Considerations on Shock

Ruminations about the Past, Present, and Future
I have no disclosures to make.

I am a full-time academic faculty member at UT Southwestern.
Essential Physiology for Understanding the Cause(s) and Treatment(s) for the Patient in Shock
Shock

“The term “shock” describes a condition that occurs when the perfusion of the body’s tissues with oxygen, electrolytes, glucose, and fluid becomes inadequate to meet the body’s needs.”
Deprived of oxygen, cells begin to use “backup” processes, which make energy for the body less efficiently and produce toxic by-products such as lactic acid. The backup (anaerobic) processes may postpone cellular death for a time.
Shock

However, the lack of oxygen is compounded by those toxic by-products because they can poison certain cellular functions, such as the production of energy by mitochondria.
Calcium Flux

1. stimulus triggers influx of calcium
2. calcium binds to ryanodine receptor, releasing stored calcium
3. calcium triggers muscle contraction
Electron Transport

- NADH → NAD⁺ + H⁺ (inside)
- Fumarate → Succinate
- ½O₂ + 2H⁺ → H₂O (outside)
- H⁺ (intermembrane space)
- ADP + H⁺ → ATP (inside)
- ATP synthesis

Flow of electrons: NADH → Succinate → Fumarate → Cyt c → O₂ → H₂O
Protecting Mitochondria

- Cyclosporin
- Sildenafil (Viagra)
Three-Dimensional Structure of the Apoptosome: Implications for Assembly.

A hub and spoke model is presented, with A showing a hub, B showing spokes, and C showing a combination of both. The diagram suggests that the hub promotes assembly of the apoptosome. This large protein complex then binds and activates procaspase-9 (Srinivasula et al., 1998; Zou et al., 1997, 1999; Li et al., 1997; Hu et al., 1999). A nonhydrolyzable ATP analog (ADP-CP) also promotes apoptosome formation. This suggests that assembly may be initiated by nucleotide binding rather than hydrolysis (Jiang and Wang, 2000).
Reperfusion Injury Salvage Kinase Pathway

ISCHAEMIC PRE- & POSTCONDITIONING

G-protein coupled ligand

GPCR

ERK 1/2 & MAPKs

PI3-K

PDK1

PI3K

IRS-1

PKB/Akt

GSK3β
eNOS

PKCθ & ζ

NO

MPTP

KATP

Mitochondria

INSULIN

FFAs

IR

GLUT-4

FAT/CD36

Long Chain Acyl CoA

Ceramide

DAG

MPTP
Oxygen Management

Considerations on the movement of oxygen from the atmosphere into the tissues of the body
Atmospheric O2 = ~ 150
Alveolar O2 = ~ 100
Arterial O2 = ~ 80 - 100
Tissue O2 = ~ 40
Tissue Damage at ~ ≤ 10
Fick Equation

- Gives “consumed oxygen”
  - \[ VO_2 = 1.38 \times \frac{(Hb)(CO)(SaO_2 - SvO_2)}{10} \]
  - (normally 240-290 cc/min)
Fick Equation

Our bodies consume a “cup” of oxygen each minute
A “pool” of oxygen in the tissues, about a quart!
In addition to the tissues!

One quart of oxygen on our hemoglobin in the normal resting state

\[ 20 \text{ cc } O_2 / 100 \text{ cc Blood} \]

\[ 5000 \text{ cc } / 100 \text{ cc } = 50 \text{ factor} \]

\[ 20 \text{ cc } x 50 = \text{ A Quart!} \]
So, with a well-oxygenated patient at the time of the beginning of the shock state, there are a total of two quarts of oxygen in the body!!!
BP = C.O. \times PVR

C.O. = HR \times SV
BP = C.O. x PVR
C.O. = HR x SV
What does a low blood pressure mean?

Either...

