EMBOLISM, INFARCTION AND SHOCK

Disseminated Intravascular Coagulation (DIC)

Characterized by the activation of coagulation within the vascular system leading to deposition of fibrin in small blood vessels and a consumption of platelets and clotting factors.

Pathogenesis
♦ Involves release of tissue factors into the circulation following tissue injury.
♦ Thrombin released in the circulation converts fibrinogen to fibrin with microthrombi formation.
♦ Microthrombi lodge in small vessels and lead to organ and tissue ischaemia.
♦ Microangiopathic haemolytic anaemia may be a result of mechanical damage to red blood cells by fibrin strands in small vessels.

Can be caused by:
♦ Infections
♦ Obstetric complications – intrauterine death, abruptio placenta and amniotic fluid embolism
♦ Shock
♦ Malignancy
♦ ABO incompatibility
♦ Snake bite
♦ Burns
♦ Miscellaneous causes

Diagnosis
♦ Clinical evidence of excessive bleeding
♦ Examination of blood film for abnormal red blood cells
♦ Decreased platelet count
♦ Coagulation tests e.g. ↑Prothrombin Time, ↑PTT (Partial ThromboplastinTime) and ↑Thrombin Time

Presence of microthrombi in blood vessels is best seen in the brain, heart, lungs and kidney.
**EMBOLISM**

An embolus is an abnormal mass of material, solid or gaseous, which is transported in the bloodstream from one part of the circulation to another and which finally impacts in the lumen of vessels too narrow to pass.

**Emboli consist of:**

- Thrombus fragments
- Air
- Nitrogen
- Fat
- Pieces of bone marrow
- Debris from atherosclerotic plaques
- Tumour cells

- 99% of emboli are derived from thrombus e.g. from the deep veins of the lower limb or pelvic veins.

- The embolus arising from a venous thrombus must impact in the pulmonary arterial tree.

**Pulmonary embolism**
Derived from a thrombus occluding a segment of the venous drainage of the lower limb.

**Predisposing factors**

- Major surgical procedure with general anaesthetic
- Prolonged immobilization
- Old age
- Contraceptive pill
- Pregnancy
- Cigarette smoking

- Pulmonary embolism may be rapidly fatal and is a major cause of sudden death

**Pathophysiology:**

- Mechanical obstruction of pulmonary vessels may produce acute right-sided heart failure (acute cor pulmonale) and sudden death.
Pathophysiology of pulmonary embolism cont’d.

Other postulated mechanisms:

♦ Vagal reflex inducing spasm of coronary and pulmonary arteries.
♦ Reflex producing marked peripheral vasodilatation.
♦ Reflex producing cardiac arrest.

Systemic embolism

♦ Systemic emboli are derived from the left side of the heart and enter the arterial circulation.

May arise in:

♦ Left atrial appendage
♦ Left ventricle e.g. in myocardial infarction and congestive cardiomyopathy.
♦ Left-sided heart valves in infective endocarditis
♦ Platelet thrombi from atherosclerotic plaques

Emboli lodge in systemic arteries in many sites including skin, lower limbs, kidneys, spleen, liver and brain.

♦ Impaction in arterial vessels can lead to ischaemia and infarction of tissues with corresponding loss of function.
♦ Infected emboli can disseminate infection to previously uninvolved organs and tissues.

Fat embolism

Most frequently associated with:

♦ Fracture of a long bone
♦ Severe burns
♦ Extensive soft tissue trauma
♦ Patients with sickle-cell anaemia who develop bone marrow necrosis

Fat globules enter veins at trauma site. Carried in circulation to the lungs where they cause sudden respiratory distress 24-72 hours after injury.

Patients may also have brain involvement when fat emboli enter the cerebral circulation – this complication is often fatal.

Brain at autopsy shows edema and many tiny haemorrhages.
Fat globules are present in cerebral capillaries.
INFARCTION

Ischaemia is the state existing when an organ has its blood supply reduced relative to its metabolic needs.

An infarct is a large area of tissue necrosis that results from ischaemia.
♦ Produced by occlusion of either the arterial supply or the venous drainage
♦ 99% of infarcts are a result of thrombo-embolism and these are almost always due to arterial occlusion.

Types of infarct
♦ Red (hemorrhagic)
♦ White or pale (anaemic)

White or anaemic infarcts
♦ Result from arterial occlusion
♦ Occurs in solid tissues
♦ Infarct may be transiently hemorrhagic but becomes pale very quickly
♦ Heart. Spleen and kidneys are typical solid organs which
   Tend to have pale infarcts

Red or hemorrhagic infarcts
♦ Tend to occur with venous occlusion
♦ Occur in soft tissues
♦ Occur in previously congested tissue
♦ Occur in tissues with double circulation
♦ Infarcted lungs show accumulation of blood within the spongy parenchyma
♦ Small intestinal infarcts are usually hemorrhagic because of rich anastomoses in the arterial supply

Infarcts are also classified as septic or bland depending on whether bacterial infection is present in the area of necrosis.

