Circulatory Disturbances
(Disturbances of Blood and Body Fluids)

by

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Lecture 1

- Hyperaemia & Congestion
- Thrombosis

Circulatory Disturbances
(Disturbances of Blood and Body Fluids)

The health of cells and tissues depends ***not only*** on an **intact circulation** to deliver oxygen and remove wastes ***but also*** on **normal fluid balance.**

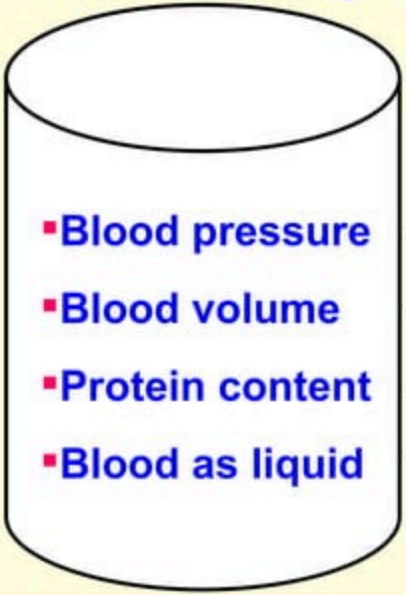
Normal fluid homeostasis includes ***maintenance of vessel wall integrity (intact circulation) as well as intravascular pressure, blood volume, and protein content (osmolarity) within certain physiologic ranges***. Therefore any change in one of these factors will affect the tissue homeostasis and may result in ***oedema*** or ***congestion***.

Normal fluid homeostasis also means ***maintaining blood as a liquid until such time as injury necessitates clot formation.*** Clotting at inappropriate sites ***(thrombosis)*** or migration of clots ***(embolism)*** obstructs blood flow to tissues & leads to cell death ***(infarction).*** Conversely inability to clot after injury results in ***haemorrhage***. Extensive haemorrhage can result in ***shock.***

Circulatory Disturbances
(Disturbances of Blood and Body Fluids)

Normal Fluid Homeostasis **Circulatory Disturbances**

- **Vessel wall integrity** → (Thrombosis or hge& shock)



- **Blood pressure** → (Congestion, oedema or shock)
- **Blood volume** → (Congestion, oedema or shock)
- **Protein content** → (Oedema)
- **Blood as liquid** → (Thrombosis, embolism, ischaemia, infarction , gangrene or haemorrhage & shock)

Hyperaemia and Congestion

Definition: Each can be defined as an increase in blood volume in a particular tissue.

Hyperaemia is an increase in blood flow in an organ or tissue due to dilatation of arteries or arterioles i.e. active hyperaemia, while congestion is passive hyperaemia due to engorgement of veins and venules by blood.

Active Hyperaemia

Physiological Condition
e.g. in skeletal &cardiac muscles in muscular exercise, in splanchnic area after eating.

Pathological Condition

e.g. in acute inflammation *(dilatation of arteries &arterioles)*

The affected tissue is redder because of engorgement with oxygenated blood.

Passive Hyperaemia (Venous Congestion)

Systemic Venous Congestion

In which blood accumulates in veins **allover the body** as in case of congestive heart failure or **sparing the lung** in case of right side heart failure

Pulmonary Venous Congestion

In which blood accumulates in **pulmonary veins** and their tributaries in case of left side heart failure or mitral stenosis

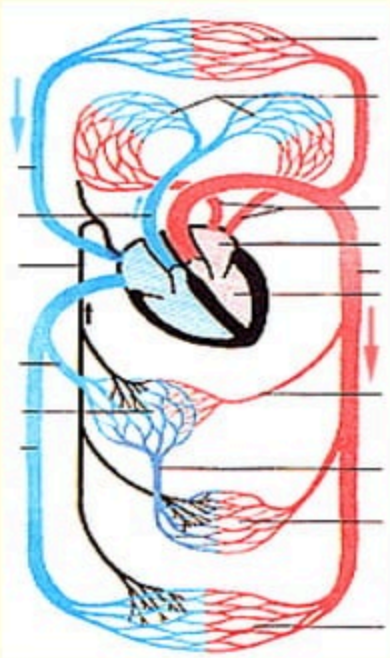
Localized V C

It is due to obstruction to blood flow in a limited area or an organ: **1.Acute** as in **mechanical obstruction** or venous **thrombosis**

2.Chronic by **pressure** on a vein **by a tumour** or by

Passive Hyperaemia (Venous Congestion)

In **rt. side heart failure:** there is **systemic venous congestion** *with sparing of the lung* while in **congestive heart failure (both sides)** there is congestion of **all** the organs including the lung.



In **lt. side heart failure:** there is **pulmonary venous congestion** but later it may cause *pulmonary hypertension* leading to **rt. side heart failure** i.e. congestive ht. failure.

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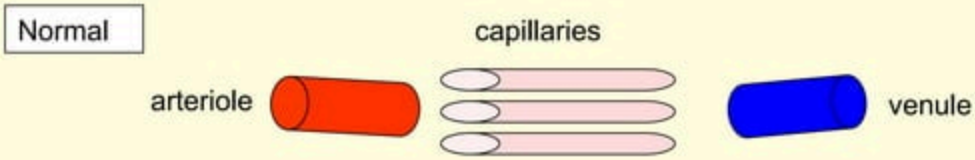
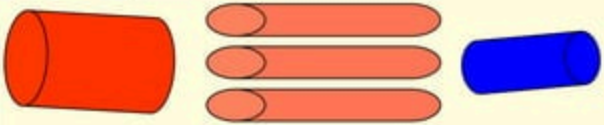


Hyperaemia → erythema

Increased inflow
e.g. exercise
&inflammation



Congestion → cyanosis & hypoxia

Local obstruction
(inside or outside),
congestive H F

Systemic Venous Congestion (Chronic Venous Congestion)

