Shock: The Physiologic Perspective

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Shock

A “rude unhinging” of the machinery of life.

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Samuel Gross (1862)
Shock

Shock is inadequate tissue perfusion.
Cellular Requirements

Oxygen

Glucose
Cellular Requirements

- Proteins
- Carbohydrates
- Lipids

Glucose
Cellular Energy Production

- **Glycolysis**
  - Glucose → Pyruvate
  - +2 ATP

- **Transition Reaction**
  - Electrons transferred by NADH

- **Citric Acid Cycle**
  - Electrons transferred by NADH
  - Electrons transferred by NADH and FADH₂

- **Electron Transport Chain**
  - +32 ATP

- **Total ATP**
  - 36 ATP

**Locations**
- Extracellular fluid
- Blood vessel
- Carrier protein
- Plasma membrane
- Cytoplasm
- Mitochondrion
Glycolysis

During the first steps, two molecules of ATP are consumed in preparing glucose for splitting.

Glucose → 2 ADP → 4 ATP

During the remaining steps, four molecules of ATP are produced.

2 Pyruvate → 2 NAD^+ → 2 NADH

The two molecules of pyruvate then diffuse from the cytoplasm into the inner compartment of the mitochondrion, where they pass through a few preparatory steps (the transition reactions) before entering the citric acid cycle.

Two molecules of nicotinamide adenine dinucleotide (NADH), a carrier of high-energy electrons, also are produced.
Transition Reaction

A molecule of NADH is formed when NAD\(^+\) gains two electrons and one proton.

Pyruvate (from glycolysis)

One carbon (in the form of CO\(_2\)) is removed from pyruvate.

NAD\(^+\)

(electron passes to electron transport chain)

A molecule of NADH is formed when NAD\(^+\) gains two electrons and one proton.

Coenzyme A

The two-carbon molecule, called an acetyl group, binds to coenzyme A (CoA), forming acetyl CoA, which enters the citric acid cycle.

Citric Acid Cycle

CoA

Acetyl CoA
Kreb’s (Citric Acid) Cycle

The citric acid cycle also yields several molecules of FADH₂ and NADH, carriers of high-energy electrons that enter the electron transport chain.

Acetyl CoA, the two-carbon compound formed during the transition reaction, enters the citric acid cycle.

The citric acid cycle yields one ATP from each acetyl CoA that enters the cycle, for a net gain of two ATP.
Electron Transport

The molecules of NADH and FADH₂ produced by earlier phases of cellular respiration pass their electrons to a series of protein molecules embedded in the inner membrane of the mitochondrion. As the electrons are transferred from one protein to the next, energy is released and used to make ATP. Eventually, the electrons are passed to oxygen, which combines with two hydrogens to form water.

Energy released is used for synthesis of ATP.
Adenosine Triphosphate (ATP)
Cellular Requirements

- **Oxygen**
  - Required for the majority of energy production derived from Krebs Cycle and Electron Transport Chain.
  - **Metabolism with Oxygen = Aerobic Metabolism**
  - **Metabolism without Oxygen = Anaerobic Metabolism**
Oxygen Transport

- **Oxygen Transport:**
  - Hemoglobin-bound (97%)
  - Dissolved in plasma (3%)

- **Monitoring:**
  - Hemoglobin-bound (SpO₂)
  - Dissolved in plasma (pO₂)
Oxygen Transport
Carbon Dioxide Transport

CO₂ transported as:
1. CO₂ dissolved = 7%
2. HbCO₂ = 23%
3. HCO₃⁻ = 70%
**Oxygen Delivery**

\[ DO_2 = \text{Normal Oxygen Delivery} \]

\[ DO_2 = Q \times CaO_2 \]

\[ DO_2 = Q \times (1.34 \times Hb \times SpO_2) \times 10 \]

Normal \( DO_2 \) is 520 to 570 mL/minute/m²
Clinical Correlation

\[ DO_2 = Q \times (1.34 \times Hb \times SpO_2) \times 10 \]

What factors can affect oxygen delivery to the tissues?

