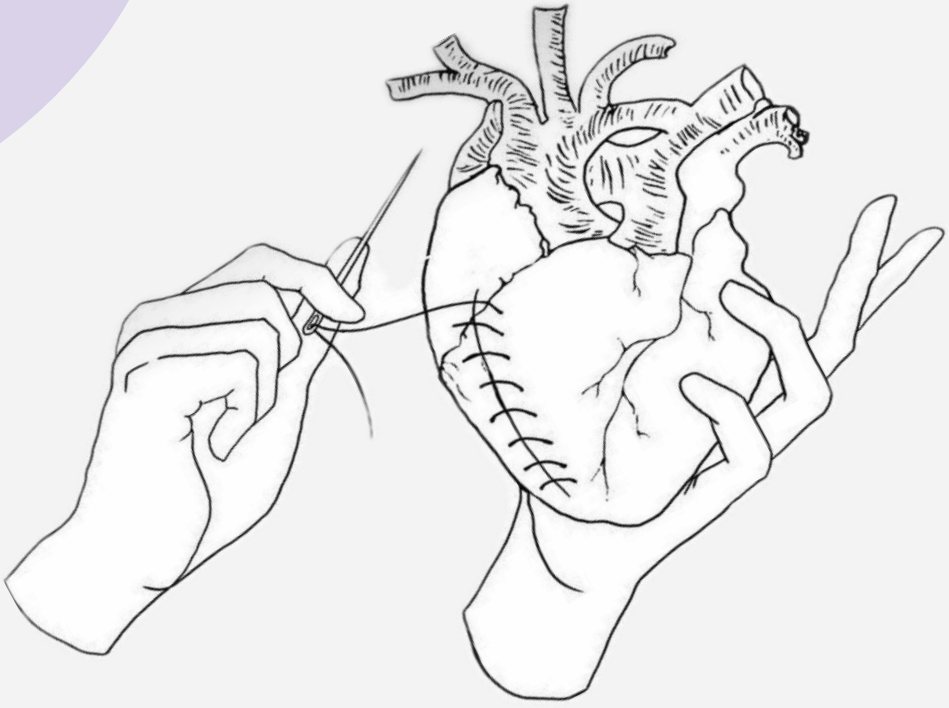
Thromboembolism



Editing file:

COLOR INDEX:

MAIN TEXT (BLACK)

FEMALE SLIDES (PINK)

MALE SLIDES (BLUE)

IMPORTANT (RED)

DR'S NOTE (GREEN)

EXTRA INFO (GREY)

Objective

Understand the basic pathology of thrombogenesis and the risk factors for development of deep vein thrombosis. Know the types of embolus than can occur and the pathology of pulmonary embolism.

Key principles to be discussed:

Pathological aspects of thrombogenesis: vessel wall abnormality, vascular stasis or turbulent flow and increased blood coagulability.

Causes of thrombus and embolism formation.

Predisposing factors for deep vein thrombosis.

Pathology of pulmonary thrombo-embolism.

Brief description of other forms of emboli like: fat embolism, air embolism, atherosclerotic plaque embolism, amniotic fluid embolism, nitrogen embolism and infective endocarditis.

Lecture outlines :

1. Understand the basic pathology of thrombogenesis. Pathological aspects of thrombogenesis: vessel wall abnormality, vascular stasis or turbulent flow and increased blood coagulability.
2. Predisposing risk factors for development of deep vein thrombosis.
3. Pathology of pulmonary thrombo-embolism.
4. Embolism. Know the types of embolus than can occur and the pathology of pulmonary embolism.
5. Brief description of other forms of emboli like: fat embolism, air embolism, atherosclerotic plaque embolism, amniotic fluid embolism.

If you want to read the lecture from Robbins click here

اللهمّ انفعنا بما علّمتنا، وعلّمنا ما ينفعنا، وزدنا علمًا وبارك لنا فيه

Hemostasis

Normal Hemostasis

- A consequence of tightly regulated process:
  - Maintain blood in a fluid, clot-free state in normal vessels.
  - Inducing the rapid formation of a localized hemostatic plug at the site of vascular injury.
- Hemostasis and Thrombosis:
  - Both hemostasis and thrombosis involve three structural and molecular components:
    - The vascular wall.
    - Platelets.
    - The coagulation cascade.

The Vascular wall

- Intact endothelial cells maintain liquid blood flow by actively:
  - Inhibiting platelet adherence.
  - Preventing coagulation factor activation.
  - Lysing blood clots that may form.
- Endothelial cell stimulation results in expression of procoagulant proteins (e.g., tissue factor vWF) that contribute to local thrombus formation.
- Loss of endothelial integrity expose underlying vWF and basement membrane collagen, both substrate for platelet aggregation and thrombus formation.
- Dysfunctional endothelial cells can produce more procoagulant factors (e.g. platelet adhesion molecules, tissue factor) or may synthesize less anticoagulant effectors (e.g., thrombomodulin, PGI2, t-PA).

Hemostasis

The Vascular wall

- Endothelial dysfunction can be induced by a wide variety of insults, for example:
  - Hypertension
  - turbulent blood flow
  - bacterial endotoxins
  - radiation injury
  - metabolic abnormalities such as homocysteinemia or hypercholesterolemia, and toxins absorbed from cigarette smoke.

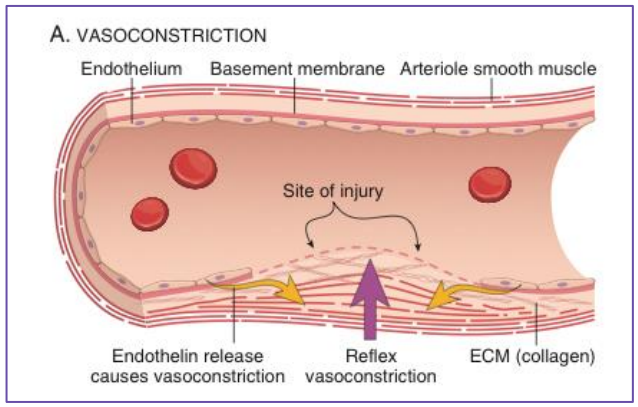
Coagulation Factors

- Coagulation occurs via the sequential enzymatic conversion of cascade of circulating and locally synthesized proteins.
- Tissue factor elaborated at sites of injury is the most important initiator of coagulation cascade.
- At the final stage of coagulation, thrombin converts fibrinogen into insoluble fibrin, which helps to form the definitive hemostatic plug.
- Coagulation is normally constrained to sites of vascular injury by:
  - Limiting enzymatic activation to phospholipid complexes provided by activated platelets.
  - Natural anticoagulants elaborated at the sites of endothelial injury or during activation of the coagulation cascade.
  - Inducing of fibrinolytic pathways involving plasmin through the activities of various PAs.

