



Pathology

Subject :

Lec no : 19

Done By : Sara Alkalabani

وَقُلْ رَبِّ زِدْنِي عِلْمًا

Hemodynamics lecture 5

Ischemia , thrombosis, arterial , venous



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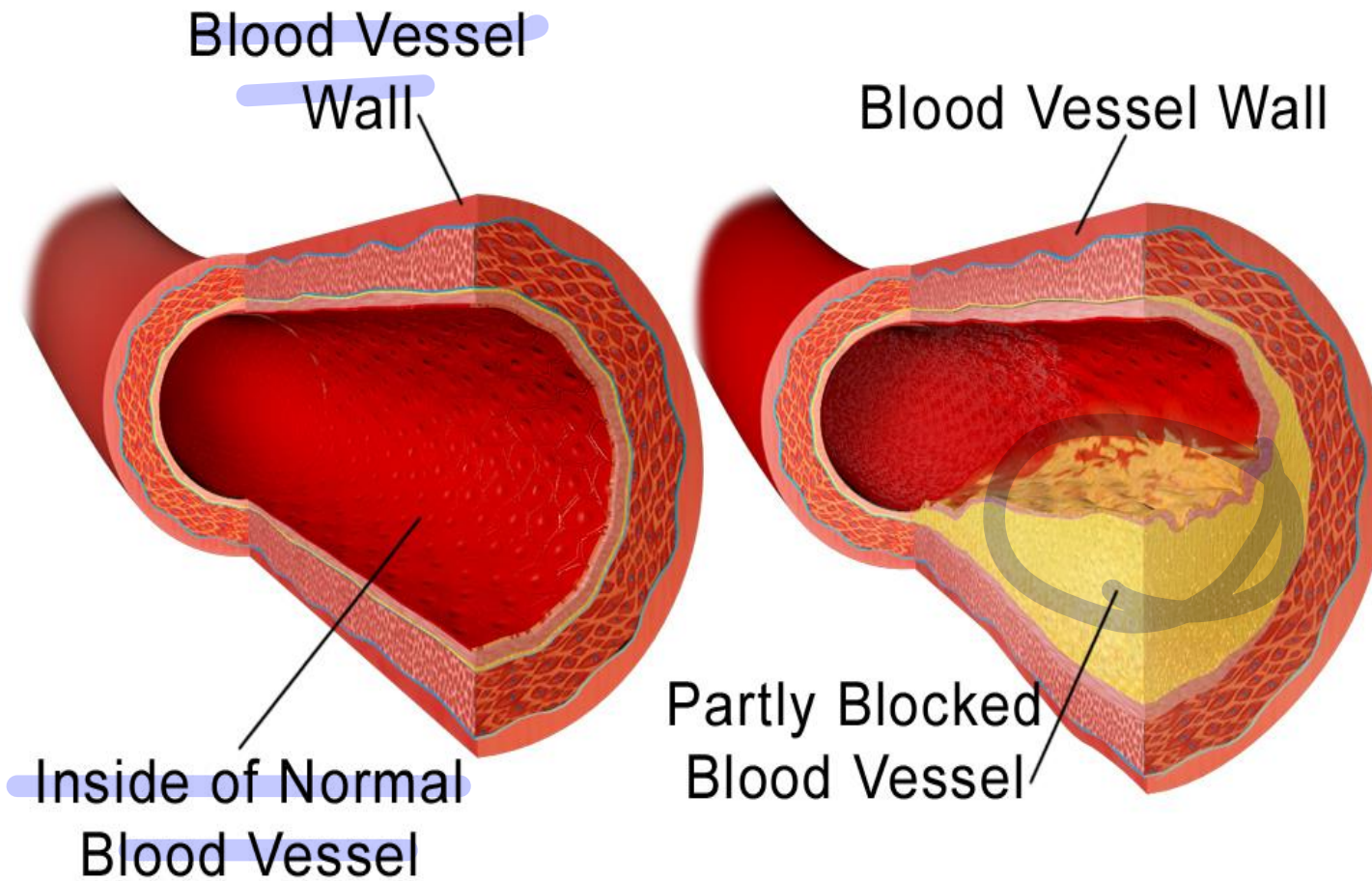
Audio 4



Causes of ischemia

- 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 → عبارة عن كتلة لىن هائى بكتلة من مكونات ادم
- 2- embolism → انس عظم باك Femur مثلا يؤدى للدهون تدخل فى مسار ادم أو أى عائق
- 3-ligation (surgical)
- Partial Gradual obstruction caused by
- 1- inflammation as in endarteritis obliterance (syphilis)
- 2-degenerative disease (atherosclerosis) تصلب شرايين (عبارة عن دهون)
- 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 تشنجات من خنومحزون - Spasm
- pressure by tumour from outside blood vessels





Normal and Partly Blocked Blood Vessel

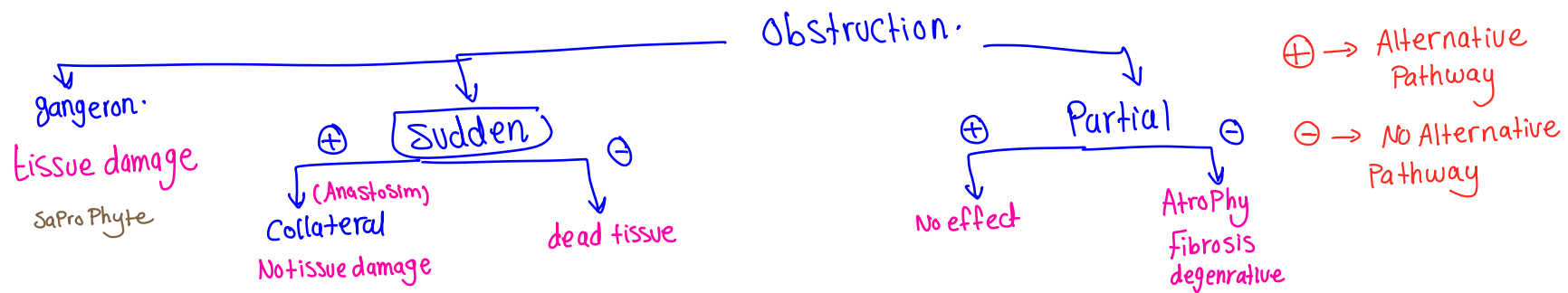


Effect of Obstruction of blood supply

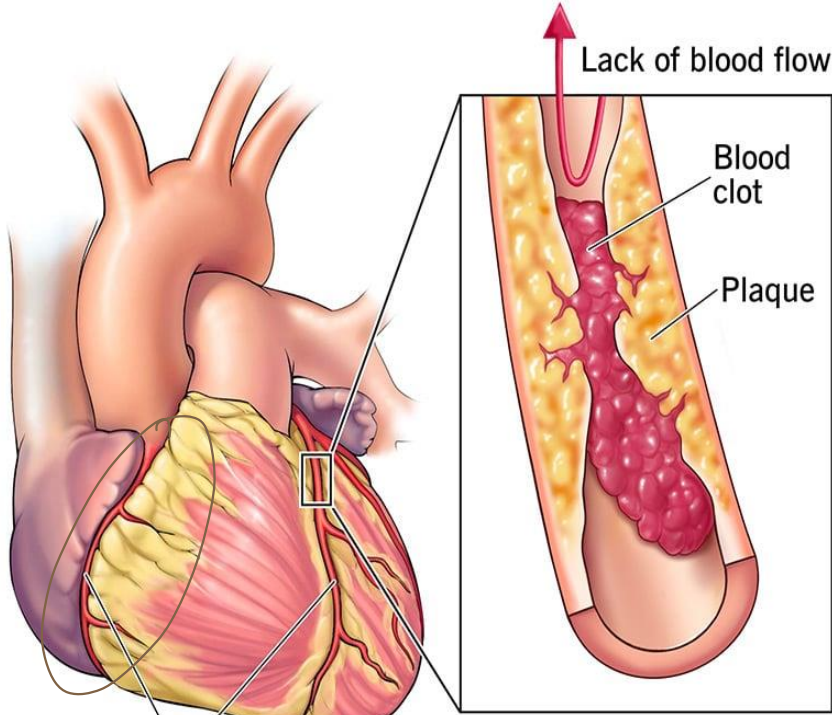
بإفترقة لو همار في حنوة هل في مسار بديل للدم؟ الكمار يكون عندهم مسار بديل لكن السباب لا / لهيك بنحكيه دائما حلقة اكبار اخذ من اصغار

- If obstruction Sudden , Complete obstruction it will lead to infarction (dead of tissue) if there is NO EFFICIENT COLLATERALS → Alternative Pathway of blood.
- Or gangrene if associated with tissue putrefaction (by bacterial action of saprophyte bact) → ^{التعفن} اسم البكتيريا اللية تتحلل غرضنيا .
- IF there is Collaterals (anastomosis)--- No effect (no tissue damage)
a cross-connection between adjacent channels, tubes, fibers, or other parts of a network
- If Obstruction Partial ,gradual without collaterals --- degenerative changes ,atrophy , fibrosis
- Partial with collateral No tissue damage





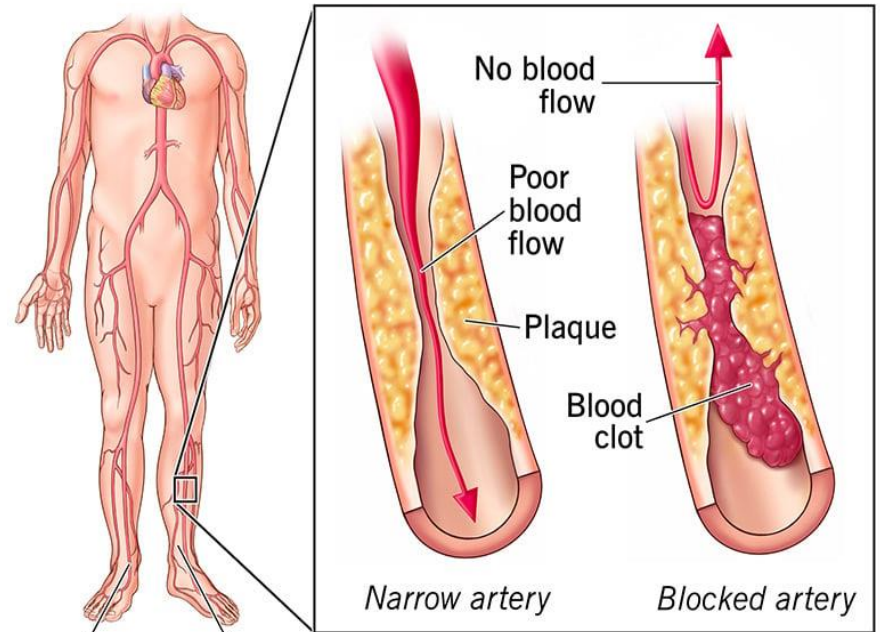
Coronary Artery Disease



Coronary arteries

Cleveland Clinic ©2022

Peripheral Artery Disease



Peripheral artery

Cleveland Clinic ©2022



Thrombosis

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

يعني تصويبه Platelet و RBCs وغيره

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

Causes of thrombosis

Virchow's triad:

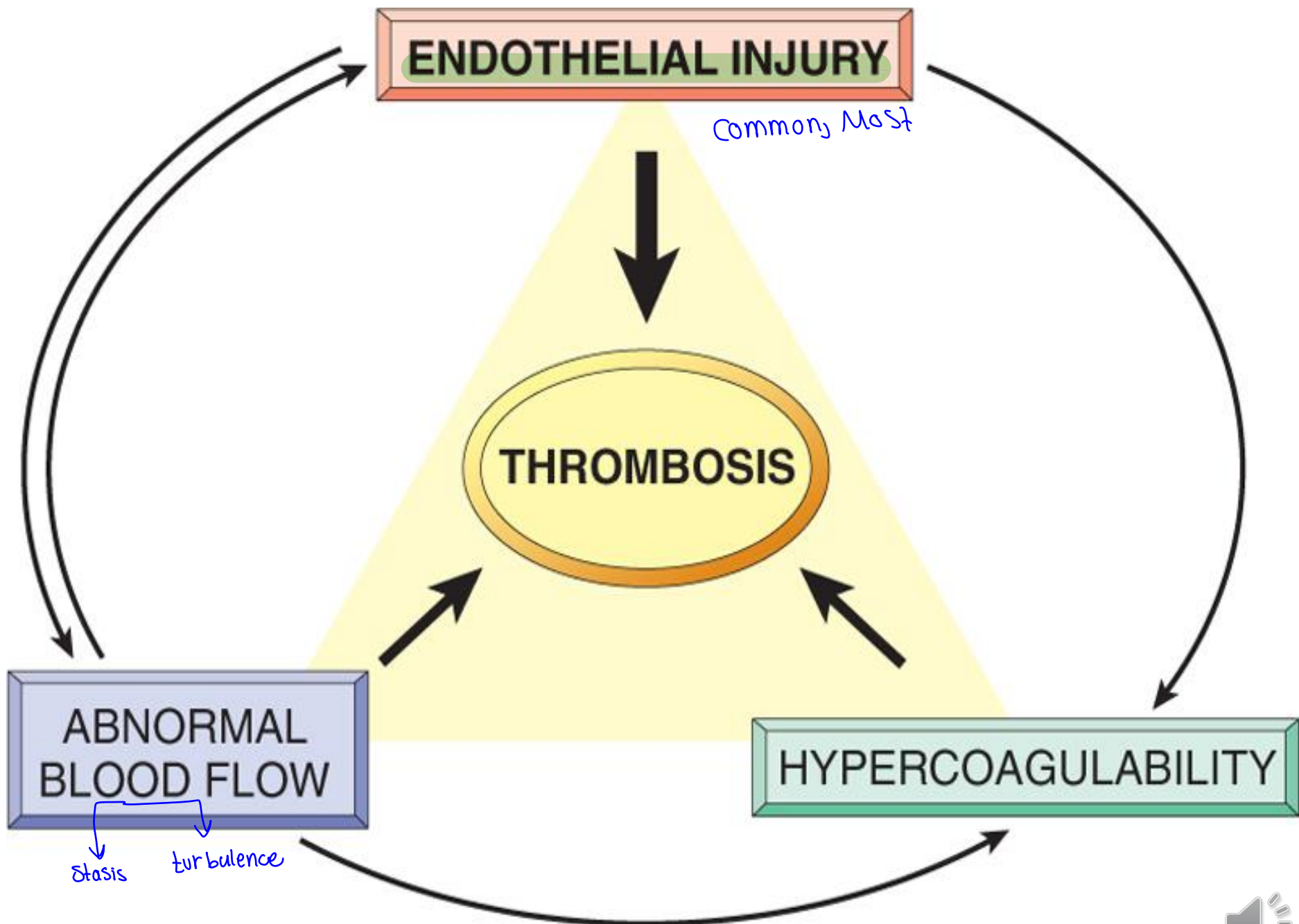
(1) Endothelial injury the most Common cause

