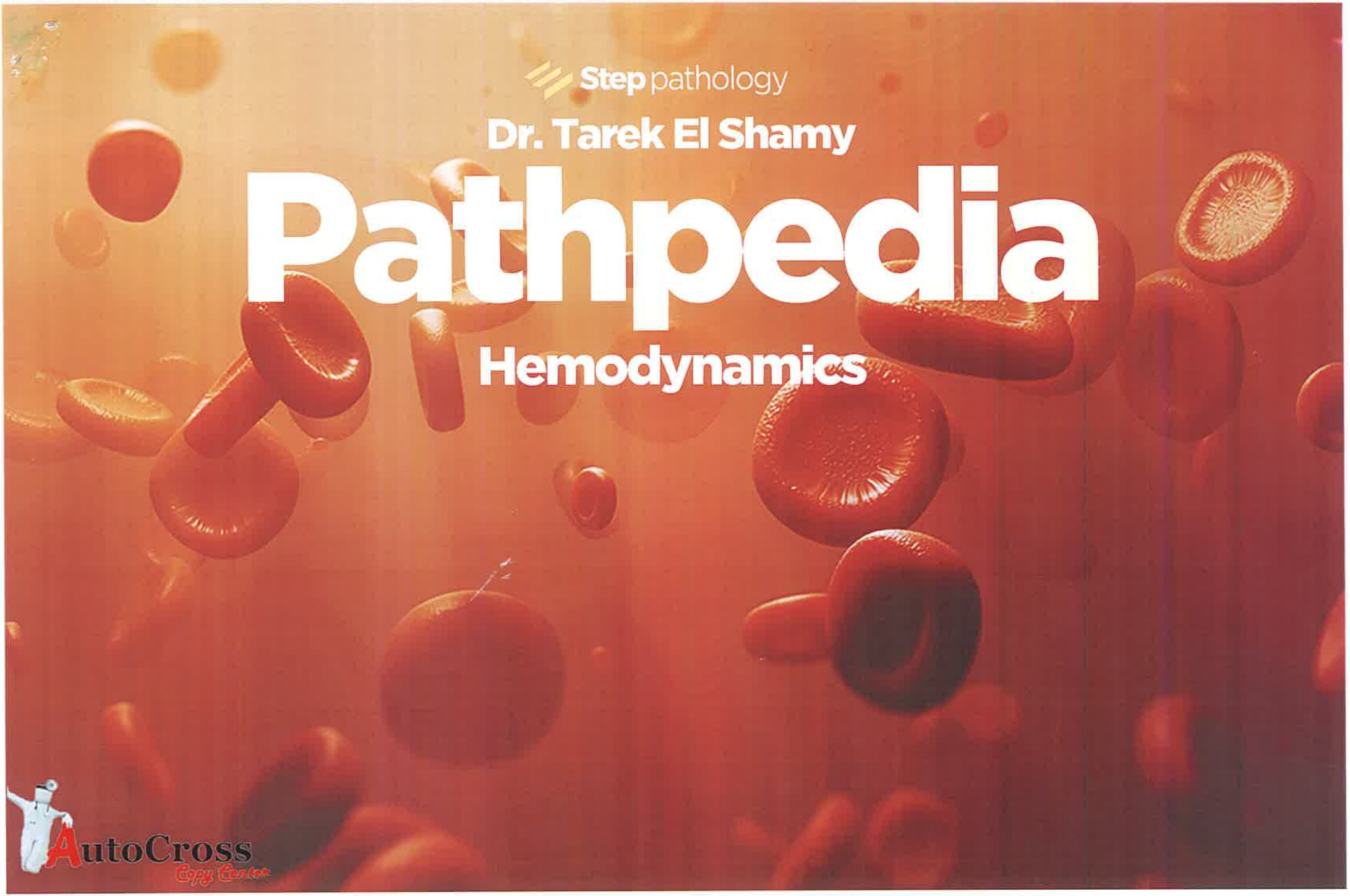


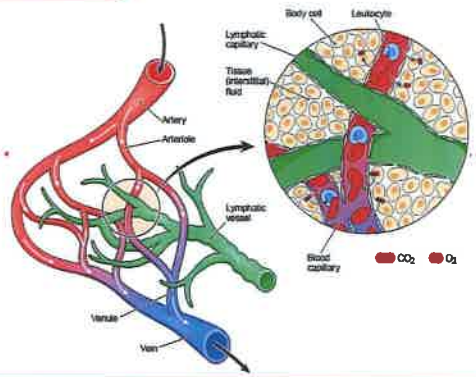
For 1st year - 2021 Edition

Hemodynamic disorders

- **Edema:** Increase fluid in the interstitial tissue spaces
- **Hydrothorax:** (pleural effusion): collection of fluid in the pleural cavity.
- **Hydropericardium:** (pericardial effusion): collection of fluid in the pericardial sac.
- **Hydroperitoneum:** (ascites): collection of fluid in the peritoneal cavity.
- **Anasarca:** severe generalized edema with marked accumulation of fluid in Subcutaneous tissue, viscera & serous cavities