Hemostasis

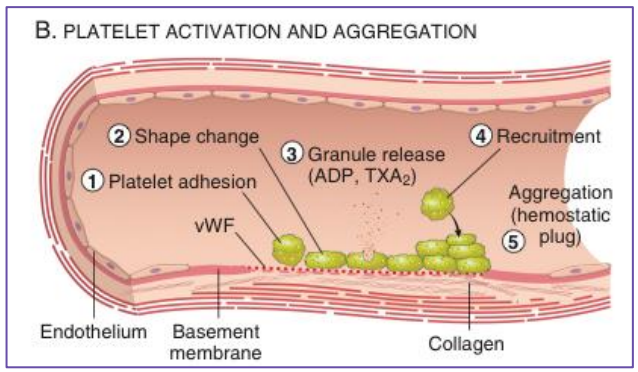
1

After vascular injury, local neurohumoral factors induce a transient vasoconstriction



2

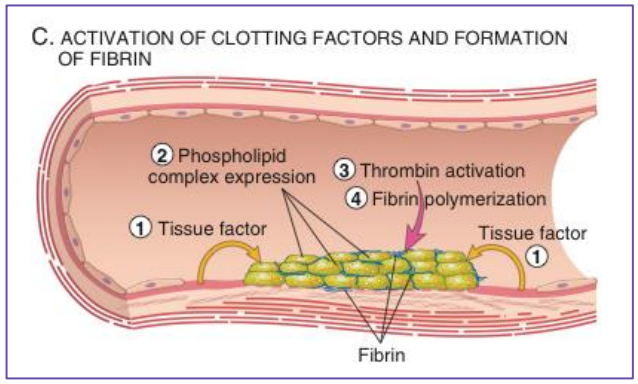
Platelets adhere (via GpIb receptors) to exposed extracellular matrix (ECM) by binding to von Willebrand factor (vWF) and are activated, undergoing a shape change and granule release. Released adenosine diphosphate (ADP) and thromboxane A2 (TXA2) lead to further platelet aggregation (via binding of fibrinogen to platelet GpIIb-IIIa receptors), to form the primary hemostatic plug.



Hemostasis

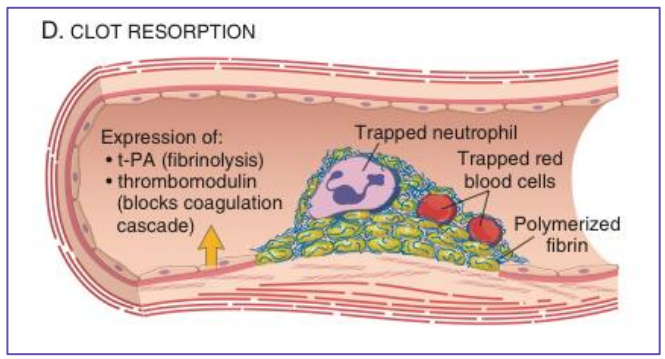
3

Local activation of the coagulation cascade (involving tissue factor and platelet phospholipids) results in fibrin polymerization, “cementing" the platelets into a definitive secondary hemostatic plug

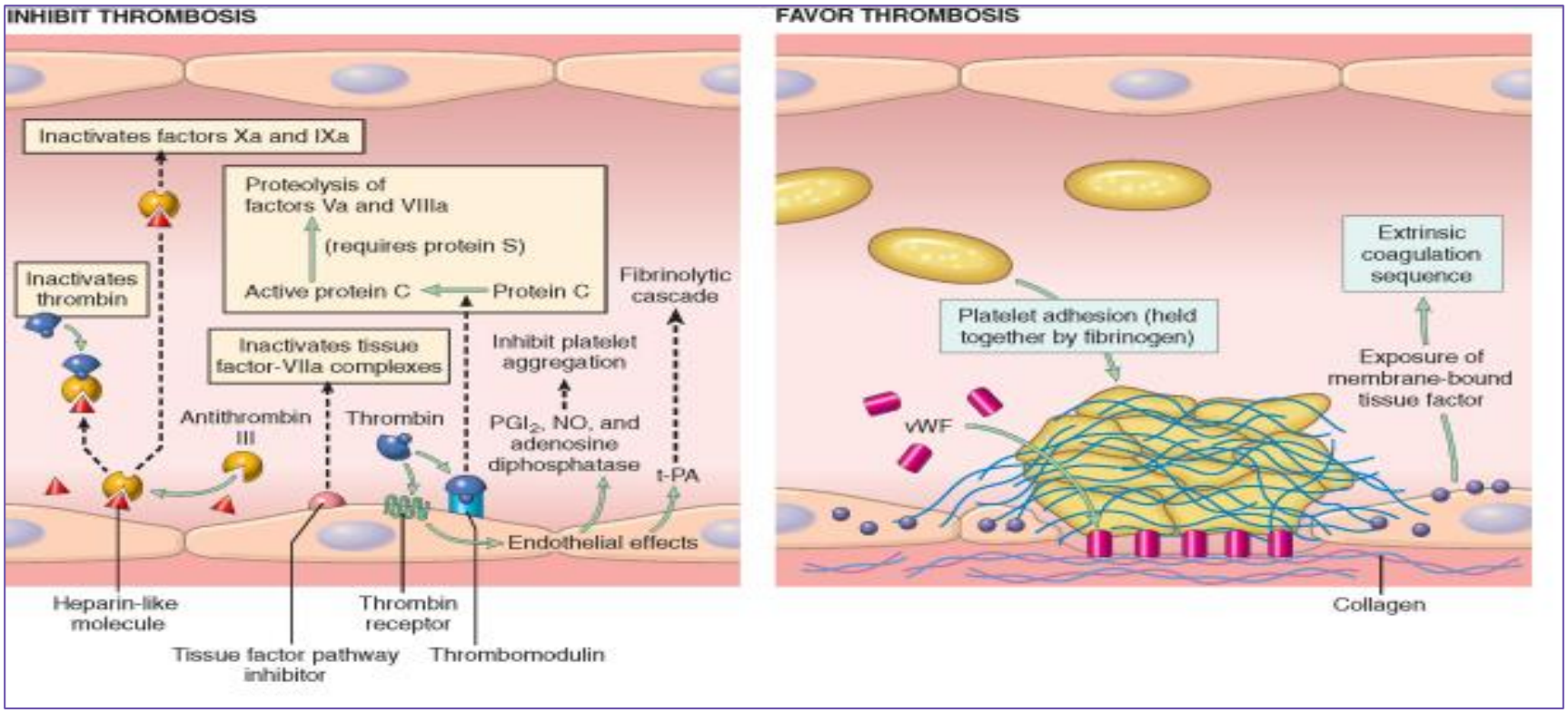


4

Counter-regulatory mechanisms, such as release of t-PA (tissue plasminogen activator, a fibrinolytic product) and thrombomodulin (interfering with the coagulation cascade), limit hemostatic process to the site of injury