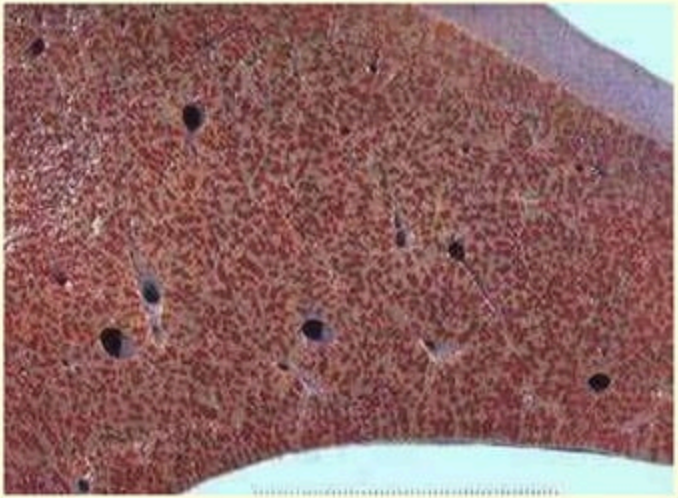
Clinical Features of congestive heart failure or Rt side heart failure :

- **Cyanosis (bluish discolouration)** in lips and nails due to the presence of reduced blood (deoxygenated blood).
- **Congested pulsating neck veins** due to increased venous pressure.
- **Oedema of lower limbs** due to increased venous pressure.
- **Enlarged tender liver**.

Pathological Features of Chronic Venous Congestion in Various Organs (Liver)

1.Liver

Gross Picture: The liver is **enlarged** , **firm** and the cut surface shows alternating **dark** areas of **congestion** with **pale** areas of **fatty change**, giving the liver the **nutmeg** appearance.

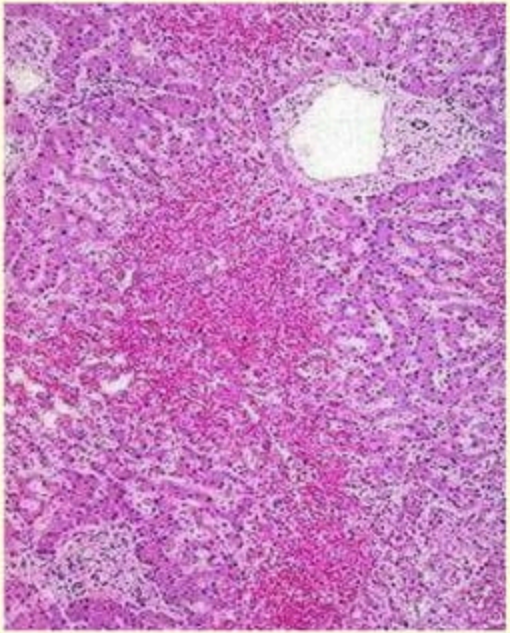


Nutmeg cut surface of the liver (dark areas of congestion alternating with pale areas of fatty change)

Pathological Features of Chronic Venous Congestion in Various Organs (Liver)

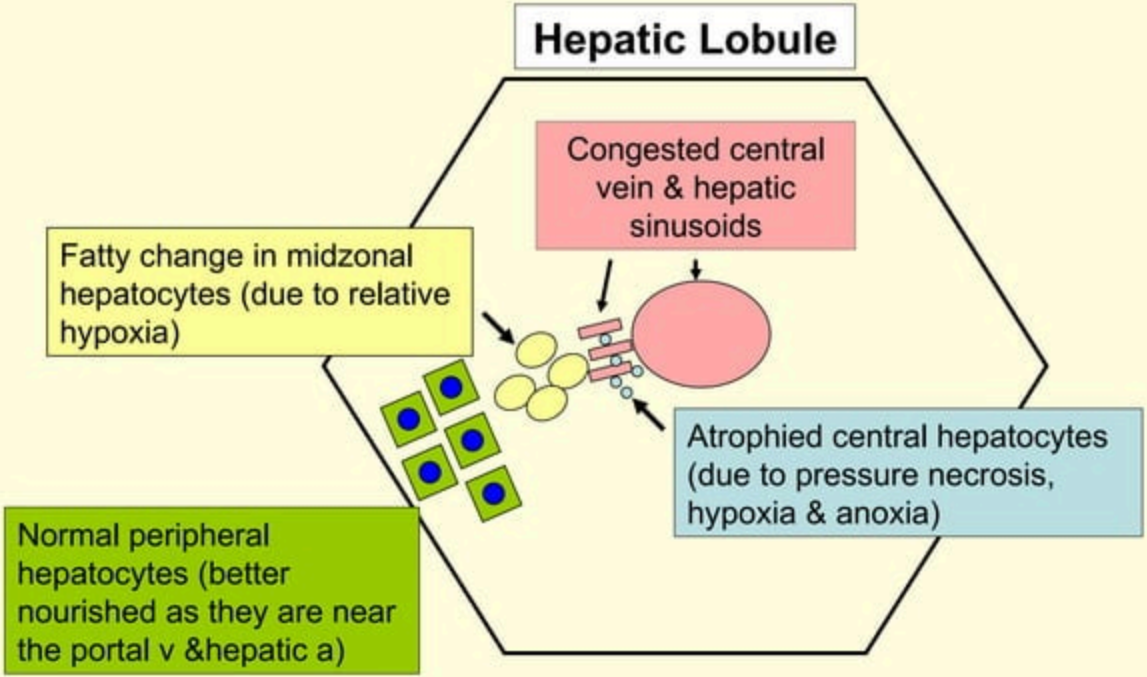
Microscopic Picture of Liver in Chronic Venous Congestion

1. The **central vein** in hepatic lobule is **congested** as well as the **hepatic sinusoids** in the central area.
2. The **central hepatocytes** will show **atrophy** and **necrosis**.
3. The **mid zonal hepatocytes** may show **fatty change** due to relative hypoxia.
4. The **peripheral hepatocytes** are **normal.**



Early CVC of liver (congestion of central vein &central hepatic sinusoids)