Factors regulating movement of fluid between intra & extra vascular compartments

- The hydrostatic pressure of capillary which tends to expel fluid into the interstitial tissues
- The osmotic pressure of plasma which tends to retain fluid within the intra-vascular compartment
- Lymphatic tissue → remove the excess amount of fluid by returning it to the circulation via the thoracic duct.



	Trasudate	Exudate
	Associated with hemodynamic derangements	Associated with inflammation
1) Protein content	<1 gm%	>4 gm%
2) Clotting	Does not clot	May clot due to presence of fibrinogen
3) Specific gravity	<1012	>1020
4) Cell	Few "or" absent	Numerous & their type depend on the type of inflammation

Causes of edema

A) ↑ capillary hydrostatic pressure:

» Local due to impaired venous outflow → deep venous thrombosis

» Generalized, due to Congestive HF [cardiac edema]

B) ↑ Capillary permeability: due to (inflammation - allergic condition [cardiac edema])

C) ↓ Colloidal OP of plasma [hypo proteinemia]

» Excessive loss of albumin in protein losing glomerulopathies [nephrotic edema]

» ↓ synthesis of albumin → in liver cirrhosis [hepatic edema] & malnutrition [nutritional edema]

D) Na & H2O retention: due to acute reduction in renal function [nephritic edema see in acute & rapidly progressive glomerulonephritis]

E) Lymphatic obstruction [lymphedema]

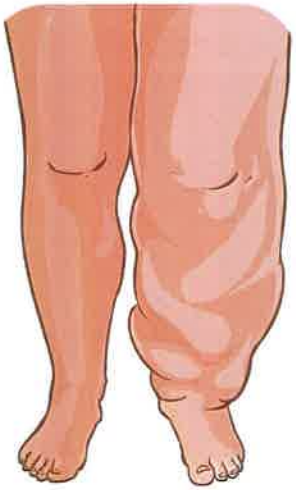
» Inflammation as in filariasis

» Obstruction of lymphatics by cancer cell → e.g.: peau d'orange in cancer breast resulting from obstruction of the superfacial lymphatics of the breast

» Surgical removal of LNs → e.g.: edema of arm following radical mastectomy

» Post-irradiation destruction of lymphatics → e.g.: edema of arm following irradiation of breast cancer

- **N.B:** Markedly edematous subcutaneous tissue may pit under pressure (Pitting edema)
- Lymphatic edema is associated with over growth of connective tissue the edematous area is firm {non pitting edema}



Type of edema

Localized edema

- **DVT in lower limb:** edema of affected leg due to localized ↑ intravascular hydrostatic pressure
- **Lymphatic obstruction.**
- **Inflammatory edema:**
  - » ↑ Vascular permeability → flow of protein into the intersitium → ↑ osmotic pressure of intersitium → retention of fluid
  - » ↑ vasodilatation of capillary → ↑ hydrostatic pressure ↑ blood flow in arterioles [active hyperemia]

Generalized edema

Renal edema:

Nephritic edema

- Seen in acute glomerulonephritis & rapidly progressive glomerulonephritis
- Due to inflammation of glomerular basement membrane → Na & H2O retention (contributory factor)
- <1 gm protein in urine
- Mild edema: (proteinuria, Haematuria and hypertension)

Nephrotic edema

- Nephrotic syndrome due to damage of glomerular basement membrane
- More severe edema:
- Heavy proteinuria → Hypoproteinemia → ↓ Plasma osmotic pressure → ↑ Movement of fluid into interstitial tissue → ↓ Blood volume → ↓ cardiac output → ↓ renal perfusion → Na & H2O retention → Further escape of fluid into tissue → More ↓ blood volume

Cardiac edema (as in CHF):

- Generalized chronic venous congestion → ↑ capillary hydrostatic pressure → ↑ transudation → edema
- ↓ cardiac output → ↓ arterial blood volume