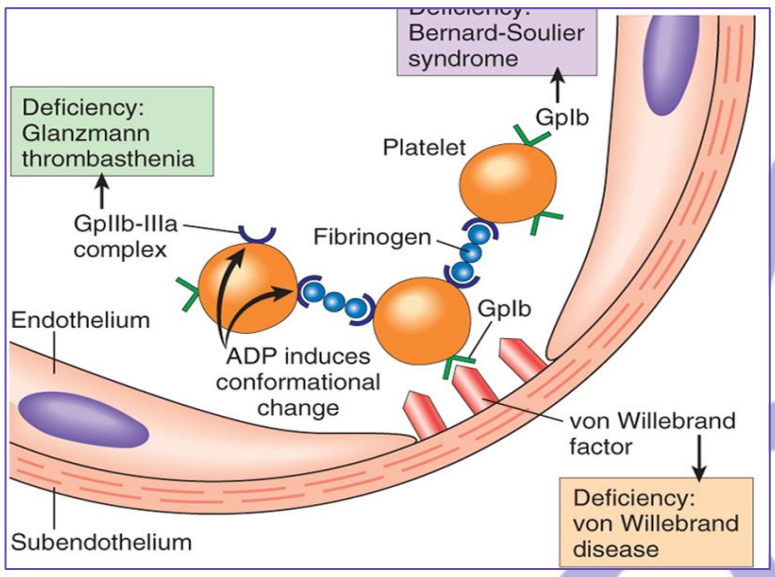


Hemostasis

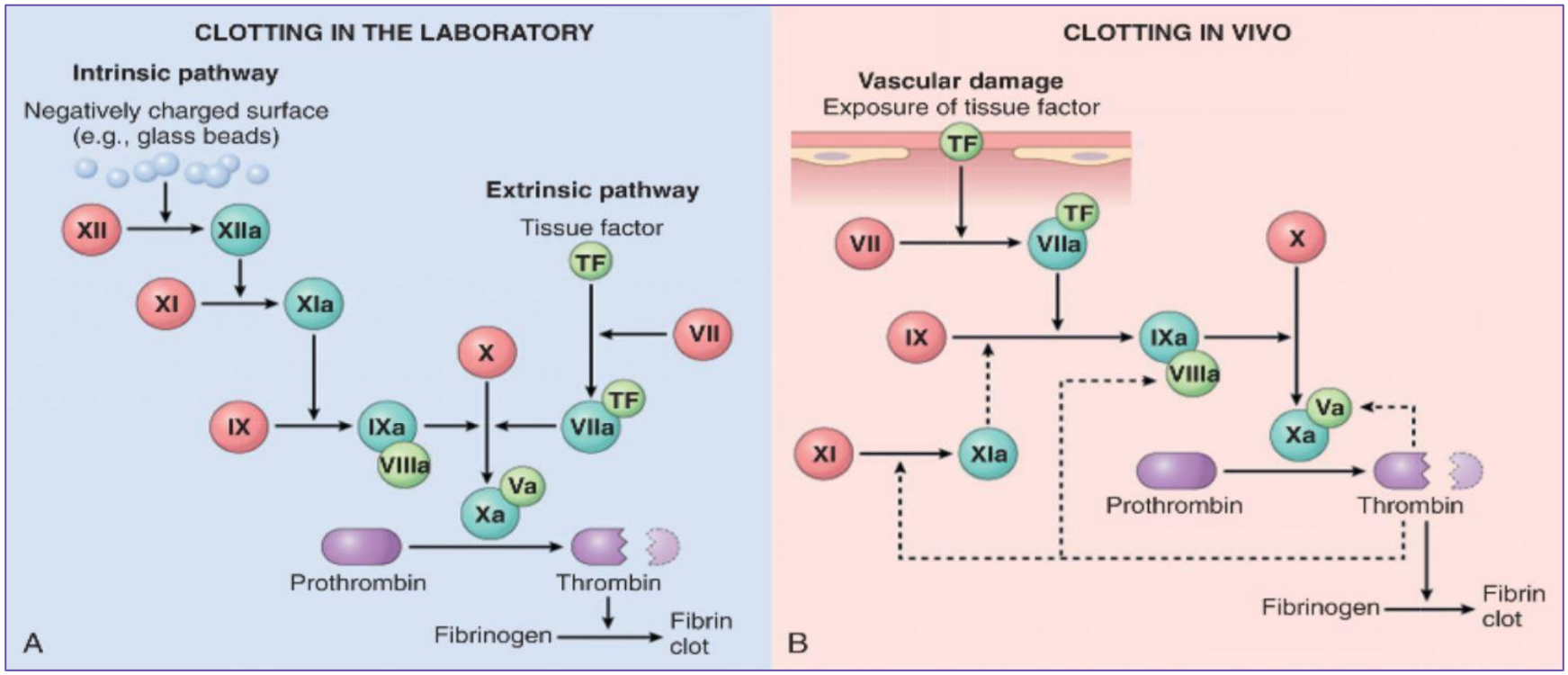


Additional reading:
Anti- and procoagulant activities of endothelium. NO, nitric oxide; PGI2, prostacyclin; t-PA, tissue plasminogen activator; vWF, von Willebrand factor. The thrombin receptor is also called a protease-activated receptor (PAR).

Platelet adhesion and aggregation:
Von Willebrand factor functions as an adhesion bridge between subendothelial collagen and the glycoprotein Ib (GpIb) platelet receptor. Aggregation is accomplished by binding of fibrinogen to platelet GpIIb-IIIa receptors and bridging many platelets together. ADP, adenosine diphosphate.



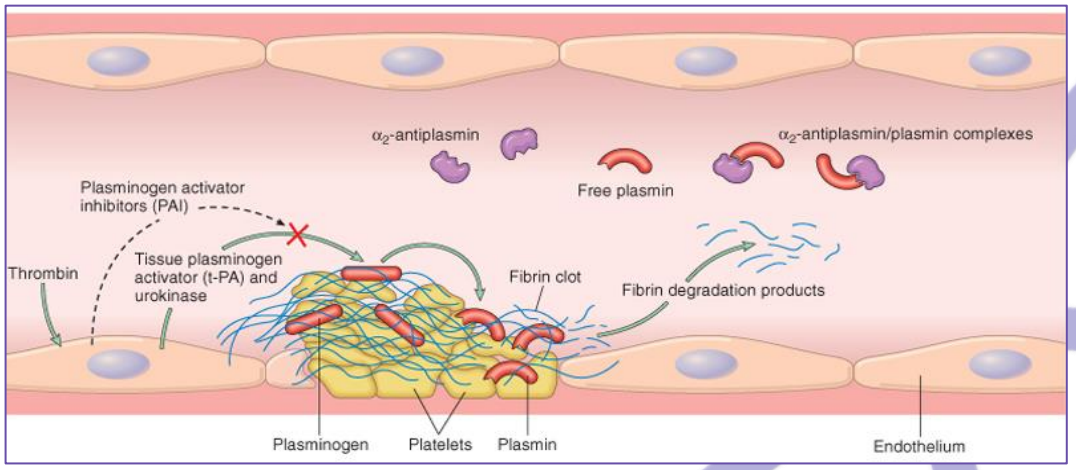
Hemostasis



The details of the diagram are additional reading

- The classical coagulation cascade. Note the common link between the intrinsic and extrinsic pathways at the level of factor IX activation. Factors in red boxes represent inactive molecules; activated factors are indicated with a lower-case a and a green box. HMWK, high-molecular-weight kininogen
- This reaction requires vitamin K as a cofactor

The fibrinolytic system, illustrating various plasminogen activators and inhibitors, major players include t-PA



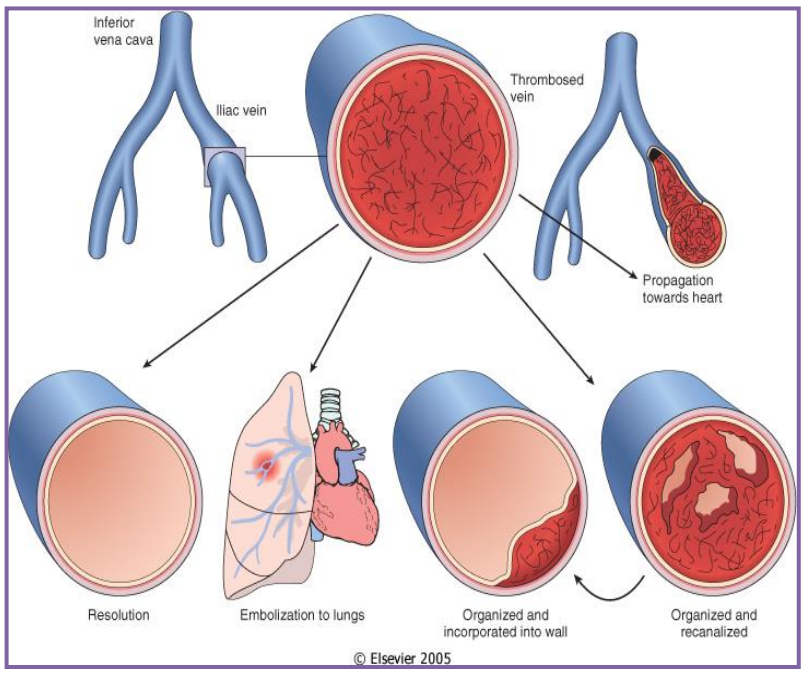
Hemostasis

Thrombus formation

- Platelet plug + Fibrin mesh
- RBCs & other cells entrapped

Thrombus Fate:

