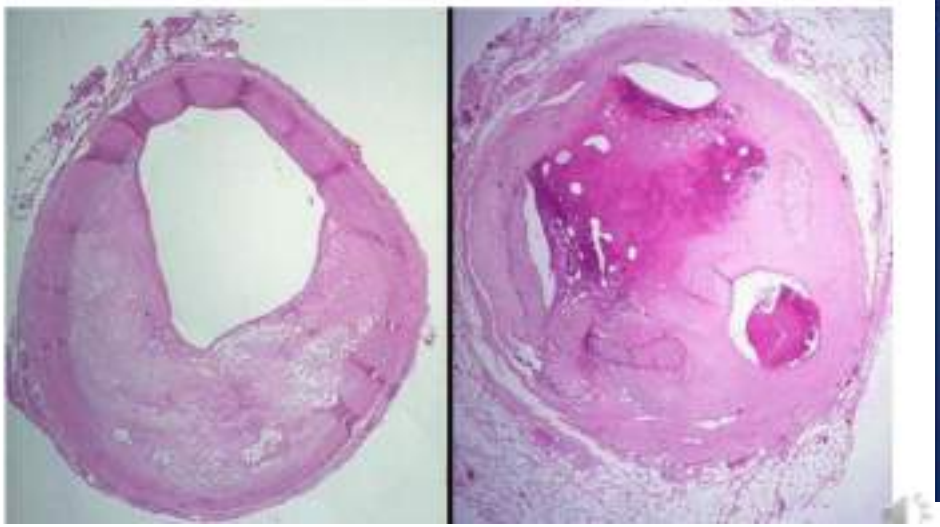
Fate of the Thrombus



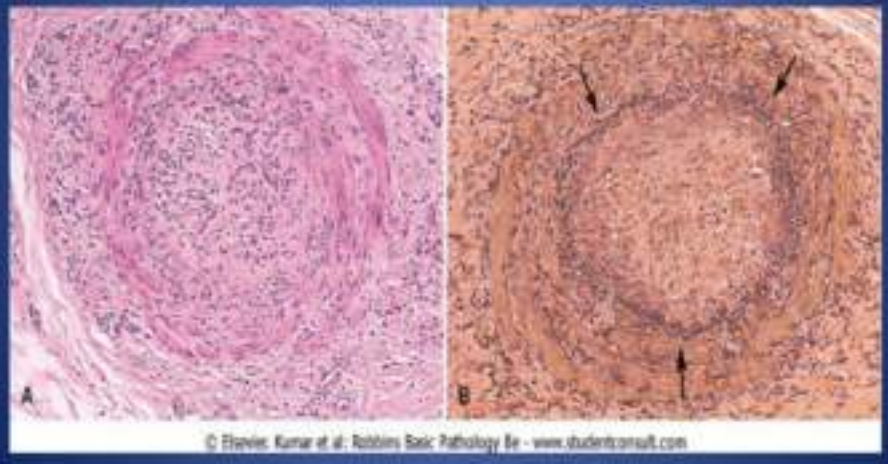
Fate of the Thrombus



Here is occlusive coronary atherosclerosis. The coronary at the left is narrowed by 60 to 70%. The coronary at the right is even worse with evidence for previous thrombosis with organization of the thrombus and recanalization such that there are three small lumens remaining.



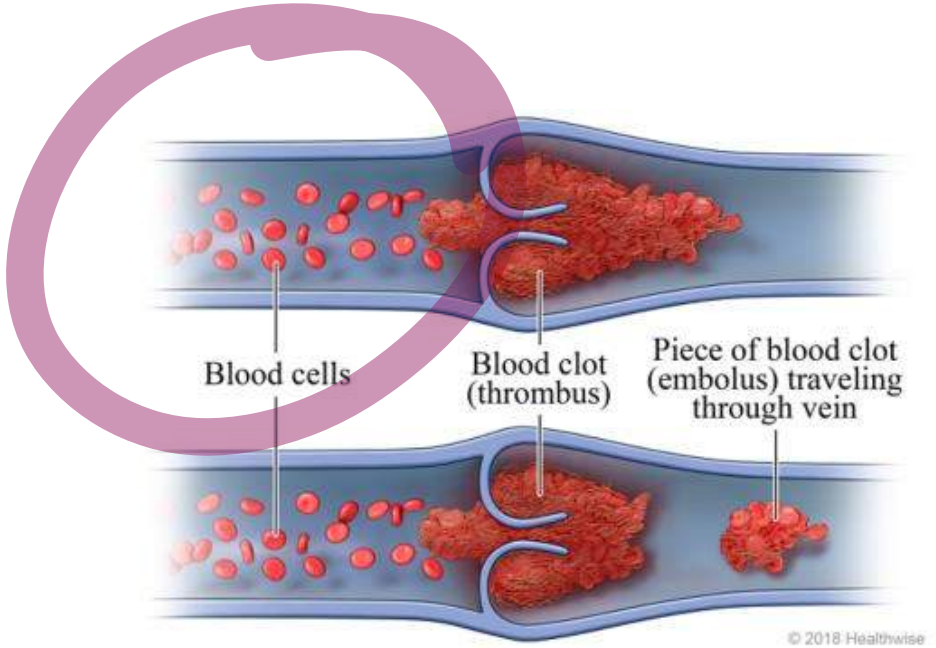
F 41 : **Artery with an old thrombus. A,** H&E stained section. **B,** Stain for **elastic tissue (black).** The original lumen is delineated by the **internal elastic lamina (3 arrows)** & is totally filled with organized thrombus .



