THROMBOSIS
This is the process whereby a thrombus is formed. A thrombus is a coagulated solid mass composed of blood constituents, i.e. platelets, fibrin of entrapped cellular elements which develops in an artery or a vein. Thrombus formation can only occur during life. This is in contrast to simple blood clotting (haemostasis), which can occur after death or in a test tube (in vitro). Similarly, a thrombus differs from a hematoma which result from hemorrhage and subsequent clotting outside the vascular system.
There are three main predisposing factors for thrombus formation (Virchow’s triad):

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

These predisposing factors are associated with particular conditions or life styles.
- **Table 1. Predisposing factors for thrombosis.**

**Examples:**

<table>
<thead>
<tr>
<th>Endothelial damage</th>
<th>Trauma, atherosclerosis, smoking, bacterial colonies.</th>
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<td>Stasis/turbulence</td>
<td>Post-operative immobility (inactive legs) and blood pooling; post myocardial infarction (sluggish blood flow around body); turbulence around atherosclerotic plaques or within aneurysms.</td>
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<td>Increased coagulability</td>
<td>Pregnancy, oral contraceptives, leukemia cancer.</td>
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THROMBOSIS IN THE ARTERIAL SYSTEM

• **Pathogenesis:**
  
  • Most commonly vessels involved in arterial thrombosis are the: coronary, cerebral, mesenteric, renal arteries and arteries of the lower extremities.
  
  • Less commonly, arterial thrombosis occurs in other disorders including inflammation of the arteries, trauma and diseases of the blood.
  
  • Thrombi are common in aneurysms.
Three factors involving arterial thrombosis:

- Damage to the endothelium, usually by atherosclerosis, disturbs the anticoagulant properties of the vessel wall and serves as the nidus for platelet aggregation and fibrin formation.

- Alterations in blood flow, whether from turbulence in an aneurysm or at the sites of arterial bifurcation is conducive to thrombosis. Slowing in narrowed arteries favors thrombosis.

- Increased coagulability of the blood, as seen in polycythemia vera or in association with some cancers, leads to an increased risk of thrombosis.
**Pathology:**
Arterial thrombus attached to the vessel wall is soft, friable and dark red, with fine alternating bands of yellowish platelets and fibrin, the so-called lines of Zahn.

- Once formed, arterial thrombi have several possible outcomes:
  - Lysis of an arterial thrombus may occur, owing to the potent thrombolytic activity of the blood.
  - Propagation of a thrombus may ensue, because the thrombus serves as the focus for further thrombosis.
  - Organization refers to the eventual invasion of connective tissue elements, which causes a thrombus to become firm and grayish white.
  - Canalization is the process by which lumina lined by endothelial cells form in an organized thrombus. The functional significance of this change is often questionable.
  - Embolization occurs when a portion or all of the thrombus become dislodged and travels through the circulation to become lodged in a blood vessel some distance from the site of thrombus formation.
Clinical Features:

- Arterial thrombosis is the most common cause of death in Western industrialized countries.
- Since most arterial thrombi occlude the vessel, they often lead to ischemic necrosis of the tissue supplied by the artery.
- Thrombosis of a coronary or cerebral artery results in a myocardial infarct (heart attack) or cerebral infarct (stroke).
- Other end-arteries that are affected by atherosclerosis and often suffer thrombosis include the mesenteric arteries (intestinal infarction), renal arteries (kidney infarcts) and arteries of the leg (gangrene).
THROMBOSIS IN THE HEART DEVELOPS ON THE ENDOCARDIUM

As in the arterial system, endocardial injury and changes in blood flow in the heart are associated with mural thrombosis, which refers to a thrombus adhering to the underlying wall of the heart. The disorders in which mural thrombosis occurs include the following:

* Myocardial infarction: Adherent mural thrombi form in the cavity of the left ventricle over areas of myocardial infarction, owing to damaged endocardium and alternations in blood flow associated with a poorly functional or a dynamic segment of the myocardium.

* Atrial fibrillation: A disorder of atrial rhythm leads to slower blood flow and impaired contractility in the left atrium.
* Cardiomyopathy: Primary diseases of the myocardium are associated with mural thrombi in the left ventricle, presumably because of endocardial injury and altered hemodynamics associated with poor myocardial contractility.