Or a combination of any of these

...from BTLS/ITLS, editions 2, 3, 4, 5, 6, 7, and 8 Fowler et al
Signs of Shock

Early
- Weak, thirsty, lightheaded
- Pale, then sweaty
- Tachycardia
- Tachypnea
- Diminished urinary output

Late
- Hypotension
- Altered LOC
- Cardiac arrest
- Death
Shock

Cardiogenic
- Rapid pulse
- Distended neck veins
- Cyanosis

Volume Loss
- Rapid pulse
- Flat neck veins
- Pale

Vasodilatory
- Variable pulse
- Flat neck veins
- Pale or pink
Signs of Shock

Early

Lactate Begins to appear during this period!!

Late

Hypotension
Altered LOC
Cardiac arrest
Death
ITLS Shock 2015 and Beyond
1. Shock Assessment: How low can you go?
ROC Pilot Trial of 200 patients with major trauma: No clear indicators!
2. TXA now recommended for traumatic hemorrhage. It is being studied for TBI.
3. Corollary:
The injured brain does not tolerate hypotension!
4. Pulse waveform analysis and tissue perfusion monitors are looming on the horizon....

........$$$$$$........
5. Serum Lactate Levels may be helpful....though remember Dr. Markov!!
Increasing survival of dogs subjected to hemorrhagic shock by administration of fructose 1-6 diphosphate.

Markov AK, Terry J 3rd, White TZ, Didlake RH, Hellems HK.

Abstract

Previous reports from this laboratory described animal experiments in which intravenous administration of fructose 1-6 diphosphate (FDP) at the onset of hypovolemia, toxemia, and trauma effected improvement in hemodynamic and metabolic parameters, attenuation of tissue damage, and a significant increase in survival. The obvious question remained: Would this agent be as effective if administered after the onset of the shock syndrome? Thus 72 anesthetized dogs were subjected to normotensive hemorrhagic shock and were subsequently treated with FDP at 30 minutes, 1 hour, 90 minutes, and 2 hours after exsanguination. Analysis of the results (as compared with vehicle-treated controls) revealed evidence of improved cardiac output and arterial pressure (p less than 0.02), conservation of effective circulatory volume, better oxygen utilization, and a significant increase in survival (p less than 0.0001). These results, in conjunction with earlier experimental and recent clinical data, indicate that the therapeutic effect of FDP in ischemic and hypoperfusion states is in part metabolically mediated by the augmentation of carbohydrate utilization. Prevention of tissue injury is in part due to the inhibition of generation of oxygen-derived free radicals by neutrophils.
6. Is there a future in trauma resuscitation for intermediary mediator modulators?

- FDP
- Vitamin C
- Nitric Oxide inhibitors
The Current Evidence:

Reaching the plane of volume resuscitation vs. worsening outcomes
The Current Evidence:

**Time-Sensitive Condition**

**System Construction:**
Can every facility provide optimal care?

**Frequency? Training?**
Thinking of the Vascular System
BP = C.O. × PVR

C.O. = HR × SV
It is with attention to all of the elements of the vascular system that evaluation and treatment are optimized.
The Approach to the Hypotensive Patient in the Modern Era

Used with gratitude from www.emdocs.net
A Systematic Approach to arriving at the Best Possible Explanation

1. HEART RATE
- Pace or Cardiovert?
- unstable brady (<40)
- unstable, non-sinus tachy (>170)

2. VOLUME
- U/S for IVC & LV volume
- hypovolemia?
- hemorrhage? → FAST, AAA?
- **IVC >> LV volume if there is obsxn to flow through heart or lungs...
- Tamponade?
- New RV infarction?
- Massive PE?
- pulmonary alveolar air trapping?
- Tension pneumothorax?