- Grow in layers (PROPAGATION)
- Be removed by fibrinolysis (resolution)
- Be organized and recanalized
- Embolize



Thrombosis

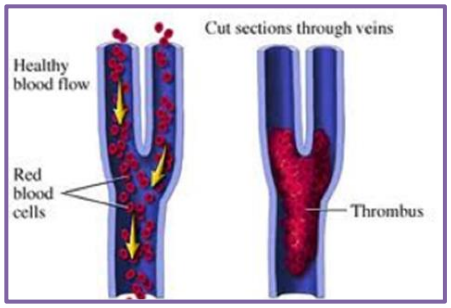
click here

Pathoma

Chapter 4 - hemostasis and related disorders
4.4- Thrombosis

Definition

- It is a process by which a thrombus is formed. It represents hemostasis in the intact vascular system.
- It is intravascular coagulation of blood and it often causes significant interruption to blood flow.
- The pathologic form of hemostasis
- Involves blood clot (thrombus) formation in uninjured vessels (or after relatively minor injury)
- Thrombosis can only occur during life
- Clotting can also occur after death or in a test tube



Thrombus

- A thrombus is a solid mass (blood clot) made up of blood constituents which develops in artery or vein. Causes obstruction of the blood flow to the organ , and that organ will undergo ischemia and necrosis.

Pathogenesis

Three primary influences called as Virchow triad predispose to thrombus formation:

- Endothelial injury
- Stasis or turbulence of blood flow
- Hypercoagulability

*It results from interaction of platelets, damaged endothelial cells and the coagulation cascade. All 3 are component of the hemostatic process.

Components of the hemostatic process

Endothelial cells	Platelets	Coagulation cascade
Integrity of endothelium is the most important factor. Endothelial cells are resistant to the thrombogenic influence of platelets and coagulation proteins. Intact endothelial cells are thromboresistant.	Maintain the integrity of the vascular endothelium and participate in endothelial repair through *PDGT. They form platelet plugs and promote the coagulation cascade through the platelet phospholipid complex (that provide an important surface for coagulation-protein activation)	Is a major contributor to thrombosis. It is a series of enzymatic conversions, that end in the formation of thrombin. Thrombin then converts the soluble plasma protein fibrinogen into the insoluble protein fibrin. And fibrin is a constituent of the thrombus.

Fibrinolysis (thrombus dissolution)

Definition

Activation of the clotting cascade induces coagulation. It also triggers the fibrinolytic cascade that limits the size of the final clot. It runs concurrently with thrombogenesis.

Function

Fibrinolytic cascade helps dissolve the thrombus and therefore restores blood flow in vessels occluded by the thrombus.

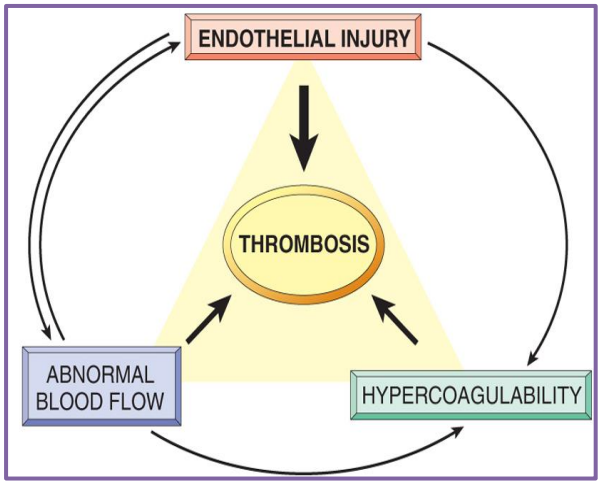
In the fibrinolytic cascade:

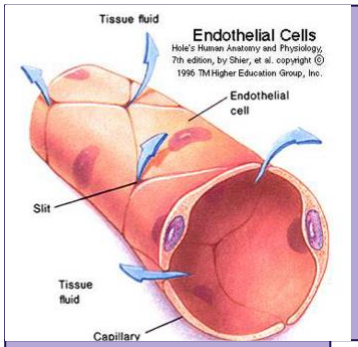
- The inactive proenzyme plasminogen is converted to active plasmin.
- Plasmin then splits the fibrin in the thrombus.
- The thrombus is dissolved by plasmin.

This is the thing that we used in patients with heart attacks who have a blood clot in their blood vessels , you try to give him fibironlytic drugs.

Virchow’s triad

Virchow's triad in thrombosis: Integrity of endothelium is the most important factor. Injury to endothelial cells can also alter local blood flow and affect coagulability.Abnormal blood flow (stasis or turbulence), in turn, can cause endothelial injury.The factors may act independently or may combine to promote thrombus formation





Endothelial cells

Definition	The endothelium is a single thick cell with the inner lining of the entire cardiovascular system (arteries, veins, and capillaries) and the lymphatic system.
Location	It is in direct contact with the blood/lymph and the cells circulating in it.
Importance	Endothelial structural and functional integrity is fundamental to the maintenance of vessel wall homeostasis and normal circulatory function.

Endothelial Injury

- Endothelial Injury is a major cause of thrombosis in the heart or arteries.
- Endothelial injury leads to:
  - Exposure of the underlying basement membrane
  - Adhesion of platelets
  - Release of tissue factor and ultimately thrombosis
- Endothelial injury can contribute to thrombosis in several clinical settings e.g:
  - Endocardial injury due to myocardial infarction
  - Ulcerated plaques in atherosclerotic arteries
  - Traumatic or inflammatory vascular injury

The following conditions lead to chronic subtle endothelial dysfunction/injury:

1. Hypertension
2. Scarred valves
3. Bacterial endotoxins
4. Radiation
5. Hypercholesterolemia
6. Cigarette smoking

Abnormal blood flow

- Abnormal blood flow: disruption of laminar blood flow can bring platelets into contact with the endothelium and promote endothelial cell activation.
- Blood is flowing in Specific speed , if this speed slows or becomes faster ether of the two will affect the thrombus formation.

  - Stasis(the blood flow becomes slow)plays a major role in the development of venous thrombi
  - Turbulence (the blood flow becomes fast) contributes to arterial and cardiac thrombosis by causing endothelial injury or dysfunction

Not coming in the exam

Additional note:

e.g. of abnormal blood flow contributing to thrombosis in several clinical settings:

- Ulcerated atherosclerotic plaques
- Abnormal aortic and arterial dilations
- Acute myocardial infarction
- Mitral valve stenosis
- Hyperviscosity syndromes
- Sickle cell anemia

Hypercoagulability

Means that the blood has higher tendency to coagulate , that will promote thrombosis

Any change of the coagulation pathways that predisposes to thrombosis

Primary (Genetic) Hypercoagulable State

Common :

- ❖ mutation in factor V gene (factor V Leiden)
- ❖ Mutation prothrombin gene
- ❖ anti-thrombin III deficiency

Rare :

- ❖ protein C deficiency
- ❖ S deficiencies

Very rare :

- ❖ fibrinolysis defects.

