AMERICAN COLLEGE OF OSTEOPATHIC INTERNIST
CRITICAL CARE BOARD REVIEW

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Disclosures

I have no disclosures, conflicts of interest related to this subject or talk.
Lecture Objectives

• Review cardiopulmonary resuscitation (CPR) as it relates to ICU medicine.

• Review the current guidelines & goals for Sepsis, Septic Shock & ARDS.

• Explain mechanical ventilation interpretation and strategies for ICU patients.

• Outline key studies used to make medical decisions in the ICU.

• Discuss studies that changed mortality in the ICU.
A middle aged man collapses at Orlando SeaWorld after hearing about the movie “blackfish”. He is unresponsive and has no pulse or respirations. Correct interventions are?

(A) Chest compression alone at 100/minute
(B) Use of AED by ACLS trained personal
(C) Provide 3 immediate shocks before CPR
(D) Establish airway and administer breaths (ABC)
Critical Care Question

You are asked to be on the ICU Stewardship Committee for infection control and antibiotics use. Which of the following evaluations have proven to be the most successful in reducing ICU infections?

(A) Education
(B) Hand washing
(C) Daily sedation vacation
(D) Nasal decontamination with Bactroban
There has been an increase in methicillin-resistant *Staphylococcus aureus* (MRSA) infections in your intensive care unit, and you are asked to provide an action plan to address this situation.

Which of the following should you recommend?

(A) Universal decolonization
(B) Gastrointestinal decolonization
(C) Targeted decolonization
(D) Patient screening and isolation

Universal Decolonization

- In this trial involving 74 ICUs at 43 hospitals, universal decolonization with the use of chlorhexidine and mupirocin was associated with a decrease in all-cause bloodstream infections.
A 69-year-old woman is brought to the emergency department from a nursing home because of confusion, fever, & flank pain.

Temperature is 38.5 C (101.3 F), pulse rate is 123 per minute, respirations are 27 per minute, and blood pressure is 82/48 mm Hg.

Physical examination reveals dry mucous membranes, costovertebral tenderness, poor skin turgor, and no edema. Leukocyte count is 15,000 and urinalysis shows 50 – 100 WBCs with many bacteria. The patient has a metabolic acidosis and high lactate levels (6 mg/dl or 0.6 mmol/L).
Case Presentation - Question

Base on the presentation which category is the patient currently in?

A. This patient has SIRS (systemic inflammatory response)
B. The case describes Sepsis
C. This is clearly severe sepsis
D. No, this is Septic Shock
Definition of Systemic Inflammation

- **SIRS** (systemic inflammatory response syndrome) - 2 of the following 4:
  - Temperature >38 or <36 degrees C
  - Heart rate > 90 beats/min
  - Respiratory Rate > 30 breaths/min or CO2 < 32 mmHg
  - WBC >12 or < 4 k cells or > 10 band forms

- **Sepsis** = Documented or suspected infection plus systemic manifestation (SIRS, Procalcitonin, CRP, ▲MS)

- **Severe Sepsis** = Sepsis plus evidence of organ dysfunction (↓ Pa/FiO2, ↓ UO, ↑ Cr, ▲Coagulation, elevated bili, ↓ cap refill)

- **Septic Shock** = Sepsis with hypotension refractory fluid resuscitation (30ml/Kg) or hyperlactatemia ( > 1mmol/L)

Cawcutt, KA & Peters, SG. Mayo Clin Proc. 2014; 89 (11);1572 - 1578
Serum lactate levels was associated with mortality, and the adjusted OR for hospital mortality increased linearly with increasing serum lactate level. An increase in serum lactate level from 2 to 10 mmol/L increased the adjusted OR for hospital mortality from 1.4 (95% CI, 1.35-1.45) to 3.03 (95% CI, 2.68-3.45).
In conjunction with appropriate antibiotics, which of the following choices is most likely to result in improved survival for this patient (Single Best Answer)?