Pathological Features of Chronic Venous Congestion in Various Organs (Liver)



Pathological Features of Chronic Venous Congestion in Various Organs (Spleen)

Chronic venous congestion can cause a form of **splenic enlargement** referred to as **congestive splenomegaly.**

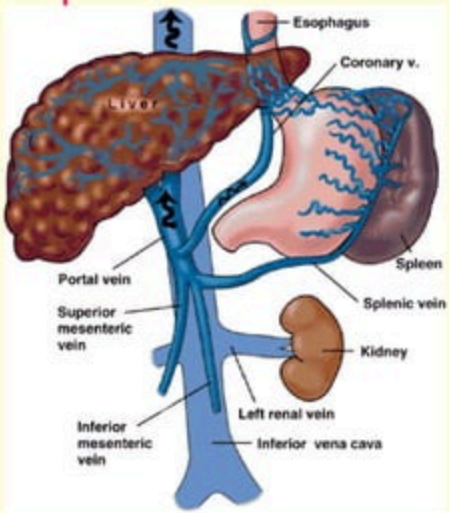
Causes of Splenic Venous Congestion:

1.Systemic or central venous congestion is encountered in right side heart failure. It produces **moderate** enlargement of the spleen that rarely exceeds **500gms.**

2.Intrahepatic causes that retard portal venous drainage as in various forms of **cirrhosis** or in **bilharzial periportal fibrosis**. These cause **striking** congestive splenomegaly. The weight of the spleen can reach to **5000gms.**

3.Extrahepatic disorders that obstruct the portal or splenic veins.

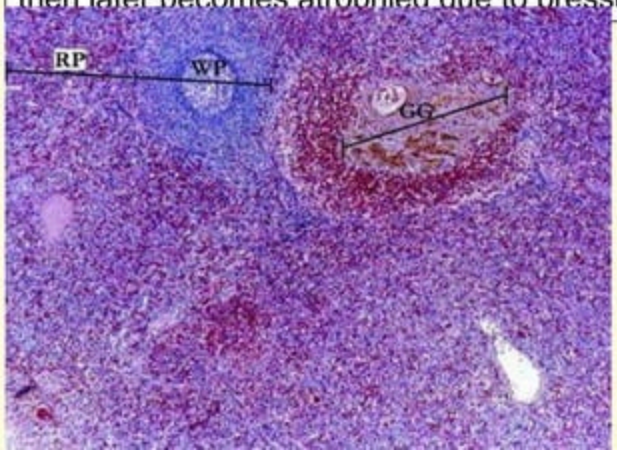
A cirrhotic liver

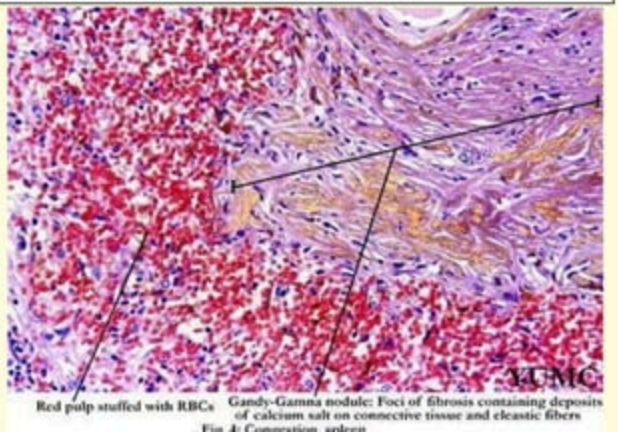


Pathological Features of Chronic Venous Congestion in Various Organs (Spleen)

2.Spleen **Gross Picture:** It is **moderately to markedly** enlarged, **firm** with **deep red to grey red** cut surface (depending on the degree of fibrosis). The **capsule is thickened**.

Microscopic Picture: The sinusoids of red pulp are **dilated** and **engorged with blood** &their walls are thickened by fibrous tissue. **Haemorrhage** may occur that will result in liberation of haemosiderin granules from haemolysed RBCs that will undergo fibrosis with formation of **fibrosiderotic nodules** called *Gamma-Gandy nodules*. The white pulp (lymphoid follicles) is first hyperplastic then later becomes atrophied due to pressure by areas of hge & fibrosis.

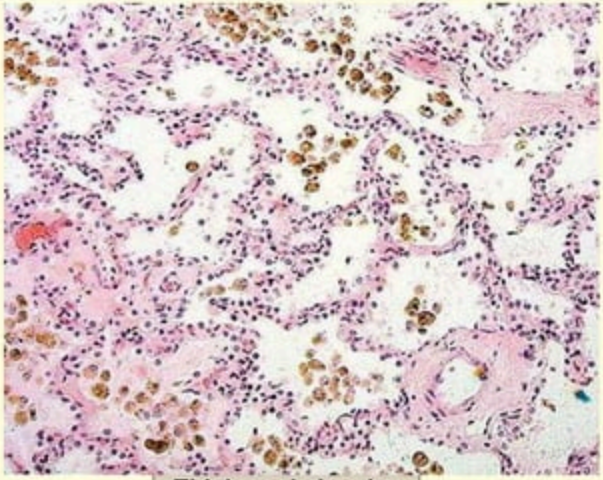




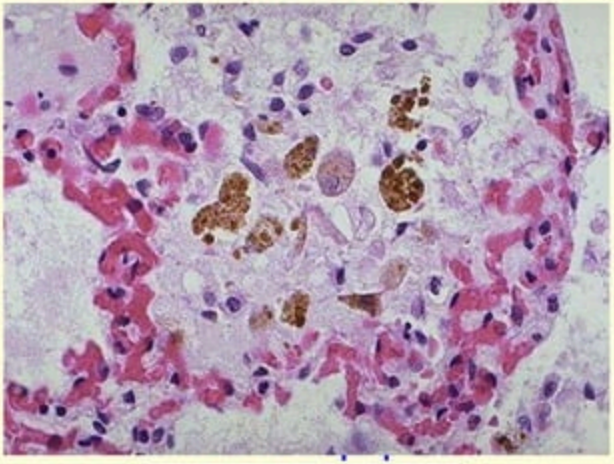
Pathological Features of Chronic Venous Congestion in Various Organs (Lung)

3.Lung **Gross Picture:** The lungs are **enlarged, heavy, firm** and **deep red** in colour **(brown induration).** Frothy blood oozes from the cut surface on squeezing.

