SHOCK

Low perfusion circulatory insufficiency leading to an imbalance between the metabolic needs of vital organs and available blood flow.

Features:
- ↓O₂ delivery to cells
- ↓removal of wastes

Key organs affected:
- Brain
- Heart
- Lungs
- Kidneys

Types of Shock
1. Hypovolemic
2. Cardiogenic* (pump failure)
3. Septic*
4. Neurogenic

* high mortality

Shock

Systemic hypoperfusion due to:
- Reduction in cardiac output
- Reduction in effective circulating blood volume

Hypotension → Impaired tissue perfusion → Cellular hypoxia

Clinical Signs of Shock
- Hypotension
- Weak, thready pulse
- Cool, clammy skin
- Tachycardia
- Altered respirations and sensorium
- Peripheral cyanosis
- Oliguria

Phases of Shock

1st (Early) Phase: Immediate problems due to medical, surgical or obstetrical catastrophe
- Electrolytes/acidosis/respiratory difficulties

2nd Phase: 1-6 days
- Renal dysfunction
- Acute tubular necrosis (ATN)
- Fluid overload
- Hyperkalemia
- Acidosis/alkalosis

3rd Phase: Diuretic phase
- 10-14 days and later
- urine volume (3L/day)
### Stages of Shock:

<table>
<thead>
<tr>
<th>Non-Progressive Stage</th>
<th>Progressive Stage</th>
<th>Irreversible Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>- compensatory reflex mechanisms activated (baroreceptors/ catechol. release)</td>
<td>- tissue hypoperfusion &amp; worsened circulatory metabolic imbalance</td>
<td>- severe cell &amp; tissue injury with no chance of recovery</td>
</tr>
</tbody>
</table>

### Congestion (Hyperemia)

Increased volume of blood in affected tissue

**Mechanism:**

- arterial and arteriolar dilatation
- flow into capillaries

### Nomenclature of Hemorrhage

- hematoma: massive clot
- hemotherax: hem. into thoracic cavity
- hemopericardium: hem. into pericardium
- hemoperitoneum: hem. into peritoneum

- petechiae: minute (1-2 mm)
- purpura: larger (1 cm)
- ecchymoses: several cm. in size; large and blotchy

### Significance of Hemorrhage

**NO CLINICAL FINDINGS:**

- 10-20% of bld. vol. lost
- slow blood loss

**HYPOVOLEMIC SHOCK:**

- larger blood losses
- more rapid bld. loss
Edema

*The abnormal accumulation of fluid in the intercellular tissue spaces or body cavities
  - localized
  - systemic

Edema fluids: nomenclature
- abdomen: ascites
- pleural cavities: effusions / hydrothorax
- pericardium: effusion
- total body: anasarca

Extravascular/Edema Fluids: Terminology

Transudate:
- low protein content
- non-inflammatory
- ultrafiltrate of plasma (mostly albumin)
- due to osmotic/hydrostatic imbalance
- no increase in vasc. permeab.
- S.G. < 1.012

Exudate:
- high protein concentration
- inflammatory
- due to altered permeab. of small bld. vessels
- S.G. > 1.020

Mechanisms of edema formation

• ↓ plasma colloid oncotic pressure
• ↑ hydrostatic pressure
• ↑ endothelial permeability
• lymphatic blockage
Thrombosis: the Virchow triad

- Endothelial injury
- Abnormal blood flow
- Hypercoagulability

Thrombosis
### Types & Fate of Thrombi

#### Types
- **Arterial:** coronary, cerebral, aorta + branches
- **Venous:** 90% in deep leg veins (also peri-uterine, peri-prostatic)
- **Mural:** heart

#### Fate
- **Propagation**
- **Embolization**
- **Dissolution**
- **Organization and recanalization**

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<th>Fate</th>
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<tr>
<td>Arterial</td>
<td>Venous thrombi (“right-sided”)</td>
</tr>
<tr>
<td>Venous</td>
<td>Arterial thrombi (“left-sided”)</td>
</tr>
</tbody>
</table>

#### Right-sided thromboemboli:
- Classic example is pulmonary emboli
- Paradoxical embolus: through patent foramen ovale to left side
- Right atrial appendage thrombi (often in mitral stenosis + atrial fibrillation)
- Pulmonary infarct (wedge-shaped region of necrotic lung) Seen in only approx. 10% of pulmonary emboli because of dual lung perfusion from bronchial arteries

#### Left-sided thromboemboli:
- Classic examples are mural thrombi in
- Left atria/ventricle or endocarditis
- Atrial appendage thrombi (often in mitral stenosis + atrial fibrillation)
Acute myocardial infarction
Disseminated Intravascular Coagulation (DIC) (Consumption Coagulopathy)

- Widespread thrombosis in microcirculation
- Platelets & fibrin in capillaries
- Mechanism: Activate *intrinsic* pathway
- Clinical: sepsis—obstetrical catastrophe—cancer—extensive tissue damage
- Hematologic: rapid consumption of fibrinogen, platelets, prothrombin, V, VIII, X
  - Generation of d-dimers ("fibrin split products")

Sepsis & Septic shock: definitions

1. **SEPSIS:** suspected or proven infection + systemic inflammatory response syndrome: fever, tachycardia, tachypnea, leukocytosis
2. **SEVERE SEPSIS:** sepsis + ORGAN DYSFUNCTION: hypotension, hypoxemia, oliguria, metabolic acidosis, thrombocytopenia, obtundation
3. **SEPTIC SHOCK:** severe sepsis + ORGAN DYSFUNCTION, HYPOTENSION, despite adequate fluid resuscitation

750,000 cases of sepsis / yr. in U.S.

Immune cell “cross-talk” in sepsis

NEJM 2003; 348: 138-150
**Toll-like receptors (TLR)**
- Family of PPR's (pattern recognition receptors)
  - TLR2: peptidoglycan
    - Gram+ org's
  - TLR 4: LPS (endotoxin)
    - Gram- org's

Roles of procoagulant-anti-coagulant balance
- Tissue factor (thromboplastin)
- Levels of:
  - Protein C
  - Protein S
  - Antithrombin III
  - Tissue factor-pathway inhibitor

**Role of innate immune response in sepsis**
- Proinflam. cytokines: TNF, IL-1
- Upregulate adhesion molecules
- Neutrophils (PMN, Mac)
- Upregulate adhesion molecules
- Systemic acute-phase response
  - Edema
  - Vasc. permeab.

**Role of adaptive immune response in sepsis**
- Th1: PROINFLAM. cytokines: TNF, IL-1
- Th2: ANTI-INFLAM. cytokines: IL-4, IL-10
- Circulatory shock
  - Hypovolemia
  - Acute lung injury
  - Renal failure
  - Myocardial contractility

**Table 1. Pathways and mediators of injury, relevant treatments, and results of sepsis models.**

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Treatment</th>
<th>Results of Sepsis</th>
</tr>
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<tbody>
<tr>
<td>Sepsis-related neutrophils</td>
<td>Anti-TNF-α</td>
<td>Negative</td>
</tr>
<tr>
<td>Intercellular adhesion</td>
<td>Interleukins I-3</td>
<td>Negative</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Endothelial permeability</td>
<td>Negative</td>
</tr>
<tr>
<td>Procoagulant</td>
<td>Prothrombin</td>
<td>Negative</td>
</tr>
<tr>
<td>Procoagulant</td>
<td>Protease-activated factor</td>
<td>Negative</td>
</tr>
<tr>
<td>Procoagulant</td>
<td>Tissue factor</td>
<td>Negative</td>
</tr>
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NEJM 2006; 355: 1699-1713