(2) Stasis or turbulence of blood flow Inactivity

(3) Blood hypercoagulability

القلب له قابليه لتكوين خثرات ←





1- Endothelial injury

most common cause of thrombus formation in the heart and arterial circulation.

Endothelium exposes subendothelial collagen, releases tissue factor, and reduces local production of PGI2 and plasminogen activators.

dynamic imbalance of the prothrombotic and antithrombotic effects of endothelium can influence clotting locally.

- The commonest cause of thrombus formation, mainly in the heart and arterial circulation.

بصير عندي حرج لأي سبب كان وينودي إي كسط endothelial ويصير فيه (collagen + Basement membrane) مكشوفات

- Loss of endothelium exposes subendothelial ECM, releases tissue factor, and reduces local production of PGI2 and plasminogen activators.

ويفرزوا عوامل حتى ليكروا الحرج ويقبل (PGI2) الة دور في توسيع الاوعية حتى تتكون بثابة وينسكن الحرج ويعمل بتحول Plasminogen Plasmin وينوب خثرة

- Any dynamic imbalance of the prothrombotic and antithrombotic effects of endothelium can influence clotting locally.

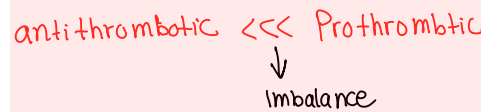
توسيع الاوعية / اقليل خثرة لونه

لبسوا خثرة

تدويه خثرة لدم / F

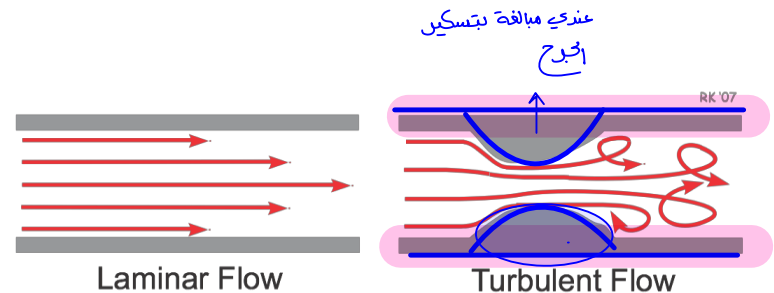
ما لبسوا خثرة

أي خلل ديناميكي في التأثيرات التخثرية والمضادة للتخثر للبطانة يمكن أن يؤثر على التخثر محلياً



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

- 1 ✓ Hypertension
- 2 ✓ Turbulent blood flow
- 3 ✓ Bacterial products
- 4 ✓ Radiation injury
- 5 ✓ Metabolic abnormalities such as hypercholesterolemia
- ✓ Toxins absorbed from cigarette smoke



حالة مزمنة

Atherosclerosis is a result of chronic endothelial injury

Cardiac + Artery **حصىب**

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.

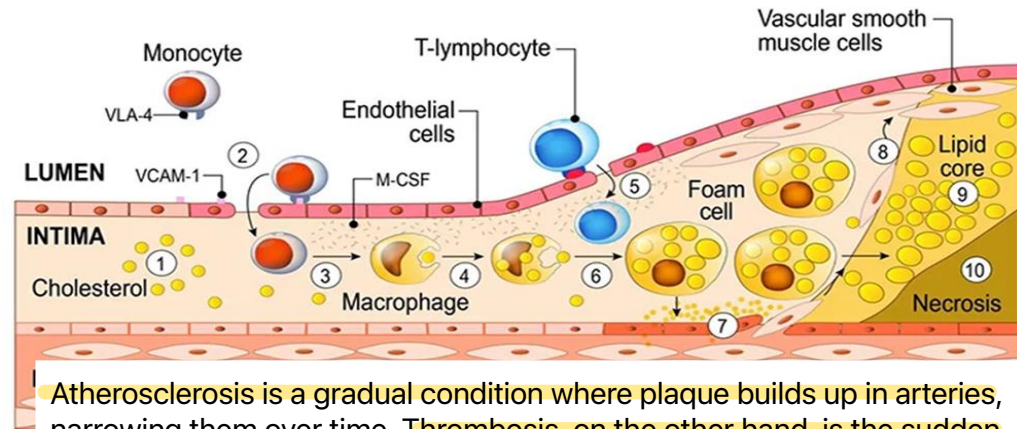
عوامل تؤدي إلى (Atherosclerosis)

①
②
③
④
⑤
اللائل غير المرصحة

أبرز لعوامل التي تؤدي لتكوين التصلبات ؟

العوامل الوراثية - اللائل غير المرصحة - الخ / كله بعض تكوين التصلبات بصفة LDL

Pathogenesis of atherosclerosis



Atherosclerosis is a gradual condition where plaque builds up in arteries, narrowing them over time. Thrombosis, on the other hand, is the sudden formation of a blood clot that can obstruct blood flow. Atherosclerosis can contribute to thrombosis by creating a surface where clots are more likely to form.



ATHEROSCLEROSIS VERSUS THROMBOSIS

Atherosclerosis is characterized by the deposition of fatty material on the inner walls of their arteries

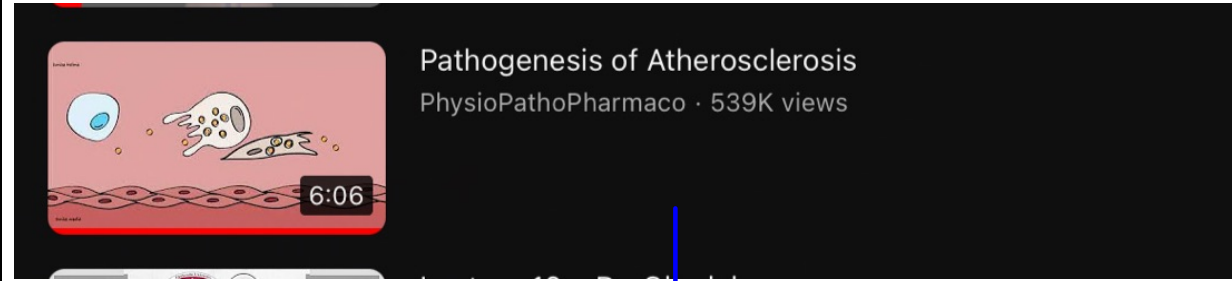
Cholesterol globules on the blood vessel walls become calcified

Caused by elevated levels of cholesterol including LDL and VLDL

Thrombosis is the local coagulation or clotting of the blood in a part of the circulatory system

The blood clot on the blood vessel wall does not become calcified

Caused by hypercoagulable status of blood composition, stasis of blood flow or damage to blood vessels



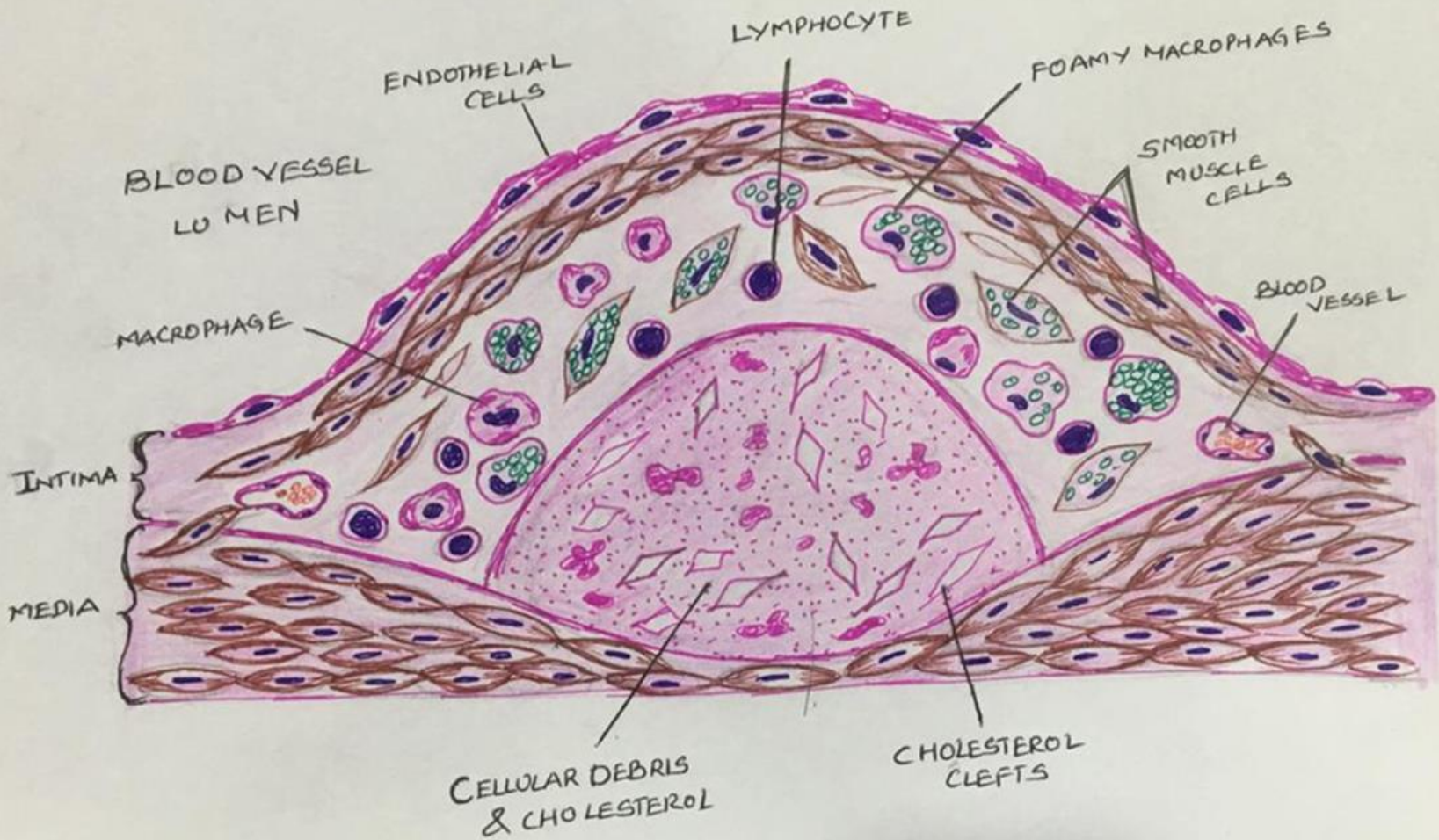
https://youtu.be/N33JsBeziEY?si=-7_O3rKq30EUm72h

ہاڈ اینڈیو خارجیں لکنہ پوجن عملیہ (Atherosclerosis)

خارجی

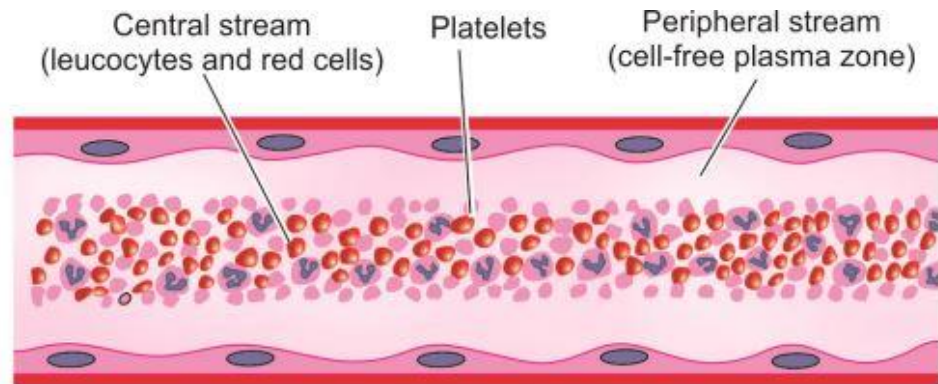
بصیرتی هجومی خلیوں (endothelial cells)

ATHEROSCLEROTIC PLAQUE



2- Alterations in Normal Blood Flow

- 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.



