**Thrombosis**

Thrombosis is defined as the formation of a solid or semisolid mass from the constituents of the blood within the vascular system during life.

Pathogenesis: thrombus formed due to the following three factors are called **Virchow’s triad**:

**A: Endothelial injury**

1. Mechanical injury: e.g rupture, torsion
2. Degeneration of endothelial cell as in atherosclerosis and aneurysm
3. Inflammation: phlebitis and arteritis

**B: Changes in blood flow: Stasis or turbulence of blood flow**

1. Arrhythmia of heart and heart failure
2. Prosthetic heart valve
3. Incompetent vascular valves (varicose vein)

**C: Changes in composition of blood:**

1. Quantitative and qualitative changes in the function platelets: eg after surgery or radiation
2. Polycythemia

**Types of thrombi:**

1. Pale thrombus: composed mainly of platelets and fibrin strands. This type is seen in arteries
2. Red thrombus: composed of platelets, fibrin strands and red blood cells. this type seen in venous thrombosis
3. According to the **presence** or **absence of pyogenic bacteria**, thrombi can be classified to **septic** and **aseptic** respectively.

**Fates (outcome) of a thrombus: thrombus can have one of the following fates:**

**A: Propagation**:

The thrombus may accumulate more platelets and fibrin & propagate to cause vessel obstruction.

**B: Embolization**:

The thrombus may dislodge and travel to other sites in the vasculature. Such a traveling thrombus is called thromboembolus. An embolus may obstruct a vessel. The obstruction leads to the death of the tissue supplied by the blood vessel. Death of a tissue due to a decreased blood supply or drainage is called infarction. Therefore, an embolus can eventually lead to an infarction of an organ. E.g pulmonary infarction can be caused by a thromboembolus from deep venous thrombosis.

**C: Dissolution:** The thrombus may be removed by fibrinolytic activity.

**D: Organization and recanalization**

**Organization** refers to the ingrowth of endothelial cells, smooth muscle cells, and fibroblasts into the fibrin-rich thrombus. Organization is accompanied by the formation of capillary channels across the thrombus, re-establishing lumen continuity to some extent. This is known as recanalization. The recanalization eventually converts the thrombus into a vasscularized mass of tissue which is later on incorporated as a subendothelial swelling of the vessel wall.

**Deep venous thrombosis (DVT):**

* Usually starts in deep veins within the calf muscles.
* Patient present with local pain, heat & edema
* Has higher incidence in middle aged & elderly people, after surgery or any patient have predisposing factors for thrombus formation
* May dislodge and cause pulmonary thromboembolism and infarction.

**Embolism**

Definition: - An embolus is a detached intravascular solid, liquid or gaseous mass that is carried by blood to sites distant from its point of origin. After traveling via the blood, the embolus can obstruct a vessel.

Causes of embolism:

An embolus can arise from:

o **Thrombus → thromboembolism**

o Platelets aggregates

o Fragment of material from ulcerating atheromatous plaque

o Fragment of a tumor

o Fat globules

o air

o Amniotic fluid in pregnant women

o Infected foreign material

**Thromboembolism:**

1. **Pulmonary thromboembolism (PTE) :** PTE is refers to the impaction of an embolus in the pulmonary arteries & their branches. Such an embolus is derived from a thrombus **in the systemic veins or the right side of the heart**.
   1. If the thrombus is large, it may block the outflow tract of the right ventricle or the bifurcation of the main pulumonary trunk (saddle embolus) or both of its branches, causing sudden death and right side heart failure (cor pulmonale).
   2. If the embolus is very small (as in 60-80% of the cases), the pulmonary emboli will be clinically silent.
   3. Embolic obstruction of medium sized arteries manifests as pulmonary haemorrhage but usually does not cause infarction because of dual blood inflow to the area from the bronchial circulation.
   4. If the cardiorespiratory condition of the patient is poor (i.e., if the patient previously had cardiac or pulmonary disease), then obstruction of a medium sized pulmonary artery by a medium-sized embolus can lead to pulmonary infarction.
   5. Recurrent thromboembolism can lead to pulmonary hypertension in the long run.
2. **Systemic thromboembolism:** Systemic emboli arise from the left side of the heart due to prosthetic heart valve, rheumatic heart valve, arrhythmia

Systemic thrombi may impact in:

1. Lower extremities (which is the commonest)
2. Brain (common and fatal)
3. Mesenteric vessels (intestinal)
4. Spleen
5. upper extremities (least one)

**Infarction**

**Infract:** is an ischemic necrosis caused by occlusion of either the arterial supply or venous drainage in a particular tissue

Causes:

1. Nearly 99% of all infarcts result from thrombotic or embolic events.
2. Local vasospasm
3. External compression (by pressure) or internal compression (eg by tumor) of the vessels.
4. Rupture or torsion of blood vessel wall

Infarcts are classified (types) depending on:

A) The basis of their color into:

1. Hemorrhagic (Red) infarcts due to venous occlusion
2. Anemic (White) infarcts due to arterial occlusion

B) The presence or absence of microbial infection into:

1. Septic infarcts
2. Bland infarcts

The development & the size of an infarct are determined by the following factors:

A. The nature of the vascular supply

B. The rate of development of occlusion

C. Suceptibility of the tissue for hypoxia

**Morphological changes of the infarcted area:**

**Gross:** All infarcts are wedge-shaped with the occluded vessel at the apex and the periphery of the organ forming the base of the wedge. The infarction will induce inflammation in the tissue surrounding the area of infarction. Following inflammation, some of the infarcts may show recovery, however, most are ultimately replaced with scars except in the brain.

