

## Shock and Hemodynamic Monitoring

Although the genesis of different forms shock can be quite varied, all forms of shock do have at least two characteristics in common: 1. All forms of shock result in impaired oxygen delivery secondary to either reduced cardiac output (cardiogenic, septic) or loss of effective intravascular volume (hypovolemic, neurogenic, anaphylactic). 2. At the cellular level, the final end pathway leading to multisystem organ failure (MSOF) is likely similar for all forms of shock and involves a immunologic response leading to microthrombosis, capillary leak, vasodilatation, and myocardial depression. This has been best studied in gram negative septic shock.

### A. Septic shock

#### a. Epidemiology<sup>1</sup>

- i. Hospitalization rates in U.S. for septicemia or sepsis doubled, from 11.6 per 10,000 population in 2000 to 24.0 per 10,000 in 2008.
- ii. Hospitalizations rates similar for males and females
- iii. 17% mortality for sepsis hospitalizations in 2008.

#### b. Pathophysiology

##### i. Gram negative sepsis

##### 1. Endotoxins in bacterial wall - lipopolysaccharides (LPS).

##### a. LPS unique to gram negative bacteria

##### b. LPS composed of:

- i. O Antigen
- ii. Core oligosaccharide
- iii. Lipid A –
  1. Responsible for most of the toxicity of gram negative bacteria.
  2. LPS binds to LPS Binding Protein (LBP). This LPS-LBP complex then binds to cell surface CD14 receptors on monocytes and macrophages.
  3. The LPS-LBP-CD14 complex then activates cells via Toll-like receptor-4 (TLR4).
  4. TLR4 then “activates” cells which eventually produce a cytokine “cascade” of proinflammatory mediators.

##### 2. Cytokine “cascade”

##### a. Tumor Necrosis Factor (TNF)

- i. First cytokine produced in response to gram negative sepsis
- ii. Principal mediator for acute response to gram negative bacteria

- iii. Major source of TNF is from activated macrophages
    - iv. TNF causes fever, cachexia, myocardial depression, and intravascular thrombosis
    - v. High levels of TNF cause septic shock and may be predictive of mortality in gram negative sepsis
    - vi. High levels of TNF cause apoptosis.
  - b. Interleukin-1 (IL-1)
    - i. Levels of IL-1 increase soon after TNF production in gram negative sepsis
    - ii. IL-1 produced by “activated” macrophages, neutrophils and endothelial cells
    - iii. IL-1 causes fever, cachexia
    - iv. IL-1 helps to increase levels of next proinflammatory cytokines in cascade, IL-2 and IL-12.
    - v. IL-1 does NOT cause apoptosis
  - c. Interleukin-10
    - i. Anti-inflammatory cytokine
    - ii. Inhibits production of IL-12
    - iii. Inhibits T-cell activation
- ii. Gram positive sepsis
  - 1. Pathogenic pathways less well understood than gram negative sepsis
  - 2. Most common organisms – Staphylococcus or Streptococcus
  - 3. Gram positive cell wall components are known to be involved in septic response
    - a. Peptidoglycans
    - b. Teichoic Acid
    - c. Likely act in a similar manner as LPS, but less potent on a weight bases.
  - 4. Gram positive bacteria can also produce exotoxins
    - a. Exotoxins from different gram positive bacteria are structurally related
    - b. Exotoxins from staph aureus the cause for toxic shock syndrome.
    - c. Exotoxins act as “superantigens” and do not require processing by antigen presenting cells in order to stimulate T cells.
      - i. Act directly with Class II major histocompatibility complex (MHC) on antigen presenting cells and T cell receptors (TCR).
      - ii. Induce activation and clonal expansion of T cells.
- c. Treatment – (2008 Surviving Sepsis Guidelines)<sup>2</sup>
  - i. Supportive Care
    - 1. Resuscitation (over the first 6 hours)