Kidney

- ↓ renal blood flow → ↑ renin-angiotensin aldosterone
- ↑ Renal Na reabsorption → ↑ H2O reabsorption → Na & H2O retention

Post pituitary

- ↑ ADH → ↑ renal H2o reabsorption → H2O retention only

→ both → ↑ plasma volume → ↑ Transudation → Edema

Hepatic edema :

- As in liver cirrhosis → ↓ plasma osmotic pressure

Nutritional edema :

- In malnutrition → ↓ plasma osmotic pressure

Clinical effect of edema

Pulmonary edema:

- Interfering with normal ventilation
- Predisposing to infection

Brain edema

Death due to:

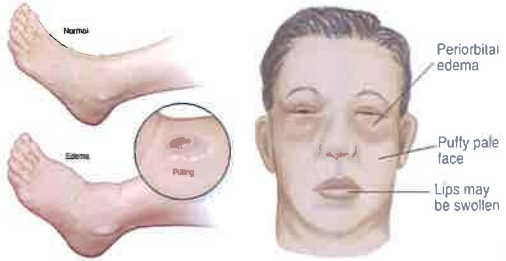
- Brain herniation
- Compression of vascular supply of the brain stem

Subcutaneous edema:

- Impair wound healing
- Impair clearance of infection

The prominent sites

- In the hydrostatic pressure is highest → influenced by gravity → legs & scrotum **(cardiac)**
- In eye lids & face **(nephritic)**
- In all part of body but early in site of loose CT → eye lid "periorbital edema" **(nephrotic)**

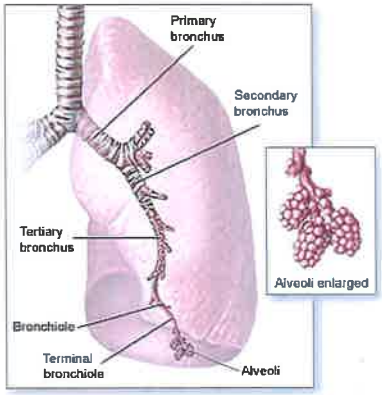


Pulmonary edema

Mainly caused by **left ventricular** failure but may also be caused by:

- **Hypersensitivity reactions**
- **Pulmonary infection**
- **Adult respiratory distress syndrome**
- **Respiratory failure**

- **The lung is heavy & the cut surface oozes:**
  A frothy blood tinged fluid → (air, edema fluid and blood)



Hyperemia & Congestion

Hyperemia

- Increased blood flow in tissue due to: Vasodilatation of arterioles → ↑ blood in arterioles & capillary
- It is active process
- Tissue appear (red) due to ↑ O2 blood

Cause:

- **Physiological**
  - » Exercise → hyperemia in skeletal & cardiac muscle
  - » Digestion → hyperemia in splanchic area
- **Pathological:** Acute inflammation

Congestion

- Increased blood in a tissue due to impaired venous return → ↑ blood in vein & capillaries
- It is passive process
- Tissue appear (blue - red) : (cyanosed) due to ↓ O2 in blood

Type & causes of congestion

1) Local venous congestion

- Impaired of venous return due to:
- Obstruction of vein by twisting
- Venous thrombus
- Pressure on vein by tumor
- Constriction of vein by fibrosis

2) Pulmonary venous congestion

- ↑ Blood in pulmonary veins & their tributaries in lung due to Mitral stenosis or left sided heart failure may be complicated by pulmonary hypertension → right sided heart failure & systemic venous congestion

3) Systemic venous congestion

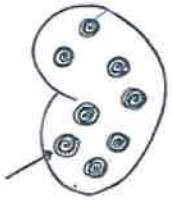
- ↑ Blood in veins all over the body except pulmonary veins

  Cause → right sided heart failure

Pathological changes in chronic venous congestion (CVC)

CVC of spleen

Grossly:



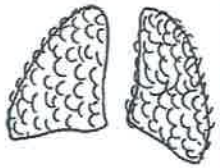
- The spleen is moderately enlarged & firm
- Cut surface is dark red show scattered brownish plagues (Fibrosiderotic "or" Gamma Gandy nodules)

Microscopically:

- The red pulp sinusoids are engorged with blood and their walls are thickened by fibrosis
- The gamma Gandy nodules are composed of:
  - » Fibrous tissue
  - » Entrapping haemosiderin due to lysis of RBCs

CVC of lungs

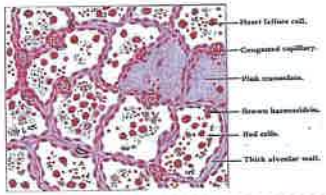
Grossly:

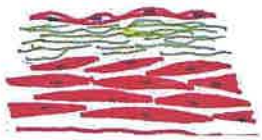


- The lungs are enlarged, heavy, firm, deep red in color
- The cut surface : ooze frothy blood on squeezing

Microscopically:

- The pulmonary venules & alveolar capillaries are engorged with blood
- The alveolar walls are thickened due to edema early & fibrosis late
- The alveolar space contain RBCs & heart failure cells (macrophage laden hemosiderin) & fluid of edema
- The pulmonary veins show medial hypertrophy & intimal fibrosis
- The pulmonary arteries & arterioles show elastosis





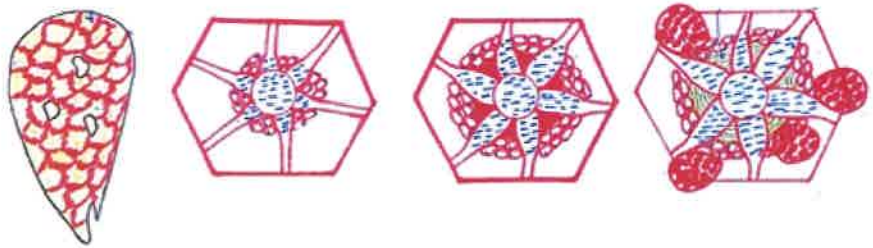
CVC of liver

Grossly:

- The liver is enlarged & firm
- Cut surface show a nutmeg appearance with dark area of congestion alternating with yellow area of fatty change

Microscopically:

- The central veins & the sinusoids are dilated with blood & hepatocytes between the sinusoids show fatty change in central zone
- With advanced condition: the sinusoidal dilation extends peripherally & the hepatocytes in the central zone become necrotic while that in the mid zone show fatty change
- In old cases: regenerative cirrhotic nodules (cardiac cirrhosis)



Clinical effect of CVC

- Cyanosis: blue color of lips due reduced hemoglobin
- Congested pulsating neck veins due to ↑ in venous pressure
- Enlarged tender liver (Rt. Hypochondrium pain)
- Edema of lower limbs: due to ↑ VP & ↑ CP & hypoxia

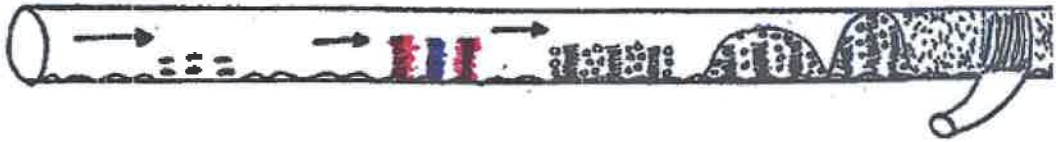
Thrombosis & Clotting

- **Thrombosis:** It is a vital process by which solid mass is formed from blood elements (platelets) within cardiovascular system during life.
- **Clotting:** Transformation of soluble fibrinogen into fibrin outside CVS or after death

Mechanism of thrombus formation

- Platelets: adhere to endothelium ➜ + of endothelium ➜ + of intrinsic coagulation pathway
- Concomitantly (Simultaneously) the release of tissue factors form injured cell ➜ + of extrinsic coagulation pathway ➜ deposition of platelets as the lines of Zahn and the space between their contain fibrin RBCs & leucocytes ➜ **(line of Zahn)** ➜ appear homogenous, hyaline under microscope, basophilic, alternating pale and dark lines

Lines of Zahn



Thrombus	Clot
Formed in CVS during life	Out CVS or after death
Formed in flowing blood	Formed in stagnant blood
Adherent to under lying vessel or heart wall	Not adherent
Firm & friable	Soft & gelatinous
Rough surface	Smooth surface

Virchow's triad

(1) Endothelial injury

- This is important for thrombus formation in the heart & arterial circulation is caused by:
- Atherosclerosis
- Inflammation
- Myocardial infarction
- Trauma

Mechanism: exposure of sub-endothelial collagen, adherence of platelets → release of tissue factor → local depletion to:

- PGI2 that inhibits platelet adhesion
- Plasminogen activators that ↑ fibrinolytic activity

(2) Alteration of blood flow

a) Turbulence:
Over atherosclerotic plagues or at sites of vascular bifurcation

b) Stasis:

- Aneurysms
- Dilated cardiac chambers
- Myocardial infarction
- polycythemia sickle cell anemia
- Varicose veins