* Endocarditis: Small thrombi, termed vegetations, may also develop on cardiac valves, usually mitral or aortic that are damaged by a bacterial infection.
THROMBOSIS IN THE VENOUS SYSTEM IS MULTIFACTORIAL

• Venous thrombosis was widely referred to as *thrombophlebitis*, implying that an inflammatory or infectious process had injured the vein. However, in recognition, there is no evidence of inflammation in most cases termed *phlebothrombosis*. Nevertheless, both terms have been replaced for the most part by the expression *deep venous thrombosis*. 
**Pathogenesis:** Deep venous thrombosis causes by the same factors that dispose toward arterial and cardiac thrombosis.

Conditions favor the development of deep venous thrombosis:

a] Stasis (heart failure, chronic venous insufficiency, post-operative immolization, prolonged bed rest).
b] Injury (trauma, surgery, childbirth).
c] Hypercoagulability (oral contraceptives, late pregnancy, cancer).
d] Advanced age (venous varicosities, phlebosclerosis).
e] Sickle cell disease.
Pathology:

- Most venous thromboses occur in the deep veins of the legs.
- The rest usually involve veins in the pelvis.
- Most venous thrombi begin in the calf.
Several potential fates:

- **Lysis**: Venous thrombi generally remain small and are eventually lysed, posing no further threat to health.

- **Organization**: Many thrombi undergo organization similar to those of arterial origin. Small organized venous thrombi may be incorporated into the wall of the vessel; larger ones may undergo canalization with partial restoration of venous drainage.

- **Propagation**: It is not uncommon for venous thrombi to serve as a nidus for further thrombosis and thereby propagate proximally to involve the large iliofemoral.

- **Embolization**: Large venous thrombi or those that have propagated proximally represent a significant hazard to life, since they may dislodge and be carried to the lungs as pulmonary emboli.
Clinical features:

- Small thrombi are ordinarily asymptomatic.
- Occlusive thrombosis of the femoral or iliac veins leads to severe
- Severe congestion, edema and cyanosis.
- Symptomatic deep venous thrombosis is treated with systemic anticoagulants.
- The function of the venous valves is always impaired in a vein subjected to thrombosis and organization.
- Chronic deep venous insufficiency is virtually inevitable.
- Small segment of the deep venous system may remain asymptomatic.
• More extensive involvement results in pigmentation, edema and induration of the skin of the leg.
• Ulceration above the medial malleolus can occur and difficult to treat.
• Venous thrombi may also pose severe hazards.
• Thrombosis of mesenteric vein can cause hemorrhagic infarction of the small bowel, thrombosis of cerebral veins may be fatal, thrombosis of hepatic veins may destroy the liver.
EMBOLISM

Embolism is the passage through the venous or arterial circulations of any material capable of lodging in a blood vessel and thereby obstructing its lumen. The usual embolus is a thromboembolus, that is a thrombus formed in one location that detaches from the vessel wall at its point of origin and travels to a distant site. An embolus is a mass of material, which is carried in the bloodstream and can become lodged within a blood vessel and block it. The material may be a solid, liquid or a gas. The effect of an embolus follow from the obstruction of blood flow to the tissues and depend on the precise site at which this occurs and whether or not there is an alternative tissue blood supply. Emboli travel through the circulatory system and obstruct the vessel lumen when the diameter prevents further passage.
Pulmonary Arterial Embolism is Potentially Fatal

- Pulmonary embolism remains an important diagnostic and therapeutic challenge.
- Pulmonary thromboemboli are reported in more than half of all autopsies.
- This complication occurs in 1 to 2% of postoperative patients over the age of 40 years.
- The risk after surgery increases with advancing age, obesity, length of the operative procedure, postoperative infection, presence of cancer and preexisting venous disease.
- Most pulmonary emboli arise from the deep veins of the lower extremities; most of the fatal ones form in the ileofemoral veins.
• Only half of patients with pulmonary thromboembolism have signs of deep vein thrombosis.
• Some thromboemboli arise from the pelvic venous plexus and others from the right side of the heart.
• The upper extremities are a rare source of thromboemboli.
• The clinical features of pulmonary embolism are determined by the size of the embolus, the health of the patient and whether embolization occurs acutely or chronically.
• Acute pulmonary embolism is divided into the following syndromes:
  • Asymptomatic small pulmonary emboli.
  • Transient dyspnea and tachypnea without other symptoms.
  • Pulmonary infarction with pleuritic chest pain, hemoptysis and pleural effusion.
  • Cardiovascular collapse with sudden death.
  • Pulmonary embolism that occurs chronically, with numerous emboli lodged in the small arteries of the lung can lead to pulmonary hypertension and right sided heart failure.
Massive Pulmonary Embolism