- a. Begin resuscitation immediately in patients with hypotension or elevated lactate.
- b. Resuscitation goals:
  - i. CVP 8-12 (for nonintubated patients)
  - ii. CVP 12-15 (for intubated patients)
  - iii. Mean arterial pressure > 65
  - iv. Urine output > 0.5 cc/kg/hr
  - v. Central venous oxygen saturation > 70% or mixed venous > 65%
- c. Vasopressors
  - i. Norepinephrine and dopamine are the initial vasopressors of choice
  - ii. Epinephrine, phenylephrine, or vasopressin should not be administered as the initial vasopressor
  - iii. Epinephrine can be used as the first alternative again in septic shock when blood pressure poorly responsive to norepinephrine or dopamine
  - iv. Vasopressin (0.03 units/min) can be added to norepinephrine
- d. Do not use low-dose dopamine for renal protection
- e. In patients requiring vasopressors, insert an arterial catheter as soon as practical
- f. Use Crystalloids or colloids
- g. Use fluid challenge technique if associated with a hemodynamic improvement
- h. Fluid challenges of 1000cc of crystalloids or 300-500cc of colloids over 30 minutes
- i. Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent hemodynamic improvement
- j. Use dobutamine in patients with myocardial dysfunction as supported by elevated cardiac filling pressures and low cardiac output
- k. Do not increase cardiac index to predetermined supranormal levels
- l. Do not use steroids to treat sepsis in the absence of shock unless the patient's endocrine or steroid history warrants it. If steroids are used, hydrocortisone dose should be < 300mg/day
- m. Recombinant human activated protein C (Drotrecogin alfa (activated)) is **NOT** recommended for treatment of severe sepsis and has been withdrawn from the market.<sup>3</sup>

## 2. Diagnosis and Source Control

- a. Two or more blood cultures

- i. One blood culture from each vascular access device in place > 48
  - b. Cultures from other sites as clinically appropriate
  - c. Imaging studies as needed to diagnose and formally evaluate for a drainable source of infection
    - i. Drainable sources of infection should be established within the first 6 hours
    - ii. Source control measures (abscess drainage, tissue debridement) should be implemented as soon as possible after initial resuscitation.
  - d. Remove intravascular access devices if potentially infected
- 3. Antibiotic therapy
  - a. Give broad spectrum antibiotics most likely active against presumed bacterial/fungal pathogens.
  - b. Begin antibiotic therapy within one hour of diagnosis of severe sepsis
  - c. Reassess antibiotic therapy daily
  - d. Duration of therapy typically limited to 7-10 days
  - e. Stop antibiotic therapy if cause is found to be noninfectious

## B. Anaphylactic Shock

- a. Pathophysiology
  - i. Immediate hypersensitivity reaction
  - ii. Circulating IgE binds to the antigen causing anaphylaxis
  - iii. Antigen-bound IgE then activates FcεRI receptor on mast cells and basophils
  - iv. IgE- FcεRI complex then mediates degranulation of mast cells and basophils, leading to the release of inflammatory mediators (such as histamine)
- b. Symptoms
  - i. Release of inflammatory mediators led to:
    - 1. Angioedema
    - 2. Contraction of smooth muscle in bronchi leading to bronchospasm
    - 3. Systemic vasodilation
    - 4. Capillary leak syndrome
    - 5. In extreme cases, complete cardiovascular collapse
  - ii. Symptoms can start minutes to hours after exposure
- c. Treatment<sup>4</sup>
  - i. Immediate supportive care (protect airway, establish IV access, volume resuscitation, etc.)
  - ii. Epinephrine is first-line treatment for severe anaphylaxis
    - 1. Can be given IM in the mid-anterolateral thigh
    - 2. Can also be given in nebulized form for laryngeal edema.
  - iii. Second-line medications

1. Antihistamines
2. Glucocorticoids
3. Nebulized bronchial dilators

#### C. Neurogenic Shock

- a. Pathophysiology
  - i. Loss of peripheral vasomotor tone secondary to injury to autonomic pathways within the spinal cord.
  - ii. Vasodilation below the level of spinal cord injury
  - iii. Unopposed vagal stimulation of heart leads to bradycardia
- b. Symptoms
  - i. Accompanied by immediate para / quadraplegia
  - ii. Extremities appear warm and well perfused
- c. Treatment
  - i. Can be poorly fluid responsive
  - ii. Phenylephrine first line vasopressor
  - iii. Atropine for critical bradycardia