Microscopic Exam.: The **alveolar septa** are thickened by congested dilated capillaries and oedema fluid followed **later** by fibrosis. As a result of microhaemorrhages, the **alveoli** contain oedema fluid, RBCs either intact or haemolysed and haemosiderin laden macrophage **(heart failure cells).**



Thickened alveolar septa (fibrosis)



heart failure cells

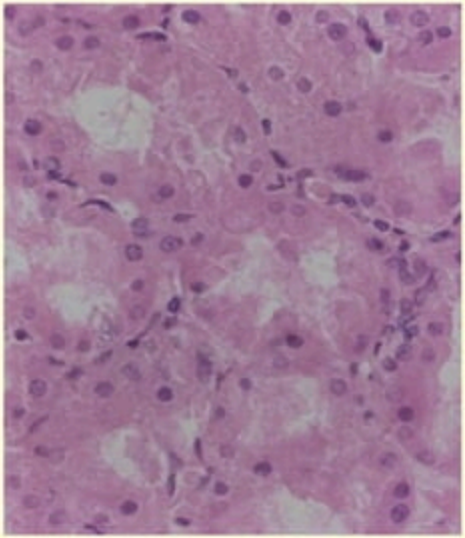
Pathological Features of Chronic Venous Congestion in Various Organs (Kidney)

4.Kidney

Gross Picture: The kidneys are slightly enlarged, firm with congested cut surface.

Microscopic Picture: the convoluted tubule cells show cloudy change or fatty change due to hypoxia.

5. Other organs as brain, adrenals stomach and intestines also show congestion.



Thrombosis

Definition **Thrombosis** is the formation of blood clot (thrombus) in an uninjuried vessels or thrombotic occlusion of a vessel after minor injury. **The thrombus** is formed of blood elements essentially platelets that develops inside the cardiovascular system during life.

Types of Thrombi

1.Pale Thrombus

- In a **flowing blood** *as in cardiac chambers or in arteries*
- Formed mainly of **platelets**
- **Firm pale reddish grey**

2. Red Thrombus

- In a **stagnant blood** *adjacent to complete vascular occlusion*
- Formed of **fibrin** entrapping RBCs, leucocytes& platelets
- **Soft dark red** and **gelatinous**

