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 $\rightarrow$ $P_{RA}^-$ $\rightarrow$ EDV (Preload) $\rightarrow$ Frank-Starling Mechanism

$P_A^-$ $\rightarrow$ CO $\rightarrow$ SV

SV $\rightarrow$ EDV or EDP or PCWP

Frank-Starling Mechanism

LV Press

LV Vol
Effects Blood Volume Loss on Arterial Pressure

(adapted from Guyton & Crowell, 1961)
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

Arterial Pressure
Pulse

Receptor Firing

Carotid Sinus

Receptor Firing Rate (% max)

Maximal Sensitivity

Mean Arterial Pressure (mmHg)
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
  – **Tonically active**
    • Receptor firing decreases ADH release leading to diuresis

• Location: Atria and Ventricles
  – **Tonically active**
    • affect vagal and sympathetic outflow similar to arterial baroreceptors
    • reinforce arterial baroreceptor responses during hypovolemia
Baroreceptor Reflexes
(Neural Activation)

- Hypovolemia
- Decreased Cardiac Output

↓ Arterial Pressure
↓ Pulse Pressure

CNS
↓ Baroreceptor Firing

↑ Sympathetic
↓ Parasympathetic

↑ Systemic Vascular Resistance
↑ Venous Tone
↑ Contractility
↑ Heart Rate

↑ P_{RA}
↑ Stroke Volume
↑ Cardiac Output
↑ Arterial Pressure
Baroreceptor Reflexes Cont.

- Redistribution of cardiac output
  - Intense vasoconstriction in skin, skeletal muscle, renal (during severe hemorrhage) and splanchnic circulations increases systemic vascular resistance
  - Coronary and cerebral circulations spared
  - Therefore, cardiac output is shunted to essential organs

- Redistribution of blood volume
  - Strong venoconstriction in splanchnic and skin circulations
  - Partial restoration of central venous blood volume and pressure to counteract loss of filling pressure to the heart
Circulating Vasoconstrictors

Hypovolemia

Decreased Cardiac Output

\[
\downarrow \text{Arterial Pressure} \quad \downarrow \text{Pulse Pressure}
\]

Baroreceptor Reflex (\(\uparrow\) Sympathetic)

\[
\uparrow \text{Arterial & Venous Tone}
\]

\[
\uparrow \text{Heart Rate} \quad \uparrow \text{Contractility}
\]

\[
\uparrow \text{P}_{RA} \quad \uparrow \text{SVR}
\]

\[
\uparrow \text{Stroke Volume}
\]

\[
\uparrow \text{Cardiac Output}
\]

Post. Pituitary

\[
\uparrow \text{AII} \quad \uparrow \text{AVP} \quad \uparrow \text{Epi}
\]

Adrenal Medulla

\[
\downarrow \text{Arterial Pressure} \quad \downarrow \text{Pulse Pressure}
\]

\[
\downarrow \text{Cardiac Output}
\]

Hypovolemia
Chemoreceptor Reflexes

- 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
- 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

• Up to 1 liter/hr can be autoinfused by this mechanism
Renal Compensation

↑ AII → ↑ Aldosterone + ↑ AVP (ADH)

↓ Na⁺ & H₂O Reabsorption

↑ Blood Volume

↑ pRA → ↑ Stroke Volume

↑ Arterial Pressure

↑ Cardiac Output

Increased Thirst
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

• Cardiogenic Shock
  – Impaired coronary perfusion causing myocardial hypoxia, systolic and diastolic dysfunction

• 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
Decompensatory Mechanisms
(Cardiogenic Shock and Sympathetic Escape)
Decompensatory Mechanisms cont.

• Systemic Inflammatory Response
  – Endotoxin release into systemic circulation
  – Cytokine formation – TNF, IL, etc.
  – Enhanced nitric oxide formation
  – Reactive oxygen-induced cellular damage
  – Multiple organ failure
  – Microvascular plugging by leukocytes and platelets

• Cerebral Ischemia
  – Loss of autonomic outflow due to severe cerebral hypoxia
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)
Resuscitation Issues
(\textit{Current Research})

- 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