#### D. Hypovolemic Shock

- a. Pathophysiology
  - i. Acute loss in intravascular volume leads to poor venous return to heart and decreased diastolic filling pressures. This leads to inadequate stroke volume and cardiac output.
  - ii. Acute intravascular volume loss usually secondary to hemorrhage or GI losses.
- b. Treatment
  - i. Replace fluid losses with isotonic fluids and blood products
  - ii. Stop acute intravascular volume loss
    1. Control sources of hemorrhage
    2. Control GI losses
      - a. Treatment of infectious diarrhea
      - b. Relief of bowel obstruction

#### E. Cardiogenic Shock

- a. Pathophysiology
  - i. Cardiac output not adequate for metabolic demands of body
  - ii. Causes
    1. Myocardial ischemia and infarction (most common).
    2. Cardiac tamponade
    3. Spontaneous cardiac dysrhythmias.
  - iii. Diagnosis
    1. History, Physical, EKG
    2. Elevated Brain-type Natriuretic Peptide (BNP)
    3. Elevated cardiac enzymes
    4. Increased cardiac filling pressures with decreased cardiac output
  - iv. Treatment
    1. Relieve tamponade
    2. Treat dysrhythmias as per ACLS protocol
    3. Inotropic agents at tolerated to improve stroke volume

4. Decrease afterload if BP allows
5. Intraaortic Balloon Pump
  - a. Decreases afterload during systole
  - b. Increases coronary artery perfusions during diastole.
6. Ventricular assist devices
  - a. Placed in parallel with ventricle
  - b. Increases cardiac output
  - c. Used as a “bridge” to heart transplantation

### Hemodynamic Monitoring

The ultimate goal of hemodynamic monitoring of critically ill patients is to better recognize the cardiovascular state of the patient, identify possible causes of cardiovascular insufficiency, and monitor response to targeted therapies.

Hemodynamic monitoring can be divided into two general categories, noninvasive and invasive.

#### A. Invasive monitoring

- a. All invasive hemodynamic monitoring devices require tubing with a continuous, unobstructed fluid column from tip of catheter to pressure transducer.
  - i. Any obstruction (air bubbles, blood clots) in system can induce error in measurements.
  - ii. Pressure transducer needs to be leveled (“zeroed”) at appropriate phlebostatic axis.
    1. Transducers positioned to low will artificially raise hemodynamic measurements.
    2. Transducers positioned to high will artificially lower hemodynamic measurements.
  - iii. Small catheter in large vessel (femoral artery catheter, PA catheter) can produce inaccurate readings secondary to “catheter whip”. Catheter whip can effect measurements of pressure by  $\pm 10$ mm Hg.
  - iv. Error can occur secondary to an overdamped or underdamped monitoring system, resulting in inaccurate transmission of pressure waveform from catheter to transducer.
    1. Overdamped system shows an attenuated systolic peak, narrow pulse pressure, and widened systolic waveform. Artificially lower systolic readings. Often from bubbles trapped in tubing.
    2. Underdamped system shows a sharp systolic peak, increased pulse pressure, and narrow systolic waveform. Artificially raises systolic readings. Often from stiff tubing that amplifies waveforms as the incoming waveform approaches the resonant frequency of the tubing system. Can lengthen tubing to correct.
    3. Can use “flush test” to determine if system is underdamped or overdamped.