A, NORMAL AXIAL FLOW

أبرز الأسباب التي تؤدي لركود الدم هي
عملية جراحية تتطلب منه يظل نائم على بطنه
أو قهوه / أشخاص يضاهم سياغروا ودائما
قاعدتين سميهم (Economy class)
ما يتكون فيه لكراسية مريحة وهي تعريض من نوميل

the lowest travel class of seating in air travel, rail travel, and sometimes ferry or maritime travel



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

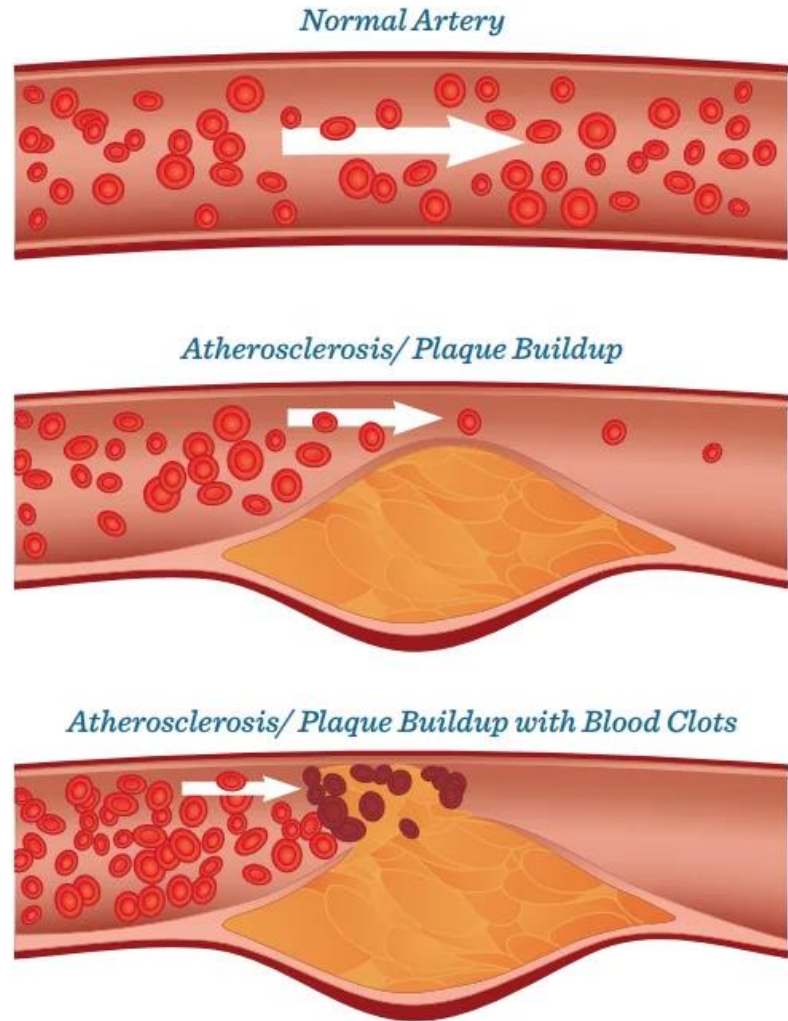
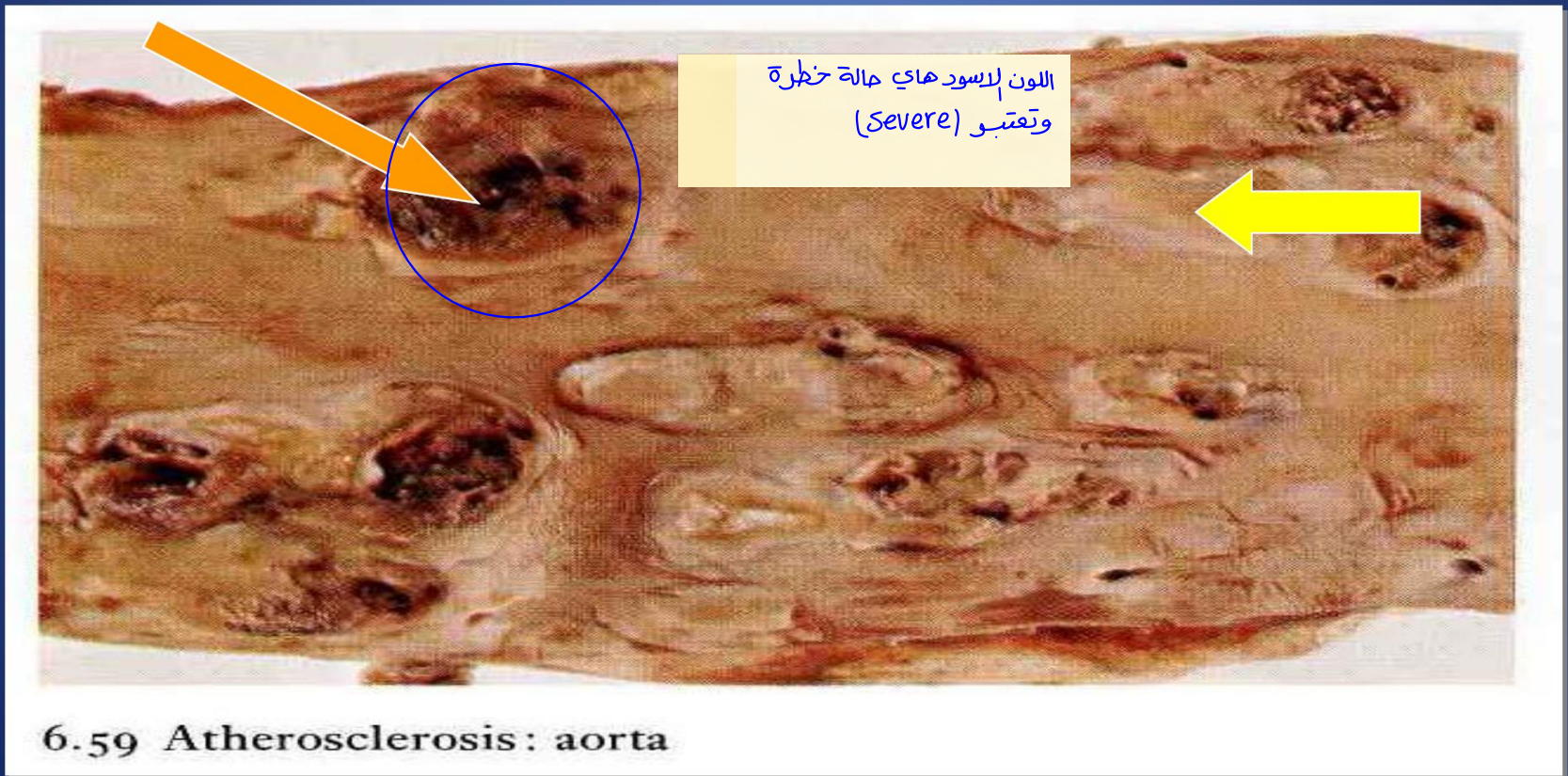


Figure 36 : Complicated atheromatous plaques, most show central ulceration, the yellow fatty debris is seen in the plaque at the top right. The brown color of the ulcerated plaques on the left is due to mural thrombosis, an important source of thromboemboli.



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



- ✓ Both promote endothelial cell activation and enhanced **procoagulant** activity.
Active ← Inactive تكون
- ✓ Stasis allows platelets and leukocytes to come into contact with the endothelium when the flow is sluggish.
لما ما يصير في حركة رج نيم التلويقة على الطرافة .
- ✓ Stasis slows the washout of activated clotting factors and **impedes** the inflow of clotting factor inhibitors.
↓

بصير ابطاء لعملية ازالة خثرة من ادم

يؤدي الركود إلى إبطاء عملية غسل عوامل التخثر المنشطة ويعيق تدفق مثبطات عوامل التخثر



Can be seen in several clinical settings:

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

2- Abnormal aortic and arterial dilations, called

↓
↑
منش طبيعي
و بلا حزمه
aneurysms (**stasis**)

↑ RBCS

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**

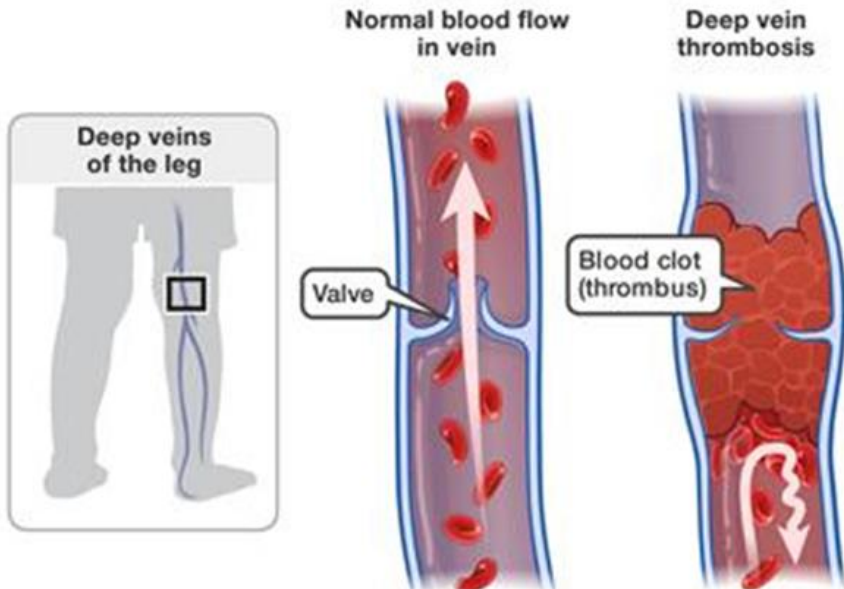
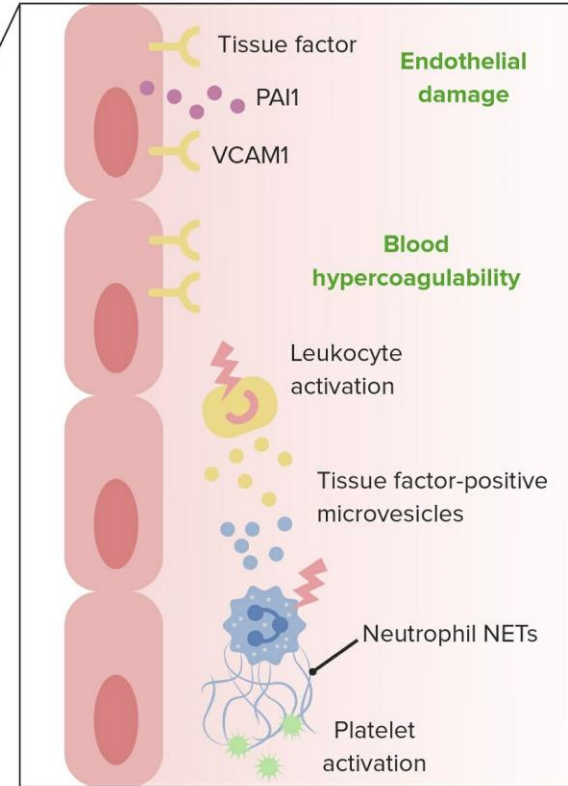
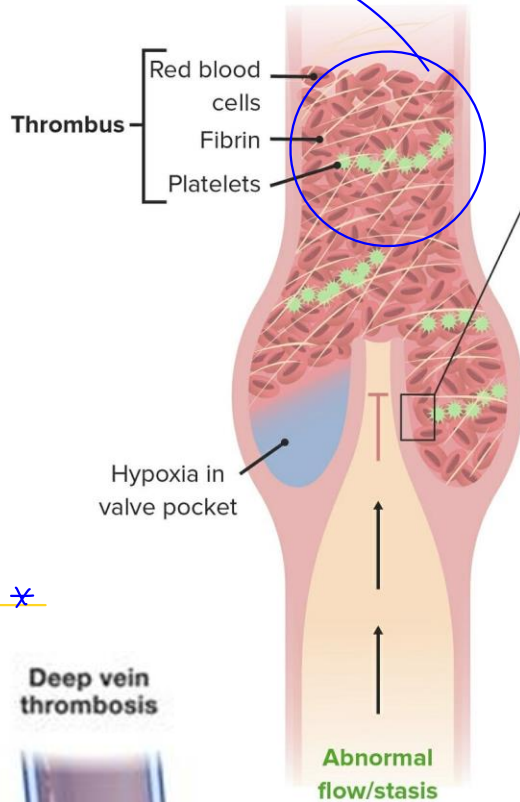
←
Rigid تكون