Secondary (Acquired) Hypercoagulable State

❖ **High risk for thrombosis**

- Prolonged bed rest or immobilization
- Myocardial infarction
- Atrial fibrillation
- Tissue damage (surgery, fracture, burns)
- Cancer
- Prosthetic cardiac valves
- Disseminated intravascular coagulation (DIC)
- Heparin-induced thrombocytopenia
- Antiphospholipid antibody syndrome (lupus anticoagulant syndrome)

❖ **Lower risk for thrombosis**

- Cardiomyopathy
- Nephrotic syndrome
- Hyperestrogenic states (pregnancy)
- Oral contraceptive use
- Sickle cell anemia
- Smoking

Thrombotic disorders

Disorder	Explanation
Anti-thrombotic (hemorrhagic)	Leading to pathological bleeding states, such as hemophilia, Christmas disease and Von Willebrand disease.
Prothrombotic	Leading to hypercoagulability with pathologic thrombosis, e.g. hereditary thrombophilia and antiphospholipid antibody syndrome. Type of hereditary thrombophilia factor V deficiency
Disseminated Intravascular Coagulation	Both **prothrombotic** and **antithrombotic** disorder characterized by widespread thrombosis and hemorrhage resulting from the consumption of platelets and coagulation factors. Very difficult to treat

	Hereditary Thrombophilia	Antiphospholipid antibody syndrome
Definition	Is a **prothrombotic** familial syndrome.	Is a **prothrombotic** hypercoagulable autoimmune multisystem disorder caused by the presence of antiphospholipid antibodies. Commonly seen in women with systemic lupus erythematosus
Characteristics	Characterized by recurrent venous thrombosis and thromboembolism	Is characterized by recurrent thrombosis and embolism and fetal loss in pregnancy. & cardiac valve vegetations & Thrombocytopenia

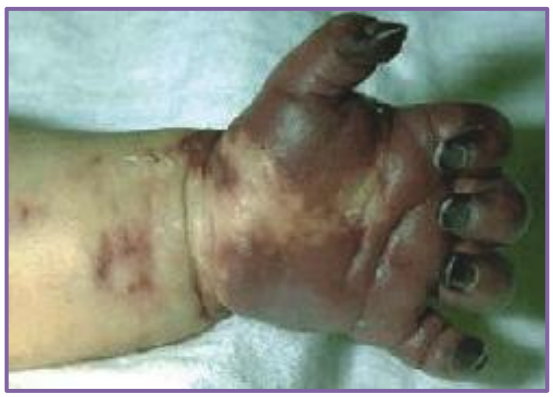
Thrombotic disorders

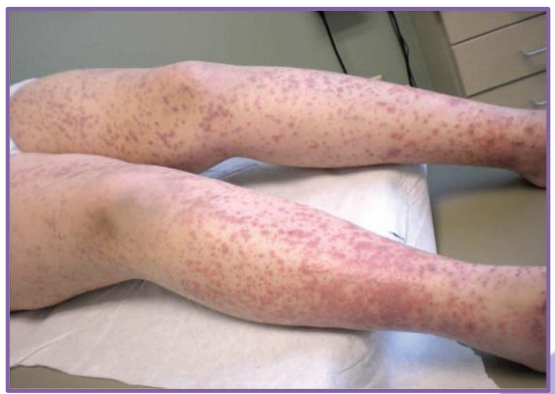
	Hereditary Thrombophilia	Antiphospholipid antibody syndrome
Notes and further information	***Factor V leiden thrombophilia*** **is genetically inherited *prothrombotic* disorder of blood.** an autosomal dominant condition which exhibits incomplete dominance. ***Factor V leiden*** is a mutated form of human factor V that causes an increase in blood clotting (hypercoagulability). In this disorder the Leiden variant of factor V cannot be inactivated by activated protein C Only a moderately increased risk of thrombosis (when otherwise healthy, patients are free of thrombotic complications) Can be caused by deficiency of antithrombotic proteins, e.g. antithrombin 3, protein C, & protein S. **Med students trying to study Pathology:** 	- Patients have prolonged partial thromboplastin time(PTT). - Fetal loss is attributable to antibody-mediated inhibition of t-PA activity necessary for trophoblastic invasion of the uterus. - The name ***Antiphospholipid antibody syndrome*** is a bit of a misnomer (Not named correctly), as it is believed that the most important pathologic effects are mediated through binding of the antibodies to epitopes on plasma proteins (e.g.prothrombin) that are somehow induced or "unveiled" by phospholipids Antiphospholipid antibody syndrome can be: • Primary, only the manifestations of a hypercoagulable state and lack evidence of other autoimmune disorders. • Secondary, Individuals with a well-defined autoimmune disease, such as ***Systemic Lupus Erythematosus*** and so this antibody is also known as lupus anticoagulant.

Disseminated Intravascular Coagulation(DIC)

Definition	Sudden or insidious (مخادع) onset of widespread fibrin thrombi and hemorrhage in the microcirculation. Is both **prothrombotic** and **antithrombotic** disorder
Morphology	Although these thrombi are not grossly visible,they are readily apparent microscopically
Complications	- Can cause diffuse circulatory insufficiency, particularly in the brain, lungs, heart, and kidneys. - It can evolve into a bleeding catastrophe: • Platelet and coagulation protein consumption (hence the synonym **consumption coagulopathy**) • At the same time, fibrinolytic mechanisms are activated
Classification	**It should be emphasized that DIC is not a primary disease (dr. emphasized more on this)** but rather a potential complication of any condition associated with widespread activation of thrombin

Picture from the Internet





Morphology of Thrombus

Thrombi are focally attached to underlying vascular surface and may develop anywhere in the cardiovascular system, the cardiac chambers, valve cusps (vegetations), arteries, or capillaries. They vary in size and shape, depending on the site of origin.

Arterial or cardiac thrombi usually begin at a site of endothelial injury (e.g., atherosclerotic plaque) or turbulence (vessel bifurcation). Venous thrombi characteristically occur in sites of stasis.

Arterial thrombi grow in a **retrograde direction** from the point of attachment (i.e. toward the heart). Venous thrombi extend **in the direction** of blood flow (i.e.toward the heart).

The propagating tail of either thrombi may not be well attached (particularly in veins) is prone to fragmentation, creating an embolus

A thrombus is made up of fibrin, platelets and red blood cell and few inflammatory cells.

Mural Thrombi

Definition

When arterial thrombi arise in heart chambers or in large blood vessels such as the aortic lumen

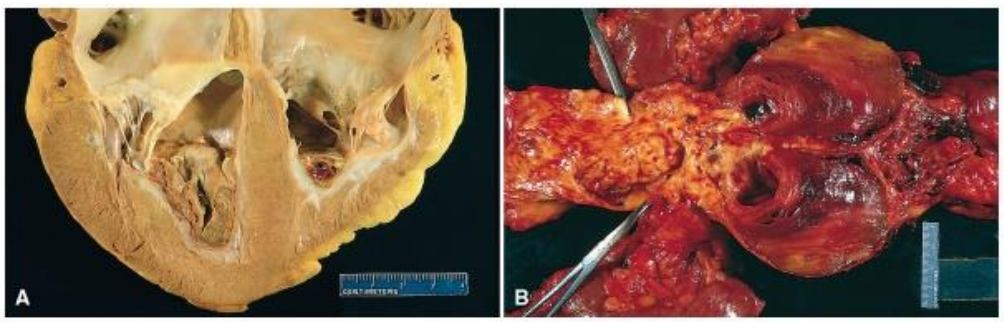
Cause

Abnormal myocardial contraction or endomyocardial injury promoted cardiac mural thrombi

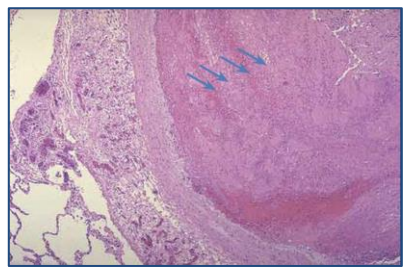
Lines of zahn

Thrombi formed in the heart or aorta may have apparent laminations, called lines of Zahn seen grossly (and microscopically) . Lines of Zahn are produced by alternating pale layers of platelets admixed with some fibrin and darker layers containing more red cells

What are the lines seen in cardiac thrombus ?
Lines of zahn



- Mural thrombi. **A**, Thrombus in the left and right ventricular apices, overlying white fibrous scar. **B**, Laminated thrombus in a dilated abdominal aortic aneurysm. Numerous friable mural thrombi are also superimposed on advanced atherosclerotic lesions of the more proximal aorta *(left side of picture)*.



