The Pathophysiology of Hemorrhagic Shock

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Learning Objectives

• Describe how acute blood loss leads to hypotension.
• Describe the compensatory mechanisms that operate to restore arterial pressure following hemorrhage.
• Describe the decompensatory mechanisms that lead to irreversible shock.
• Describe the rationale for different medical interventions following hemorrhage.
General Definition of Hemorrhagic Shock

A clinical syndrome resulting from decreased blood and oxygen perfusion of vital organs resulting from a loss of blood volume.
Hemorrhagic Shock
(Initial Uncompensated Responses)

Blood Loss → ↓ CVP → ↓ EDV (Preload)

↓ PA ← ↓ CO ← ↓ SV

Frank-Starling Mechanism

Graphs showing relationships between SV, EDV or EDP or PCWP, and LV Press, LV Vol.
Effects Blood Volume Loss on Mean Arterial Pressure

(Adapted from Guyton & Crowell, 1961)
Classes of Hemorrhagic Shock

• Class I hemorrhage (loss of 0-15%)
  – Little tachycardia
  – Usually no significant change in BP, pulse pressure, respiratory rate

• Class II hemorrhage (loss of 15-30%)
  – HR >100 beats per minute, tachypnea, decreased pulse pressure

• Class III hemorrhage (loss of 30-40%)
  – Marked tachycardia and tachypnea, decreased systolic BP, oliguria

• Class IV hemorrhage (loss of >40%)
  – Marked tachycardia and decreased systolic BP, narrowed pulse pressure, markedly decreased (or no) urinary output
  – Immediately life threatening
Compensatory Mechanisms

- Baroreceptor reflexes
- Circulating vasoconstrictors
- Chemoreceptor reflexes
- Reabsorption of tissue fluids
- Renal reabsorption of sodium and water
- Activation of thirst mechanisms
- Cerebral ischemia
- Hemapoiesis
Arterial Baroreceptors

Klabunde, RE, *Cardiovascular Physiology Concepts*, Lippincott Williams & Wilkins, 2004
Autonomic Responses to Baroreceptor Activity

- Arterial baroreceptor firing inhibits sympathetic outflow and stimulates parasympathetic outflow.
- Therefore, reduced firing, which occurs during hemorrhage, leads to sympathetic activation and parasympathetic inhibition.

Klabunde, RE, *Cardiovascular Physiology Concepts*, Lippincott Williams & Wilkins, 2004
Effects of 8% Blood Loss on Aortic Pressure in Anesthetized Dogs (Effects of Baroreceptor Denervation)

(Adapted from A.J. Edis, 1971)
Cardiopulmonary Baroreceptors

• Location: Venoatrial Junction
  – Tonic activity
    • Receptor firing decreases ADH (vasopressin) release leading to diuresis and vasodilation
    • Hemorrhage → increase ADH (reduced urine formation and increased vasoconstriction)

• Location: Atria and Ventricles
  – Tonic activity
    • affect vagal and sympathetic outflow similar to arterial baroreceptors
    • reinforce arterial baroreceptor responses during hypovolemia
Baroreceptor Reflexes

Blood Loss
→ ↓ Central Venous Pressure
→ ↓ Stroke Volume
→ ↓ Cardiac Output
→ ↓ Arterial Pressure
→ ↓ Baroreceptor Firing

+ ↑ Systemic Vascular Resistance
+ ↑ Venous Tone
+ ↑ Sympathetic
+ ↓ Parasympathetic
+ ↑ Heart Rate
+ ↑ Contractility

Klabunde, RE, *Cardiovascular Physiology Concepts*, Lippincott Williams & Wilkins, 2004
Baroreceptor Reflexes Cont.

• Redistribution of cardiac output
  – Intense vasoconstriction in skin, skeletal muscle, renal (during severe hemorrhage) and splanchnic circulations increases systemic vascular resistance, which attenuates the fall in arterial pressure
  – Coronary and cerebral circulations spared
  – Therefore, cardiac output is shunted to essential organs

• Redistribution of blood volume
  – Strong venoconstriction in GI, hepatic and skin circulations
  – Partial restoration of central venous blood volume and pressure to counteract loss of filling pressure to the heart
Importance of Changes in Venous Tone

Blood Loss
- ↓ Central Venous Pressure
- ↓ Stroke Volume
- ↓ Cardiac Output
- ↓ Arterial Pressure
  - ↓ Baroreceptor Firing
  - ↑ Sympathetic
  - ↓ Parasympathetic
    - ↑ Heart Rate
    - ↑ Contractility
  - ↑ Systemic Vascular Resistance
  - ↑ Venous Tone
Central Venous Pressure During Hemorrhage

- Hemorrhage decreases blood volume and decreases CVP (A → B)
- Peripheral venous constriction decreases venous compliance (B → C), which increases CVP and shifts blood volume toward heart
- Increased CVP increases ventricular preload and force of contraction (Frank-Starling mechanism)
Humoral Compensatory Mechanisms

Blood Loss

↓ Arterial Pressure

+ CVP
+ CO
+ Symp
Adrenal Medulla

↑ Blood Volume

+ Thirst
+ SVR
+ Symp
Kidney

↑ Vasopressin

↑ Angiotensin II

↑ Renin

↑ Catecholamines
(Epi, NE)

↑ Renal Na⁺ & H₂O Retention

↑ Aldosterone

↑ Blood Volume

Pituitary

Adrenal Cortex
Importance of Humoral Compensatory Mechanisms

• Angiotensin II, vasopressin and catecholamines reinforce sympathetic mediated vasoconstriction to help maintain arterial pressure by
  – increasing systemic vascular resistance
  – decreasing venous compliance, which increases ventricular preload and enhances stroke volume

• Angiotensin II, aldosterone and vasopressin act on the kidneys to increase blood volume
Chemoreceptor Reflexes

• Peripheral chemoreceptors
  – Carotid bodies
  – Aortic bodies

• Central chemoreceptors
  – Medulla (associated with cardiovascular control “centers”)
Chemoreceptor Reflexes cont.

