Disturbance of Circulation
Hemodynamic Disorder

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Thrombosis

**Definition:**

- Thrombosis is the formation of solid or semi-solid blood clot within the non-interrupted cardiovascular system during life.
- The blood clot is adherent to the vessel wall.
- The solid or semi-solid blood clot mass is called thrombus, pleural (thrombi).
Causes of thrombosis:

There are three main predisposing factors for thrombus formation *(Virchow’s triad)*:

1. Damage to the endothelial lining of a blood vessel.
2. Relative stasis or turbulence of blood flow.
3. Increased coagulability of blood.

*These predisposing factors are associated with particular conditions or life styles.*
Etiology and Pathogenesis

ENDOTHELIAL INJURY

THROMBOSIS

ABNORMAL BLOOD FLOW

HYPERCOAGULABILITY

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HYPERCOAGULABILITY

- Major surgery / trauma
- Malignancy
- Pregnancy (post-partum)
- Inherited thrombophilia
- Infection and sepsis

CIRCULATORY STASIS

- Immobility
- Venous obstruction (obesity, tumour, pregnancy)
- Varicose veins
- Atrial fibrillation or left ventricular dysfunction
- Congenital abnormalities affecting venous anatomy (e.g., May-Thurner and Paget-Schroetter syndrome)
- Low heart rate (bradycardia) and low blood pressure

VASCULAR DAMAGE

- Thrombophlebitis
- Cellulitis
- Atherosclerosis
- Indwelling catheter / heart valve
- Venepuncture
- Physical trauma, strain or injury
- Microtrauma to vessel wall

BLOOD

VEssel

FLOW
A. VASOCONSTRICION

Endothelium  Basement membrane  Arteriole smooth muscle

Site of injury

Endothelin release causes vasoconstriction

Reflex vasoconstriction

ECM (collagen)
B. PRIMARY HEMOSTASIS

1. Platelet adhesion
2. Shape change
3. Granule release (ADP, TXA₂)
4. Recruitment
5. Aggregation (hemostatic plug)

Endothelium
Basement membrane
Collagen

vWF
C. SECONDARY HEMOSTASIS

1. Tissue factor
2. Phospholipid complex expression
3. Thrombin activation
4. Fibrin polymerization

Fibrin

(from Robbins Basic Pathology, 2003, a litter be changed)
D. THROMBUS AND ANTITHROMBOTIC EVENTS

Release of:
- t-PA (fibrinolysis)
- thrombomodulin (blocks coagulation cascade)

Trapped neutrophil
Trapped red blood cells
Polymerized fibrin
Steps in the formation of a thrombus
• ABNORMALITIES OF BLOOD FLOW
• TURBULENCE
  – Endothelial injury
  – Local areas of stasis
  – Disrupt laminar flow
    • Moves platelets from center of flow to the vessel wall
    • Prevent dilution of activated clotting factors by flowing blood
    • Slow down the inflow of clotting factor inhibitors
    • Promotes endothelial cell activation
• Morphological types of thrombi

(1) Pale Thrombus

Constitution:
alternating layers of platelet

Location:
Arteries, cardiac valves and the initiative part of venous thrombus
(2) red thrombus

Constitution:
Coagulated red blood cells

Location:
At the end part of venous thrombus.
RED THROMBUS
Platelets: Role in Thrombosis

High Flow
- Fibrin
- RBCs
- Platelets

Slow Flow
- Fibrin
- RBCs
- Platelets

White Thrombus
- RBCs, red blood cells.

Coagulation Thrombus

(3) mixed thrombus

Constitution: fibrin with meshed red blood cells between platelet layers

Location: at the middle part of venous thrombus, ball thrombus in cardiac atrium.
(4) Fibrin thrombus (Microthrombus)

Constitution: fibrin

Location: microcirculation in case of DIC
Disseminated intravascular coagulation (DIC)

- This term refers to sudden or insidious onset of widespread fibrin thrombi (myriads of fibrin thrombi) within the microcirculation due to a variety of disorders ranging from obstetric complications to advanced cases of malignant tumors.

- DIC is not a primary disease but rather is a secondary potential complication of any condition associated with widespread activation of thrombin.

- The DIC thrombi are not visible on gross inspection; however they are readily apparent microscopically.
Arterial thrombi:

➢ Arterial thrombi are usually occlusive, firmly adhered to the arterial wall, grayish-white in color and friable.
➢ They are composed of a tangled meshwork of platelets, fibrin, RBCs and WBCs.
➢ The most common sites of arterial thrombi in human patients (in descending order) are coronary, cerebral and femoral arteries.
Arterial Thrombi Morphology

- Adherent masses of blood that demonstrate areas of pale alternating with areas of red
  - Lines of Zahn
Arterial Thrombi Morphology
Thrombi Morphology: Venous

- Venous thrombi
  - Usu occlusive
  - Red (because they form in stasis syndrome and have more associated enmeshed RBCs)
  - Long forming a cast of vein with markings on them from venous valves
  - Red blood cells alternating with peripheral areas of fibrin
Venous Thrombi: Clinical
Marked passive congestion of the left lower leg in a patient with a deep venous thrombus.

