HEMODYNAMIC DISORDERS
THROMBOEMBOLIC DISEASE, AND SHOCK

Haemostasis is the process that keeps blood in its fluid state and within the confines of the vasculature.

Successful haemostasis depends on:

- Vessel wall (constrict to limit blood loss)
- Platelets (formation of platelet plug)
- Coagulation system (via thrombin)
- Fibrinolytic system (breakdown of fibrin)

I. Edema and Effusion

1. Edema generally refers to fluid accumulation in interstitial tissue. When due to purely hemodynamic changes the fluid is a transudate.
2. Anasarca - systemic edema and effusions due to hemodynamic cause(s). Transudate.
3. Ascites - generally refers to fluid accumulation in the peritoneal cavity; clinically may refer to a transudate type of fluid (hemodynamic).
4. Effusion refers to fluid accumulation in a body cavity.

Pathogenesis of transudate:

1. Increased intravascular hydrostatic pressure. Increased intravascular pressure in capillaries and venules “pushes” water, electrolytes and a small amount of low Molecular Weight (MW) protein molecules out of the vessels and into adjacent interstitial tissue and/or body cavities.

Example: Increased pressure in the left ventricle of the heart (left-sided heart failure) is transmitted backwards to the left atrium, pulmonary veins and then to the pulmonary capillaries. The result is the formation of transudate in the septal and then in the alveolar spaces; called pulmonary edema. The causes include:

- Impaired venous return
- Congestive heart failure
- Constrictive pericarditis
- Ascites (liver cirrhosis)
- Venous obstruction or compression
- Thrombosis
- External pressure (e.g., mass)
- Lower extremity inactivity with prolonged dependency
- Arteriolar dilation

2. **Reduced intravascular osmotic pressure. Most often this is due to hypoalbuminemia.**
   - **Examples:**
     - Liver disease (e.g. cirrhosis) results in a marked reduction in albumin synthesis.
     - Renal disease (e.g. nephrotic syndrome) results in a marked loss of albumin.
     - Malnutrition
     - Protein-losing gastroenteropathy

3. **Increased pressure in lymphatic vessels**
   - **Example:** Radical mastectomy in which the excision of axillary lymph nodes blocks the normal drainage of lymph and results in the accumulation of fluid in the patient’s arm. Also, could be:
     - Inflammatory
     - Neoplastic
     - Postsurgical
     - Postirradiation

4. **Sodium Retention**
   - Excessive salt intake with renal insufficiency
   - Increased tubular reabsorption of sodium
   - Renal hypoperfusion
   - Increased renin-angiotensin-aldosterone secretion

II. **HYPEREMIA or CONGESTION**

1. **Active.** Dilatation of arteries/arterioles results in increased blood flow (perfusion) of a tissue or organ. The tissue appears red. This was the mechanism for the “redness” of acute inflammation.
2. **Passive.** Impaired venous drainage results in stasis and the accumulation of deoxygenated blood. The tissue has a bluish color due to the accumulation of deoxygenated hemoglobin.

Either of these may be acute or chronic. The term “congestion” is sometimes used to describe a hyperemic organ or tissue.

**Example:** Passive hyperemia resulting in acute or chronic passive congestion of the liver or spleen. The organs are enlarged and the liver may be tender.

### III. HEMORRHAGE: These are the most important lesions related to coagulation disorders:

1. **Petechiae** - pinhead size; **Purpura** - up to 1 cm.; **Ecchymoses** - larger
2. **Hematoma** - a mass composed of blood infiltrating soft tissue.
3. **Hemothorax / hemopericardium / hemoperitoneum** - blood within the respective body cavity.

### IV. THROMBUS (The process is called thrombosis)

**Thrombosis** is the solidification of a formed mass of blood components within the circulatory system. It requires the interaction of all cells within the vasculature and endothelial cells, as well as circulating elements, such as platelets and the clotting cascade. Clotting is a balance between two opposing forces: those favoring the formation of a stable thrombus, and those factors causing breakdown of the clot.

**Patho-physiology of thrombus formation**

Injury to the vascular endothelium causes factors that facilitate and inhibit thrombus.

- **a. Facilitation**
  - Exposure of tissue factor from injured cells activates factor VII
  - Exposure of the thrombogenic subendothelial collagen activates factor XII
  - Platelets deposit and aggregate due to collagen exposure and generation of thrombi

- **b. Inhibition**
  - Increased prostacyclin (PGI2) and nitryl (NO2) inhibit platelet aggregation
  - Synthesis of plasminogen activator promotes fibrinolytic activity
c. Predisposing factors

- **Abnormalities of the vessel wall**: Damage to the endothelium/vascular wall e.g. atherosclerosis, vascular trauma.
- **Abnormalities of blood flow**: Stasis of blood flow (varicose veins, prolonged bed rest).
- **Abnormalities of the blood constituents**: Hypercoagulable state, and increased blood viscosity (dehydration).