اللون شاحب للدم دلالة أنه مخلوط
Platelets + RBCs + Fibrin

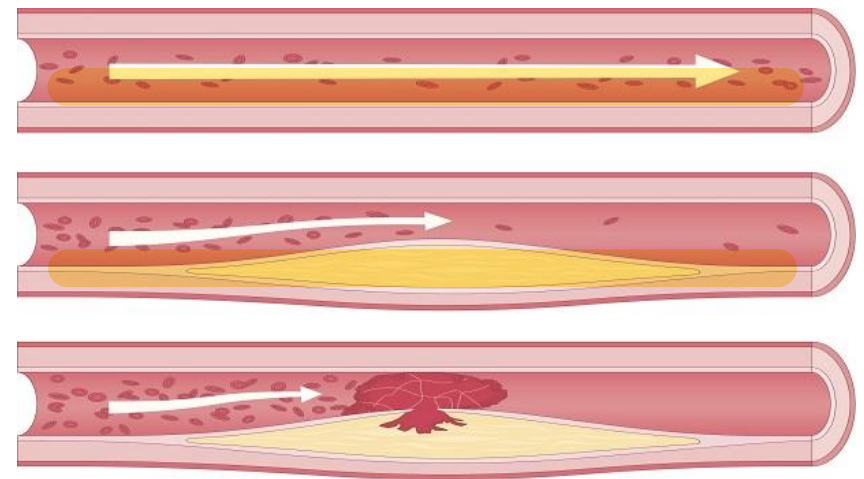
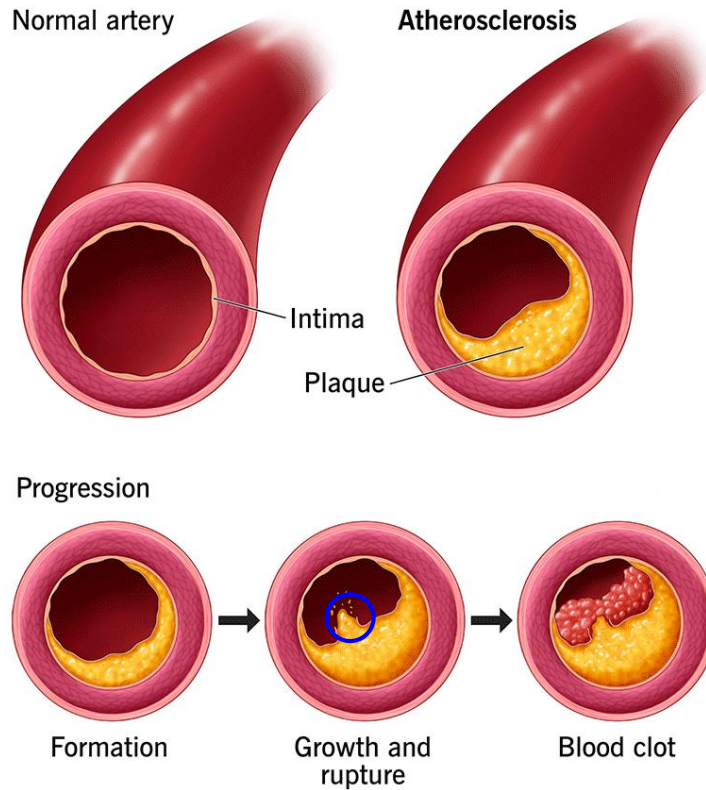
Stasis is a major contributor to the development of venous thrombi

* مخلوط الدم مرتبط مع تحلطات بالدورة



1- Ulcerated atherosclerotic plaques (turbulent)

Atherosclerosis

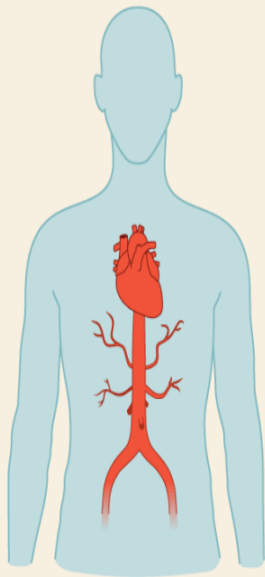


2- Abnormal aortic and arterial dilations, called

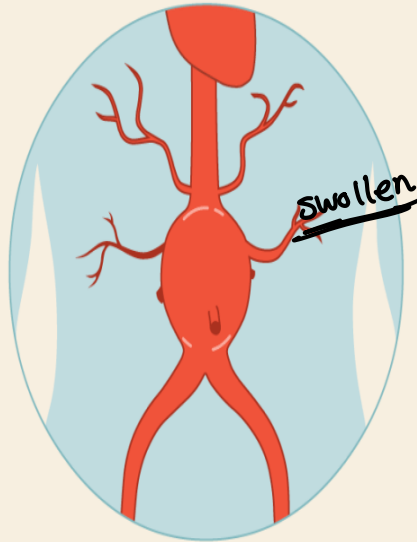
انقباض كل الكبيبات ←
وهي حالة severe

aneurysms (stasis)

Abdominal Aortic Aneurysm



Normal aorta

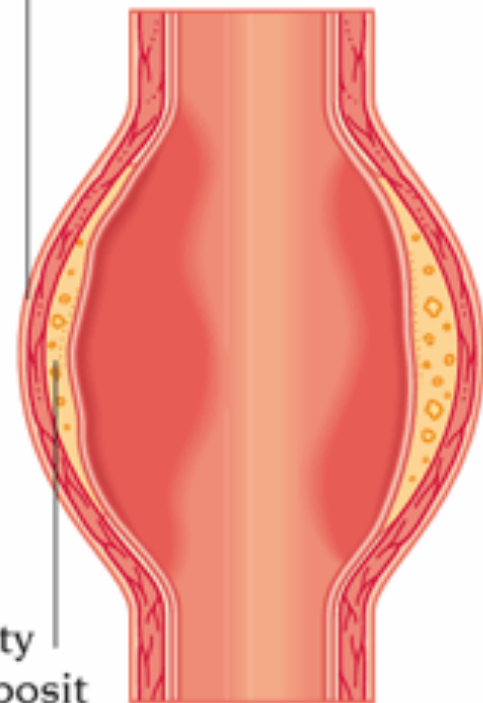


Aorta with large abdominal aneurysm

healthline

ANEURYSM

Weakened, bulging artery wall

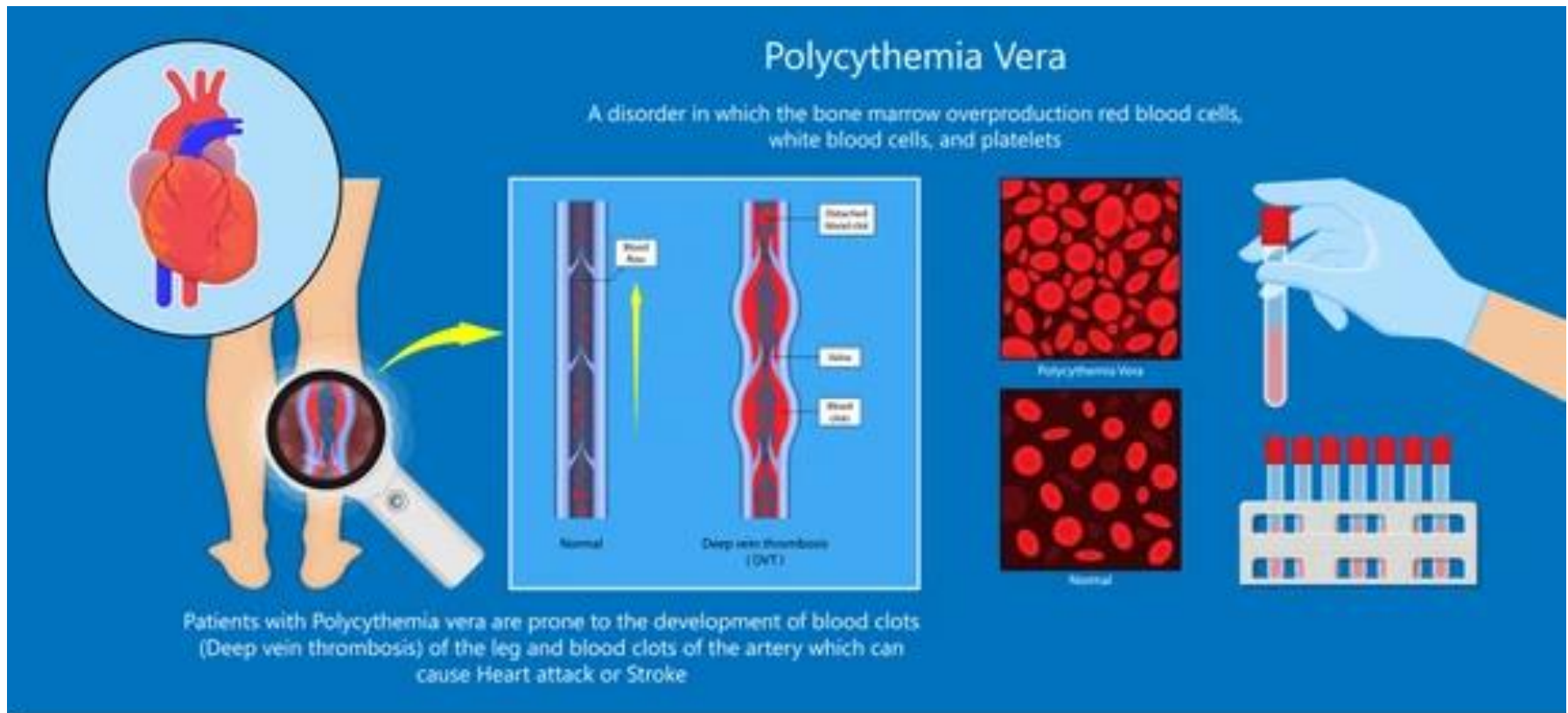


Fatty deposit

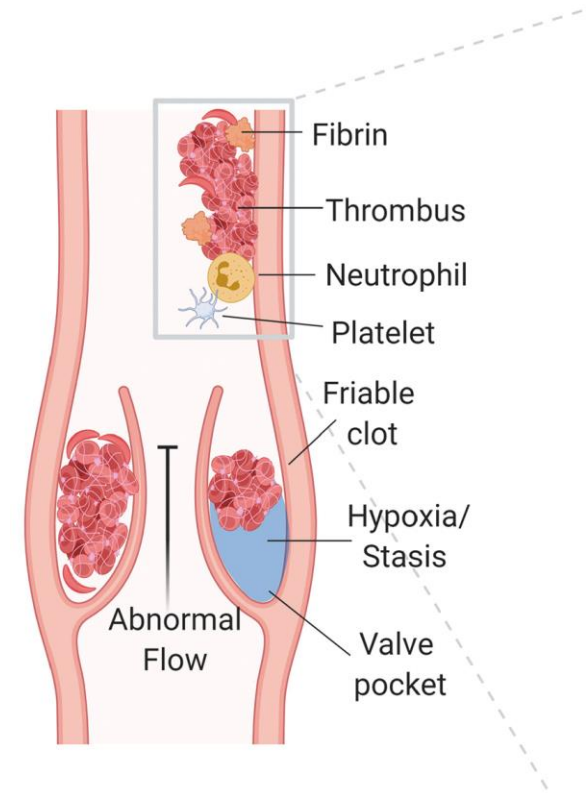
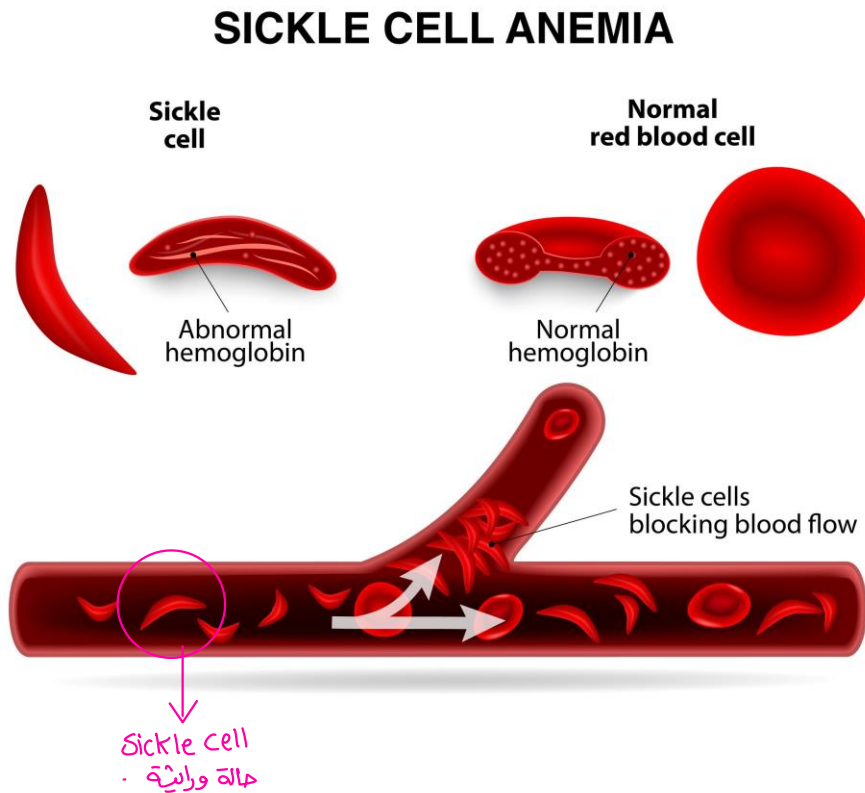


3-Hyperviscosity syndromes (such as **polycythemia**) increase resistance to flow and cause small vessel stasis

الدم مارج يعرف يتحرك



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



3- Hypercoagulability

Venous

- 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

Natural anti coagulation.