Surgical dissection of the thrombus.
Fate of thrombosis:

1) *Propagation*; The thrombus propagates by accumulation of more platelets and fibrin, resulting in obstruction of the affected blood vessel.

2) *Embolization*; The thrombus detaches from the blood vessel wall and transports as an embolus to other sites in the cardiovascular system.

3) *Dissolution (lysis)*; The thrombus is dissolved by the fibrinolytic activity.

4) *Organization*; Shrinking of the thrombus due to gradual in-growth of fibrous connective tissue.

5) *Recanalization*; Resulting in formation of a pathway between the two ends of the thrombus and thus permits the blood to flow through it.
VENOUS THROMBI FATES

- Inferior vena cava
- Thrombosed vein
- Propagation towards heart
- Resolution
- Embolization to lungs
- Organized and incorporated into wall
- Organized and recanalized

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Differentiation between arterial thrombi, venous thrombi and postmortem clot according to their morphology

<table>
<thead>
<tr>
<th>Features</th>
<th>Arterial thrombi</th>
<th>Venous thrombi</th>
<th>Postmortem clot</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Adherence to the B.V. wall:</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>2 Formation of cast in the B.V. lumen:</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>3 Consistency:</td>
<td>Friable and firm</td>
<td>Firm</td>
<td>Rubbery and gelatinous</td>
</tr>
</tbody>
</table>
| 4 Color:                                      | Mixture of red and gray | Red and shiny | **Lower part:** Dark red.  
**Upper part:** Yellow (looks like chicken fat). |
| 5 Presence of the interlacing dark and pale lines of Zahn: | +++              | +              | -               |
Embolism

Definition:
Embolism is the process by which a detached intravascular solid, liquid, or gaseous mass is carried by the blood to a site distant from its point of origin.
Pathogenesis (Types of embolism)

(1) Thromboembolism:

Detached thrombi cause the commonest type of embolism. The detached thrombus may be of venous, arterial, or cardiac origin.

1. Systemic thromboembolisms → arterial or cardiac origin.

2. Pulmonary thromboembolisms → venous origin from deep limb thrombous.
Common locations in which venous and arterial emboli cause infarction and the anatomical routes by which they reach these organs.
Pulmonary Thromboembolism

- 20-25 per 100,000 hospitalized patients
- May be fatal if 60% of pulmonary circulation is obstructed (acute cor pulmonale)
- Saddle PE straddles the bifurcation of the main PA
- Sequelae: Sudden death, clinically silent – resolution – organization, shortness of breath, pulmonary infarction
- Pathogenesis: Deep venous thrombi usual cause – often following immobilization-bed rest from hospitalization
Saddle Pulmonary Thromboembolism
Extensive Pulmonary Embolism

Thrombus in leg can break off and travel to heart and lungs

Right pulmonary artery may become occluded by emboli

Left pulmonary artery may become occluded by emboli

No oxygenated blood can return to the heart, completely shutting down the circulatory system

Extensive pulmonary emboli may lodge in right lung

Extensive pulmonary emboli may lodge in left lung

Blood entering heart from vena cava

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Events leading to stroke

Atheromatous plaque

Emboli

Thrombus

Brain
(2) Fat embolism:

(a) Fractures of long bones and/or operative manipulation of fractures;
(b) Trauma to adipose tissue or fatty liver;
(c) Acute pancreatitis.

Fat emboli tend to be small and they often cause small infarcts adjacent to capillaries at the sites where they lodge in.
Fat embolism
(3) Gaseous embolism

a) Mismanaged intravenous infusions.

b) Operations in which large veins are opened.
Meninges air embolism
(4) Amniotic fluid embolism

- The uterine contractions that occur during childbirth can sometimes cause amniotic fluid to be driven through the placental bed into the maternal circulation.
- This can cause acute respiratory distress and shock. It may be fatal.
Amniotic fluid
(5) Tumor fragments

(6) Infective agents

(7) Athermanous plaques;
Infarction

Definition:
An infarct is an area of ischemic necrosis within a tissue or an organ, produced by occlusion of either its arterial supply or its venous drainage.
Etiology and Pathogenesis:

- Occlusion of a major artery is most often the result of atherosclerosis and its complications (thrombosis, and/or embolism).