Complications of Thrombi

- Occlusion (Obstruction) of blood vessels
  - Veins: Congestion and edema distal to obstruction
  - Arteries: Ischemia and infarcts in areas supplies by the vessel.

- Embolization



Venous Thrombosis (Phlebothrombosis)

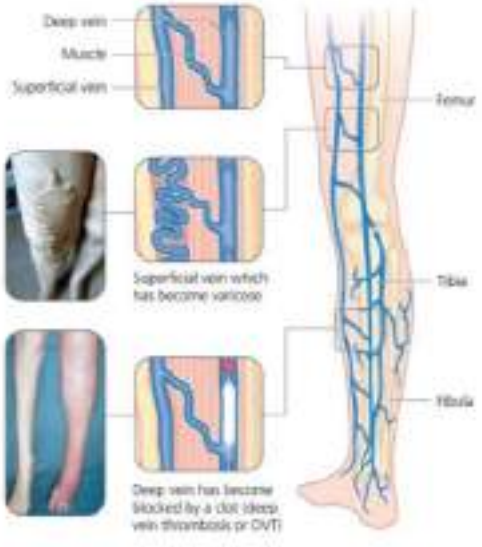
Mostly in **superficial** or **deep veins** of the legs

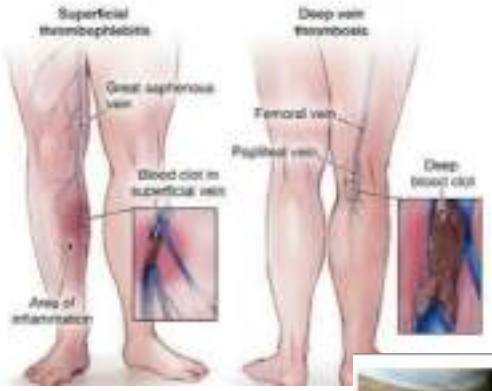
- Superficial vein thrombosis occur in the saphenous system (varicosities).

  Manifestations: local congestion, swelling (edema), pain, tenderness, infections of overlying skin and development of varicose ulcers. Rarely embolize

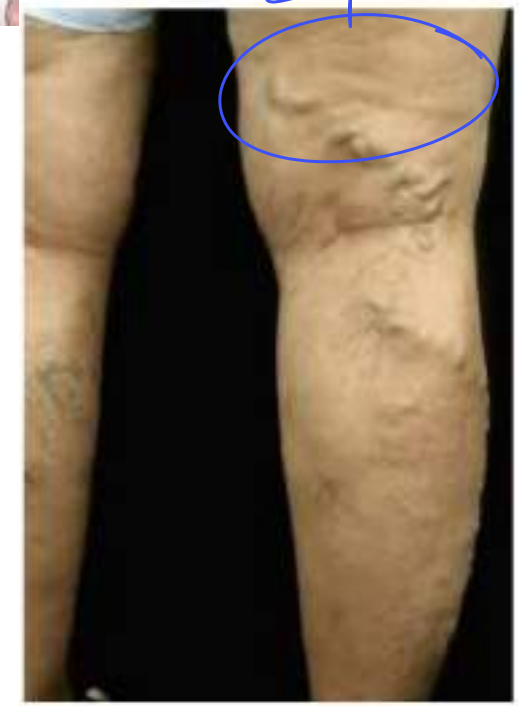
- Deep vein thrombosis(In the larger veins at or above the knee joint) *is more serious*; it may lead to pulmonary emboli, causes edema, pain and tenderness

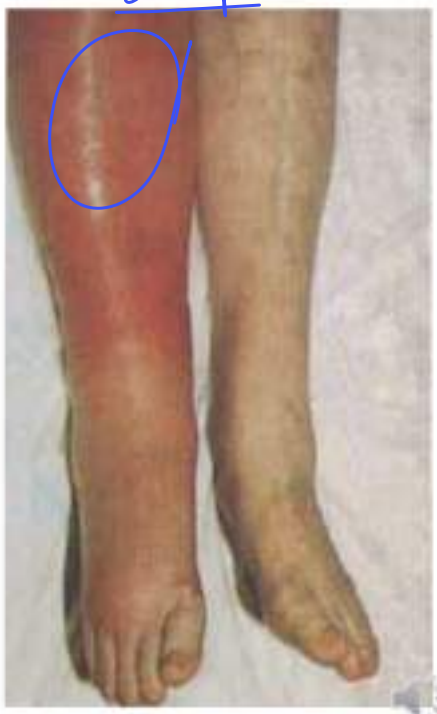
Superficial and deep vein thrombosis





Superficial deep





Venous Thrombosis (Phlebothrombosis)

- Venous obstruction often is circumvented by collateral channels.
- Consequently, DVTs are entirely asymptomatic in approximately 50% of patients and are recognized after they have embolized to the lungs.