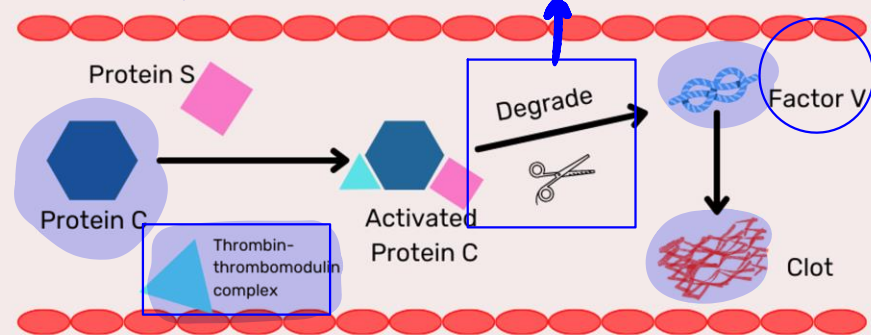
تغيير بـ Coagulation ← يقاوم AntiCoagulation



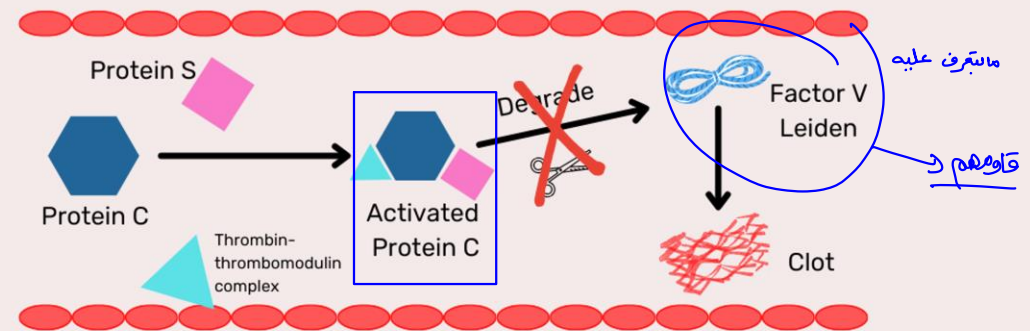
Factor v Leiden mutation

Pathophysiology of Factor V Leiden Gene Mutation

يقوموا Factor v دور من البقتر .



NORMAL PHYSIOLOGY



FACTOR V LEIDEN G1691A 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.

تتضمن لـ
thrombosis
أكثر من غيرها.

بعد العملية

2. Prolonged bed rest or immobilization

economy class Trip
العاسية تكون صنيقة وما يجرها.

3. Disseminated cancers, release of mucin in adenocarcinoma predisposes to thrombus formation (migratory thrombophlebitis or Trousseau's syndrome).

حالة سرطانات
الغدة بتفرز مادة

اسمها mucin
الهادور في تكوين
الجلطات

4. Advancing age: due to increased platelet aggregation and reduced release of PGI₂ from endothelium.



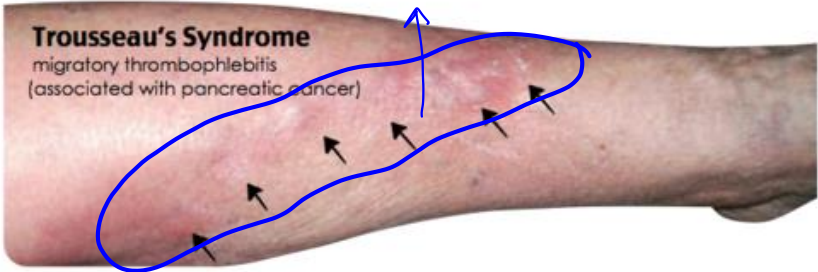
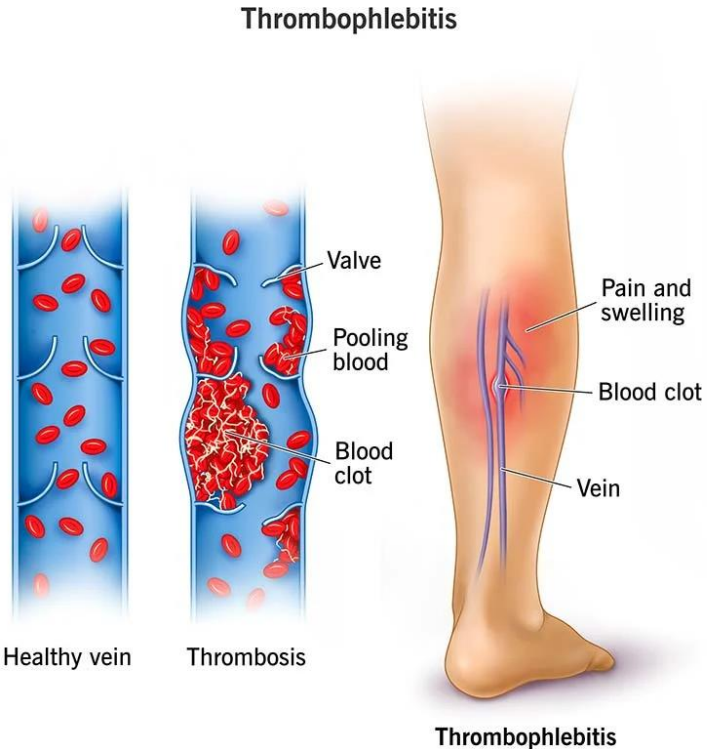
Migratory thrombophlebitis or

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**.

متعلق بسرطان غدة البنكرياس

مصاحبة حالات سرطان



Atery
end of the vessel

يمكن تكون ب vein أو

Thrombi ✖

- Thrombi can have grossly (and microscopically) apparent laminations called **lines of Zahn:**

ما يشوخصها
في
Venous
Thrombosis

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.**

قبل الوفاة

بعد الوفاة

فائرة (lines of Zahn)

يمكن التمييز بين تجلط الدم قبل الوفاة والتخثر اللطيف
جلطات غير مغلقة تتشكل في حالة ما بعد الوفاة

هذه عبارة عن thrombi بتصير في إحدى حجرات القلب ولها القدرة تنقل من مكان لآخر



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.

مهمّة هاي لصورة للعلة و لنظري

Lines of Zahn :- عبارة عن خطوط

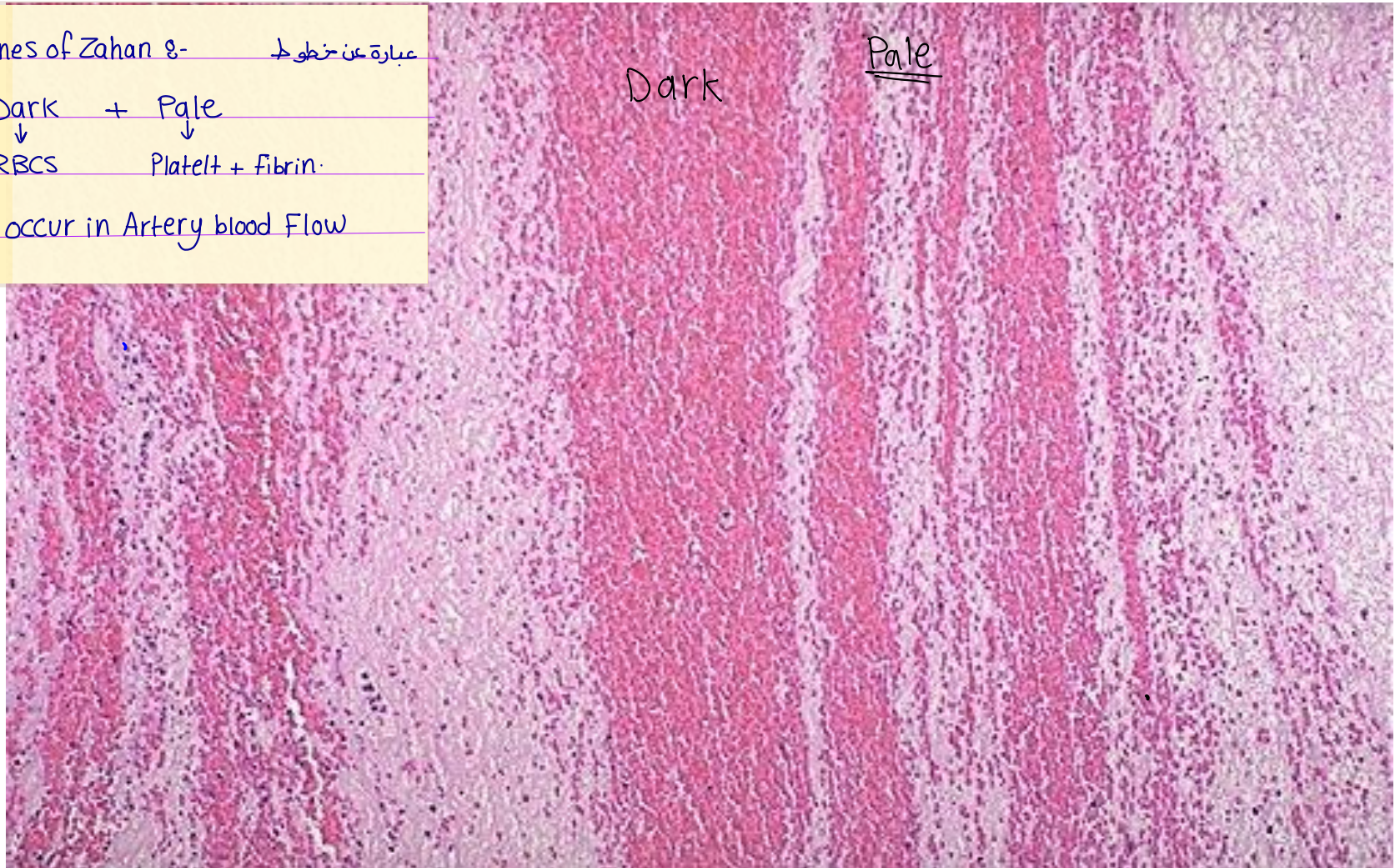
Dark + Pale

↓ ↓
RBCs Platelet + fibrin

occur in Artery blood Flow

Dark

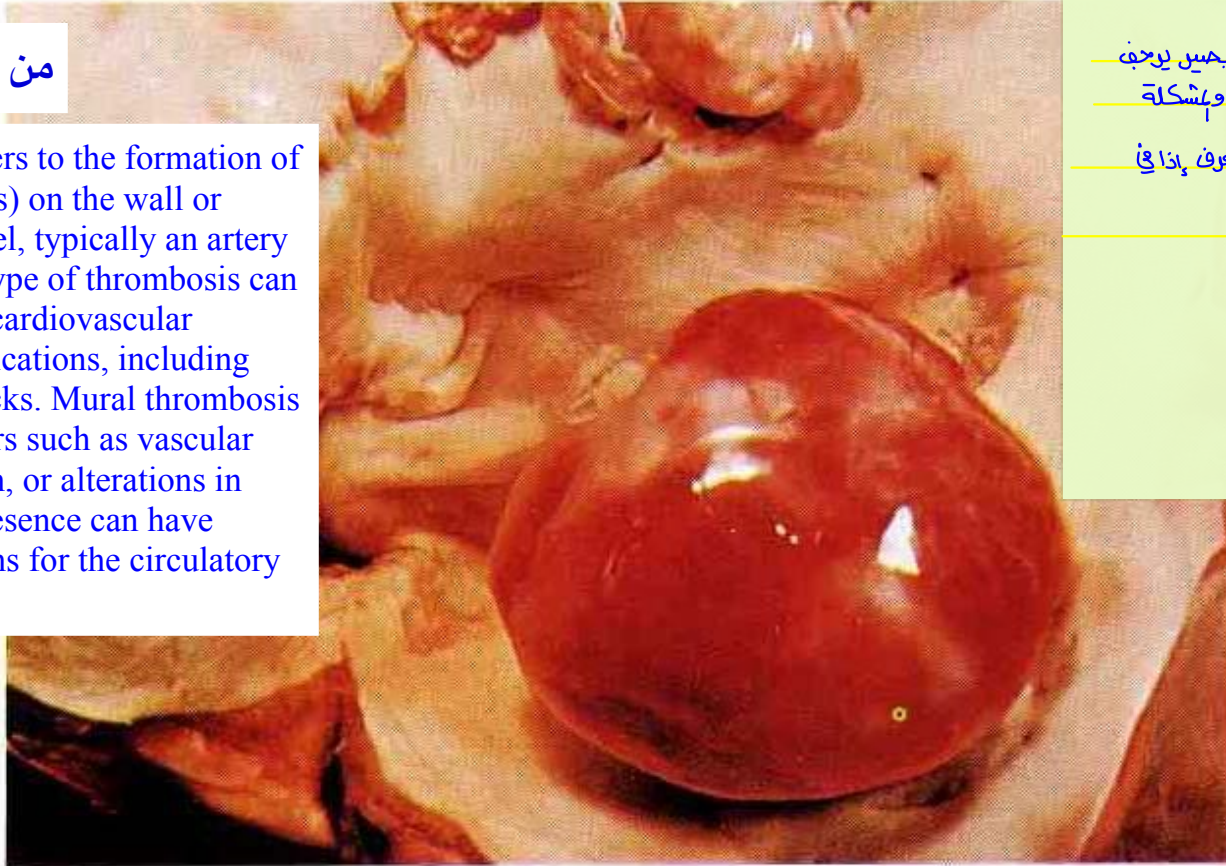
Pale



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.