- Rarely, arterial spasm can be severe enough to cause arterial occlusion and infarction.
Classification of infarction

(1) White infarcts (anemic infarcts):

Occur in situations where there is a single blood supply,

① with arterial occlusion,

② in solid tissue with a blood supply that divides in a tree-like configuration e.g. heart, kidneys & spleen.
Triangular Pale infarct
Myocardial Infarction (MI.)
(2) **Red infarcts (hemorrhagic infarcts):**

① With venous occlusion;
② In loose tissues;
③ In tissues with a double circulation e.g. lung & liver.
④ In tissues previously congested.
Pulmonary Red infarcts
Infarction due to venous obstruction
Infarction

- Microscopically see coagulative necrosis
Cerebral Infarction (Stroke)
Shock (Cardiovascular Collapse)

Shock is a systemic hypoperfusion (impaired tissue perfusion with arterial blood), due to either reduction in cardiac output or reduction in the affective blood volume.
It represents the final event for a number of potentially lethal conditions include:

1. Severe hemorrhage
2. Extensive trauma or burns
3. Large myocardial infarction
4. Massive pulmonary embolism
5. Microbial septicemia
Calcifications of shock:

1. Hypovolemic shock
2. Cardiogenic shock  Most common
3. Septic shock
4. Neurogenic shock
5. Anaphylactic shock  Less common
1. Hypovolemic shock: 
Is a systemic hypoperfusion resulting from loss of blood volume due to extensive hemorrhage or from large loss of plasma volume due to extensive vomiting, diarrhea or from severe burns.
Hypovolemic shock is an emergency condition in which severe blood and fluid loss make the heart unable to pump enough blood to the body. This type of shock can cause many organs to stop working.

What Causes Hypovolemic Shock?

- About 20% or more lost amount of blood in the body
- Excessive diarrhea
- Excessive sweating
- Severe burns
- Protracted and excessive vomiting

Blood loss can be due to:

- Bleeding from cuts, cuts or wounds
- Bleeding from injuries, blunt traumatic injuries due to accidents or seizure activity
- Internal bleeding from the gastrointestinal tract or ruptured ectopic pregnancy

What are the Symptoms?

- Blue lips & fingernails
- Anxiety
- Chest pains
- Rapid heart rate
- Shallow breathing
- Low urine output

The greater and more rapid the blood loss, the more severe the symptoms of shock.
2. Cardiogenic shock:

Is a systemic hypoperfusion resulting from myocardial pump failure, this may be caused by intrinsic myocardial damage (infarction), ventricular arrhythmias, extrinsic compression (cardiac tamponade) or outflow obstruction.
Causes of cardiogenic shock
3. Septic shock:
Is a systemic hypoperfusion caused by systemic microbial infection. Most commonly this occur in case of G –ve infection (endotoxic shock).
4. Neurogenic shock:
Neurogenic shock is a less common systemic hypoperfusion that may occur in case of anesthetic accident or spinal cord injury, which result in loss of vascular tone and peripheral pooling of blood.
NEUROGENIC SHOCK

Any factor that stimulates parasympathetic activity or inhibits sympathetic activity of vascular smooth muscles can cause neurogenic shock, which results in widespread and massive vasodilation.

Causes of neurogenic shock:
- Spinal cord injury above T5
- Spinal anesthesia
- Vasomotor center depression (e.g., severe pain, drugs, hypoglycemia)

Symptoms of neurogenic shock consist of low systemic vascular resistance, excessive parasympathetic activity, and bradycardia.
4. Anaphylactic shock: Anaphylactic shock is a less common systemic hypoperfusion initiated by generalized immunoglobulin-E mediated hypersensivity reaction, it is associated with systemic vasodilatation and increase vascular permeability, lead to sudden increase in vascular capacity which can not be fill by normal circulatory volume.
ANAPHYLACTIC REACTION

Causes:
- Insect Stings (bee, wasp, ant)
- Medication Reaction
- Food Allergy (peanuts, eggs, shellfish)

- Rapid Onset
- Dyspnea
  - Tight Throat
  - Bronchospasm
  - Laryngeal Edema
- Feelings of Apprehension
- Tingling and Swelling in Mouth, Face, Throat and Tongue
  - Itching
  - ↓ BP
  - Tachycardia
- Loss Of Consciousness

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Fainting (Vasovagal attack), Primary shock:

- It’s a common fainting attack which is occur in susceptible individual by emotional upset or trauma which may be minor, and its mediated by nervous mechanisms.

- The patient feels faint, looks pale with cold sweat and may be vomit. The pulse slaws and the blood pressure falls, the consciousness will be lost.

- At this stage nervous reaction quickly begins and recovery is soon complete.

- On very rare occasions death occurs due to complete cardiac inhibition by vagal action.