- Consequence of the release of a large deep venous thrombus from a lower extremity.
- Patient succumbs immediately on getting out of bed for the first time.
- The muscular activity dislodges a thrombus that formed as a result of the stasis associated with prolonged bed rest.
- Excluding deaths related to surgery, massive pulmonary embolism is the most common cause of death after major orthopaedic surgery and is the most frequent nonobstetric cause of postpartum death.
- It is also a common cause of death for those suffering chronic heart and lung diseases and those who are subjected to prolonged immobilization.
• Pulmonary embolus often lodges at the bifurcation of the main pulmonary artery (saddle embolus).

• Multiple smaller emboli may lodge in secondary branches and prove fatal.

• With acute obstruction of more than half of the pulmonary arterial tree, the patient often experiences immediate severe hypotension (or shock) and may die within minutes.
Pulmonary Infarction

• Small pulmonary emboli are not ordinarily lethal.
• Tend to lodge in peripheral pulmonary arteries and in some patients (15-20% of all pulmonary emboli), they produce infarcts of the lung.
• Pulmonary infarction is usually seen in the context of congestive heart failure or chronic lung disease, because the normal dual circulation of the lung ordinarily protects against ischemic necrosis since the bronchial artery pumps blood into the necrotic area, pulmonary infarcts are typically hemorrhagic.
• Tend to be pyramidal with the base of the pyramid on the pleural surface.
• Patients experience cough, stabbing pleuritic pain, shortness of breath and occasional hemoptysis.

• Pleural effusion is common and often bloody.

• With time, the blood in the infarct is resorbed, and the center of the infarct becomes pale.

• Granulation tissue forms on the edge of the infarct, after which it is organized to form a fibrous scar.
Pulmonary Embolism Without Infarction

- Since the lung has a dual circulation, supplied by both the bronchial arteries and the pulmonary emboli do not produce infarcts.
- Most small emboli do not attract clinical attention, a few lead to a syndrome characterized by dyspnea, cough, chest pain and hypotension.
- Rarely (3%), recurrent pulmonary emboli produce pulmonary hypertension by mechanizal blockage of the arterial bed.
- Reflex vasoconstriction and bronchial constriction, owing to release of vasoactive substances may contribute to a reduction in size of the functional pulmonary vascular bed.
• Patients have the clinical and radiological findings of pulmonary infarction due to thromboembolism.
• The lesion resolves instead of contracting to leave a scar.
• Hemorrhage and necrosis of the lung tissue in the affected area occur, but the tissue framework remains.
• Collateral circulation maintains the viability of the tissue and enables its regeneration.
Fate of Pulmonary Thromboemboli

• Small pulmonary emboli may completely resolve, depending on:
  • a] embolic load
  • b] adequacy of the pulmonary vascular reserve
  • c] state of the bronchial collateral circulation
  • d] activity of the thrombolytic process.

• Alternatively, thromboemboli may become organized and leave strings of fibrous tissue attached to the vessel wall in the lumen of pulmonary arteries.

• Radiological studies have indicated that half of all pulmonary thromboemboli are resorbed and organized within 8 weeks with little narrowing of the vessels involved.
Paradoxical Embolism

• Paradoxical embolism refers to emboli that arise in the venous circulation and bypass the lungs by traveling through an incompletely closed foramen ovale, subsequently entering the left side of the heart and blocking flow to the systemic arteries.

• Since the pressure in the left atrium usually exceeds that in the right, most of these cases occur in the context of a right to left shunt.
SYSTEMIC ARTERIAL EMBOLISM OFTEN CAUSES INFARCTS

**Thromboembolism**

- The heart is the most common source of arterial thromboemboli which usually arise from mural thrombi.
- These emboli tend to lodge at points where the vessel lumen narrows abruptly.
- The viability of the tissue supplied by the vessel depends on the availability of collateral circulation and on the fate of the embolus itself.
- The thromboembolus may propagate locally and lead to a more severe obstruction or it may fragment and lyse.
Organs that suffer the most from arterial thromboembolism include the following:

- **Brain**: Arterial emboli to the brain cause ischemic necrosis of brain tissue.