Clinical effects

Clinical effects depend on the site of thrombosis. Thrombi are significant because:

they are potential sources of emboli

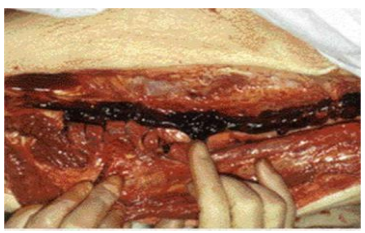
They cause obstruction of arteries and veins

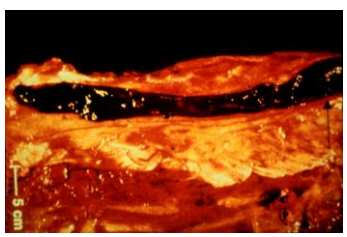
Lead to ischemia —> necrosis—> infraction

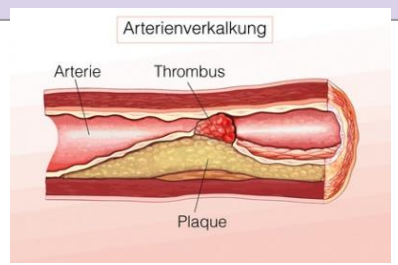
Clinical effects depend on the site of thrombosis:

Venous thrombi have capacity to embolize to the lungs and can cause death.

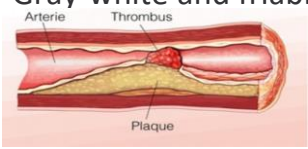
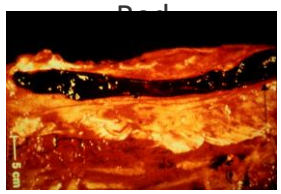
Arterial thrombi embolize in the systemic circulation and can cause vascular obstruction at critical sites and cause serious consequence e.g. ischemia and necrosis.







Types of thrombi

Types & Characteristics	Arterial Thrombi click here	venous Thrombi <phlebothrombosis> click here
Nature	Usually occlusive	Almost invariably occlusive, and often occurs at sites of stasis taking the shape of the vein
Setting	Usually superimposed on a **ruptured atherosclerotic plaque**,and are firmly adherent to the injured arterial wall. but other vascular injuries (vasculitis, trauma) may be the underlying cause.	these thrombi form in a relatively static environment(sluggish venous circulation) , they contain more enmeshed erythrocytes (and relatively few platelets) and are therefore known as RED or **stasis thrombi**
Most affected sites	**Most common** sites in descending order, are coronary, cerebral, and femoral arteries. Arterial or cardiac thrombi usually begin at sites of turbulence or endothelial injury	Veins of the lower extremities (90% of cases) • Upper extremities, periprostatic plexus, or the ovarian and periuterine veins can also be affected • Under special circumstances, they can also occur in the dural sinuses, portal vein, or hepatic vein.
Gross appearance	Gray-white and friable 	

Thrombi on heart valves

Thrombi on heart valves are called vegetations

Thrombi on heart valve

Infective vegetations

Infective endocarditis: bacterial or fungal blood-borne infections may result in the development of large thrombotic masses on heart valves.

Patients with Systemic Lupus Erythematosus (**SLE**) can have noninfective, verrucous (**Libman-Sacks**) endocarditis.

Sterile vegetations

Nonbacterial thrombotic endocarditis (marantic): is non infective vegetations on valves in patients with:

- hypercoagulable states
- Subtle endothelial abnormalities
- And some patients with malignancy and other debilitating diseases.

DVT

click here

	Deep vein thrombosis
Definition	**Venous thrombosis that arises in the deep veins of the legs.** They occur with stasis or in hypercoagulable states. Often associated with **inflammation** and then it is termed **thrombophlebitis**.
Site	Common in **deep the larger leg veins** at or above the knee, (e.g. Popliteal, femoral, and iliac veins).
Clinical features	DVTs can cause local pain and edema, Clinical venous obstructions from DVTs can be rapidly offset Features by collateral channels. But it can be **asymptomatic** in approximately 50% of affected individuals,and it will be recognized only in retrospect after embolization.
Complications	**DVT** may embolize to the lungs giving rise to pulmonary embolism with resultant **pulmonary infarct.**

Predisposing factors for DVT

Bed rest and **immobilization**

Congestive heart failure:

➔ Causes impaired venous return.

Trauma, surgery, and burns:

➔ immobilize and are also associated with vascular insults, procoagulant release from injured tissues, increased hepatic synthesis of coagulation factors, and altered t-PA production

Tumors:

➔ associated inflammation and coagulation factors (tissue factor, factor VIII)

➔ procoagulants (e.g., mucin) release

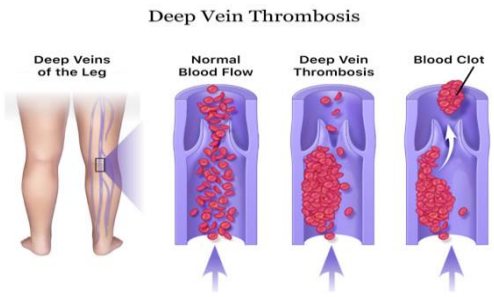
Advanced age:

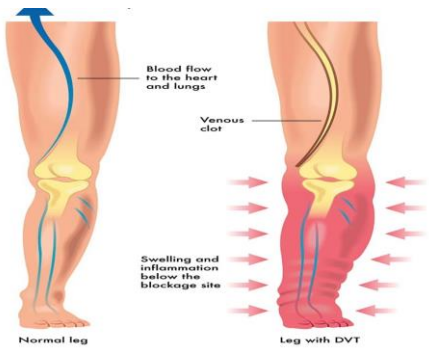
➔ (Regardless of the specific clinical setting)

Pregnancy:

➔ The potential for amniotic fluid infusion into the circulation at the time of delivery can cause thrombogenesis.

➔ late pregnancy and the postpartum period are also associated with systemic hypercoagulability.





Postmortem clots

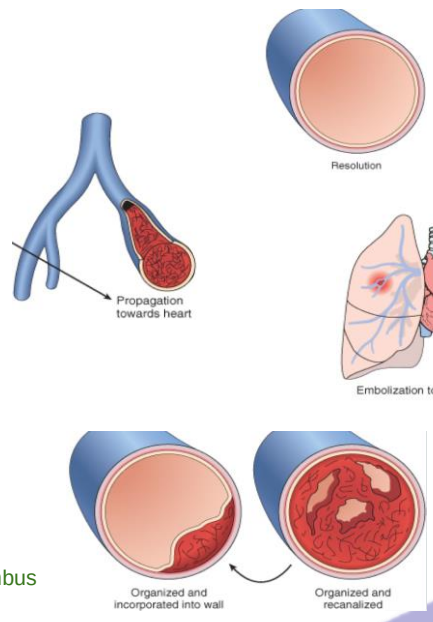
Mortem : death

➢ Postmortem clots may be confused with venous thrombi

Differences	Postmortem clot	Venous thrombus
Feel	Gelatinous	Firm
Morphology	Has **dark red dependent portion** where red cells have settled by gravity and a **top layer of yellow "chicken fat"**	On cut section revel vague strands of **pale gray fibin** Sectioning typically reveals gross and/or microscopic **lines of Zahn.**
Attachment	**Not attached** to the underlying wall	Almost always has a point of attachment.