- Cardiac Output (Q)
- Available Hemoglobin (Hb)
- Oxygen Saturation (SpO_2)
Oxygen Uptake

\[ \text{VO}_2 = Q \times 13.4 \times \text{Hb} \times (\text{SpO}_2 - \text{SvO}_2) \]
Oxygen Extraction Ratio

\[ O_2\text{ER} = \frac{VO_2}{DO_2} \times 100 \]

Normal \( O_2\text{ER} = 0.2-0.3 \) (20 to 30\%)
Metabolic Demand

• **MRO$_2$**:  
  - 1. The metabolic demand for oxygen at the tissue level.  
  - 2. The rate at which oxygen is utilized in the conversion of glucose to energy and water through glycolysis and Kreb’s cycle.
Shock

\[ \text{VO}_2 \geq \text{MRO}_2 = \text{Normal Metabolism} \]

\[ \text{VO}_2 < \text{MRO}_2 = \text{SHOCK} \]
Shock

• Causes of Shock:
  • **Inadequate oxygen delivery:**
    • Inadequate respiration and oxygenation
    • Inadequate hemoglobin
    • Inadequate fluid in the vascular system
    • Inadequate blood movement
  • **Impaired oxygen uptake**
Shock

- Causes of Shock:
  - Inadequate nutrient delivery:
    - Inadequate nutrient intake
    - Inadequate nutrient delivery
    - Inadequate fluid in the vascular system
    - Inadequate blood movement
  - Impaired nutrient (glucose) uptake
Shock

• **Causes of Shock:**
  
  • **Inadequate oxygen delivery**
    - Inadequate respiration and oxygenation
      - Respiratory failure (mechanical, toxins)
    - **Inadequate hemoglobin**
      - Hemorrhage or anemia
    - **Inadequate fluid in the vascular system**
      - Hemorrhage or fluid loss (burns, vomiting, diarrhea, sepsis)
    - **Inadequate blood movement**
      - Cardiac pump failure
  
  • **Impaired oxygen uptake**
    - Biochemical poisoning (hydrogen cyanide)
Shock

• Impaired oxygen uptake

• Cyanide:
  • Inhibits metal-containing enzymes (i.e., cytochrome oxidase)
  • Halts cellular respiration
Shock

• **Causes of Shock:**
  
  • **Inadequate nutrient delivery**
    • Inadequate nutrient intake
      • Malnutrition, GI absorption disorder
    • Inadequate nutrient delivery
      • Malnutrition, hypoproteinemia
  
  • Inadequate fluid in the vascular system
    • Hemorrhage, fluid loss (burns, vomiting, diarrhea)
  
  • Inadequate blood movement
    • Cardiac pump failure
  
• **Impaired nutrient (glucose) uptake**
  • Lack of insulin (Diabetes Mellitus)
Shock (Types)

- Hemorrhagic
- Respiratory
- Neurogenic
- Psychogenic
- Cardiogenic
- Septic
- Anaphylactic
- Metabolic
Shock (Classifications)

• Physiological classifications better describe underlying problem:
  • Cardiogenic Shock
  • Hypovolemic Shock
  • Distributive Shock
    • Spinal Shock
    • Septic Shock
    • Anaphylactic
The pathway to shock follows a common metabolic pattern.
Pathogenesis of Shock

Impaired Glucose Usage → Inadequate Tissue Perfusion → Impaired Oxygen Usage

- Increased Serum Glucose Levels
  - Increased Pyruvic Acid
  - Increased Lipid Breakdown (Lipolysis)
  - Increased Glucose Production
  - Increased Glycogen Breakdown
  - Increased Triglycerides and Fatty Acids
  - Increased Protein Breakdown
    - Increased Serum Alanine
    - Decreased Serum Albumin
    - Increased Amino Acids
    - Decreased Colloid Osmotic Pressure
    - Loss of Intravascular Fluid

- Release of Catecholamines, Cortisol, and Growth Hormone
  - Decreased Energy Reserves

- Acidosis Causes Decreased Oxygen Affinity for Hemoglobin
  - Increased Lactic Acid
  - Metabolic Acidosis

