Pathophysiology of shock
Definition of shock

Hypoperfusion of organs and tissues, which in turn results in insufficient supply of oxygen and nutrients for cellular function.
Shock:

- An inadequate delivery of oxygen and substrates create the cellular injury, induces the production and release of inflammatory mediators.
- Compromise perfusion through functional and structural changes within the microvascular circulation, leading to impaired perfusion and cellular injury.
- Maldistribution of blood flow compromising cell perfusion.
Cellular Responses:

- Anaerobic glycolytic pathway
- Severe shock
- Impaired function of Na/K-ATPase
- Intra cellular and extracelular accumulation of lactic acid
- Limited amounts of ATP
- Mitochondria activity depressed and lysosomal membranes may rupture
- Intracellular accumulation of sodium and loss of potassium
- Cellular edema and increased cell membrane permeability

- Cell death and the release of intracellular contents into the extracellular space
- Release of enzymes and intracellular destruction
Compensatory Mechanisms:

1. Immediate:
   A) the sympathetic nervous system
   B) the renin-angiotensin mechanism

- Increase heart rate and stimulate constriction of blood vessels
- Maintain cardiac output and blood pressure
- Alpha and beta receptors
- Beta 1 receptors - increase in heart rate and force of myocardial contraction;
- Beta 2 receptors - vasodilation of the skeletal muscle beds and relaxation of the bronchioles
- Vasoconstriction
renin-angiotensin mechanism:

- Increase in sodium and water retention by the kidneys.
- Increase in norepinephrine, angiotensin II, vasopressin, and endothelin.
- Local release of vasoconstrictors: norepinephrine, angiotensin II, vasopressin, and endothelin.
- Increased production of oxygen free radicals.
- Vasoactive inflammatory mediators such as histamine.
- Cellular metabolism is impaired.
- Excessive lactic acid and hydrogen ions.
- Arterial and venous vasoconstriction.
- A decrease in tissue perfusion and insufficient supply of oxygen.
### Chart 20-1: Classification of Circulatory Shock

**Cardiogenic**
- Myocardial damage (myocardial infarction, contusion)
- Sustained arrhythmias
- Acute valve damage, ventricular septal defect
- Cardiac surgery

**Hypovolemic**
- Loss of whole blood
- Loss of plasma
- Loss of extracellular fluid

**Obstructive**
- Inability of the heart to fill properly (cardiac tamponade)
- Obstruction to outflow from the heart (pulmonary embolus, cardiac myxoma, pneumothorax, or dissecting aneurysm)

**Distributive**
- Loss of sympathetic vasomotor tone (neurogenic shock)
- Presence of vasodilating substances in the blood (anaphylactic shock)
- Presence of inflammatory mediators (septic shock)
Types of Shock:
Cardiogenic shock occurs when the heart fails to pump blood sufficiently to meet the body’s demands.

Clinically, it is defined as decreased cardiac output, hypotension, hypoperfusion, and indications of tissue hypoxia despite an adequate intravascular volume.
Causes of cardiogenic shock:

- myocardial infarction,
- myocardial contusion,
- acute mitral valve regurgitation
- papillary muscle rupture,
- sustained arrhythmias,
- severe dilated cardiomyopathy,
- cardiac surgery.
Cardiogenic Shock

- Clinically is defined as
- Decreased CO, hypotension, hypoperfusion, indications of tissue hypoxia
Pathophysiology:

Cause
- Decreased myocardial contractility
- Increased afterload, excessive preload
- Mediators, neurotransmitters

Decreased SV, CO

Insufficient perfusion

Decreased cardiac function

Renin-Ag-Aldosteron

Impaired coronary artery perfusion

Increase in intracardiac pressures
Clinical Features of Cardiogenic Shock

- Lips, nail beds, and skin-cyanotic → stagnation of blood flow and increased extraction of oxygen from Hb
- Urine output decreases ← lower renal perfusion pressures and the increased release of aldosterone.
- Elevated preload ← CVP and PCWP
- Neurologic changes (alteration in cognition or consciousness) ← low cardiac output and poor cerebral perfusion
CARDIOGENIC SHOCK

Cardiogenic shock is the inability of the heart to maintain cardiac output necessary to meet body needs. Extra strain on the heart causes decreased tissue perfusion.

Clinical Symptoms
- Tachycardia
- Anxiety and delirium
- Increased preload
- Pulmonary congestion
- Decreased cardiac output
- Dusky skin color
- Decreased blood pressure
- Narrow pulse pressure
- Oliguria
- Dyspnea

Causes
- Systolic dysfunction
- Diastolic dysfunction
- Arrhythmias
- Structural problems
Hypovolemic Shock

It is characterized by diminished blood volume such that there is inadequate filling of the vascular compartment.
Causes of hypovolemic shock:

- Acute loss of 15-20% of the circulating blood volume
- External loss of whole blood (hemorrhage), plasma (severe burns), or extracellular fluid (severe dehydration or loss of gastrointestinal fluids with vomiting or diarrhea
- Internal hemorrhage
- Third-space losses
Acute bleeding or other conditions leading to decrease in blood volume