- **Intestine**: In the mesenteric circulation, emboli cause infarction of the bowel, a complication that manifests as an acute abdomen and requires immediate surgery.

- **Lower extremity**: Embolism of an artery of the leg leads to sudden pain, absence of pulses, and a cold limb. In some cases, the limb must be amputated.

- **Kidney**: Renal artery embolism may infarct the entire kidney but more commonly results in small peripheral infarcts.

- **Heart**: Coronary artery embolism and resulting myocardial infarcts are reports but are rare.
• **Air embolism**

• Air may be introduced into the venous circulation through neck wounds, thoracocentesis, punctures of the great veins during invasive procedures or hemodialysis.

• Small amounts of circulating air in the form of bubbles are of little consequence, but quantities of 100 ml or more can lead to sudden death.

• Air bubble tend to coalesce and physically obstruct the flow of blood in the right side of the heart, the pulmonary circulation and the brain.

• Bubble of air appears as empty spaces, can be seen in the capillaries and small vessels of the lung.
• Persons exposed to increased atmospheric pressure such as scuba divers and workers in underwater occupations are subject to decompression sickness, a unique form of gas embolism.
• Air embolism is the second most common cause of death in sport diving.
• Acute decompression sickness, commonly known as “the bends” is characterized by temporary muscular and joint pain, owing to small vessel obstruction in these tissues. However, involvement of the cerebral blood vessels may be severe enough to cause coma or even death.
• Caisson disease refers to decompression sickness in which the vascular obstruction causes multiple foci of ischemic necrosis of bone, particularly affecting the head of the femur, tibia and humerus.
Amniotic Fluid Embolism

- Refers to the entry of amniotic fluid containing fetal cells and debris into the maternal circulation through open uterine and cervical veins.

- The disorder usually occurs at the end of labor when the pulmonary emboli are composed of the solid epithelial constituents (squames) contained in the amniotic fluid.

- On clinical presentation, it can be dramatic with the sudden onset of cyanosis and shock followed by coma and death.

- Minor amniotic fluid embolism is probably a common asymptomatic event, since autopsies of mothers who have died of other causes in the perinatal period frequently show evidence of this complication.
Fat Embolism

- Describes the release of emboli of fatty marrow into damaged blood vessels following severe trauma to fat containing tissue, particularly accompanying bone fractures.

- Cases of severe fat embolism are marked by the development of fat embolism syndrome, which appears 1 to 3 days after the injury. In its most severe form, which may be fatal which is characterized by respiratory failure, mental changes, thrombocytopenia and widespread petechiae.

- It is usually considered a direct consequence of trauma, with fat entering ruptured capillaries at the site of the fracture.
Bone Marrow Embolism

- Bone marrow emboli to the lungs, complete with hematopoietic cells and fat are often encountered at autopsy after cardiac resuscitation, a procedure in which fractures of the sternum and ribs commonly occur.
- They also occasionally occur after fractures of the long bones.
- In most cases, no symptoms are attributed to bone marrow embolism.
Miscellaneous Pulmonary Emboli

- Intravenous drug abusers who use talc as a carrier for illicit drugs may introduce it into the lung via the bloodstream.
- Talc emboli produce a granulomatous response in the lungs.
- Cotton emboli are common and are due to cleansing of the skin prior to venipuncture.
- Schistosomiasis may be associated with the embolization of ova to the lungs from the bladder or the gut in which case they incite a foreign body granulomatous reaction.
- Tumor emboli are occasionally seen in the lung during hematogenous dissemination of cancer.
# Types of Embolism and Their Sources

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<td>Amniotic fluid</td>
<td>Uterus at delivery: it can embolize to lungs via the uterine veins or placenta.</td>
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<td>Nitrogen</td>
<td>Inadequate decompression in deep sea divers; emboli cause problems in lungs, heart, spinal cord and skeleton.</td>
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<td>Air</td>
<td>Deliberate or accidental surgical Introduction of air into circulation e.g. into great vein in chest.</td>
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<td>Fat</td>
<td>Complicated bony fractures; emboli to lungs, brain and kidney.</td>
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INfarction

Defined as the process by which coagulative necrosis develops in an area distal to the occlusion of an end-artery.