3. CONTRACTION
- ECG & U/S for LV fxn
- Volume in lumen during diastole?
- LV walls collapse well in systole?
- Is volume truly going forward?
  (listen for regurg murmur & rales)

** When 1-3 are okay, then volume is going forward ... so consider peripheral vasodilation +/- mitochondrial dysfxn

Cervical spinal cord compression?
Anaphylaxis?
Fulminant liver failure?
Sepsis?
Mitochondrial poison (Cyanide, CO)?
1. Heart Rate (HR):

- **Approach:** Look at the HR on the monitor.
- **Increased or decreased HR can lead to hypotension.**
- **Tachycardia:** In general, unstable, non-sinus HR > 170 (threshold varies with compliance of LV and age of pt) can result in hypotension.
  - Physiology:
    - ↑ HR -> ↓ stroke volume because there is **less time for diastolic filling** -> ↓ Cardiac Output (HR x SV) -> hypotension
    - Additionally, since less time is spent in diastole, the ventricular myocardium has **inadequate relaxation time** to allow flow through intramyocardial perforating coronary branches. This leads to **ischemia of the LV subendocardium**. Ischemia can progress from the subendocardium to more superficial layers of the LV myocardium and result in **poor contractile function** -> hypotension
    - Also, diffuse ischemia can produce heterogeneous myocyte repolarization patterns -> re-entrant arrhythmia or fibrillation.
  - The key is to differentiate between tachycardia as a **response to hypotension** or tachycardia as the **cause of hypotension**.
    - Typically HR > 170 starts to affect diastolic filling and can result in hypotension -> suspect tachycardia as the **cause of hypotension**.
    - Typically HR < 170 does not affect diastolic filling -> suspect tachycardia as the **response to hypotension**.
      - Of note: AFib w/ RVR may result in hypotension at lower HR thresholds because short diastolic filling is compounded by loss of atrial contraction, and hence LV filling is solely passive. In this setting, non-compliant LVs may fail to fill at HRs as low as 140.
- **Bradycardia:** In general, unstable HR < 50 can result in hypotension.
  - Physiology: ↓ Heart Rate -> ↓ Cardiac Output -> Hypotension
  - Differential: Know your tachyarrhythmias and bradyarrhythmias, but in general treat appropriately -> cardiovert or pace the patient.
2. Volume Status:

- Assess this **after** you’ve determined that the HR is a **result of hypotension**, not the cause (since rapid heart rates impair diastolic filling and will enlarge the IVC as volume remains peripherally).
- **Physiology:** ↓ Volume Status → ↓ Stroke Volume → ↓ Cardiac Output → Hypotension
- **Approach:** Do a quick bedside physical examination, then grab your ultrasound probe to assess the **inferior vena cava (IVC)** and **left ventricle (LV) volume**.
  - **Physical examination:**
    - Look at the patient’s face.
      - Dry mucous membranes?
      - Sunken eyes?
    - Feel the extremities.
      - Abnormal skin turgor (ie tenting when pinched)?
      - Poor capillary refill (ie > 2 seconds)?
      - Weak pulse?
      - Cool extremities?
  - **IVC/LV Ultrasound**
1. Flat/collapsed IVC (anteroposterior diameter of the IVC < 2 cm in size with > 50% collapse with respiratory variation) with hyperdynamic LV.
   - Differential: Hypovolemia vs. Hemorrhage.
     - Is this due to hypovolemia from dehydration?
     - Hemorrhage from a ruptured AAA/ectopic/GI Bleed?
       - FAST the patient
         - Abdominal aorta > 3 cm indicates AAA
         - Abdominal or pelvic free fluid
         - Serial bedside HGB testing
       - Treatment: Fluid/blood resuscitation

2. Plethoric / plump, non-compressible IVC, which is significantly greater than LV volume.
   - Ask yourself if there is an obstruction to the flow through the heart or the lungs? -> Obstructive shock
   - Differential: Cardiac tamponade vs. RV infarction vs. severe pulm HTN/massive pulmonary embolism (PE) vs. asthmatic alveolar air trapping vs. tension pneumothorax (PTX)
     - Ultrasound findings to look for:
       - Anechoic fluid surrounding heart with diastolic collapse -> cardiac tamponade
       - RV strain (RV/LV ratio > 0.9, “D sign”) -> Pulmonary HTN of some cause (massive PE? Alveolar air trapping?)
       - Lack of lung sliding or “bar code” sign -> PTX
     - Treatment: Depends on underlying cause