**Features**:

1. Intravascular
2. Adherent to the luminal surface of the vessel.
3. Mass of coagulated blood composed of platelets, fibrin and entrapped cells and other plasma proteins. Early lines of Zahn are present: alternating layers of platelets and fibrin.

**Distinguish from**:

1. *In vitro* clot
2. Postmortem clot - does not adhere to the vessel wall.
3. Clotting of a hematoma or hemorrhagic exudate.

**Outcome: Consequences of thrombosis**

1. **Lysis**. The role of fibrinolytic agents in the blood.
2. **Propagation**. Enlargement and extension of the thrombus.
3. **Organization**. Fibrosis of the thrombus.
4. **Recanalization**. During organization new channels may form within the thrombus; these may allow renewed blood flow through the obstructed vessel.

**Complications**:

1. Reduced blood flow to a tissue/organ resulting in ischemic injury or infarction.
2. Fragments of thrombus break off and result in thromboembolization.

**Clinical consequences**

1. arterial thrombosis (tissue infarction distally)
2. venous thrombosis (oedema, due to impaired venous drainage)
3. embolism
Disseminated intravascular coagulation (DIC)

DIC occurs as a complication of many disease states, most notably Gram-negative sepsis - endotoxin effect. Also obstetric complications, metastatic cancer, extensive trauma - all associated with extensive tissue necrosis.

Clotting factors become activated inside the blood vessels due to endotoxins released by the bacteria and a disseminated consumption of clotting factors is produced; as a consequence, the patient starts bleeding through mucosae, skin and blood internal vessels. The presence of fibrin split products in the blood is diagnostic of DIC.

Effects of thrombosis

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<tr>
<th>Arterial</th>
<th>Venous</th>
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<tr>
<td>ischaemia</td>
<td>congestion</td>
</tr>
<tr>
<td>infarction</td>
<td>oedema</td>
</tr>
<tr>
<td>depends on the site and</td>
<td>ischaemia</td>
</tr>
<tr>
<td>collateral circulation</td>
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Embolism is the occlusion of a vessel (either artery or vein) by a mass. Most commonly, they are thrombi that have dislodged from their site of formation and have lodged in a distal lumen occluding blood flow.

1. **Pulmonary emboli** often originate from deep vein thrombosis in the low legs and less often from deep pelvic veins
2. **Systemic emboli** are formed in the arterial circulation; most arise in the heart
3. **Paradoxical emboli** cross over from the right side to the left side of the heart through septal defects and gain access to the systemic circulation
4. **Other types of emboli** include gas emboli (e.g. Caisson's disease), fat emboli (e.g. associated with bone fractures), amniotic fluid emboli, bone chips, and tumour cells

DVT (Deep Vein Thrombosis)

**Predisposing factors**

- oral contraceptives
- severe burns
- cardiac failure
- disseminated cancer
- immobility / best rest
- post-operative
- pregnancy and post-partum
V. EMBOLISM or EMBOLUS (the process is called embolization)

- A particle/mass which is carried in the blood stream as far as its size will allow. It becomes lodged at that point and obstructs the vessel.

- Thrombo-embolus is the most common type. Thromboemboli arise from thrombi and range in size from microscopic to those which are large enough to occlude major arteries.

- Thromboemboli may occur in either arteries or veins. Like thrombi they may undergo lysis, propagation, organization and/or re-canalization and can result in ischemic injury and infarction.

- The most common type of venous thromboembolus arises from a thrombus in the deep leg veins. Fragments of the thrombi travel to the lung where they occlude the pulmonary artery and may result in infarction in the lung. In general the term “embolus” (e.g. pulmonary embolus) is synonymous with “thromboembolus.”

- Systemic arterial thromboemboli usually arise from mural thrombi in the heart either as a consequence of valvular disease or after a myocardial infarction. Ruptured thrombi travel via the systemic arterial system to such organs as the brain, kidneys, spleen and extremities. They usually result in infarction(s) in those sites.

Amniotic fluid emboli - amniotic fluid infusion syndrome

1. Occur during labor or immediately postpartum.
2. Rare but frequently fatal. They are a major cause of maternal mortality.
4. Tear in placental membranes and rupture of uterine veins results in an “infusion” of amniotic fluid and particulate matter into the maternal venous circulation.

Air/Gas emboli

1. May occur during delivery-abortion, chest wall/lung trauma: Air injected intravenously is likely to be absorbed while air injected intra-arterially is more likely to act as an embolus and result in infarction.
2. May occur as the result of a rapid change in atmospheric pressure, e.g. in divers. While diving, increased ambient pressure allows increased gas to dissolve in the blood. With too rapid decompression coming to the surface, gas comes out of solution and forms bubbles in the blood - especially nitrogen. These bubbles act as emboli. This type of situation is known as decompression sickness, “the bends” or Caisson disease.