The necrotic zone is termed an infarct.

Infarcts of vital organs such as the heart, brain and intestine are serious medical conditions and are major causes of morbidity and mortality.
Pathology:

- The gross and microscopic appearance of an infarct depends on its location and age. Upon arterial occlusion, the area supplied by the vessel, rapidly becomes swollen and deep red. Microscopically, vascular dilation and congestion and occasionally interstitial hemorrhage are noted. Subsequently, several types of infarcts are distinguishable by gross examination.

- Pale infarcts are typical in the heart, kidneys and spleen, although certain infarcts in the kidney may be cystic. Dry gangrene of the leg due to arterial occlusion is actually a large pale infarct.
• Red infarcts may result from either arterial or venous occlusion and are also characterized by coagulative necrosis. However, they are distinguished by bleeding into the necrotic area from adjacent arteries and veins. It occurs principally in organs with a blood supply such as the lungs, small intestine and brain.

• In the brain, an infarct typically undergoes liquefactive necrosis and may become a fluid-filled cyst and referred to as cystic infarct.

• A septic infarct results when the necrotic tissue of an infarct is seeded by pyogenic bacteria and becomes infected.

• Pulmonary infarcts are not uncommonly infected, presumably because the necrotic tissue offers little resistance to inhaled bacteria. A septic infarct may become a frank abscess.
Infarction Specific Location is often Fatal

- *Myocardial Infarcts* are transmural or subendocardial. A transmural infarct results from complete occlusion of a major extramural coronary artery. Subendocardial infarction reflects prolonged ischemia caused by partially occluding, atherosclerotic, stenotic lesions of the coronary arteries when the requirement for oxygen exceeds supply. This infarct may be pale or red, depending upon the extent of reflow of blood into the infarcted area.
• **Pulmonary Infarcts**: Only about 10% of pulmonary emboli elicit clinical symptoms referable to pulmonary infarction, usually after occlusion of a middle-sized pulmonary artery. Infarction occurs only if the circulation from the bronchial arteries inadequately compensates for the loss of the supply from the pulmonary arteries. Often found in congestive heart failure, although stasis in the pulmonary circulation may contribute.
• **Cerebral Infarcts:** Infraction of the brain may result from local ischemia or a generalized reduction in blood flow. The latter often results from systemic hypotension as in shock, and produces infarctions in the border zones between the distributions of the major cerebral arteries. The occlusion of a large artery produces a wide area of necrosis which may ultimately resolve as a large fluid-filled cavity in the brain.
• **Intestinal Infarcts:** The earliest tissue changes in intestinal ischemia are necrosis of the tips of the villi in the small intestine and necrosis of the superficial mucosa in the large intestine. More severe ischemia leads to hemorrhagic necrosis of the submucosa and muscularis but not the serosa. Infarction is defined as death of tissue caused by ischemia or lack of oxygen. It may result from a partial or complete reduction of the blood supply (arterial infarction) or diminished drainage of blood from the tissue (veinous infarction). The shape and size of the infarct depends on the territory normally supplied or drained by the occluded blood vessel. The appearance of an infarct varies, depending on how long the process has been going on. The vast majority of infarcts are arterial in nature and are caused by thrombosis or embolism.
SHOCK

Shock is a condition in which profound haemolytic and metabolic functions of the body are depressed due to severe and acute reduction in cardiac output and effective circulating blood volume resulting in inadequate perfusion. There is progressive cardiovascular collapse characterised by hypotension, hyperventilation and clouding of consciousness. Subsequently there is oliguria.
There are many causes, conveniently grouped under three main headings:

1. **HYPOVOLAEMIC** (i.e. diminished blood volume) associated with:
   - (i) Severe haemorrhage – external or internal
   - (ii) Severe injury – especially fractures of bones and crushing of tissues.
   - (a) Trauma
   - (iii) Surgical procedures – especially if anaesthesia is not adequate, spinal cord injury – neurogenic shock (acute brain or spinal cord injury).
   - (iv) Burning – especially where extensive surface damage allows loss of a large amount of exudate.
   - (b) Dehydration – in cases of severe vomiting or diarrhea.