3. Distended, non-collapsing IVC with dilated LV
   - Move on to cardiac cause in step 3

4. Normal IVC with diameter >2cm but <50% collapse with respiration
   - May trial a small bolus of volume if lung auscultation is clear
   - Move on to cardiac cause in step 3
3. Cardiac Performance:

- Assess this after you’ve determined that step 1 and 2 are normal. That is, the HR is not the cause of diastolic limitations to myocardial blood flow, intravenous volume is adequate, and there is no obstruction to flow through the thoracic circuit.
- Physiology: ↓ Cardiac Contractility -> ↓ Stroke Volume -> ↓ Cardiac Output -> Hypotension
- Approach: Assess myocardial performance by cardiopulmonary physical examination, ECG, and bedside ultrasound to assess left ventricular (LV) function.
  - Physical examination
    - High-pitched holosystolic murmur radiating to axilla?
    - Diastolic murmur at RUSB radiating to LLSB?
    - Systolic murmur at RUSB radiating to neck?
    - Crackles/rales?
    - Elevated JVP or obvious JVD?
    - Peripheral edema?
  - Ultrasound – Short axis parasternal view
    - Do the LV walls collapse well in systole?
      - If not, there is decreased LV contractility/EF
        - Treatment: inotropy to move blood forward +/- vasopressors to increase SVR/diastolic pressure and hence coronary perfusion.
        - Is volume truly going forward? -> Acute mitral regurgitation (MR) or acute aortic regurgitation (AR)
          - Murmur and rales on exam with multiple B lines on lung sonography
  - Differential: Cardiogenic shock ( Decompensated heart failure, acute MI, acute MR, acute AR)
4. Systemic Vascular Resistance:

- If 1-3 are okay, then the pt is hypotensive despite a HR allowing diastolic filling of LV lumen and coronary arteries, adequate intravenous volume, no obstruction through the pulmonary circuit and hence adequate LV diastolic volume, and adequate contractile function with forward flow out the aortic root. In this setting, there must be a component of peripheral vasodilation to explain low intravascular tone at the measured artery.
- Physiology: Since blood pressure is a balance of cardiac output and systemic vascular resistance, decreasing SVR can result in hypotension.
- Approach:
  - Physical examination
    - How do the extremities feel? Are they warm and vasodilated? Or are they cold, clamped and vasoconstricted?
  - Differential: Distributive shock (sepsis, anaphylaxis, vasodilatory medication overdose, neurogenic shock, fulminant liver failure, and other causes of severe acidemia including toxic ingestion, inherent metabolic disturbance, or mitochondrial poisons like cyanide, hydrogen sulfide, & carbon monoxide).
- Treatment: Depends on underlying cause
Follow a Four Step Systematic Approach

1. Heart Rate
2. Volume Status
3. Cardiac Performance
4. Systemic Vascular Resistance
Evaluating Heart Rate as a Cause of Shock

1. ↑ HR -› ↓ stroke volume because there is less time for diastolic filling -› ↓ Cardiac Output (HR x SV) -› hypotension
Evaluating Heart Rate as a Cause of Shock

2. Since less time in diastole, the ventricular myocardium has inadequate relaxation time to allow flow through *intra-myocardial* perforating coronary branches. *This leads to ischemia of the LV* -> *poor contractile function* -> *hypotension*
Evaluating Heart Rate as a Cause of Shock

Bradycardia:
In general, unstable HR < 50 can result in hypotension.