Pathology
♦ All infarcts tend to be wedge-shaped with the apex of the wedge pointing to the focus of vascular occlusion.
♦ The base of the infarct is formed by the external aspect of the organ.
♦ The outline of the infarct is at first ill-defined.
♦ After 24 hours it is well-defined and of firmer consistency than the surrounding normal tissue.
Pale infarcts remain yellow-white and hemorrhagic infarcts remain darker than the adjacent normal parenchyma.

Characteristic microscopic change is *ischaemic coagulative necrosis*.

Cytological changes may be absent if the vascular occlusion occurs a few hours prior to the death of the patient e.g. in myocardial infarcts.

The brain is a notable exception to this pattern. Ischaemic necrosis leads to liquefaction of the brain substance.

If sepsis is present, an abscess develops in the infarct followed by organisation.

**Factors determining the development of infarcts**

1. Nature of vascular supply.
2. Rate of development of the occlusion.
3. Susceptibility of tissue to hypoxia.

**SHOCK**

A state of *prolonged tissue hypoperfusion* due to reduction of blood volume or cardiac output, or redistribution of blood, resulting in an *inadequate effective circulating volume*.

**Major types of shock**

1. **Cardiogenic shock** caused by failure of the myocardial pump due to
   - Primary myocardial damage (infarction)
   - Arrhythmias
   - External pressure (cardiac tamponade)
   - Outflow obstruction (pulmonary embolism)

2. **Hypovolemic or hemorrhagic shock**, due to inadequate blood or plasma volume caused by
   - Hemorrhage
   - Large fluid losses e.g. severe burns
   - Trauma

3. **Septic shock**, caused by
   - Bacteria
   - Viruses
   - Fungal infections,
   - Most commonly gram-negative bacteria (endotoxic shock) or dengue fever

4. Anaphylactic shock.
5. Neurogenic shock.
Pathogenesis of shock

Factors in tissue perfusion:
1. Systemic arterial pressure.
2. Peripheral vascular resistance.
3. Patency of tissue capillary bed.

Hypovolemia
Leads to fall in stroke volume and cardiac output

♦ Hemorrhage – external or internal.
♦ Excess fluid loss – severe vomiting and diarrhoea.
♦ Burns – fluid loss and vasoactive mediators released in severe tissue injury.
♦ Vasodilatation – vasoactive mediators and sympathetic nervous system.

Cardiogenic shock (pump failure)
♦ Myocardial infarction leads to low cardiac output
♦ Cardiogenic shock occurs in massive infarcts and leads to reduced coronary artery perfusion pressure → increased myocardial dysfunction.
♦ Outflow obstruction. Best example is massive pulmonary embolism.
  1. If more than 50% of the vascular bed is occluded then right ventricular failure intervenes.
  2. Large segment of lung that is ventilated but not perfused with blood i.e. a ventilation-perfusion mismatch.
  3. Shock is the third component. A fall in pulmonary venous return leads to a fall in cardiac output.

♦ Cardiac tamponade: rapid accumulation of fluid - usually blood – in the pericardial sac leading to increased pericardial pressure which eventually causes decompensation in the heart and produces a dramatic fall in cardiac output. Often fatal.

Shock and infection

Causes:
♦ Gram-negative bacteria
♦ Gram-positive bacteria
♦ Spirochaetes
♦ Rickettsia
♦ Viruses - dengue
♦ Fungi - candida
♦ Parasites - malaria

Septic shock is a term reserved for shock due to gram-negative septicaemia.
Gram-negative “endotoxic” shock

♦ Endotoxin is a lipopolysaccharide (LPS) in the outer part of the cell wall of many gram-negative bacteria.
♦ LPS can elicit features of shock, fever, hypotension, haematological and biochemical abnormalities.
♦ Tumour necrosis factor (TNF) is thought to mediate the actions of LPS. It is a cytokine which can reproduce the actions of endotoxin.

Morphology of shock - Hypoxic failure of multiple organ systems

♦ Brain – develops ischaemic encephalopathy.
♦ Heart – sub-endocardial hemorrhage and/or necrosis.
♦ Kidneys – acute tubular necrosis.
♦ Lungs – Acute Respiratory Distress Syndrome (ARDS).
♦ Gastro-intestinal tract – mucosal hemorrhages and necrosis.
♦ Liver – fatty change and centrilobular hemorrhagic necrosis.

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