This will repair the neural control of vasomotor tone, vasodilation → ↓ effective circulating blood and plasma volume i.e. as that seen in hypovolaemic shock.
2. **CARDIOGENIC**
   - Acute diseases of the heart – especially myocardial infarction, pulmonary embolism, myocarditis or cardiac tamponade and atrial myxoma – in which there is a sudden fall in cardiac output. In addition ↓ Blood volume ↓ venous return.

3. **BACTERIAL** (Septic, bacteraemic, endotoxic). In serious bacterial infections (especially Gram-negative organisms, e.g. E. coli and bacteroides). The loss of effective circulating blood causes tissue and cell damage, and, at the same time, initiates reactive changes in the circulation. These two mechanisms combine to cause the shock syndrome.

4. **Anaphylactic shock** mediated by IgE. Widespread vasodilation and ↑ vascular permeability.
REACTIVE CHANGES – EARLY STAGE

These changes are concerned with the maintenance of an adequate cerebral and coronary circulation and are effected by a redistribution of the blood in the body as a whole.

Acute Hypovolaemia

- Reduced Central Venous Pressure (CVP)
- Reduced Cardiac Filling
- Reduced Cardiac Output
- Reduced Arterial Pressure

Peripheral Receptors

Central Receptors

- Sympathetic Nerve Stimulation
- Adrenal Medulla Stimulation

Cathecholamines +++

Vasoconstriction

- Arterioles and Venules

Alimentary tract

Skin

Kidney

Oliguria

MAINTENANCE OF BLOOD PRESSURE AND CONSERVATION FLUID

Diminished secretion
At the same time, the circulations in the brain and heart are protected by auto-regulartory mechanisms. They are not subject to the generalized vasoconstriction.

Instead:

- **CEREBRAL** maintains satisfactory dilatation of blood vessels.
- **CORONARY** dilatation ensures flow down to blood pressure of 50-60mmHg.

If the loss of circulating fluid volume is great, the limits of the compensatory mechanism are exceeded and the patient goes into a state of severe shock.

**ADVANCED STAGE**

The patient is now listless, pale and cold, the face is pinched and the lips blue. The pulse is rapid and weak and the blood pressure is low.
Condition in Vascular Bed

Capillary bed

Normal

Arteriole

Venule

Vascular perfusion in tissues in balance

Constriction

Early Shock (Compensatory phase)

Arteriole

BP rises

Vascular perfusion of tissues diminished

Constriction Continues

Advanced Shock (Compensatory Mechanism failing)

Dilatation

Arteriole

BP falls

Capillaries Open

Fluid leaves capillaries – sludging of blood

Vascular perfusion of tissues seriously diminished

TISSUE HYPOXIA
ADVANCED STAGE (Continued)

Thus, from the beginning of the shock process, all the body tissues, with the exception of the brain and the heart, suffer from hypoxia. This sets up vicious circles which aggravate the condition.

**HYPOXIA**

- Damage to cells and tissues
- Production of vasodilator (e.g., enzymes, kinins and Prostaglandinis)
  - Capillary endothelial damage
    - Increased permeability
      - Loss of fluid to tissue spaces substances
        - Loss of circulating fluid (HYPOVOLAEMIA)
  - Loss of circulating fluid (HYPOVOLAEMIA)

**FALL IN BP**
2. When the blood pressure falls below 50-60 mmHg, the autoregulatory control of the cerebral and coronary circulation fails. Serious damage to the brain (p. 194) and heart may occur.
CHANGES IN THE BLOOD AND CELL METABOLISM

As well as these basic circulatory disturbances, important changes in the blood and cellular metabolism occur in shock.

**Blood coagulation system**

- Acute Hypoxia → Damaged endothelium → Coagulation Cascade triggered → May proceed To formation of Fibrin → Disseminated Intravascular Coagulation (DIC)

**Cellular metabolism**

- Acute hypoxia → Pyruvic and Lactic acid Build up → METABOLIC ACIDOSIS
- Acute hypoxia → Inhibition Of respiratory And energy Utilization systems → HYPERGLYCAEMIA
- Glucose → Water → K+
- Failure of ‘sodium pump’ → Na

AGGRAVATION OF WATER AND ELECTROLYTE DISTURBANCE
HEART
There are two main ways in which heart failure may be associated with shock:
1. In hypovolaemic and bacteraemic shock, heart failure is a complication.
2. In cardiogenic shock, acute heart failure is the CAUSE of shock.