Physiology:
↓ Heart Rate -> ↓ Cardiac Output -> Hypotension
Evaluating Hypovolemia as the Cause of Shock

Physiology: ↓ Volume Status -> ↓ Stroke Volume -> ↓ Cardiac Output -> Hypotension

Approach: Do a quick bedside physical examination, then grab your ultrasound probe to assess the inferior vena cava (IVC) and left ventricle (LV) volume.
Evaluating Hypovolemic Shock

Physical examination:
- Look at the patient’s face.
  - Dry mucous membranes?
  - Sunken eyes?
- Feel the extremities.
  - Abnormal skin turgor (i.e., tenting when pinched)?
  - Poor capillary refill (ie > 2 seconds)?
  - Weak pulse?
  - Cool extremities?
Evaluating Hypovolemia as the Cause of Shock

**IVC/LV Ultrasound:**

Flat/collapsed IVC (anteroposterior diameter of the IVC < 2 cm in size with > 50% collapse with respiratory variation) with **hyperdynamic left ventricle [LV]**

Differential: Hypovolemia vs. Hemorrhage.

Is this due to hypovolemia from dehydration?

Plethoric / plump, non-compressible IVC, which is significantly greater than LV volume.

Ask yourself if there is an obstruction to the flow through the thorax ("obstructive, or mechanical, shock")
Evaluating Hypovolemia as the Cause of Shock

Distended, non-collapsing IVC with dilated LV:
Move on to cardiac cause in step 3

Normal IVC with diameter >2cm but <50% collapse with respiration:
May trial a small bolus of volume if lung auscultation is clear, then Move on to cardiac cause in step 3
Evaluating Cardiac Performance as the Cause of Shock

Assess this after you’ve determined that step 1 and 2 are normal:

...that is, the HR is not the cause of diastolic limitations to myocardial blood flow, intravenous volume is adequate, and there is no obstruction to flow through the thoracic circuit....
Evaluating Cardiac Performance as the Cause of Shock

**Physiology:** ↓ Cardiac Contractility -> ↓ Stroke Volume -> ↓ Cardiac Output -> **Hypotension**
Evaluating Cardiac Performance as the Cause of Shock

**Approach:** Assess myocardial performance

- Cardiopulmonary physical examination
- Electrocardiogram
- Bedside ultrasound to assess left ventricular (LV) function
Evaluating Systemic Vascular Resistance as the Cause of Shock

**Physiology**: Since blood pressure is a balance of cardiac output and systemic vascular resistance, decreasing SVR can result in hypotension.
Evaluating Systemic Vascular Resistance as the Cause of Shock

Approach: Physical examination
How do the extremities feel? Are they warm and vasodilated?
Or, are they cold & vasoconstricted?
Evaluating Systemic Vascular Resistance as the Cause of Shock

**Differential**: Distributive shock (sepsis, anaphylaxis, vasodilatory medication overdose, neurogenic shock, fulminant liver failure, and other causes of severe acidemia including toxic ingestion, inherent metabolic disturbance, or mitochondrial poisons like cyanide, hydrogen sulfide, & carbon monoxide).
http://www.emdocs.net/hypotensive-ed-patient-sequential-systematic-approach/
Summary Thoughts: Shock 2015 and Beyond
The Understanding of Basic Physiology must ALWAYS guide Evaluation and Management
Can we bring the comprehensive process of patient assessment to the field?

If not now, when?

Pace or Cardiovert?
unstable brady (≤40)
unstable, non-sinus tachy (>170)

1. HEART RATE

2. VOLUME

U/S for IVC & LV volume
hypovolemia?
hemorrhage? → FAST, AAA?
**IVC >> LV volume if there is obsxn to flow

3. CONTRACTION

ECG & U/S for LV fxn
Volume in lumen during diastole?
LV walls collapse well in systole?
Is volume truly going forward?
(listen for regurg murmur & rales)

4. SVR ↓
** When 1-3 are okay, then volume is going forward ... so consider peripheral vasodilation +/- mitochondrial dysfxn

Cervical spinal cord compression?
Anaphylaxis?
Fulminant liver failure?
Sepsis?
Mitochondrial poison (Cyanide, CO)?
For now and into the distant future….
Every patient is your teacher…
You have to search for the lesson