📌 chat gpt من

Mural thrombosis refers to the formation of a blood clot (thrombus) on the wall or lining of a blood vessel, typically an artery or a large vein. This type of thrombosis can contribute to various cardiovascular conditions and complications, including strokes and heart attacks. Mural thrombosis may result from factors such as vascular damage, inflammation, or alterations in blood flow, and its presence can have significant implications for the circulatory system.



بجس عندي مشكلة في القلب وبعيس يرجف
دون Contract ويؤدي إلى ركود وبمشكلة
لازم نعمل فحص (ECo) حتى تعرف إذا في
عنا (thrombosis) أو لا

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.

التخثر الوريدي

متشابكة



Arterial thrombi

Venous thrombi

Etiology

Endothelial damage
or turbulence

Stasis and hyperco-
agulable states



Lines of Zahn

Prominent

Less prominent

RBCs اور جمل

Color

Gray

Red

Occlusive

Yes

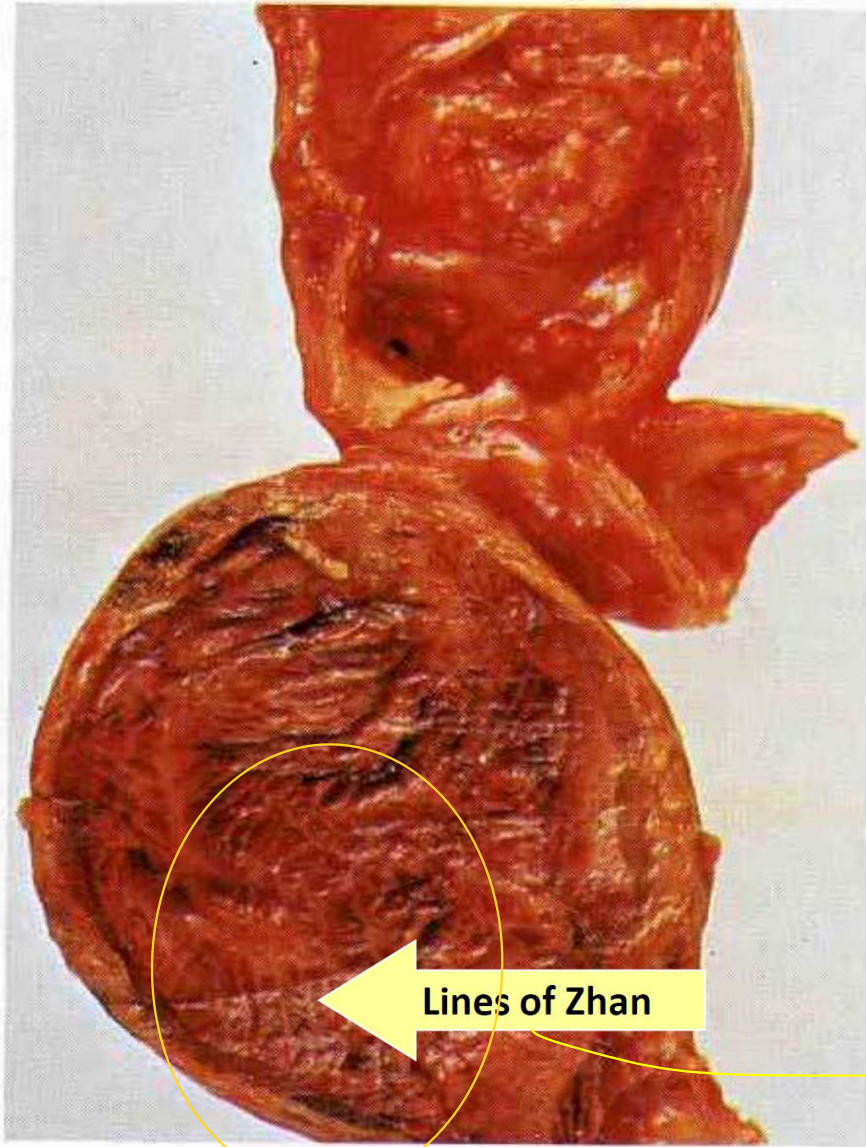
Yes

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.

هون في خنوط



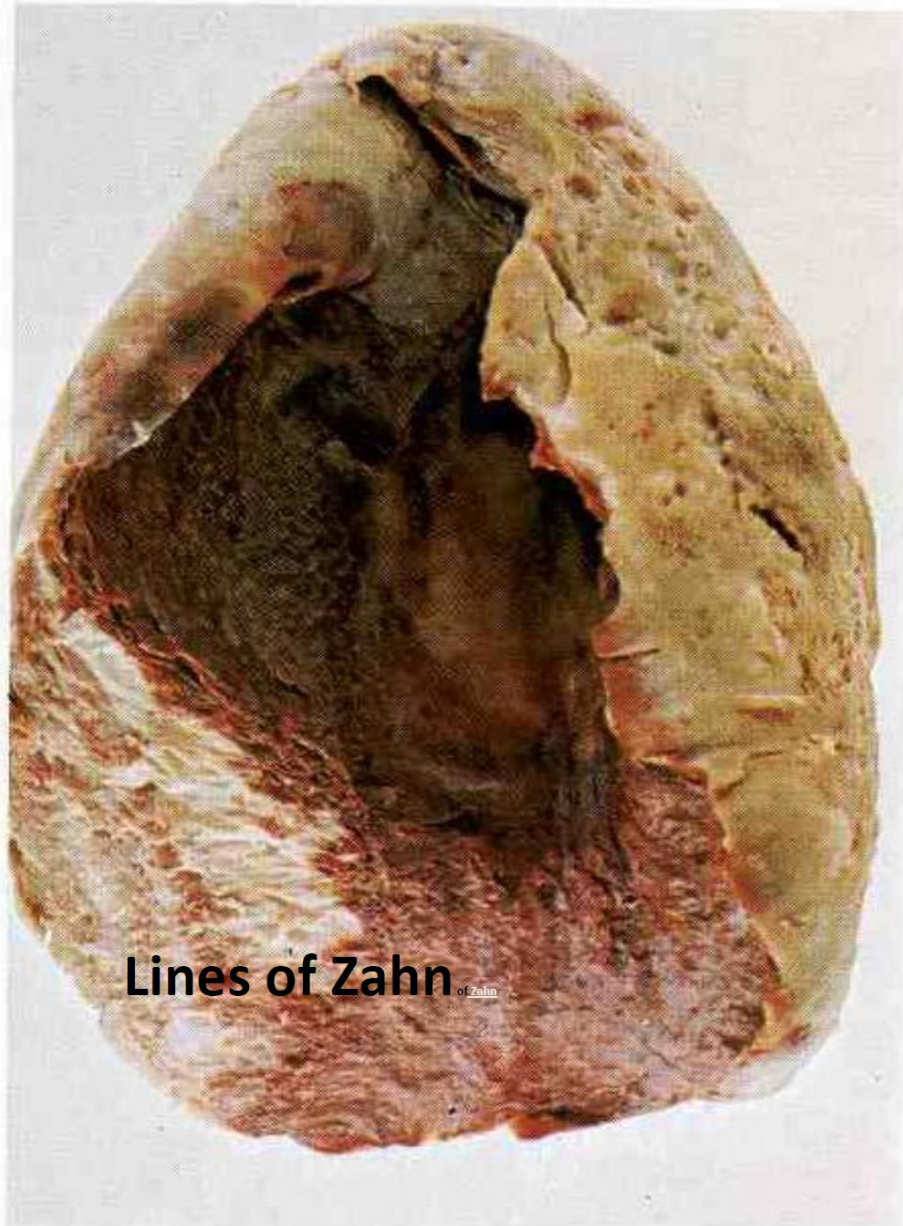
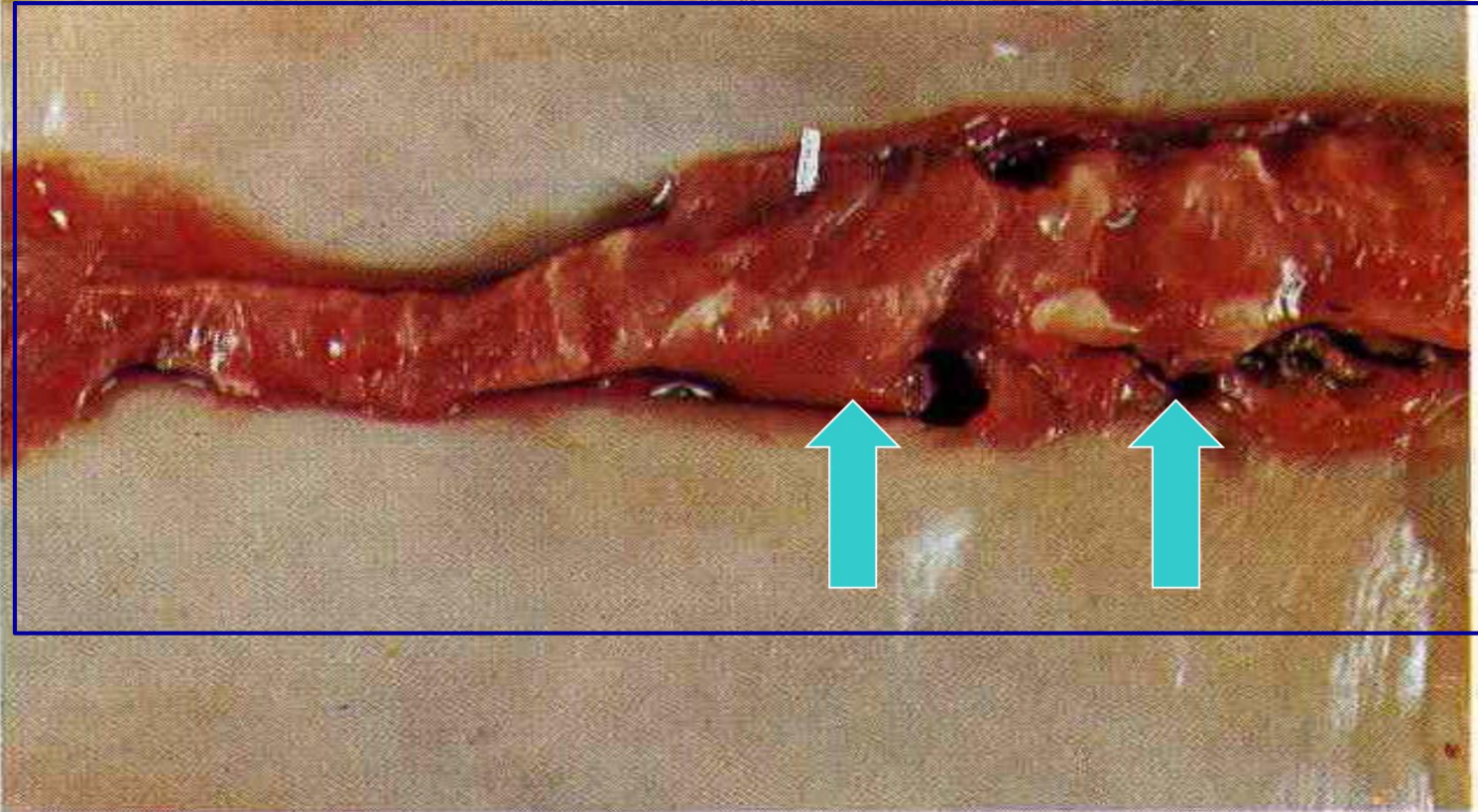


Fig. 38 : Large thrombus, (measuring **20X12X12** cm) removed from an atheromatous abdominal aortic aneurysm (AAA). The laminated structure (lines of Zahn) of the thrombus is clearly evident (lower left).



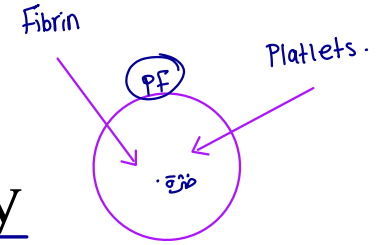
F 39 : Venous Thrombosis. The inferior vena cava contains a long pale tapering thrombus .Thrombus is mural & firmly attached to the vein wall.



6.30 Thrombosis: inferior vena cava



Fate of the Thrombus



تكاثر

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.

من إقلبه للدمج

بعكس لإيانه

2. **Embolization:** Fragment of thrombus is transported elsewhere in the vasculature.

تنتقل إمكان إين

3. **Dissolution:** In newly formed thrombus, activation of fibrinolysis may lead to its rapid shrinkage and complete dissolution.