(3) Hypercoagulability

a) Genetic cause:
Mutation in factor V gene & prothrombin gene

b) Acquired cause:

- Prolonged bed rest
- Surgery
- Cancer
- Fracture
- Burns

Stasis & turbulence cause thrombus as follow:

- Disrupt laminar flow → bring platelet to adhere to endothelium
- Promote endothelial cell activation → predisposing to local thrombosis & leucocytes adhesion
- Prevent dilution of activated clotting factors by fresh-following blood
- Retard the inflow clotting factors inhibitors & permit the build up of thrombi

Pathogenesis of thrombosis:

- Cardiac failure & trauma → stasis
- Hyper-estrogenic stats [ex: pregnancy] → ↑ hepatic synthesis of coagulation factors & ↓ synthesis of anti thrombin III
- Cancer → release procoagulant tumor products
- Old age → ↑ platelets aggregation & ↓ PGI2
- In SLE → there is release of anti phospholipid antibodies that induce platelets aggregation & (-) PGI2 & protein C synthesis

Morphology of thrombosis:

Pale thrombus:
- Formed In rapidly flowing blood (eg. Arteries)
- From platelets
- It is firm & pale reddish grey

Red thrombus:
- Formed in stagnant blood (eg. adjacent to complete vascular occlusion)
- From RBCs, fibrins WBCs
- Soft, dark red & smooth outer surface
- Undistinguished from blood clot

Mixed thrombi:
- Formed in slowly flowing blood: alternating layers of pale & red thrombi
- Or Vascular anastomosis: red thrombi interrupted by pale thrombi

Sites of thrombosis

Venous thrombosis

1) Phlebo thrombosis
- In superficial veins (eg saphenous system in presence of varicosities)
- Deep veins ex. femoral veins following (Tumors, Bed rest , Puerperal & postpartum states, CHF)
- The thrombus progress in blood flow direction i.e. towards the heart
- Stasis occur proximal to occlusion of vein by thrombus that cause clotting of blood up to level of tributary occludes lumen of vein
- Stasis & clotting propagated proximally by repeated thrombosis & clotting

Thrombophlebitis
- The thrombus result from damage of endothelium by inflammation (Septic – Chemicals)
- Septic thrombi invaded by micro organisms from vessels wall fragmented to **(septic emboli)**

3) Migratory thrombophlebitis (Trousseau's syndrome)
- Recurrent attacks of multiple venous thrombosis of changing sites
- occur in association with various forms of cancer ex: (cancer pancreas) due to release of procoagulant substances by cancer cells

Thrombosis in the heart

1) In dilated Left atrium in Mitral Stenosis:
- Attached to the wall (mural thrombosis), Free in atrial lumen, Plug mitral valve (ball-valve thrombus)

2) On cardiac valves (vegetations)

3) On the endocardium lining ventricle in myocardial infarction (mural thrombus)

Thrombosis of arteries

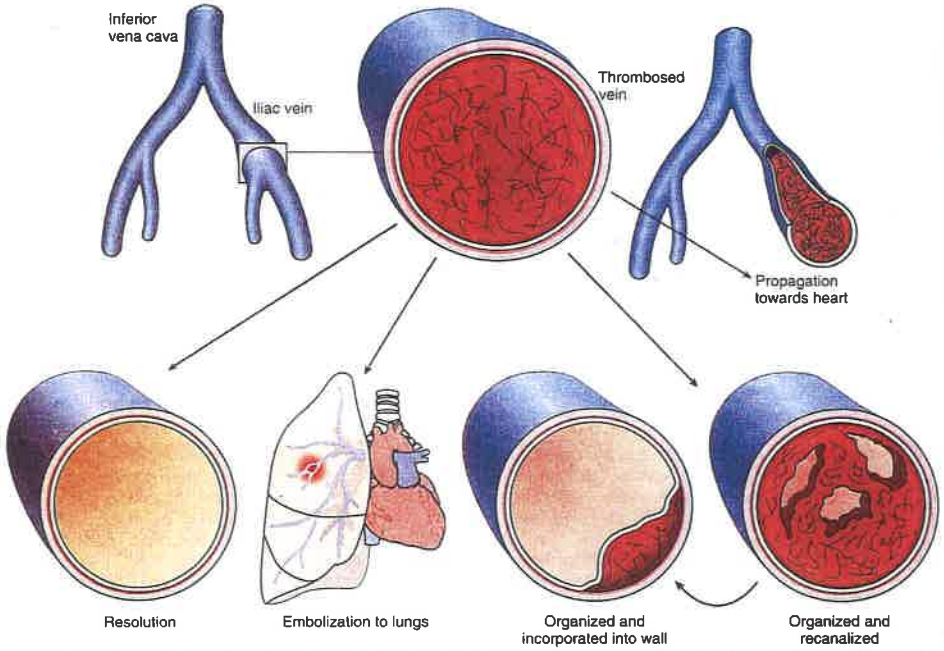
At site of:
- Endothelial injury due to atheroma, turbulence (arterial bifurcation) or stasis (aneurysm)
- In small arteries e.g.:
- Coronary & cerebral → **May occlude lumen → (occluding thrombi)**