- Anaerobic Metabolism
  - Decreased Energy (ATP)
  - Decreased Sodium/Potassium Pump
  - Influx of intracellular sodium and water

- Cellular Edema
  - Cellular Rupture

- Release of Digestive Lysosomal Enzymes
- Inflammatory Response
- Activation of Clotting Cascade
Pathogenesis of Shock

Glucose → ATP

2 Lactate → 2 Pyruvate

NAD+ → NADH

ADP + Pi → ATP
Cardiogenic Shock

The heart cannot pump enough blood to meet the metabolic demands of the body.
Cardiogenic Shock

• Loss of contractility:
  - AMI
  - Loss of critical mass of left ventricle
  - RV pump failure
  - LV aneurysm
  - End-stage cardiomyopathy
  - Myocardial contusion
  - Acute myocarditis
  - Toxic global LV dysfunction
  - Dysrhythmias/heart blocks

• Mechanical impairment of blood flow:
  - Valvular disease
  - Aortic dissection
  - Ventricular septal wall rupture
  - Massive pulmonary embolus
  - Pericardial tamponade
Cardiogenic Shock

Pathogenesis of Cardiogenic Shock

**Systolic Dysfunction**
- Decreased Cardiac Output
  - Activation of Renin/Angiotensin System
- Decreased Stroke Volume
  - Antidiuretic Hormone (ADH) Release
  - Increased Aldosterone
- Myocardial Dysfunction
  - Catecholamine Release
  - Increased Systemic Vascular Resistance

**Diastolic Dysfunction**
- Increased Left Ventricular End-Diastolic Pressure (LVEDP)
  - Pulmonary Congestion

**Flowchart**
- Increased Blood Volume
- Increased Preload
  - Increased Heart Rate
  - Increased Stroke Volume
  - Increased Cardiac Work
  - Increased Myocardial Oxygen Use
  - Decreased Cardiac Output
    - Decreased Ejection Fraction
    - Decreased Tissue Perfusion
    - Impaired Cellular Metabolism
Hypovolemic Shock

Fluid (blood or plasma) is lost from the intravascular space.
# Hypovolemic Shock

## Trauma:
- Solid organ injury
- Pulmonary parenchymal injury
- Myocardial laceration/rupture
- Vascular injury
- Retroperitoneal hemorrhage
- Fractures
- Lacerations
- Epistaxis
- Burns

## GI Tract:
- Esophageal varices
- Ulcer disease
- Gastritis/esophagitis
- Mallory-Weiss tear
- Malignancies
- Vascular lesions
- Inflammatory bowel disease
- Ischemic bowel disease
- Infectious GI disease
- Pancreatitis
Hypovolemic Shock

- **GI Tract:**
  - Infectious diarrhea
  - Vomiting

- **Vascular:**
  - Aneurysms
  - Dissections
  - AV malformations

- **Reproductive Tract:**
  - Vaginal bleeding
    - Malignancies
    - Miscarriage
    - Metrorrhagia
    - Retained products of conception
    - Placenta previa
  - Ectopic Pregnancy
  - Ruptured ovarian cyst
Hypovolemic Shock
Neurogenic Shock

- Interruption in the CNS connections with the periphery (spinal cord injury).
- Form of distributive shock.
Neurogenic Shock

- Spinal cord injury
- Spinal anesthetic
Neurogenic Shock

\[ \text{BP} = \text{CO} \times \text{PVR} \]

\[ \text{CO} = \text{HR} \times \text{SV} \]

\[ \text{BP} = (\text{HR} \times \text{SV}) \times \text{PVR} \]
Neurogenic Shock

Pathogenesis of Neurogenic Shock

- Spinal Cord Injury
  - Autonomic Nervous System Imbalance
    - Massive Vasodilation
      - Decreased Systemic Vascular Resistance
        - Massive Vasodilation
        - Massive Vasodilation
          - Inadequate Cardiac Output
            - Decreased Tissue Perfusion
              - Impaired Cellular Metabolism
Anaphylactic Shock

- Shock resulting from widespread hypersensitivity.
- Form of distributive shock.
Anaphylactic Shock