تذوب

Plasmongen → Plasmin

تذوب خثرة

Murai

بس يروح على لإطراف
بجمل غوغريتا

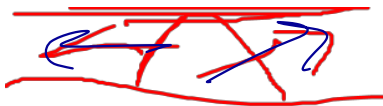


Outcomes of thrombosis (Fates):

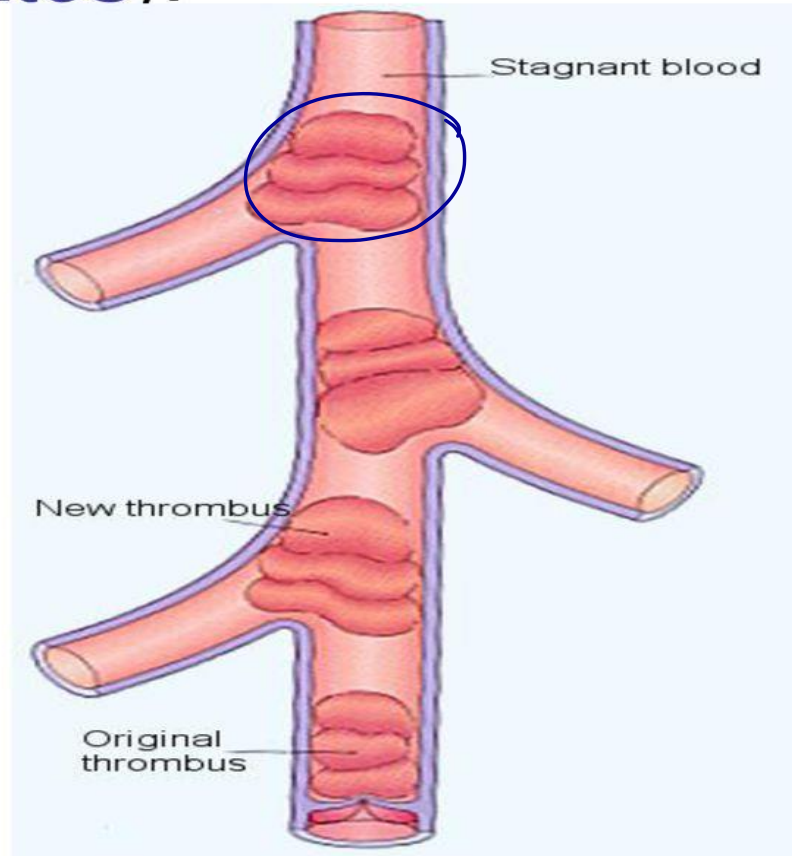
▪ Propagation

– progressive spread of thrombosis

Retro ← distally in arteries
Antero ← proximally in veins



↓
حول كتلة الدم بعين clot



Fate of the Thrombus

وبعدها يفتحوا قنوات فيها
سيعمل جزء ملان بالفايبرين ويتصل ثابتة / ويعبر من منها الدم

4. Organisation and recanalization:

- Older thrombi become organized by the ingrowth of endothelial cells, smooth muscle cells, and fibroblasts into the fibrin-rich thrombus

خلق لسعيرات في مكان الخثرة / ذي كانه تبكيف مع الوضع

- In time, capillary channels are formed and create conduits along the length of the thrombus, thereby reestablishing the continuity of the original lumen.

وسم للكتيريا

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.

النتيجة

- مع مرور الوقت، تتشكل القنوات الشعرية وتكون قنوات على طول الخثرة، وبالتالي إعادة استمرارية التجويف الأصلي.

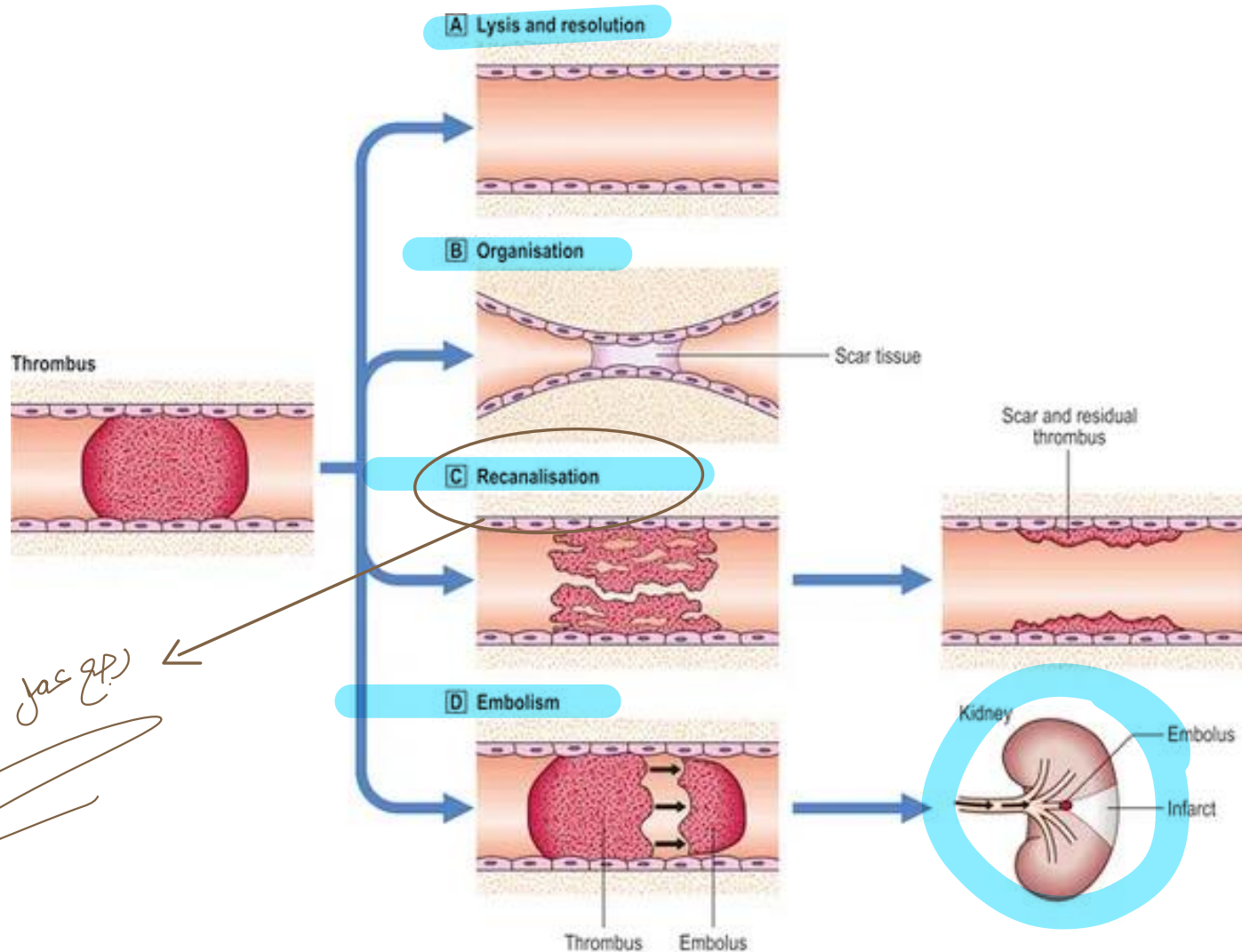
5. البذر البكتيري للخثرة: يعمل بمثابة وسط زرع، وقد تؤدي العدوى