Thrombosis of capillaries

- **Develop in:**
- Acute inflammation • Vasculitis • DIC

Fate of the thrombus

- Dissolution by fibrnolytic activity → rapid shrinkage and lysis of recent thrombi
- Organization & recanalization → organization is replacement of thrombus by granulation tissue that is then replaced by fibrosis that can contract and make capillary channels which communicates the blood columns
- Calcification: may be visualized as radio-opaque shadow in X-ray **(Phlebolith)**
- Propagation mainly in venous thrombi towards the heart
- Embolization due to fragmentation of the thrombus



Clinical effect of thrombus

- Obstruction:
  - » Arteries → ischemic necrosis ex: (myocardial infarction – cerebral infarction – gangrene of limb)
  - » Veins → congestion & edema in distal vascular ends
- Embolization:
  - » Infarcts
  - » Pyemic abscesses - (septic emboli)
  - » Massive pulmonary embolism

Disseminated intravascular coagulation (DIC)

Causes:

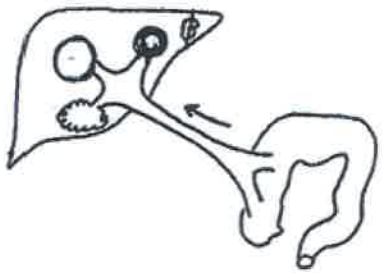
- » Obstetric complications
- » Advanced malignancy

- It is sudden onset of wide spread fibrin thrombi in the micro circulation → diffuse circulatory ischemia → brain, lungs, heart & kidneys
- There is a rapid consumption of platelets & coagulation proteins with the increase of fibrinolytic mechanism → serious bleeding

Embolism

- Detached intravascular solid, liquid, or gaseous mass carried by blood from its point to a distant point where it get lodged in a blood vessels which is too small to permit its further passage.

Tumor emboli



Parasitic emboli

Fat emboli

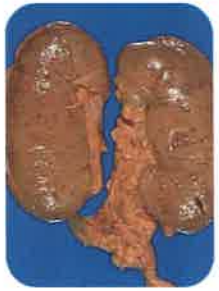
Air emboli

Types & effects of emboli

Thrombotic emboli | Air emboli | Amniotic fluid embolism | Fat emboli | Parasitic emboli | Tumor emboli

Thrombotic emboli

- 99% of emboli & derived from fragmentation of thrombus



Effects depend on:

- Septic or bland (aseptic)
- Size
- Organ embolized

Types:

- **Septic emboli** → pyemic abscesses
- **Aseptic emboli** that may be:
  - » Large emboli from venous thrombus impacts in **main trunk of the pulmonary artery**, across its bifurcation or major branch → sudden death due to acute right ventricular failure → if sudden obstruction ≥ 60% of its out flow in left ventricular cardiac output & cardiogenic shock **(massive pulmonary embolism)**
  - » Smaller emboli derived from venous thrombus or from Right side of the heart impact in small branches of pulmonary Artery → lung infarction in case of chronic venous congestion
- N.B.: Most pulmonary emboli 60-80% small, silent → go organization & fibrosis.

Air emboli

- **Air enter circulation through:**
  - » Tubal insufflations
  - » Following chest wall injury
  - » Wounds involving the large veins of neck
- Large amount >100 ml mixed with blood will form frothy masses can obstruct the right ventricle or pulmonary artery → death from acute right sided heart failure

Decompression sickness (caissons):

- Normally air is breathed at high pressure as deep sea → ↑ gas dissolved in blood & tissue
- If the diver ascends too rapidly → gases come out of solution → form bubbles in the blood (gas emboli make many clinical effect) involving:
  - » Muscle
  - » Joint
  - » CNS
  - » CVS
  - » Respiratory system