Compensatory mechanisms

Mechanisms to maintain cardiovascular function

Heart
- Increased heart rate and cardiac contractility

Blood vessels
- Vasocostriction of vessels in skin and nonvital organs

Mechanisms to maintain blood volume

Hypothalamus
- Stimulation of thirst
  - Posterior pituitary
  - Stimulation of ADH release

Liver
- Constriction of veins and sinusoids with mobilization of blood stored in liver

Kidney
- Sodium and water retention
  - Release of aldosterone

Adrenal cortex
- Release of aldosterone

Decreased urine output
Clinical features:

- Depend on severity and are related to:
  - 1. Low peripheral blood flow
  - 2. Excessive sympathetic stimulation
    - thirst
    - increased heart rate
    - cool and clammy skin
    - decreased arterial blood pressure
    - decreased urine output
    - changes in mentation
Laboratory tests:

- Hb level is normal
- Ht increases
- Low pH
- Lactic acid increases
- Metabolic acidosis
- Coagulopathy
- Hypothermia
- Circulatory failure
Pathophysiology of clinical features

- Increased heart rate
- Pulse becomes weak and thready \( \Rightarrow \) vasoconstriction and reduced filling of the vascular compartment;
- Thirst \( \leftarrow \) decreased blood volume and increased serum osmolality;
- Arterial blood pressure decreases;
- Respiration becomes rapid and deep \( \Rightarrow \) compensates metabolic acidosis
- Decreased venous return to the heart and a decreased CVP
- Peripheral veins may collapse
- Cool and mottled skin \( \leftarrow \) sympathetic stimulation
- Urine output decreases
- Restlessness, agitation, and apprehension
Distributive shock or vasodilatory shock is characterized by loss of blood vessel tone;
- Enlargement of the vascular compartment;
- Displacement of the vascular volume away from the heart;
- Central circulation

- Normovolemic shock!
Distributive Shock

Causes:
1. a decrease in the sympathetic control of vasomotor tone
2. release of excessive vasodilator substances
3. prolonged and severe hypotension due to hemorrhage (irreversible or late-phase hemorrhagic shock);

- Neurogenic shock
- Anaphylactic shock
- Septic shock
Neurogenic shock

- Caused by decreased sympathetic control of blood vessel tone due to a defect in the vasomotor center in the brain stem or the sympathetic outflow to the blood vessels
  - (spinal cord injury, brain injury, depressant action of drugs, general anesthesia, hypoxia, or lack of glucose);
Imbalance between sympathetic and parasympathetic stimulation

Massive vasodilation

Decreased vascular tone

Decreased systemic vascular resistance

Causes of neurogenic shock:

- Spinal cord injury above T5
- Spinal anesthesia
- Vasomotor center depression (e.g., severe pain, drugs, hypoglycemia)
Anaphylactic (Systemic) Reactions

A systemic life-threatening hypersensitivity reaction characterized by widespread edema, vascular shock, difficulty breathing.
Systemic Anaphylaxis

- **Aetiology:**
  - injection of an antigen;
  - insect sting;
  - absorption across the epithelial surface skin or gastrointestinal mucousa.
Anaphylactic Shock

Signs and symptoms of Anaphylaxis

- Swelling of the conjunctiva
- Runny nose
- Swelling of lips, tongue, and/or throat
- Heart and vasculature: fast or slow heart rate, low blood pressure
- Skin: hives, itchiness, flushing
- Pelvic pain
- Central nervous system: lightheadedness, loss of consciousness, confusion, headache, anxiety
- Respiratory: shortness of breath, wheezes or stridor, hoarseness, pain with swallowing, cough
- Gastrointestinal: crampy abdominal pain, diarrhea, vomiting
- Loss of bladder control

Causes:
- Food
- Medication (antibiotics)
- Venom from animals (bugs, snakes, etc.)
- Allergic reactions

Treatment:
- EpiPen (Epinephrine)
- Histamine (pharmaceutical drug)
- 911

How to Prevent it:
The most common cause of this kind of shock are allergic reactions. To counteract the severity of the reaction in the future, immunotherapy is the way to go. The person is gradually vaccinated with progressively larger doses of the allergen, small enough so that the body's immune system can counteract it on its own, conditioning the body.

Glogster by Nick Termini and Zack Assenmacher
Manifestations:

- Itching
- Hives
- Skin erythema
- Laryngeal edema
- Bronchospasm
- Respiratory distress
- Vomiting
- Abdominal cramps
- Diarrhea
- Shock
- Die
Septic shock

The most common type of vasodilatory shock that is associated with severe infection and the systemic response to infection
As suspected or proven infection, plus a systemic inflammatory response (e.g., fever, tachycardia, tachypnea, and elevated white blood cell count, altered mental state, and hyperglycemia in the absence of diabetes.