- Increasingly important when mean arterial pressure falls below 60 mmHg (i.e., when arterial baroreceptor firing rate is at minimum)
- Acidosis resulting from decreased organ perfusion stimulates central and peripheral chemoreceptors → sympathetic activation
- Stagnant hypoxia in carotid bodies enhances peripheral vasoconstriction
- Respiratory stimulation may enhance venous return (abdominothoracic pump)
Reabsorption of Tissue Fluids

- Capillary pressure falls
  - Reduced arterial and venous pressures
  - Increased precapillary resistance
  - Transcapillary fluid reabsorption (up to 1 liter/hr autoinfused)

- Capillary plasma oncotic pressure can fall from 25 to 15 mmHg due to autoinfusion thereby limiting capillary fluid reabsorption

- Hemodilution causes hematocrit to fall which decreases blood viscosity
Changes in Starling Forces Following Hemorrhage

Starling Equation for Fluid Balance

\[ FM = K \cdot A \left[ (P_C - P_T) - (\pi_C - \pi_T) \right] \]

Normal

Starling Equation for Fluid Balance

\[ FM = K \cdot A \left[ (P_C - P_T) - (\pi_C - \pi_T) \right] \]

Hemorrhage (early)

\[ P_C \text{ decreases due to:} \]

\[ \downarrow P_A \text{ & } P_V, \downarrow R_V/R_A \]
Cerebral Ischemia

• When mean arterial pressure falls below 60 mmHg, cerebral perfusion decreases because the pressure is below the autoregulatory range

• Cerebral ischemia produces very intense sympathetic discharge that is several-fold greater than the maximal sympathetic activation caused by the baroreceptor reflex
Decompensatory Mechanisms  
“Progressive Shock”

- **Cardiogenic Shock**
  - Impaired coronary perfusion causing myocardial hypoxia, systolic and diastolic dysfunction, arrhythmias

- **Sympathetic Escape**
  - Loss of vascular tone (↓SVR) causing progressive hypotension and organ hypoperfusion
  - Increased capillary pressure causing increased fluid filtration and hypovolemia

- **Cerebral Ischemia**
  - Loss of autonomic outflow due to severe cerebral hypoxia
• **Metabolic Acidosis**
• **Rheological** –
  – Increased microvascular viscosity
  – Microvascular plugging by leukocytes and platelets
  – Intravascular coagulation
• **Systemic Inflammatory Response**
  – Endotoxin release into systemic circulation
  – Cytokine formation – TNF, IL, etc.
  – Enhanced nitric oxide formation
  – Reactive oxygen-induced cellular damage
  – Increased capillary permeability
  – Multiple organ failure
Decompensatory Mechanisms
(Cardiogenic Shock and Sympathetic Escape)

↓ Cardiac Output
↓ Inotropy
↓ Coronary Perfusion
↓ Arterial Pressure
↑ Sympathetic Vasoconstriction
↑ Tissue Hypoxia

Vasodilation
Time-Dependent Changes in Cardiac Function

- Dogs hemorrhaged and arterial pressure held at 30 mmHg
- Precipitous fall in cardiac function occurred after 4 hours of severe hypotension

(adapted from Crowell et al., 1962)
## Comparison of Different Forms of Shock

<table>
<thead>
<tr>
<th></th>
<th>Cardiogenic Shock</th>
<th>Hemorrhagic Shock</th>
<th>Septic Shock</th>
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<tbody>
<tr>
<td><strong>CV Origin</strong></td>
<td>Cardiac</td>
<td>Volume</td>
<td>Vascular</td>
</tr>
<tr>
<td><strong>Cardiac Output</strong></td>
<td>↓</td>
<td>↓</td>
<td>↑↓</td>
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<tr>
<td><strong>Vascular Resistance</strong></td>
<td>↑</td>
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<tr>
<td><strong>Blood Volume</strong></td>
<td>↑</td>
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<tr>
<td><strong>Management</strong></td>
<td>Mechanical Inotropes Vasopressors Vasodilators</td>
<td>IV Fluids/Blood Vasopressors</td>
<td>IV Fluids Antibiotics Vasopressors Inotropes</td>
</tr>
</tbody>
</table>
Resuscitation Issues

- Reducing reperfusion injury & systemic inflammatory response syndrome (SIRS)
  - Anti-inflammatory drugs
  - NO scavenging and antioxidant drugs
- Resuscitation fluids
  - Crystalloid vs. non-crystalloid solutions
  - Isotonic vs. hypertonic solutions
  - Whole blood vs. packed red cells
  - Hemoglobin-based solutions
  - Perfluorocarbon-based solutions
  - Fluid volume-related issues
Resuscitation Issues cont.
(Current Research)

• Efficacy of pressor agents
• Hypothermic vs. normothermic resuscitation
• Tailoring therapy to conditions of shock
  – Uncontrolled vs. controlled hemorrhage
  – Traumatic vs. atraumatic shock
Review Learning Objectives

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