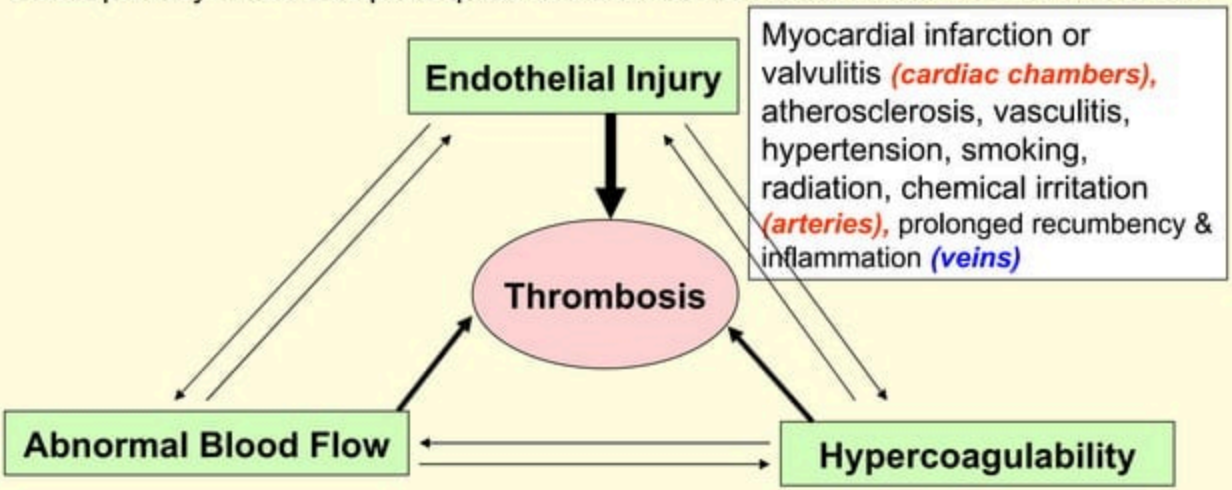
3.Mixed Thrombus

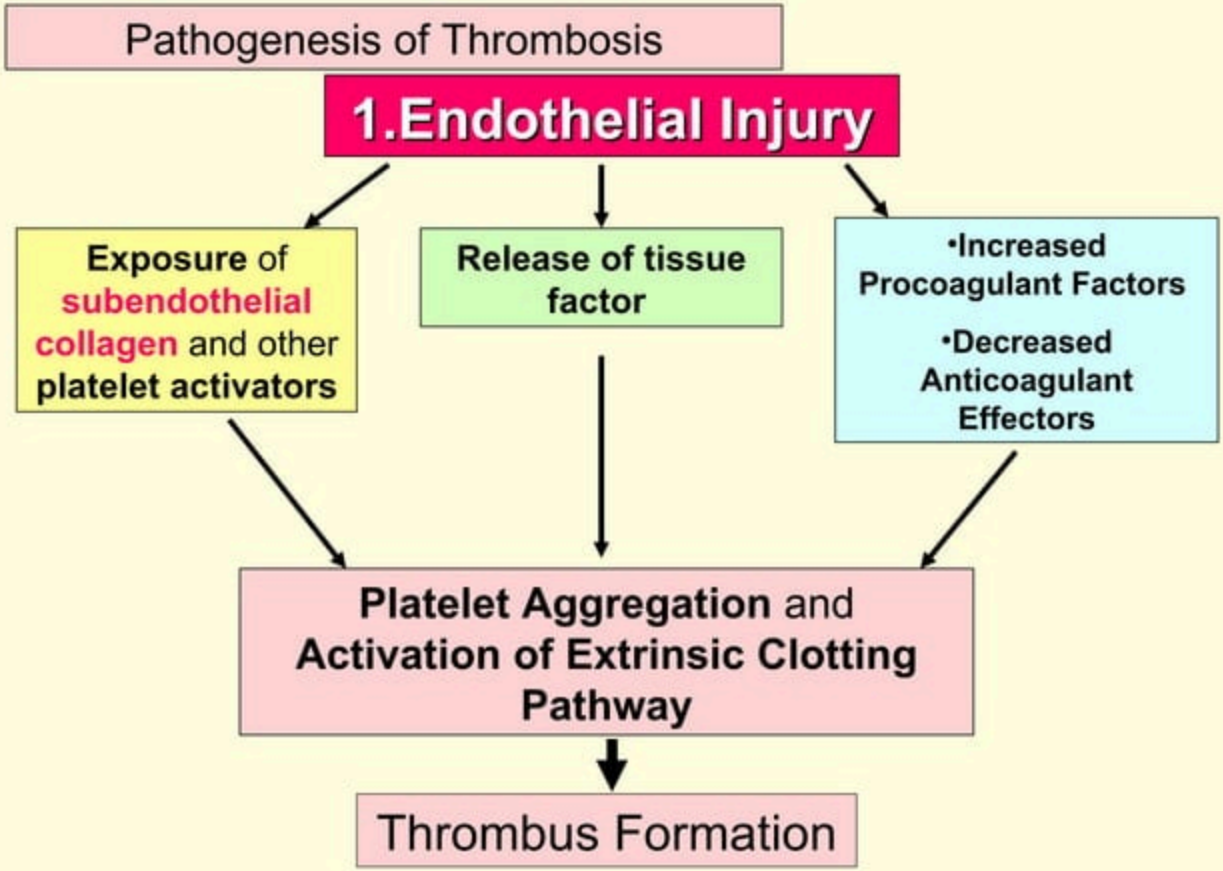
- In a **slowly flowing blood** usually in veins & arteries
- Formed of **alternating layers of platelets** and **fibrin** entrapping RBCs and leucocytes.
- **Alternating red &pale layers**

Thrombosis

Pathogenesis (Causes= Predisposing Factors)

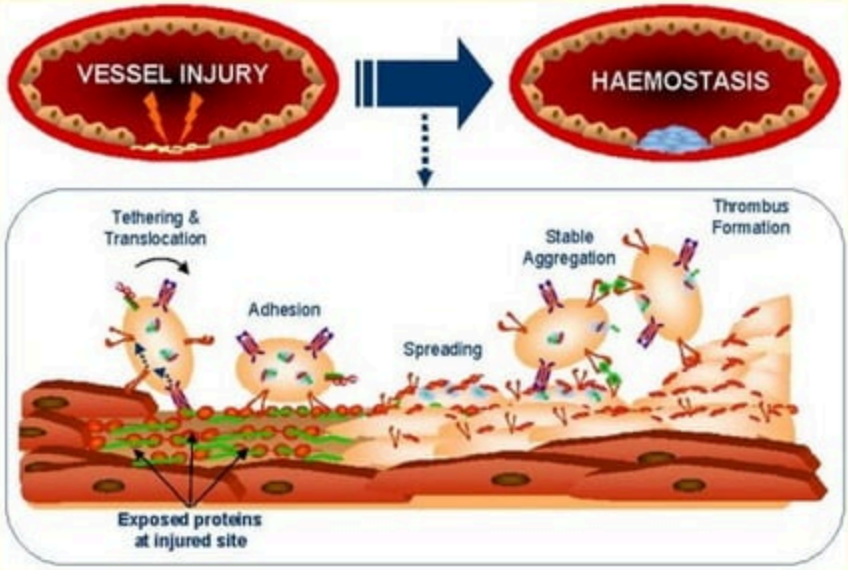
Three primary influences predispose to thrombus formation called **Virchow's triad**




Pathogenesis of Thrombosis
1.Endothelial Injury
Exposure of subendothelial collagen and other platelet activators
Release of tissue factor
•Increased Procoagulant Factors
•Decreased Anticoagulant Effectors
Platelet Aggregation and Activation of Extrinsic Clotting Pathway
Thrombus Formation

Pathogenesis of Thrombosis

1.Endothelial Injury



Pathogenesis of Thrombosis

Normal blood flow is ***laminar*** such that the **platelets flow centrally in the lumen**, separated from the endothelium by a slower moving clear zone of plasma.

2.Abnormal Blood Flow (Turbulence & Stasis)

Disrupt the laminar flow bringing the platelets into contact with the endothelium

Promote endothelial cell activation

Prevent the dilution of the activated clotting factors by fresh flowing blood

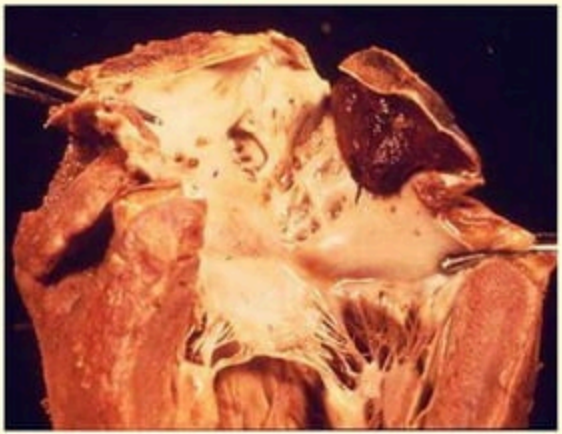
Retard the inflow clotting factors inhibitors

Thrombus Formation

Pathogenesis of Thrombosis

2.Abnormal Blood Flow (Turbulence & Stasis)

Iliac artery aneurysm with laminated thrombus



Left atrial mural thrombus in a case of rheumatic mitral stenosis

Pathogenesis of Thrombosis

3.Hypercoagulability: It is any alteration of the coagulation pathways that predispose to thrombosis.