- v. Catheter whip and overdamped / underdamped systems effect diastolic / systolic pressure readings more than mean pressure readings. Therefore, the mean arterial pressure is usually the most accurate measurement in invasive blood pressure monitoring.
- b. Invasive Blood Pressure Monitoring (via arterial line)
  - i. Advantages
    - 1. Continuous, instantaneous measurements of SBP, DBP, MAP
    - 2. Ability to easily and repeatedly sample arterial blood
  - ii. Disadvantages
    - 1. SBP increases and DBP decreases the further away the site of measurement is from the aortic root (brachial > radial > femoral)
    - 2. Complications of intraarterial catheters
      - a. Infection
      - b. Thrombosis / embolization
      - c. Arterial injury
- c. Direct arterial catheter placement is the standard for blood pressure monitoring in hemodynamically unstable patients<sup>2</sup>
- d. Invasive Intravascular Volume / Cardiac Function Monitoring
  - i. All intrathoracic vascular pressures are measured at end expiration
    - 1. Waveforms measured at the highest point in respiratory variation in nonintubated patients.
    - 2. Waveforms measured at the lowest point in respiratory variation in mechanically ventilated patients.
  - ii. Central venous waveforms
    - 1. “a” wave- due to right atrial contraction. Correlates with P wave on EKG
    - 2. “c” wave- due to tricuspid valve prolapsing into the right atrium during early right ventricular contraction. Correlates with end of the QRS on EKS
    - 3. “v” wave- due to blood filling right atrium with a closed tricuspid valve. Correlates with ending of T wave on EKG.
  - iii. Central Venous Catheter
    - 1. Advantages
      - a. Can measure central venous pressure (CVP) and central venous oxygenation (ScvO<sub>2</sub>).
      - b. CVP used by Surviving Sepsis Guidelines for guiding resuscitation
      - c. Shown to improve outcome when used in Early Goal Directed Therapy in the Treatment of Severe Sepsis and Septic Shock<sup>5</sup> based on values of CVP and continuous ScvO<sub>2</sub>.
    - 2. Disadvantages
      - a. Requires skill for placement of catheter
      - b. Complications of central venous line placement
        - i. Infection
        - ii. Pneumothorax

- iii. Bleeding
  - iv. Thrombosis
  - v. Air emboli
  - vi. Arterial puncture
- c. Use of cardiac filling pressures to guide volume and hemodynamic management is criticized by some authors<sup>6</sup>
- iv. Pulmonary artery catheter
  1. Measures pulmonary artery pressure and pulmonary artery occlusion pressure via continuous fluid column and pressure transducer.
  2. Measures right ventricular cardiac output via thermodilution technique.
    - a. A solution that is colder than the central venous blood is injected via the proximal catheter port (30cm from tip).
    - b. In patients with decreased cardiac output, the cold solution will take longer to reach the thermistor at the end of the PA catheter (4cm from tip), and will move past the thermistor slowly. In patients with an increased cardiac output the cold solution will take a shorter time to reach the thermistor and move past the thermistor quickly.
    - c. Therefore, the cardiac output is inversely proportional to the change in temperature over time. If temperature / time measurements are plotted on a graph the cardiac output will be equal to the area under the curve.
  3. Advantages
    - a. Can directly measure pulmonary artery pressures, pulmonary artery occlusion pressure, right ventricular cardiac output, and mixed venous oxygenation.
    - b. Can indirectly calculate SVR, PVR, CI, oxygen delivery, oxygen consumption.
  4. Disadvantages
    - a. Requires skill for placement of central venous access and then floating PA catheter through right side of heart
    - b. Cardiac arrhythmias during insertion
    - c. Can have all the complications of central venous line placement in addition to:
      - i. Rare pulmonary artery rupture
      - ii. Increased rates of catheter related sepsis
  5. PA Catheter Controversy
    - a. Prospective randomized trials have failed to show improvement in mortality with the use of PA catheters in patients with:
      - i. Shock and ARDS<sup>7</sup>
      - ii. High Risk Surgical Patients<sup>8</sup>
      - iii. Acute Lung Injury<sup>9</sup>
    - b. PA Catheter use decreased by 65% from 1993 to 2004.<sup>10</sup>



- v. Arterial waveform analysis
  - 1. Stroke volume variation (SVV)
    - a.  $SVV = (SV_{\max} - SV_{\min}) / SV_{\text{mean}}$
    - b. Uses variations in stroke volume caused by changes in intrathoracic pressure during the respiratory cycle.
    - c. As intravascular volume decreases, stroke volume variation increases.
    - d. Has been validated in mechanically ventilated patients only.
    - e. Arrhythmias can dramatically affect SVV