النتيجة إلى إضعاف جدار الوعاء الدموي، مما يؤدي إلى تكوين تمدد

الأوعية الدموية الفطري



Fate of the Thrombus



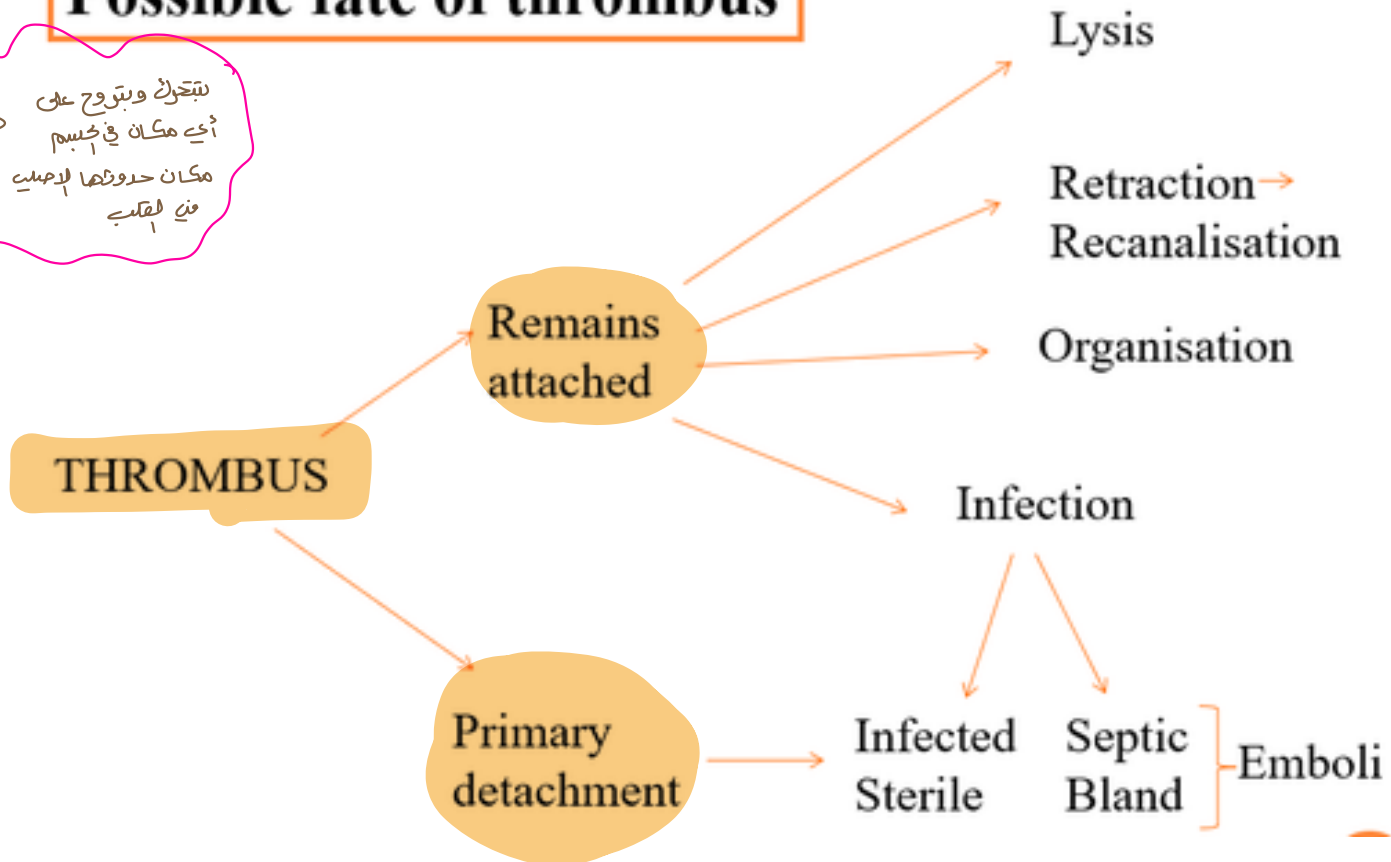
ثرومبوس (جاس) قوہ اولیٰ



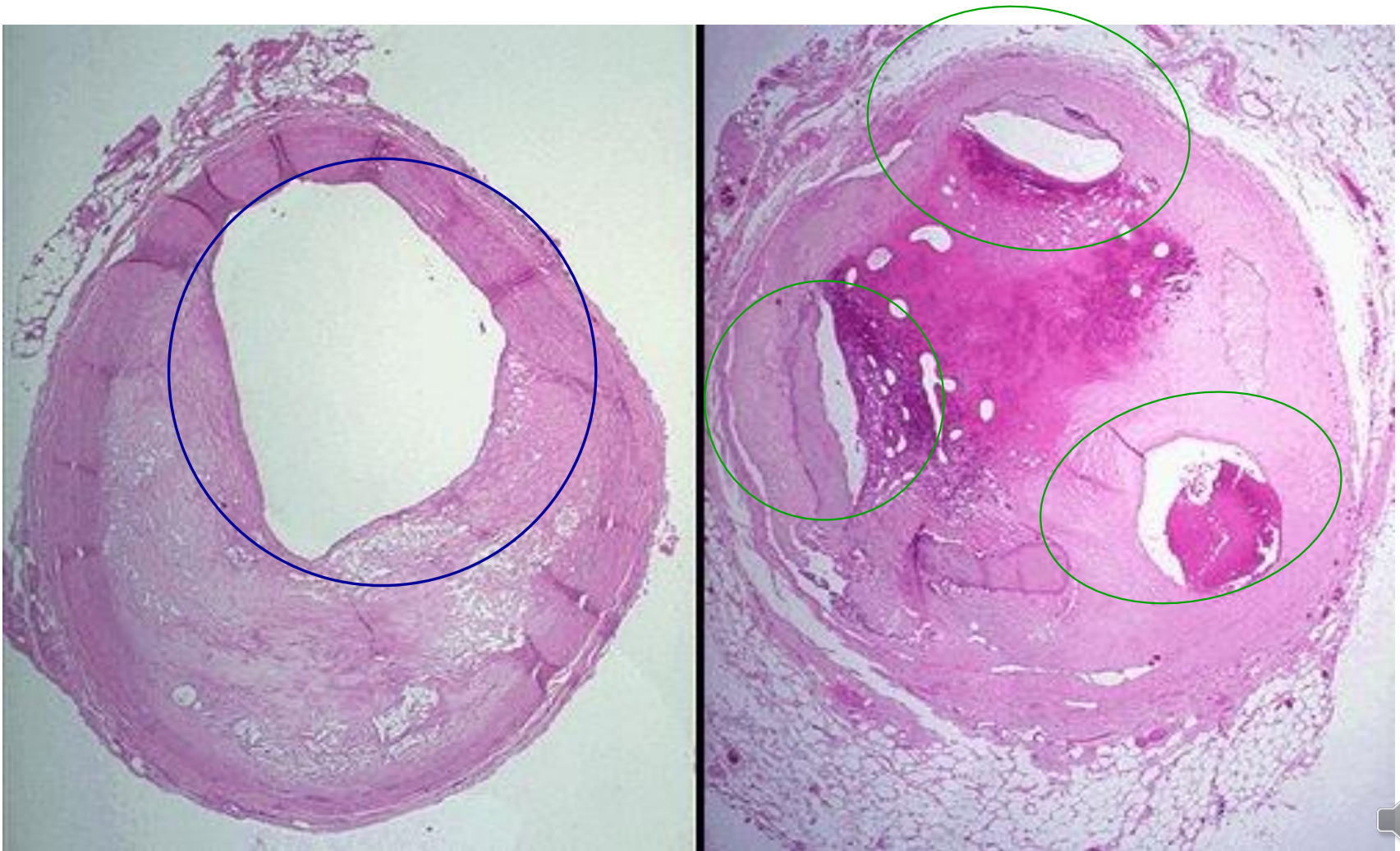
Fate of the Thrombus

Possible fate of thrombus

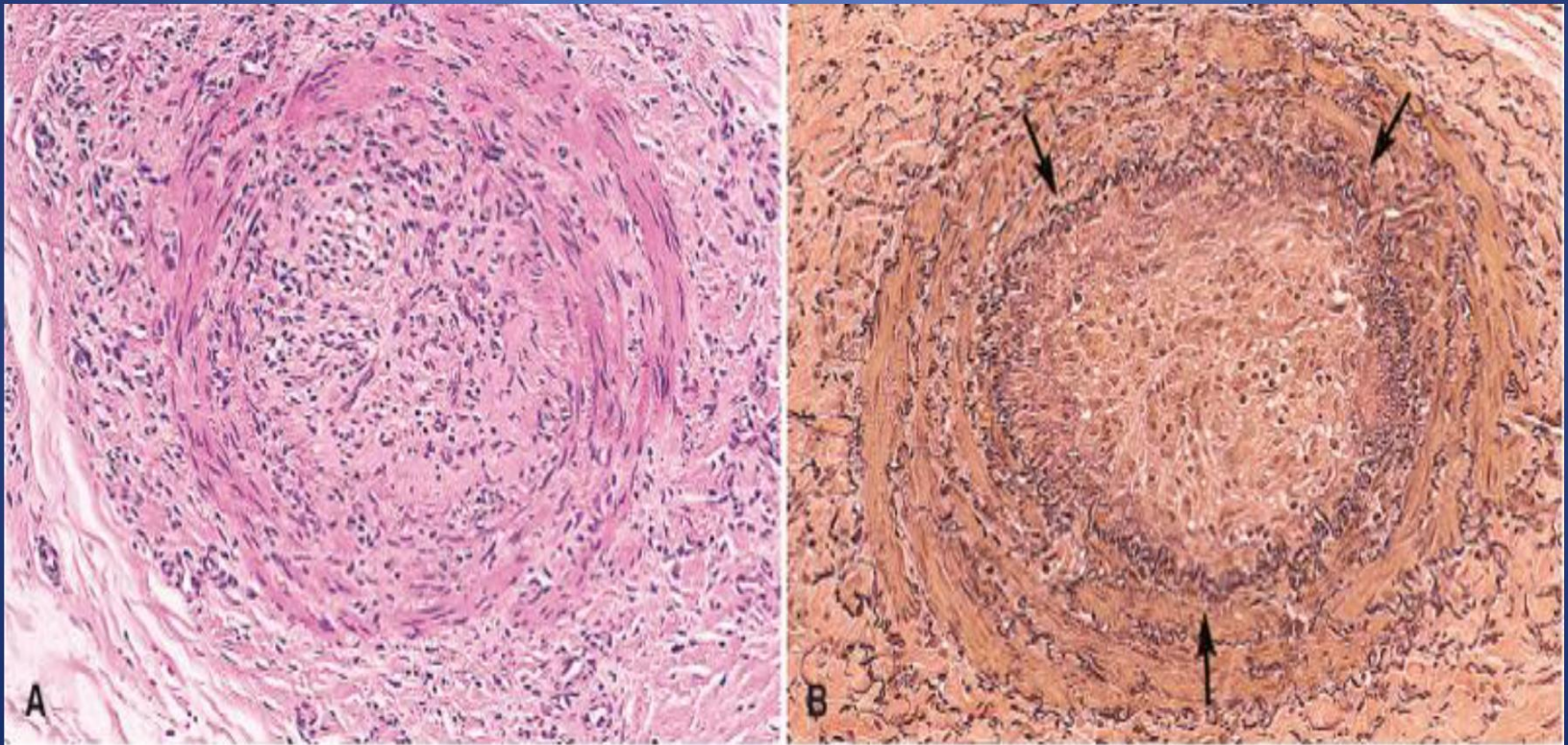
Mural thrombosis → يتكون ويترواح على
أى مكان في جدار
مجان حدودها لإصلية
فوق القلب



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 .



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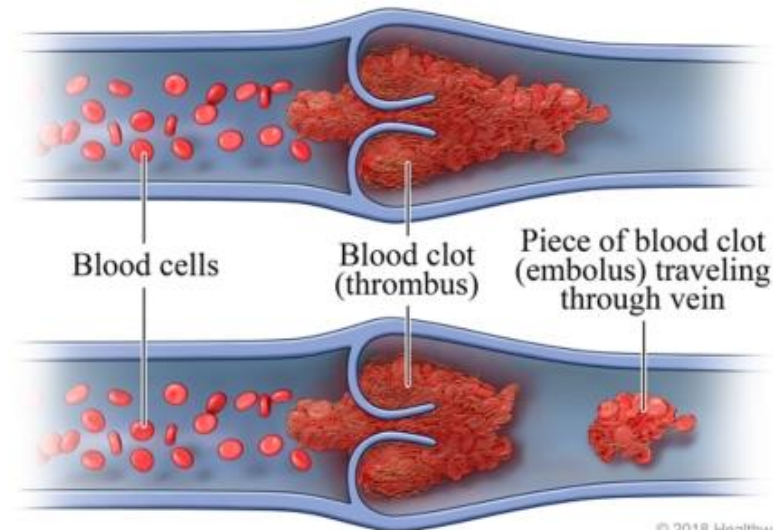
Complications of Thrombi

- Occlusion (Obstruction) of blood vessels

Veins: Congestion and edema distal to obstruction

Arteries: Ischemia and infarcts in areas supplies by the vessel.

Embolization



هو بالاصل ما يغذي
هو يعمل تصريف
فالنتيجة وذمة
هاد بزود جسم في
الغذاء / النتيجة
infraction
بصير تتحرك
في جسم
مثل Mural

(Femoral vein) → Thrombosis
Main vein
لا يصير فيه Thrombosis
الرجل كلها يصير لونها
أبيض سموها
(Milk leg)
بسبب الوذمة

Venous Thrombosis (Phlebothrombosis)

في منطقة -
Below knee / Deep thrombosis
هنا يتخوف وخطرة ما يتحرك .

حكيما أنها بتصاب
الاطراف

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

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

← موهن لدوائه / الجمل واقفة / عامل وراثي / الحمل .
طبيعة العمل
تكون نمكان معين

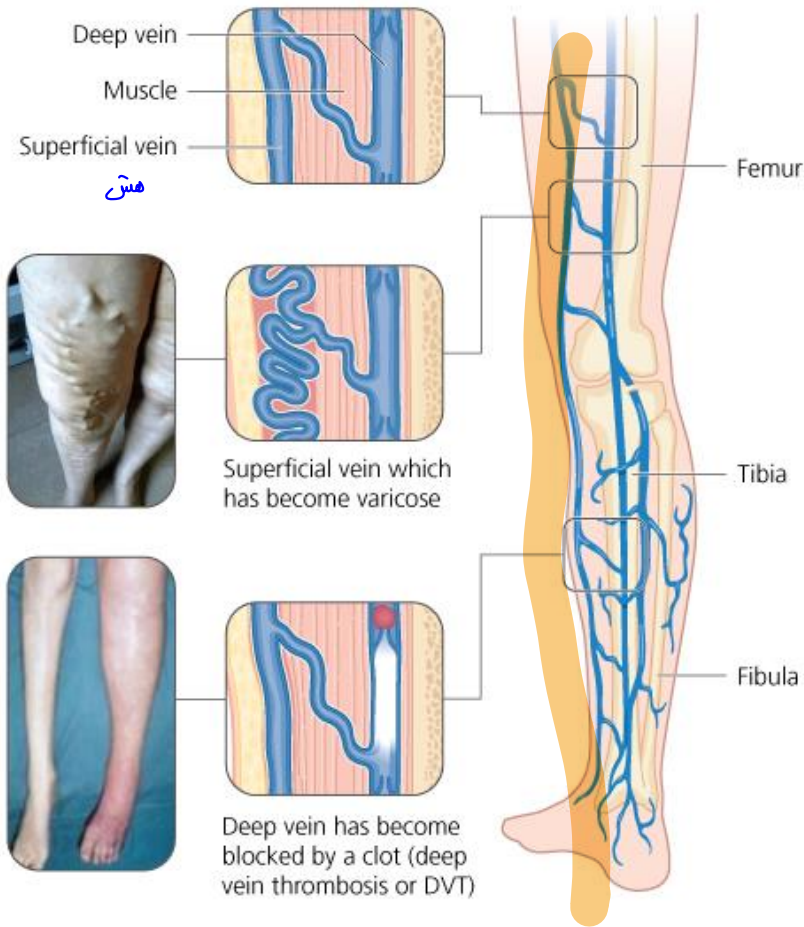
Manifestations: **local congestion, swelling (edema), pain, tenderness, infections of overlying skin and development of varicose ulcers.** Rarely embolize

نادر ما تنتقل من مكان لآخر

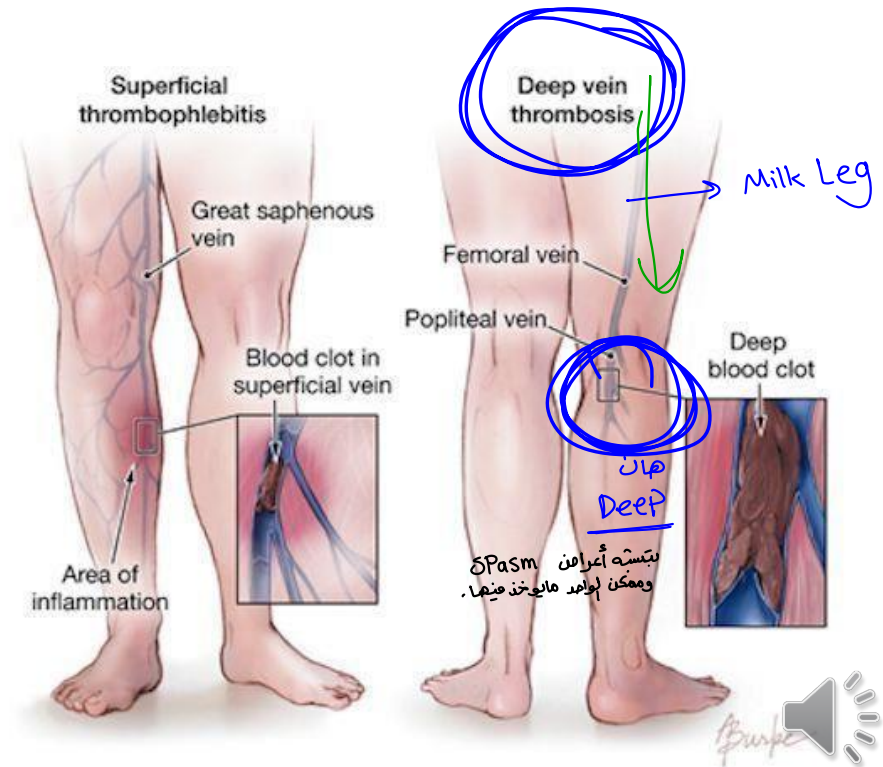
هنا حالة خطيرة

- **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





Venous Thrombosis (Phlebothrombosis)

thrombosis of Placenta cause abortion.

لروح بلاغتي مسار بديل وهذا المسار
بجانبه ما يعرف بالعمامة اي يكون
صافية Deep / وماح تفحص
بالاطا تفحص بغيره للرثة -

- 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.