Amniotic fluid embolism

- Rare maternal complication of child birth but often fatal
- Due to introduction of amniotic fluid into maternal circulation via tears in the placental membrane & uterine veins
- Amniotic fluid produce DIC due to its high thromboplastic activity
- DIC result in marked hypofibrinogenemia (consumptive coagulopathy) → fatal uterine hemorrhage

Parasitic emboli

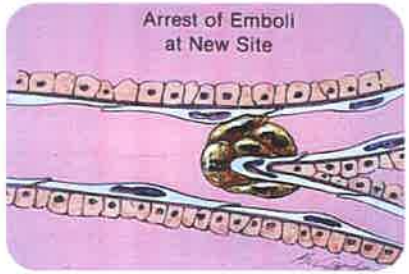
- Ova of schistosoma mansoni in Large intestine enter portal circulation → liver → schistosomal hepatic fibrosis
- Larva of eshicnococcus granulosus in large intestine → portal circulation → hydatid cyst
- Vegetative form of entameba histolytica in Large intestine to liver → ameobic liver abscess

Fat embolism

- Consisting of fat globules with may enter circulation from:
  - » Bone marrow following fracture of the long bone
  - » From the subcutaneous tissue following trauma
- **Most cases have no symptoms but rare patients (1%) may develop:**
  - » Pulmonary insufficiently with tachypnea, dyspnea & tachycardia
  - » Neurological symptoms: restlessness
  - » Anemia & thrombocytopenia
- These symptoms appear (1-3) day after injury
- Fatal in 10% of cases

Tumor emboli

- Composed of malignant cells lead to 2ry metastasis



Ischemia

- Decreased arterial blood supply to apart which may complete or partial

Complete arterial occlusion

Causes:

- Thrombosis or embolism (99%)
- Swelling of an atheroma by hemorrhage
- Arterial spasm (e.g. ergot poisoning & Reynaud's disease)
- Compression of artery by edema, tumor, hernial strangulation
- Twisting of artery (e.g. in testicular torsion, bowel volvulus)

Effect:

- **Nature of blood supply:**
  - » Complete arterial occlusion → ischemic necrosis in organs supplied by end arteries ex: (central retinal, cerebral, coronary, renal, splenic & mesenteric arteries). Present of diseased anastomotic collaterals by (atheroma fibrosis & calcification) cannot supply the ischemic part
  - » Organ with an efficient collateral circulation → resistant relatively the complete ischemia
  - » Organ with dual blood supply ex: [lung (pulmonary & bronchial), liver (portal & hepatic)] →relatively resistant to complete ischemia
- **Oxygen content of blood:** the infarction maybe developed in presence of an efficient collateral circulation in patients with CHF or anemia
- **Susceptibility of tissue to hypoxia:** (eg. neurons & cardiac muscle) → die within 3 & 30 min of arterial occlusion due to hypoxia, while fibroblast may viable for hours after occlusion
- **Rate of development of occlusion:** slowly developing occlusion are less likely to produce infarction due to they provide more time to development collateral pathway ex: collateral coronary circulation

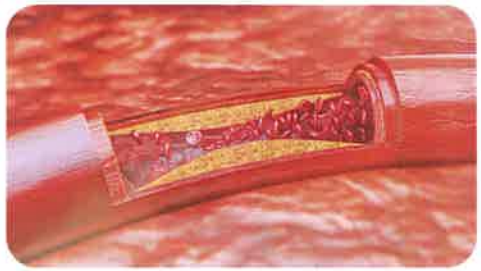
Partial arterial occlusion

Causes:

- Atheroma
- Proliferative change in intima of arteries as: (hypertension & obliterative endarteritis)

Effect:

- Atrophy & loss of parenchymatous cells accompanied by overgrowth of fibrous tissue (heart & kidney in atherosclerosis)
- Intermittent pain due to failure of removal waste products from ischemic tissue ex: (angina pectoris in atherosclerosis of coronaries & intermittent claudication in atherosclerosis of lower limb arteries)
- Infarction in patient with sever anemia or CHF due to ↓ O2 content



Infarction

- It is an area of ischemic necrosis resulting from occlusion of arterial blood supply or less commonly the venous drainage in organ with a single venous out flow (testis & ovary)

Morphology

Red infarcts (hemorrhagic):

- Tissue with dual circulation (lung)
- Previously congested tissue
- Venous occlusion → ovarian torsion
- Loose tissue allow to collect of blood in infarcted area → small intestine & lung

Pale infarcts (white/anemic):

- Occur in arterial occlusion
- Solid organs → heart, spleen kidney
- Limits hemorrhage from necrotic capillaries in the infarcted area