Mechanisms

- Poor coronary circulation When BP falls to critical level
- Impaired Respiratory function
- Chemicals released From damaged tissue (esp. pancreas)
- Peripheral vasconstriction

HYPOXIA

Mechanism

- Acute fall in cardiac output
- Tissue Hypoxia

SHOCK reaction

Depresses activity Of myocardium Increases strain on myocardium

Note: Venous return to Heart (CVP) not reduced fluid replacement not required. The commonest condition is Myocardial infarction.
LUNGS

Respiratory function is seriously disturbed in 2 main ways:

1. Changes in the rate and depths of breathing
   - Metabolic acidosis → Respiratory Centre → Hyperventilation

   Oxygen lack ------→ peripheral receptors

2. Circulatory changes in the lung
These occur when compensatory mechanisms are failing.
There is congestion and oedema, patchy to begin with but becoming confluent. At autopsy the lungs are heavy and wet. This condition is called ‘shock lung’ or adult respiratory distress syndrome (ARDS).
Early patchy changes throughout the lungs:

Alveoli full

Of red cells and

Fluid

Neutrophils are ‘sequestered’ in alveolar capillaries
The mechanisms initiating and progressively augmenting the damage are complex and interacting:

1. **ENZYMES AND VASO-ACTIVE AUGMENTING FACTORS**
   - SUBSTANCES from damaged tissues
   - ENDOTOXINS from Gram-negative sepsis
   - Damaging agents (e.g. superoxides) from sequestered neutrophils

   +

   **AUGMENTING FACTORS**
   - (a) Oxygen therapy
   - (b) Some forms of drug therapy
   - (c) Cardiac failure with pulmonary edema
   - (d) Disseminated intravascular coagulation

   ↓

   DAMAGE alveolar epithelium and capillary endothelium

   ↓

   ALVEOLAR EDEMA and HAEMORRHAGE
2. There may also be:
   (a) Patchy alveolar collapse and
   (b) Formation of hyaline membranes

Epithelial damage

\[ \text{Cessation of surfactant action} \]

- Alveolar collapse
- Hyaline membranes

3. If the patient survives, the organization is followed by fibrosis: the end result in severe cases may be a combination of fibrosis, emphysema and bronchoelecctasis.
KIDNEYS

• The secretory function of the kidneys is always disturbed in shock. This is due to the general circulatory collapse and hypotension but it may be aggravated by the secretion of renin and angiotensin by the kidney, aldosterone by the adrenal and antidiuretic hormone by the posterior pituitary. These hormones are secreted in an attempt to retain fluid and restore the blood volume, but by inducing vasoconstriction they will tend to increase renal damage.
Mechanism: Increased breakdown of body proteins (esp in traumatic shock)

FALL IN BLOOD PRESSURE

Decreased glomerular filtrate (GF) → Retention of → WASTE PRODUCTS (Uraemia)

Tubular ischemia (hypoxia)
Depression of function
Oliguria (less than 400 ml urine/d)

Tubular necrosis (esp. distal Tubule:'lower nephron’ GF
Completely reabsorbed

ANURIA → SEVERE PROGRESSIVE URAEMIA

(failure of urine formation: less than 100 ml/d)

In such cases, at post mortem the kidneys are pale and swollen and the architectural Marking are blurred.
ADRENALS

• In addition to the release of aldosterone in response to changes in kidney function and fluid electrolyte balance, the adrenal CORTEX secretes increased quantities of gluocorticoids and the MEDULA a great increase of catecholamines (adrenaline, etc).

• Occasionally in severe shock, adrenal haemorrhage occurs particularly when the blood coagulation mechanism is disturbed or if there is overwhelming bacterial infection.
ALIMENTARY TRACT
• Acute ulceration of the stomach and duodenum may complicate shock – the mechanism is not known. (Clurling’s or stress ulcers). Haemorrhage of varying severity may also occur, especially from the colon.

BRAIN
• During the compensated phase of shock, relatively mild cerebral ischaemia is associated with changes in the state of consciousness. When the blood pressure falls to below 50-60 mHg, the brain suffers serious ischaemic damage which can amount to actual infarction in the ‘boundary zones’ of the cerebral cortex (and cerebellum).
• There may also be more diffuse cerebral damage.
POST MORTEM APPEARANCES IN SHOCK

- These are very variable.
- Often the changes in the organs are not striking, and the continuing presence of the initiating cause of the shock is the most important finding.
- Organ damage of the types described above may be present in varying degree and combination.
• **FAINTING (VASOVAGAL) ATTACK – (PRIMARY SHOCK)**

• What used to be called ‘primary shock’ is in fact the common fainting attack which is brought on in susceptible individuals by emotional upset or trauma which may be minor, and is mediated by nervous mechanisms. The patient feels ‘faint’, becomes pale often with a cold sweat and may vomit. The pulse slows and the blood pressure falls: consciousness is lost.