Primary (Genetic):

- Factor5 Mutations
- Prothrombin Mutation
- Antithrombin3 Deficiency
- Protein C or S Deficiency

Secondary (Acquired):

- Prolonged bed rest or immobilization
- Myocardial Infarction
- Tissue Damage (surgery, fracture, burns)
- Cancer
- Prosthetic Cardiac Valves
- Disseminated Intravascular Coagulation
- Atrial Fibrillation
- Cardiomyopathy
- Hyperoestrogenic States & Contraceptive Pills
- Sickle Cell Anemia
- Smoking
- Systemic Lupus Erythematosis

Thrombosis

Morphology

•Thrombi may develop **anywhere inside the cardiovascular system** i.e. heart, arteries, veins and capillaries.

•They are **variable in size** and **shape** depending on the **site of origin** and the **causes of their development.**

•An **area of attachment** to the underlying vessel or heart wall frequently firmest at the **site of origin is characteristic of all thrombi**.

Arterial or Cardiac Thrombi

▪They usually begin at a site of **endothelial injury** or **turbulence** (atherosclerotic plaques or other forms of injury as vasculitis or trauma).

▪They tend to grow in a **retrograde direction** from the point of attachment.

▪They are **firmly attached** to the injured endothelium.

▪They are **pale** and composed of platelets, fibrin, RBCs, & leucocytes.

Venous Thrombi

▪They characteristically occur in sites of **stasis.**

▪They extend in the **direction of blood flow**, that is toward the heart.

▪The propagating tail **may not be well attached** and is prone to fragment, creating an embolus (to the lung).

▪They are either of **mixed or red type** more RBCs due to sluggish blood flow.

Venous Thrombosis

Phlebothrombosis

It commonly occurs in veins of lower limbs following operations, congestive heart failure, delivery, and severe injury due to:

- **Slowing of circulation** as a result of lack of muscular activity ***(stasis).***
- **Damage to the intima by pressure** on calf muscles in recumbency ***(endothelial injury& change in blood flow).***
- **Increased number and adhesiveness of the platelets** ***(hypercoagulability).***

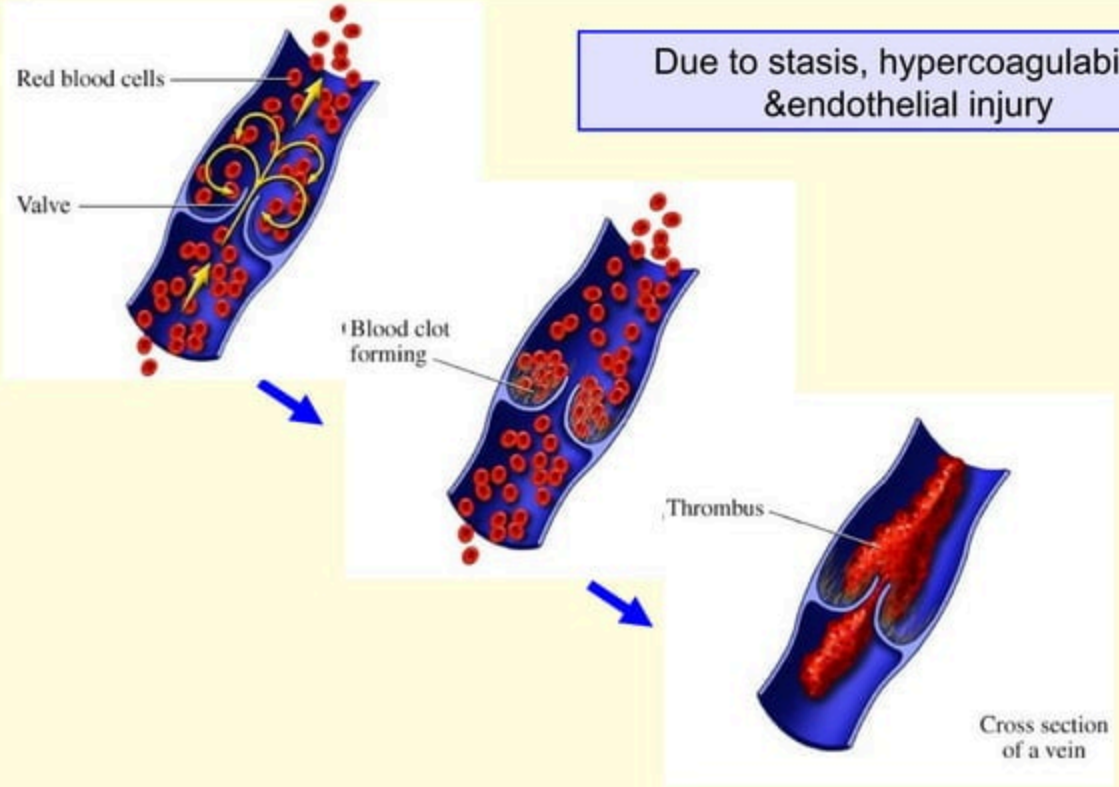
Thrombophlebitis

It results from damage of endothelium due to **inflammation of the vein**, either **bacterial or nonbacterial:**

- **Septic** or **bacterial thrombophlebitis** The thrombus is invaded by microorganisms from the vessel wall, then become fragmented and circulate in blood steam as septic emboli to form pyaemic abscesses wherever they settle.
- **Nonseptic (nonbacterial)** thrombophlebitis which is induced by ionizing radiation or chemicals.