## B. Noninvasive

- a. Noninvasive Blood Pressure Monitoring– via sphygmomanometer
  - i. Auscultation based measurements (via stethoscope)
    - 1. Based on Korotkoff sounds
    - 2. Accuracy is operator dependent
    - 3. Cuff mismatching
      - a. Length of pressure bladder in cuff should be at least 80% circumference of arm.
      - b. Cuff too small – BP falsely elevated
  - ii. Oscillatory based measurements (automatic Dynamat BP cuff)
    - 1. Based on an oscillatory algorithm which senses changes in pressure transmitted from artery to inflated cuff
    - 2. Accuracy not operator dependent
    - 3. Oscillatory sensing decreases with decreasing blood pressure, so accuracy is lower in hypotensive patients

## C. Noninvasive Intravascular Volume / Cardiac Function Monitoring

- a. Bedside ultrasound
  - i. Advantages
    - 1. Can look at RV / LV to assess cardiac function
    - 2. Can look at IVC to assess intravascular volume
      - a. Measure absolute diameter
      - b. Measure change in diameter during respiratory variation
    - 3. Can be repeated without danger to patient
  - ii. Standardized Exams
    - 1. BEAT = Bedside Echocardiographic Assessment in Trauma/Critical Care<sup>11</sup>
      - a. Can calculate cardiac output, pericardial or pleural effusion, IVC diameter and respiratory variation.
    - 2. FREE = Focused Rapid Echocardiographic Examination.<sup>12</sup>
      - a. Can calculate ejection fraction, IVC diameter and respiratory variation
  - iii. Disadvantages
    - 1. Has not been shown to improve patient outcomes
    - 2. Operator dependent
- b. Esophageal Doppler Probe

- i. Advantages
  - 1. Only semi-invasive
  - 2. Can measure SV and CO continuously
- ii. Disadvantages
  - 1. Has not been shown to improve patient outcomes

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<sup>1</sup> CDC NCHS Data Brief. No.62, June 2011

<sup>2</sup> Dellinger RP, et.al. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med 2008; 36:296-327

<sup>3</sup> FDA Drug Safety Communication: Voluntary market withdrawal of xigris due to failure to show a survival benefit. Published 10-25-2011. < <http://www.fda.gov/Drugs/DrugSafety/ucm277114.htm>>. Accessed May 13, 2012.

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<sup>5</sup> Rivers E, et.al. Early Goal-Directed Therapy in the Treatment of Severe Sepsis and Septic Shock. N Engl J Med 2001; 345:1368-77

<sup>6</sup> Osman D, et.al. Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge. Crit Care Med. 2008 Jan;35(1):64-8.

<sup>7</sup> Richard C, et.al. Early Use of Pulmonary Artery Catheter and Outcomes in Patients with Shock and Acute Respiratory Distress Syndrome. JAMA. 2003; 290(20):2713-20.

<sup>8</sup> Sandham JD, et.al. A Randomized, Controlled Trial of the Use of Pulmonary-Artery Catheters in High-Risk Surgical Patients. N Engl J Med 2003; 348:5-14.

<sup>9</sup> Pulmonary-Artery versus Central Venous Catheter to Guide Treatment of Acute Lung Injury. N Engl J Med. 2006;354:2213-24.

<sup>10</sup> Wiener RS, et.al. Trends in the Use of the Pulmonary Artery Catheter in the United States, 1993-2004. JAMA 2007; 298(4):423-29.

<sup>11</sup> Gunst M, et.al. Accuracy of Cardiac Function and Volume Status Estimates Using the Bedside Echocardiographic Assessment in Trauma/Critical Care. J Trauma. 2008; 65(3):509-16

<sup>12</sup> Ferrada P. Transthoracic Focused Rapid Echocardiographic Examination: Real-time Evaluation of Fluid Status in Critically Ill Trauma Patients. J Trauma. 2011; 70(1):56-64.