• **Drugs:**
  - Penicillin and related antibiotics
  - Aspirin
  - Trimethoprim-sulfamethoxazole (Bactrim, Septra)
  - Vancomycin
  - NSAIDs

• **Other:**
  - *Hymenoptera* stings
  - Insect parts and molds
  - X-Ray contrast media (ionic)

• **Foods and Additives:**
  - Shellfish
  - Soy beans
  - Nuts
  - Wheat
  - Milk
  - Eggs
  - Monosodium glutamate
  - Nitrates and nitrites
  - Tartrazine dyes (food colors)
Anaphylactic Shock

Pathogenesis of Anaphylactic Shock

1. Exposure to Antigen at Some Point in Life
2. Repeat Exposure to Same Antigen
   - Large Release of Antibody IgE
   - Increased Capillary Permeability
   - Edema
3. Massive Release of Histamine, Prostaglandins, Kinins
   - Peripheral Vasodilation
   - Decreased Systemic Vascular Resistance
   - Relative Hypovolemia
   - Decreased Cardiac Output
   - Decreased Tissue Perfusion
   - Impaired Cellular Metabolism
4. Bronchoconstriction
   - Laryngospasm
   - Gastrointestinal Cramps, Vomiting, Diarrhea
Septic Shock

- Component of systemic inflammatory response syndrome (SIRS).
- Form of distributive shock.
Septic Shock

• Patient has nidus of infection.
• Causative organism releases:
  • **Endotoxin**
    • Toxic shock syndrome toxin-1
    • Toxin A (*Pseudomonas aeruginosa*)
  • **Structure Components**
    • Teichoic acid antigen
    • Endotoxin
  • **Activates immune system cascade**
2016 Consensus Definitions:

- **Sepsis:** Life-threatening organ dysfunction caused by a dysregulated host response to infection.

- **Septic shock:** Sepsis with circulatory and cellular/metabolic abnormalities profound enough to substantially increase mortality.
2016 Consensus Clinical Criteria:

• **Sepsis.** Suspected or documented infection and an acute increase ≥ 2 SOFA points.

• **Septic shock:** Sepsis and vasopressor therapy needed to elevate MAP ≥ 65 mm Hg and lactate ≥ 2 mmol/L (18 mg/dL) after adequate fluid resuscitation.
# Septic Shock

## Sequential Organ Failure Assessment (SOFA) Score

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurologic (GCS)</strong></td>
<td>13-14</td>
<td>10-12</td>
<td>6-9</td>
<td>&lt; 9</td>
</tr>
<tr>
<td><strong>Pulmonary PaO(_2/)FiO(_2)</strong></td>
<td>&lt; 400</td>
<td>&lt; 300</td>
<td>&lt; 200 With Respiratory Support</td>
<td>&lt; 100 With Respiratory Support</td>
</tr>
<tr>
<td><strong>Cardiac MSAP</strong></td>
<td>&lt; 70</td>
<td>Dopamine ≤ 5 or Dobutamine (whatever dose)</td>
<td>Dopamine &gt; 5 or Epinephrine ≤ 0.1 or Norepinephrine ≤ 0.1</td>
<td>Dopamine &gt; 15 or Epinephrine &gt; 0.1 or Norepinephrine &gt; 0.1</td>
</tr>
<tr>
<td><strong>Renal Creatinine or Diuresis</strong></td>
<td>1.2-1.9</td>
<td>2.0-3.4</td>
<td>3.5-4.9</td>
<td>&gt; 5.0</td>
</tr>
<tr>
<td><strong>Platelets</strong></td>
<td>&lt; 150</td>
<td>&lt; 100</td>
<td>&lt; 50</td>
<td>&lt; 20</td>
</tr>
<tr>
<td><strong>Bilirubin</strong></td>
<td>1.2-1.9</td>
<td>2.0-5.9</td>
<td>6.0-11.9</td>
<td>&gt; 12.0</td>
</tr>
</tbody>
</table>
Septic Shock

- qSOFA:
  - An alteration in mental status.
  - A decrease in systolic blood pressure of < 100 mm Hg.
  - A respiration rate greater than > breaths/min.
Stages of Shock

- **Compensated**
  - The body’s compensatory mechanisms are able to maintain some degree of tissue perfusion.