Venous Thrombosis

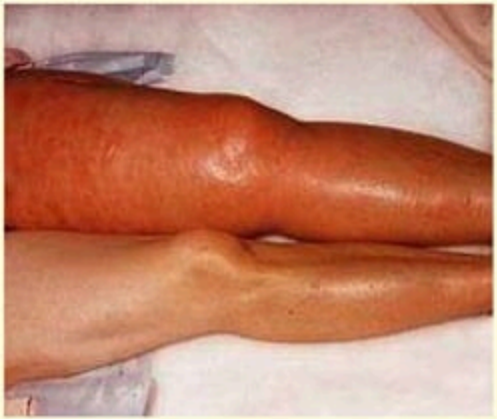
Due to stasis, hypercoagulability &endothelial injury



Venous Thrombosis

3.Hypercoagulability: It is any alteration of the coagulation pathways that predispose to thrombosis.

Swollen, painful, dusky red left lower limb



A case of deep venous thrombosis (DVT) in a patient suffering from systemic lupus erythematosus

Migratory Thrombophlebitis (Trousseau's Syndrome)

Disseminated cancers or certain types of malignancy as ***pancreatic carcinoma*** are sometimes associated with **repeated attacks of multiple venous thrombosis at different and changing sites due to** the procoagulant factors formed by cancer cells. This is referred to as **migratory thrombophlebitis or Trousseau's syndrome.**

Capillary Thrombosis

It is formed mainly of **fused RBCs** and are seen in some types of **vasculitis** and in disseminated intravascular coagulopathy **(DIC).**

Disseminated Intravascular Coagulopathy

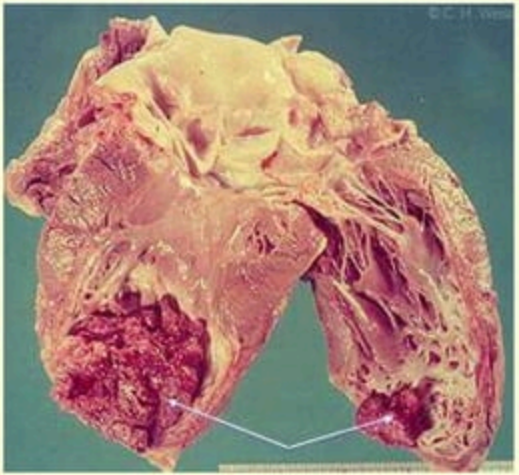
A variety of disorders ranging from obstetric complications to advanced malignancy may be complicated by DIC, **the sudden onset of widespread fibrin thrombi in the microcirculation.**

With the development of the multiple thrombi, there is rapid concurrent **consumption of platelets & coagulation proteins** (consumption coagulopathy); at the same time the **fibrinolytic mechanisms are activated**, and as a result an **initially thrombotic disorder can evolve into a serious bleeding disorder.**

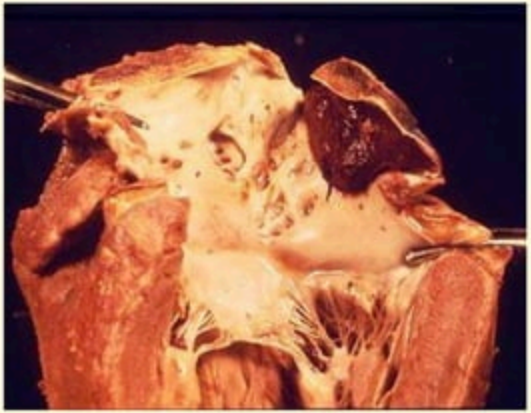
Thrombosis

Sites of Thrombosis

in heart (atria , ventricles & on valves); in arteries ; in veins ; and in capillaries.



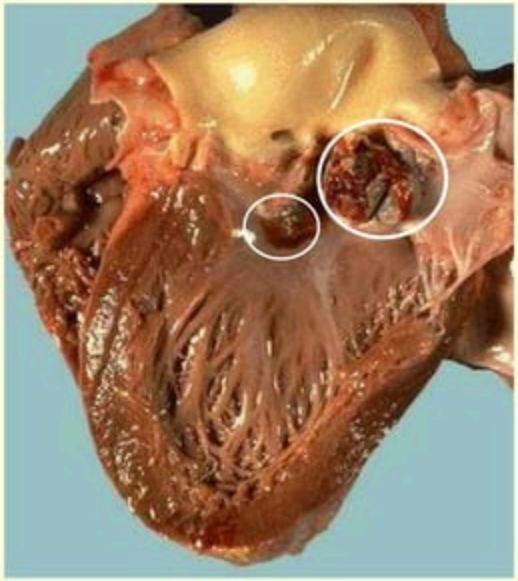
Large mural thrombus on top of myocardial infarction

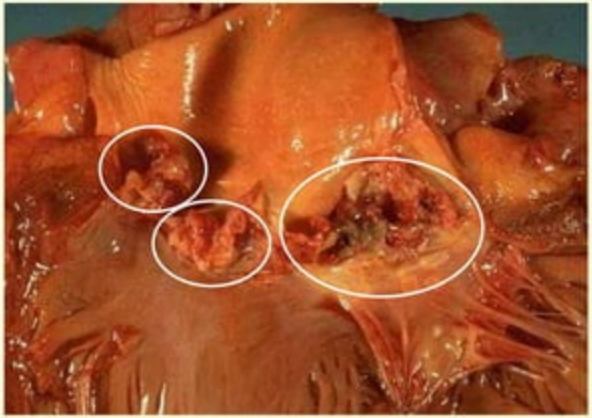


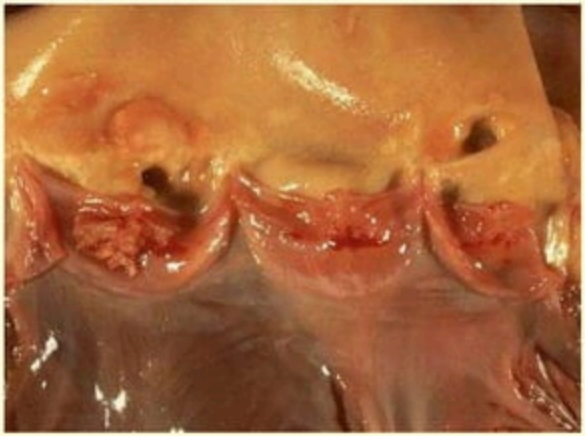
Left atrial mural thrombus in a case of rheumatic mitral stenosis