**Severe sepsis** - as sepsis with organ dysfunction (e.g., hypotension, hypoxemia, oliguria, metabolic acidosis, thrombocytopenia, or obtundation)

**Septic shock** - as severe sepsis with hypotension, despite fluid resuscitation
**The Sepsis Continuum**

- **SIRS**
  - A clinical response arising from a nonspecific insult, with \( \geq 2 \) of the following:
    - \( T > 38^\circ C \) or \( < 36^\circ C \)
    - \( HR > 90 \) beats/min
    - \( RR > 20 \) /min
    - \( WBC > 12,000 / \text{mm}^3 \) or \( < 4,000 / \text{mm}^3 \) or \( > 10\% \) bands

- **Severe Sepsis**
  - SIRS with a presumed or confirmed infectious process

- **Septic Shock**
  - Sepsis with organ failure
  - Refractory hypotension
Sepsis and septic shock

1. Cellular activation
2. Release of cytokines
3. Recruitment of neutrophils and monocytes
4. Involvement of neuroendocrine reflexes
5. Activation of compliment, coagulation, and fibrinolitic systems
Manifestations:

- Arterial hypotension;
- Warm and flushed skin
- Hypovolemia due to arterial, venous dilatation and leakage of plasma into the interstitial spaces
- Abrupt changes in cognition or behavior due to reduced cerebral blood flow
- Fever,
- Increased leukocytes
- Metabolic acidosis
Obstructive shock

Circulatory shock that results from mechanical obstruction of the flow of blood through the central circulation (great veins, heart, or lungs)
Obstructive shock

- **Causes:**
  1. dissecting aortic aneurysm
  2. cardiac tamponade
  3. pneumothorax
  4. atrial myxoma
  5. evisceration of abdominal contents into the thoracic cavity due to ruptured hemidiaphragm
  6. pulmonary embolism
Obstructive shock

Pathogenesis

- Elevated right heart pressure due to impaired right ventricular function
- Pressures are increased despite impaired venous return to the heart

Manifestations

- Elevation of CVP
- Jugular vein distention
Complications of shock:

1. Acute Lung Injury/Acute Respiratory Distress Syndrome
2. Acute Renal Failure
3. Gastrointestinal Complications
4. Disseminated Intravascular Coagulation
5. Multiple Organ Dysfunction Syndrome
It is a potentially lethal form of pulmonary injury that may be either the cause or result of shock.
Acute Lung Injury/Acute Respiratory Distress

- Rapid onset of profound dyspneea that occurs 12 to 48 hours
- Respiratory rate and effort of breathing increases;
- Profound hypoxemia (impaired matching of ventilation and perfusion, greatly reduced diffusion of blood gases across the thickened alveolar membranes)
Pathophysiology of (ARDS)

- Cytokines
  - Activation of neutrophils
    - Accumulates in pulmonary vasculature
      - Injury to endothelial cells
        - Leakage of fluid and plasma proteins in alveolar spaces
          - Atelectasis
          - Impaired gas exchange
          - Decrease compliance (stiffness)
          - Decrease surfactant
ARDS - PATHOGENESIS

Insult (direct or indirect)

Activation of inflammatory cells & mediators

Damage to alveolar capillary membrane

Increased permeability of alveolar capillary membrane

Influx of protein rich edema fluid and inflammatory cells into air spaces

Dysfunction of surfactant
Acute renal failure:

Renal ischemia

→ Vascular effects

Increased cytosolic $\text{Ca}^{2+}$ in afferent arterioles of the glomerulus

Increased sensitivity to vasoconstrictor and renal nerve stimulation; impaired autoregulation

$\Uparrow$ Endothelial injury

$\downarrow$ NO derived from eNOS

$\Uparrow$ ET

$\downarrow$ PGs

$\Uparrow$ Inflammatory mediators (TNF-$\alpha$, IL-18)

Endothelial ICAM-1 and P-selectin

$\Uparrow$ Neutrophil adhesion

$\Uparrow$ Oxygen radicals

$\downarrow$ GFR
G.I Complication

- Constriction of vessels supplying GIT for redistribution of blood flow
  - Severe Decrease mucosal perfusion
    - GIT ulceration
    - Bleeding
Disseminated Intravascular Coagulation

**PATHOPHYSIOLOGY**

- Stimulus
- Tissue destruction (Extrinsic pathway)
- Endothelial injury
- Tissue factor
- Endotoxin
- Factor XII activation (intrinsic pathway)

**Thrombin generation**

- Intravascular fibrin deposition
- Plasmin activation
- Platelet consumption
- Thrombocytopenia

**Thrombosis**

- Hemolytic anemia
- Tissue ischemia

- Fibrin degradation products (inhibit thrombin and platelet aggregation)
- Fibrinolysis
- Clotting factor degradation

**Bleeding**
Hypovolaemia

Endogenous vasoconstrictors

Splanchnic hypoperfusion

Gut mucosal hypoperfusion

Ischaemia-reperfusion injury

Exogenous vasoconstrictors

Gut mucosal barrier disruption

Increased mucosal permeability to bacteria/endotoxin

Activation of inflammatory pathways

MODS