**Microscopy:**

The dominant histologic feature of infarction is ischemic coagulative necrosis. The brain is an exception to this generalization, where liquifactive necrosis is common.

Clinical examples of infarction:

**A. Myocardial infarction**

ª Usually results from occlusive thrombosis supervening on ulcerating atheroma of a major coronary artery.

ª Is a white infarct.

ª Can cause sudden death, cardiac failure, etc...

**B. Cerebral infarcts**

ª May appear as pale or hemorrhagic

ª A fatal increase in intracranial pressure may occur due to swelling of large cerebral infarction, as recent infarcts are raised above the surface since hypoxic cells lack the ability to maintain ionic gradients & they absorb water & swell.

ª Is one type of cerebrovascular accidents (CVA) or stroke which has various clinical manifestations.

**C. Lung infarcts**

ª Are typically dark red & conical (wedge-shaped).

ª Can cause chest pain, hemoptysis, etc…

**Disseminated Intravascular Coagulation (DIC)**

Definition: -DIC is an acute or chronic thrombohemorrhagic disorder occurring as a result of progressive activation of coagulation pathway beyond physiologic set point secondary to a variety of diseases resulting in failure of all components of hemostasis. Hence the other term for DIC is **consumption coagulopathy.**

**Etiology and Pathogenesis**

**DIC is not a primary disease**: It is a coagulopathy that occurs in the course of variety of clinical conditions. DIC follows massive or prolonged release of soluble tissue factors & /or endothelial-derived thromboplastin into the circulation which lead to activation of coagulation system

Therefore, DIC results from pathologic activation of the extrinsic &/or intrinsic pathways of coagulation or impairment of clot inhibiting influences by different causes. Two major mechanisms activating the coagulation pathway to cause DIC are:

(1) Release of tissue factor or thromboplastic substance into the circulation

(2) Widespread injury to the endothelial cells.

**Tissue thromboplastin substance may be derived from a variety of sources such as:**

**A: Massive trauma**, severe burns & extensive surgery. The major mechanism of DIC is believed to be autoinfusion of thromboplastin from the tissues.

**B: Obstetric conditions** in which thromboplastin derived from the placenta, dead retained fetus,

**C: Cancers such as acute** leukaemia, adenocarcinoma

**D: Gram negative sepsis** (an important cause of DIC) in which bacterial endtoxins releasing tissue factor from monocytes.

**Endothelial injury: Widespread endothelial injury may result from: -**

1. Deposition of antigen-antibody complexes as it occurs in systemic lupus erythematosus
2. burns
3. Hypoxia, acidosis
4. shock

**Shock**

Definition: **Shock** is a state in which there is failure of the circulatory system to maintain adequate cellular perfusion resulting in widespread reduction in delivery of oxygen & other nutrients to tissues. In shock, the mean arterial pressure is less than 60 mmHg or the systolic blood pressure is less than 90 mmHg.

**Classification of shock**

Shock can be divided into:

**A. Hypovolemic shock**

**B. Cardiogenic shock**

**C. Distributive shock**

**A. Hypovolemic shock**

**Definition: This is shock caused by reduced blood volume. Reduction in circulating blood volume results in the reduction of the preload which leads to inadequate left ventricular filling, reflected as decreased left & right ventricular end diastolic volume and pressure**. **Causes of hypovolemic shock include:**

**a) Haemorrhage b) Diarrhea & vomiting c) Burns d) Trauma**

Cardiogenic shock

Definition: This is shock that results from severe depression of cardiac performance. It primarily results from pump failure [myocardial failure].

Causes of cardiogenic shock can be divided into:

1. Myopathic:
2. Acute myocardial infraction. Usually shock occurs in this conditioin if ≥ 40% of the left ventricular mass & more on the right ventricle is involved by infarction.
3. Mycocarditis
4. Dilated cardiomyopathy/hypertrophic cardiomyopathy
5. Mechanical

a) Left ventricle outflow obstruction E.g.Aortic stenosis, hypertrophic cardiomyopathy

b) Reduction in forward cardiac output E.g. Aortic or mitral regurgitation

c) Arrhythmia

d) Pericardial tamponade (gross fluid accumulation in the pericardial space) results in a decreased ventricular diastolic filling → ↓CO

**C. Distributive shock**

Definition: Distributive shock refers to a group of shock subtypes caused by profound peripheral vasodilatation despite normal or high cardiac output.

**Causes of distributive shock**

1) Septic shock – the commonest among the group & clinically very important.

2) Neurogenic shock: Usually occurs in the setting of anaesthetic procedure [cephalo-caudal migration of anaesthetic agent] or spinal cord injury owing to loss of vascular tone & peripheral pooling of blood.

3)Anaphylactic shock : Initiated by generalized IgE – mediated hypersensitivity response, associated with systemic vasodilatation & increased vascular permeability.

4)Endocrine shock - This is a type of shock that typically occurs in adrenal insufficiency.

Stages of shock

Uncorrected shock passes through 3 important stages:

**Stage 1: An initial nonprogressive phase**

It is also called a period of early compensatory period, during which compensatory mechanisms are activated & perfusion of vital organs maintained.

Compensatory mechanisms include:

1. Increase heart rate
2. Peripheral vasoconstriction
3. Renal Na+ and water retention

**Stage 2: Progressive stage (Established shock)**

1. This is characterized by tissue hypoperfusion with onset of worsening circulatory & metabolic imbalances including acidosis.
2. There is a widespread tissue hypoxia.
3. Anaerobic glycolysis results in excessive lactic acid production.
4. Impaired carbohydrate metabolism causes a fall in production of ATP
5. DIC.

**Stage 3. An irreversible stage**

• A sage at which, even if hemodynamic disorders are corrected survival is not possible.