Fate of Thrombus

- Resolution
- Propagation (growing)
- Embolism
- Organization and recanalization
  - In middle of thrombus Building blood vessels between the thrombus
- Organization and incorporation into the wall.
  - Building blood vessels and clump together and push the thrombus away



Embolism

click here

Pathoma

Chapter 4 - hemostasis and related disorders
4.5- embolism

Definition

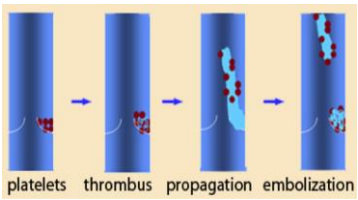
An embolus (pleural: emboli) is a detached intravascular solid, liquid, or gaseous mass that is carried by the blood to a site distant from its point of origin

1. Majority (Virtually 99%) of the emboli **represent some part of a dislodged thrombus**, hence the commonly used term thromboembolism
2. the emboli is lodged in vessels too small to permit further passage, it results in partial or complete vascular occlusion leading to ischemic necrosis of distal tissue (infarction)
3. Depending on the site of origin, emboli may lodge in the pulmonary or systemic circulations

Types of embolism

Types of embolism

- Pulmonary thromboembolism
- Systemic thromboembolism
- Fat embolism : bits of bone marrow
- Air embolism : bubbles of air or nitrogen
- atherosclerotic debris (cholesterol emboli
- tumor fragments
- Amniotic fluid embolism



PULMONARY THROMBOEMBOLISM

click here

Description

Site of lodging & Occlusion

- Embolus get lodged in the pulmonary vasculature.
- **Depending on the size:** it may occlude main pulmonary artery, or impact across the bifurcation **(saddle embolus)** or pass out into smaller, branching arterioles of the pulmonary circulation.
- **Paradoxical embolism:** embolus may pass through interatrial or interventricular defect to gain access to the systemic circulation. Rare

Complications

- Frequently multiple emboli (perhaps sequentially, or as a shower of smaller emboli from a single large thrombus).
- In general, the patient who has had one pulmonary embolus is at high risk of having more.
- Most (60-80%) are clinically **silent** because they are small. – they eventually become organized and become incorporated into the vascular wall – in some cases, organization of the thromboembolism leaves behind a delicate, bridging fibrous web
- Sudden death, right heart failure (cor pulmonale) occurs and cardiovascular collapse when more than 60% of the pulmonary circulation is obstructed by emboli.
- Embolic obstruction of medium-sized arteries can cause pulmonary hemorrhage but usually **not** pulmonary infarction:
- the lung has a dual blood supply and the intact bronchial arterial circulation continues to supply blood to the area.
- Embolic obstruction of small end-arteriolar pulmonary branches usually does result in associated infarction.

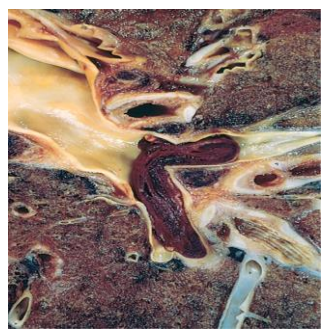
Many emboli occurring over a period of time may cause:
– pulmonary hypertension -> right ventricular failure

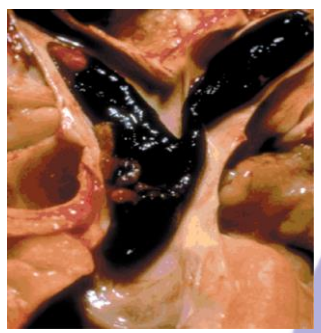
Origin & Pathway

- In more than 95% of cases, venous emboli originate from **deep leg vein thrombi** above the level of the knee through progressively larger channels and pass through the right side of the heart entering the pulmonary vasculature.

Pictures

Embolus derived from a lower extremity deep venous thrombosis and now impacted in a pulmonary artery branch





SYSTEMIC THROMBOEMBOLISM

Description

Site of lodging & Occlusion

- refers to emboli traveling within the **arterial circulation.**
- Most arise from an intracardiac mural thrombi (80%).
- Major sites are the lower extremities (75%) and the brain (10%). the intestines, kidneys, and spleen affected to a lesser extent
- 2/3 of which are associated with Lt ventricular wall infarct.
- 1/4 with dilated left atria (e.g. secondary to mitral valve disease).
- **The remainder originates from:**
- Aortic aneurysms
- Thrombi on ulcerated atherosclerotic plaques
- Fragmentation of valvular vegetations.

Complications

- Consequences depend on the extent of **collateral vascular supply** in the affected tissue, the **tissue's vulnerability** to ischemia, and the **caliber of the vessel** occluded.
- **Causes infarction** of tissues supplied by the artery.

FAT EMBOLISM

Description

Site of lodging & Occlusion

- Microscopic fat globules may be found in the circulation after **fractures of long bones** (which have fatty marrow) or, rarely in **soft tissue trauma and burns.**
- **Fat is released by marrow or adipose tissue** injury and enters the circulation through rupture of the blood vessels and act as embolus..

Complications

- Although fat and marrow embolism occurs in some 90% of individuals with severe skeletal injuries, fewer than 10% of such patients show any clinical findings.
- **Fat embolism syndrome** is characterized by pulmonary insufficiency, neurologic symptoms, anemia, and thrombocytopenia.

Seen in patients women who have total body burn

AIR EMBOLISM

Description	
Site of lodging & Occlusion	- **Gas bubbles within the circulation can obstruct vascular** flow almost as readily as thrombotic masses can(and cause distal ischemic injury) acting as thrombotic masses. - Bubbles may coalesce to form frothy masses sufficiently large to occlude major vessels. - Air may enter the circulation during obstetric procedures or as a consequence of chest wall injury.
Complications	An excess of 100 cc (ml) is required to have a clinical effect. E.g. : **Decompression sickness.**

Decompression sickness :

Description	Decompression sickness is a type of air embolism. • It occurs when individuals are exposed to sudden changes in atmospheric pressure • Scuba and deep sea divers, underwater construction workers, and individuals in unpressurized aircraft with rapid ascent are all at risk.
Causes	When air is breathed at high pressure (e.g., during a deep-sea dive) increased amounts of gas (particularly **nitrogen**) become **dissolved** in the blood and tissues. If the diver then **ascends (depressurizes) too rapidly** the nitrogen expands in the tissues and bubbles out of solution in the blood which leads to gas emboli.
Complications & symptoms	- can induce focal ischemia in a number of tissues: - brain and heart - skeletal muscles, causing pain (the bends) - In the lungs, respiratory distress, (the chokes)
Treatment	Placing the individuals in a compression chamber where the **barometric pressure may be raised**, thus forcing the gas bubbles back into solution followed by subsequent slow decompression.

A more chronic form of decompression sickness is called **caisson disease** in which, persistence of gas emboli in the skeletal system leads to multiple foci of ischemic necrosis; the more common sites are the heads of the femurs, tibia, and humeri.

AMNIOTIC FLUID EMBOLISM

Description

Site of lodging & Occlusion

-A grave and uncommon complication of labor and the immediate postpartum period
- **Caused by infusion of amniotic fluid or fetal tissue into the maternal circulation** via a tear in the placental membranes or rupture of uterine veins.