Maybe septic or aseptic

- Septic infarction develop as result of either:
  - » Impaction of septic emboli from septic vegetation or thrombus
  - » Infection of infarcted tissue change to abscess

Infarcts are often wedge shaped

- Bass of it direct towards the surface of organ & its apex towards hilum, If the base serosal surface there is covered by fibrinous inflammation

Infarcts are surrounded by:

- Rim of hyperemia (congestion) due to acute inflammation at margin → induced by necrotic tissue with congestion & infiltration of neutrophils & Macrophage → gradual removal of infarcted tissue and replaced by granulation tissue

The necrosis of infarct is a coagulative type in all infarcts except:

- CNS, which the necrosis is liquefactive → because the necrotic area undergoes rapid liquefaction & eventually appear → cavity filled with clear fluid & surrounded by layer of gliosis from astrocytes

Clinical significance of infarction

Myocardial infarction may:

- Death due to arrhythmia, acute LF & cardiogenic shock
- CHF following replacement of infarct by fibrous tissue

Cerebral infarction:

- Hemiplegia due to destruction of the pyramidal tract

Infarction of the lung

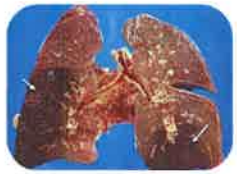
- Hemopytsis → hemorrhage into alveolar spaces with expectoration of blood
- Chest pain & friction rub

Infarction of kidney

- Hematuria
- Senile kidney (atherosclerotic kidney) → if infarction is repeated over long period

Infarction of intestine

- Acute intestinal obstruction
- Severe toxemia → (gangrene)



Hemorrhage

- It is escape the blood outside the CVS

Causes

Rupture of an artery or vein:

- Trauma
- Atherosclerosis, aneurysm, varicose veins
- Inflammation
- Neoplasia

Capillary bleeding:

- Due to Minor trauma in:
  - » CVC
  - » Hemorrhagic disease

Clinical aspect depend on:

- Volume of blood loss
- Rate of blood loss
- Site of bleeding
  - » Rapid loss >20% of blood volume → hypovolemic shock, while slow loss have little effect
  - » Also relatively mild bleeding in brain may death

Classification

According to site:

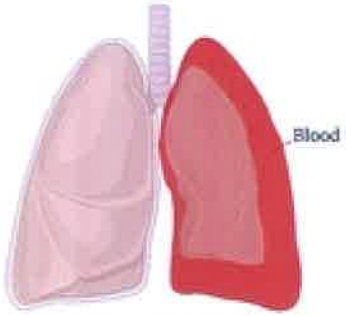
- External → in which blood escape outside of the body
- Internal → in which blood accumulates within a tissue or in body cavities

According to size:

- Petichiae → pinpoint flat round red spot under skin caused by intradermal hemorrhage, also occur in MMS & serosal surfaces
- Purpura → bleeding into the surface of skin > 3mm, its color varies with duration of lesions early purpura is red & then darker & then purple then brown yellow as it fodes
- Bruise (Eschymoses) → it is discoloration of skin consisting of large irregularly formed haemorrhagic area >1 cm
- Hematoma → is a large blood accumulation in soft tissue ex: mediastinum "or" retro peritoneum

Blood accumulation in body cavity:

- Hemothorax (pelura)
- Hemopericardium (pericardium)
- Hemoperitoneum
- Hemoarthrosis (joints)



Hemothorax

Shock

- It means failure of circulatory system to maintain adequate perfusion & oxygenation of vital organs due to sudden sever reduction of COP or circulatory blood volume

	Causes (clinical examples)	Mechanisms
1) Cardiogenic	• Myocardial infarction • Ventricular rupture • Arrhythmia • Cardiac tamponed • Pulmonary embolism	• Failure of myocardial pump resulting from intrinsic myocardial damage • Extrinsic pressure • Obstruction of outflow
2) Hypovolemic	• Hemorrhage • Fluid loss (vomiting & diarrhea & burns)	• Inadequate blood or plasma volume
3) Septic	• Overwhelming microbial infections • Endotoxin shock • Gram positive septicemia	• Peripheral VD& pooling of blood • Endothelial activation / injury • Leucocyte – induced damage • DIC
4) Anaphylactic	• Hypersensitivity response	• Generalized vasodilatation & ↑ vascular permeability by an IgE-mediated hypersensitivity response
5) Neurogenic	• Spinal cord injury • Anesthetic accident	• Loss of vascular tone & peripheral pooling of blood