- **Decompensated**
  - The body’s compensatory mechanisms fail to maintain tissue perfusion (blood pressure falls).

- **Irreversible**
  - Tissue and cellular damage is so massive that the organism dies even if perfusion is restored.
Clinical Findings

• What is the first physiological factor in the development of shock?
  • $\text{VO}_2 < \text{MRO}_2$
• So, what are the first symptoms you would expect to find?
  • ↑ respiratory rate
  • ↑ heart rate
Clinical Findings

- What is often the second physiological response to the development of shock?
- Peripheral vasoconstriction
- What symptoms would you expect to see?
  - pale skin
  - cool skin
  - weakened peripheral pulses
Clinical Findings

• As shock progresses, what physiological effects are seen?
• End-organ perfusion falls
• What symptoms would you expect to see?
  • altered mental status
  • decreased urine output
Clinical Findings

• As compensatory mechanisms fully engage, what signs and symptoms would you expect to see?
  • tachycardia
  • tachypnea
  • pupillary dilation
  • decreased capillary refill
  • pale cool skin
Clinical Findings

• When compensatory mechanisms fail, what signs and symptoms would you expect to see?
  • hypotension
  • falling $\text{SpO}_2$
  • bradycardia
  • loss of consciousness
  • dysrhythmias
  • death
Cardiogenic Shock

• **Treatment:**
  • Oxygen
  • Monitors
  • Nitrates (if possible)
  • Morphine or fentanyl
  • Pressor support (dopamine or dobutamine)
  • If no pulmonary edema, consider small fluid boluses
  • IABP
  • Definitive therapy (fibrinolytic therapy, PCI, CABG, ventricular assist device, cardiac transplant)
Hypovolemic Shock

- **Treatment:**
  - Oxygen
  - Supine position
  - Monitors
  - IV access
  - Fluid replacement
  - Pressor support (rarely needed)
  - Correct underlying cause
Hypovolemic Shock

- **Fluid replacement:**
  - **Hypovolemia:**
    - Isotonic crystalloids
    - Colloids
  - **Hemorrhage:**
    - Whole blood
    - Packed RBCs
    - Isotonic crystalloids
    - Colloids
Caveat:

- If shock due to trauma, and bleeding cannot be controlled, give only enough small fluid boluses to maintain radial pulse (SBP≈ 80 mm Hg).
- If bleeding can be controlled, control bleeding and administer enough fluid or blood to restore normal blood pressure.
Neurogenic Shock

• **Treatment:**
  - ABCDE
  - Fluid resuscitation with crystalloid.
  - PA catheter helpful in preventing overhydration.
  - Look for other causes of hypotension.
  - Consider vasopressor support with dopamine or dobutamine.
  - Transfer patient to regional spine center.
Anaphylactic Shock

• **Treatment:**
  • Airway (have low threshold for early intubation)
  • Oxygenation and ventilation
  • Epinephrine (IV, IM)
  • IV Fluids (crystalloids)
  • Antihistamines
    • Benadryl
    • Zantac
  • Steroids
  • Beta agonists
  • Aminophylline
  • Pressor support (dopamine, dobutamine or epinephrine)
Septic Shock

Treatment:
- Airway and ventilatory management
- Oxygenation
- IV fluids (crystalloids)
- Pressor support (dopamine, norepinephrine)
- Empiric antibiotics
- Removal of source of infection
- NaHCO₃?
- Steroids?
- Anti-endotoxin antibodies
Shock Treatments

- Not supported by clinical evidence:
  - MAST/PASG
  - High-dose steroids for acute SCI
  - Trendelenburg position

- Less important than formerly thought:
  - Pressure infusion devices
  - IO access
Summary

• To understand the shock, you must first understand the pathophysiology.
• Once you understand the pathophysiology, then recognition of the signs and symptoms and treatment becomes intuitive.