Fat emboli - fat embolism syndrome

1. Scattered fat emboli are commonly found at autopsy following severe bone fractures.
2. A small percentage of such cases manifest fat embolism syndrome. This is characterized by the onset, 1 - 3 days after the trauma, of acute respiratory insufficiency, often accompanied by neurological signs which may progress to coma. Cutaneous petechiae are common. Death occurs in about 10% of cases. At autopsy globules of fat are found in the small vessels of the lungs, brain and other organs.
3. As in amniotic infusion syndrome, fat emboli syndrome is thought to be due to more than just the mechanical effects of the emboli and chemical injury appears to play a role.

Other types of emboli:

1. **Atherosclerotic plaque** - especially from the aorta to the kidneys.
2. **Tumor** - in cancer patients.
3. **Bone marrow** - especially after trauma, e.g. resuscitative effort with fracture of the sternum. Its finding is considered a terminal event not necessarily responsible for death.
4. **Trophoblastic cells** in the lungs of pregnant women. Considered to be a non-pathologic event.

VI. **INFARCT** (the process is called infarction)

1. An area of ischemic necrosis which typically results from obstruction of the corresponding artery by a thrombus or an embolus. Typically wedge-shaped and pale (“**white infarct**”) - unless there is some associated hemorrhage ( e.g. in the lung).
2. Infarction is an irreversible process and healing occurs by fibrosis.

3. Does total arterial obstruction always result in infarction? No - if there is a dual or **collateral blood supply**.

4. Can infarction occur in the absence of total arterial obstruction? Yes - all that is needed for infarction to occur is for the oxygen supply to be insufficient to sustain the life of the affected tissue. This may occur, for example, as the result of partial obstruction ischemic injury exacerbated by hypoxemia and/or by increased needs for oxygen by the tissue. We will say more about this when we discuss myocardial infarction.

5. Infarcts due to systemic venous obstruction are much less common than arterial. Obstruction of a vein allows blood to enter the tissue - but not exit; this leads to severe passive congestion, hemorrhage and infarction. Venous infarcts are typically hemorrhagic (“**red infarct**”).

6. Factors which modify the development of an infarct include the type of vascular supply, the rate of development of the obstruction, the vulnerability of the tissue to hypoxia, and the oxygen concentration of the arterial blood supply.

**V. SHOCK** – is the systemic **hypoperfusion** of cells and tissue. It is characterized by marked hypotension (tachycardia) with increased pulse rate. Aerobic cellular metabolism switches to anaerobic with increased lactate production (lactic acidosis).

**Four types**

1. **Cardiogenic** - reduced cardiac output, e.g. as the result of a large myocardial infarct.
2. **Hemorrhagic / hypovolemic** - reduced blood volume, e.g. massive fluid loss.
3. **Septic** - most often Gram-negative bacteremia. Endotoxins are mediated by tumor necrosis factor and other chemical mediators results in a frequently irreversible situation of systemic vasodilatation, endothelial damage and direct injury to cells.
4. **Neurogenic**, e.g. anaesthesia with severe widespread peripheral vasodilatation. Very uncommon.

**Stages**

1. **Non-progressive** - reflex compensatory mechanisms result in the perfusion of vital organs.
2. **Progressive** - hypoperfusion of tissues with increasing circulatory and metabolic imbalances.
3. **Irreversible** - despite temporary interventional correction of hemodynamic defects, cellular and tissue injury are so severe as to preclude survival.

**Major sites of injury**

- Brain - hypoxic encephalopathy
- Lungs - “shock lung” - adult respiratory distress syndrome (ARDS)
- Kidneys - acute tubular necrosis
- G.I. - hemorrhagic necrosis of the mucosa

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<tr>
<th>Type of Shock</th>
<th>Clinical Examples</th>
<th>Principal Mechanism</th>
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<td>- Ventricular rupture</td>
<td>Failure of myocardial pump owing to intrinsic myocardial damage, extrinsic pressure, or obstruction to outflow</td>
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<td>- Arrhythmia</td>
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<td>- Cardiac tamponade</td>
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<td></td>
<td>- Pulmonary embolism</td>
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<td></td>
<td>- Myocardial infarction</td>
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<tr>
<td>Hypovolemic</td>
<td>- Hemorrhage</td>
<td>Inadequate blood or plasma volume</td>
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<td></td>
<td>- Fluid loss, e.g., vomiting, diarrhea, burns, or trauma</td>
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<tr>
<td>Septic</td>
<td>- Overwhelming microbial infections</td>
<td>Peripheral vasodilation and pooling of blood; endothelial activation/injury; leukocyte-induced damage; disseminated intravascular coagulation; activation of cytokine cascades</td>
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<tr>
<td></td>
<td>- Endotoxic shock</td>
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<td>- Gram-positive septicemia</td>
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