• At this stage, nervous reaction quickly begins, and with a simple fainting attack recovery is soon complete. On very rare occasions, sudden death occurs due to complete cardiac inhibition by vagal action.

• Because the nervous mechanisms of the fainting attack only play a minor part in the early stages of true shock the term ‘primary shock’ is now obsolete.
SHOCK IN BURNS AND SCALDS

Mechanism

1. The immediate reaction is NERVOUS – PAIN and stimulation of afferent nerves, followed by An INFLAMMATORIY RESPONSE evoked by the burnt tissues.

Massive exudation and Loss of PROTEIN-RICH fluid $\rightarrow$ HYPOVOLAEMIA $\rightarrow$ SHOCK (sludging of blood in capillaries)

This mechanism explains why the SEVERITY of the shock is roughly proportional to the exuding SURFACE AREA and not to the depth of the burn, and why PLASMA transfusion is indicated.
Other factors are chemical mediators derived from the burnt tissue.

1. Complications which aggravate the shock.
   (a) Infection

   Burnt tissues $\rightarrow$ Susceptible to infection $\rightarrow$ BACTERIAL SHOCK
   - Esp. Staph. Aureus
   - Strep. Pyogenes
   - Gram-neg. bacilli
   (e.g. Pseudomonas)

   (b) Anaemia

   Haemolysis of red cells
   At burnt site and later $\rightarrow$ ANAEMIA
   If sludging is severe
ANAPHYLACTIC SHOCK

• This is an acute reaction caused by hypersensitivity of the host to exogenous protein.

BACTERIAL SHOCK

Causes

1. Bacteria

• In modern practice, the GRAM-NEGATIVE BACTERIA, especially the coliform group, are the commonest causes, and the shock is caused by ENDOTOXINS.

• Other organisms which may or may not be associated with endotoxins can also produce shock, e.g. staphylococci, streptococci and menigococci.
2. Associated conditions

- (a) Serious primary bacterial infection, e.g. sepsicaemia, peritonitis – potentiated by deficiency in immune status and liver disease where detoxification is impaired.

- (b) Bacterial shock may complicate pre-existing shock due to other causes, e.g. burns.

- (c) Bacterial shock may complicate relatively trivial surgical procedures, especially in the gastrointestinal and urinary tracts in the presence of infection.
Occasionally, especially in bacterial infection where endotoxin is not produced, there is a generalized arteriolar dilatation with a fall in BP, but the cardiac output is maintained and the patient has a warm, pink skin.
The **OUTCOME** of **SHOCK**

There are 3 possibilities, depending on several factors:

1. **RECOVERY** – after convalescence which may be long.

2. **SURVIVAL** – with permanent damage to various organs.

3. **DEATH**
<table>
<thead>
<tr>
<th>FACTORS FAVOURING RECOVERING</th>
<th>FACTORS FAVOURING PROGRESSION OF SHOCK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Availability of Early Treatment of the Initiating cause the hypovolaemia</td>
<td>Delay in treatment</td>
</tr>
<tr>
<td>Youth</td>
<td>2. Failure to remove the initiating cause</td>
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<tr>
<td>Good general health</td>
<td>3. Old age</td>
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<tr>
<td></td>
<td>Poor general health</td>
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<td>4. Pre-existing cardiovascular and lung disease.</td>
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<td></td>
<td>5. Onset of complications, esp. infection and organ damage</td>
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</tbody>
</table>
IRREVERSIBLE SHOCK

• Theoretically, at some stage in its evolution, shock becomes irreversible due to the severity of vascular impairment and tissue damage. In medical practice, no certain indications are available as to when this point is reached. Measurements of blood pressure and central venous pressure indicate the severity of the vascular disturbance, but many severe cases respond to modern sophisticated treatment. However, the basic essentials remain the early transfusion of fluid and the removal of the original cause of the shock.