Sites of Thrombosis

Aortic **Valve**
Thrombi=vegetation





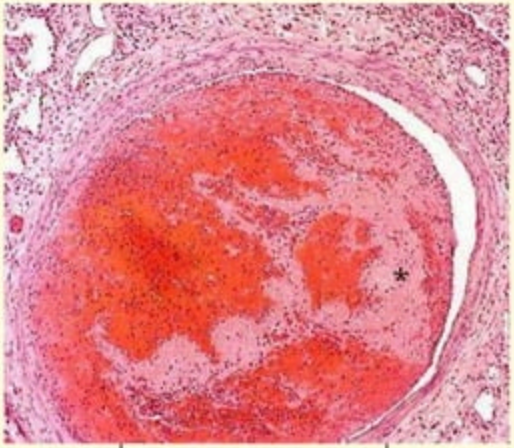


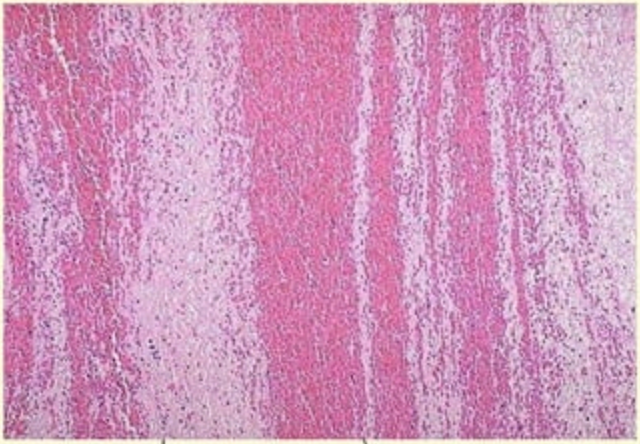
Sites of Thrombosis

Multiple thrombi on atheromatous patches in aorta

The Microscopic Picture of a Thrombus

Apparent laminations called **lines of Zahn** are seen formed of **pale layers** of **platelets and fibrin** that alternate with **darker layers** containing **more red cells**.



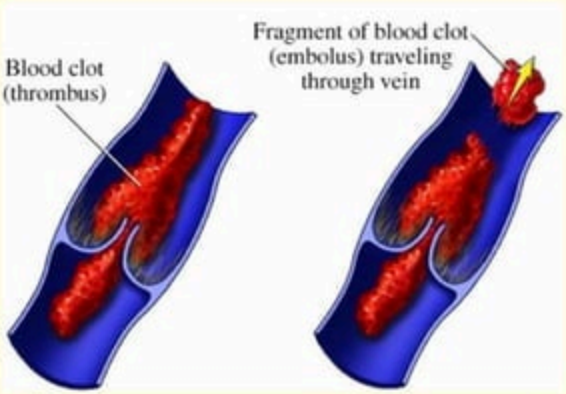


Fate of the Thrombus

If the patient survives the immediate effects of a thrombotic vascular obstruction, thrombi undergo some combination of the following **four events**

1.Propagation: the thrombus may accumulate more platelets and fibrin eventually **obstructing** other critical vessel.

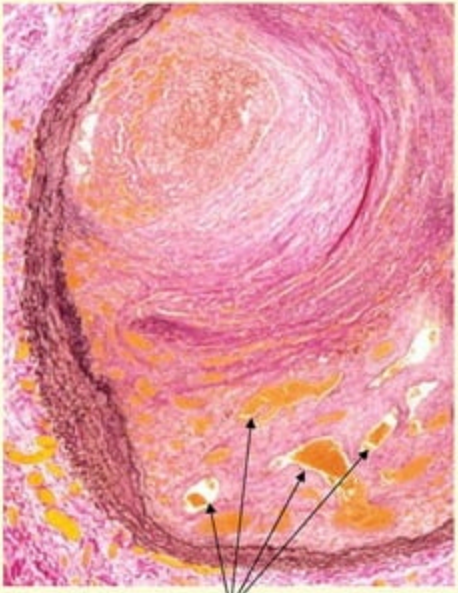
2.Dissolution: Thrombi may be **removed** by the fibrinolytic activity.



3.Embolization: Thrombi may dislodge as **thrombotic emboli.**

Fate of the Thrombus

4.Organization and Recanalization:
Thrombi may induce inflammation and fibrosis (organization) and may eventually **recanalize.**



Organization &Recanalization
(multiple capillary channels)

Questions to be answered after studying

Give Reasons for the Following Statements:

- Traveling in an airplane for a **long period** of time predisposes to **deep venous thrombosis.**
- **Blushing of face** after **exercising** or **being feverish.**
- **Recurrent attacks of deep venous thrombosis** in a patient suffering from **pancreatic carcinoma**.
- Presence of **vegetations** on **mitral valve** and the **posterior wall of left atrium in rheumatic mitral stenosis.**
- **Atherosclerosis** can be complicated by **thrombosis.**
- **Myocardial infarction** can be complicated by **mural thrombosis.**
- Presence of **left atrial thrombosis** in **atrial fibrillation**.
- Serious (fatal) **bleeding disorder** can occur in **disseminated intravascular coagulopathy.**
- **Aortic aneurysm** (localized dilatation) can be complicated by **thrombosis.**
- **Prolonged immobilization** may predispose to **thrombosis**.
- **Nutmeg appearance of liver** in **right side heart failure**.
- Presence of **haemosiderin laden macrophage** in alveoli in **left side heart failure**.