Very common on not developed countries

Complications

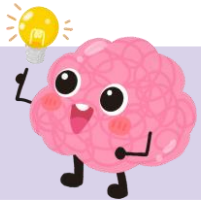
- **Microscopy:** presence in the pulmonary microcirculation of squamous cells shed from fetal skin, fetal hair, fetal fat,etc.
- Characterized by **sudden severe dyspnea**, **cyanosis**, and **hypotensive shock**, followed by **seizures and coma.**
- Marked pulmonary edema and diffuse alveolar damage are also present. Systemic fibrin thrombi indicative of DIC can also be seen.

Origin & Pathway

- If the patient survives the initial crisis, pulmonary edema develops, along with disseminated intravascular coagulation, owing to release thrombogenic substances from amniotic fluid.

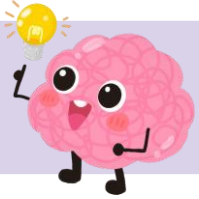
Summary

Types of embolism		
Types	**Characteristics**	**Description**
Pulmonary Embolism	Site & occlusion	Depending on the size: occlude main pulmonary artery, or Site of lodging impact across the bifurcation (saddle embolus) or pass out into & Occlusion - Paradoxical embolism: embolus may pass through interatrial or interventricular defect to gain access to the systemic circulation.
	Complications	- multiple emboli - Another PE - Sudden death - Embolic obstruction of medium-sized arteries can cause pulmonary hemorrhage but usually not pulmonary infarction:
Systemic Thrombo-embolism	Site & occlusion	In the arterial circulation - Major sites are the lower extremities (75%) and the brain (10%). - Most arise from an intracardiac mural thrombi (80%).
	Complications	Consequences depend on the extent of collateral vascular supply in the affected tissue
Fat m Embolism	Site & occlusion	after fractures of long bones & soft tissue trauma and burns.
	Complications	Fat embolism syndrome is characterized b pulmonary insufficiency, neurologic symptoms, anemia, and thrombocytopenia.
Amniotic Embolism	Site & occlusion	Caused by infusion of amniotic fluid or fetal tissue into the maternal circulation via a tear in the placental membranes or rupture of uterine veins.
	Characteristics	Characterized by sudden severe dyspnea, cyanosis, and hypotensive shock, followed by seizures and coma.
	Complications	If the patient survives the initial crisis, pulmonary edema develops, along with disseminated intravascular coagulation,
Air & Occlusion Embolism	Site & occlusion	Gas bubbles within the circulation can obstruct vascular flow
	Complications	An excess of 100 cc (ml) is required to have a clinical effect.



KEYWORDS

Hypercoagulability	• mutation in factor V(gene factor V Leiden) • prothrombin gene, • antithrombin III deficiency • protein C or S deficiencies, • fibrinolysis defects.
Hereditary Thrombophilia	• prothrombotic familial syndrome. • Factor V leiden thrombophilia • deficiency of antithrombotic proteins, e.g. antithrombin 3, protein C, & protein S.
Antiphospholipid antibody syndrome	• autoimmune multisystem disorder • Patients have prolonged partial thromboplastin time (PTT). • sometimes associated SLE • lupus anticoagulant.
Mural Thrombus	• Thrombus in heart / large arteries • Lines of Zahn
Arterial Thrombi	• ruptured atherosclerotic plaque • coronary, cerebral, and femoral arteries. • Gray-white and friable
Venous Thrombi	• enmeshed RBCs • lower extremities • Red
Deep vein Thrombosis	• Late veins • bed rest / immobilization • Tumors • Pregnancy • Surgery



KEYWORDS

Pulmonary Embolism	• Deep vein thrombosis • Most common complication of DVT
Fat Embolism	• Fracture of long bone • Massive burns
Amniotic Embolism	• Complicated delivery • Tear in the placenta • Abnormalities in the placenta • Pulmonary edema • Diffuse alveolar damage
Air Embolism	• Chest wall injury • Decompression sickness.

Answers:
1- D 2- A 3- C 4- D 5- B

MCQ

1- “Thrombosis can only occur during life” what are the implications of that sentence?			
A) Help in diagnosis of DIC	B) Determine the cause of death	C) Differentiate between a thrombus and a clot	D) B & C
2- Which of the following has a lower risk of thrombosis?			
A) Pregnancy	B) Prolonged bed rest	C) Myocardial infarction	D) Antiphospholipid antibody syndrome
3- Which of the following is a fate of Thrombus?			
A) Immobilize	B) Become cancer	C) Embolize	D) Be removed by Human Factor V
4- Disseminated intravascular disease is a Sudden Insidious onset of widespread fibrin thrombi in the Macrocirculation. Which one of the above words is wrong?			
A) Sudden	B) Insidious	C) Thrombi	D) Macrocirculation
5- An embolus can be all of the below except?			
A) Solid	B) Thrombus	C) Liquid	D) Gaseous

Answers:
6- C 7- D 8- D 9- B 10- D

MCQ

6- have capacity to embolize to the lungs and can cause death.			
A) Arterial thrombi	B) Hypotension	C) Venous thrombi	D) Hypertension
7- Hereditary Thrombophilia can be caused by deficiency of which of the following?			
A) Protein C	B) Protein A	C) Protein S	D) Answers A & C
8- In thrombus, the dark lines of zahn are due to:			
A) Coagulated fibrin	B) Aggregated proteins	C) Aggregated platelets	D) Aggregated RBCs
9- The major factors predisposing to thrombogenesis include all of the following except:			
A) Pattern of blood flow	B) Arterial blood flow	C) Hypercoagulability	D) Endothelial injury
10- Thrombosis due to Hypercoagulability is seen in:			
A) Cancer	B) Atrial fibrillation	C) Sickle cell anemia	D) All mentioned

Answers:
1- B 2- D 3- A 4- B

Cases

1- Dr. Aziz was performing an autopsy to determine the cause of death for a patient who died suddenly. He quickly determined that the cause of death was thrombosis, what did dr.Aziz see?			
A) Postmortem clots	B) Lines of Zahn	C) DVT	D) Pulmonary Edema
2- A 28-year-old female is postoperative day one after an emergency C-section of her term infant. She had no other complications during pregnancy and has no other past medical problems. Which of the following factors puts her at an increased risk of developing a deep vein thrombosis?			
A) Increased Hypercoagulability	B) Increased Cardiac output during labor	C)Physiologic Anemia	D)Increased Plasma volume during pregnancy
3- A 45 year old male presented to the ER after a major accident which caused his right Femur to be fractured. The doctors were really worried because the pt had increased risk of developing which type of the following emboli?			
A) Foreign bodies embolism	B) cholesterol embolism	C) amniotic fluid embolism	D) Fat embolism
4- After an operation on a 67 year old male patient, who was on bed rest before the operation for 2 weeks. The attending physician prescribed him heparin and warned him that if he moved his right leg, he might end up with a pulmonary embolism. The pt was stubborn and did not follow instructions, he walked out of the hospital to get some falafel from the nearby shop, when he came back he complained to the nurse that he couldn't breath and he has chest pain. Which of the following was the physician worried about and tried to solve?			
A) Paradoxical embolism	B) Deep vein thrombosis which may lead to PE	C) Congestive heart failure	D) The heparin not working properly

Pathology team

Shahad Alshehri

Hessa Alamer

Muhannad Alotaibi

Joud alahmari

Abdulaziz Nasser

Norah albahily

Abdulaziz Alobathani

Shoug Albattah

Faris Alturaiki

Marwah Ahmed

Tariq Alshamrani

Ritaj alsubaie

Waleed Alanazi

Elaaf Albadi

Abdulaziz Alanazi

Contact us at : pathology.444ksu@gmail.com