(A) 25% albumin infusion  
(B) Aggressive & early fluid resuscitation with crystalloid  
(C) Maintaining a hemoglobin level above 10 mg/dl  
(D) Maintaining a PaCO2 below 50 mm Hg  
(E) IV steroids
The Effects of Antibiotics On Survival

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock.

Case Presentation - Answer
Goal Directed Therapy

To emphasize that aggressive fluid resuscitation is a life saving & time sensitive intervention for sepsis patients, regardless of the type of monitoring device.

Case Presentation - Answer
Directed Therapy

Interventions

- ScvO2 Group
  - Resuscitation Protocols
  - resuscitated to normalize
  - Central venous pressure, mean arterial pressure, ScvO2 of at least 70%;

- Lactate Clearance Group
  - Central venous pressure, mean arterial pressure, lactate clearance of 10%.

Equivalence ≠ in:
- Mortality: 17% v. 23% (EGDT)
- Hospital LOS: 11% v. 12% (EGDT)
- MSOF: 25% v. 22% (EGDT)

Study protocol was continued until all goals or for up to 6 hours.

The ProCESS Investigators
Protocolized Care for Early Septic Shock Trial

All 3 arms of the study mortality was < 21%
Protocolized Care for Early Septic Shock Trial

- Mortality rates in the EGDT study vs the ProCESS & ARISE trials?
  - EGDT = 31% - 47%
  - ProCESS = 18.2% - 21%, 60 day mortality rate
  - ARISE = 18.6% - 18.8%, 90 day mortality rate
Management in Sepsis (ProMISe) Trial
Protocolized Care for Septic Shock Trial

• Pragmatic, open, multi center, randomized controlled trial of 56 emergency departments in the United Kingdom
• 1260 patients were assigned to EGDT (6-hour resuscitation protocol) vs “usual” care

• Outcomes = Primary: All-cause mortality at 90 days
  • Total IVFs in 6 (ml) 2226 ± 1443 v. 2022 ± 1271
  • Arterial Catheters 74.2% v. 62.2%
  • Central Venous Catheters (CVC) 92.1% v. 50.9%
  • Vasopressors 53.3% v. 46.6%
  • Transfusions 8.8% v. 3.8%
  • Dobutamine 18.1% v. 3.1%
  • 90 Day Mortality 29.5% v. 29.2%

The Sequential Organ Failure Assessment (SOFA) Score (Predictor of morbidity severity and mortality estimation) at 6 hours was higher in the EGDT arm vs “usual” care arm (6.4 ± 3.8 vs 5.6 ± 3.8).

Number of patients requiring advanced cardiovascular support was 37.0% in the EGDT arm vs 30.9% in the “usual” care arm (p = 0.026).

Number of days in the ICU was 2.6 days in the EGDT arm vs 2.2 days in the “usual” care arm (p = 0.005).

The average cost of care was $17,647 in the EGDT arm vs $16,239 in the “usual” care arm, but this was not statistically significant (p = 0.26).
<table>
<thead>
<tr>
<th>Trial Name</th>
<th>ProCESS</th>
<th>ARISE</th>
<th>ProMISe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title</strong></td>
<td>A Randomized Trial of Protocol-Based Care for Early Septic Shock</td>
<td>Goal-Directed Resuscitation for Patients with Early Septic Shock</td>
<td>Protocolised Management in Sepsis (ProMISe)</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>U.S. 31 Emergency Departments</td>
<td>Australia/New Zealand 51 Emergency Departments</td>
<td>U.K. Multi-Center</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>1935 adult subjects with septic shock (refractory hypotension or LA ≥ 4mmol/L)</td>
<td>1600 adult sepsis subjects with septic shock (refractory hypotension or LA ≥ 4mmol/L)</td>
<td>1260 adult sepsis subjects with septic shock (refractory hypotension or LA ≥ 4mmol/L)</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>EGDT</td>
<td>EGDT</td>
<td>EGDT</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>Protocol-Based Care (no CVC) Usual Care</td>
<td>Usual Care</td>
<td>Usual Care</td>
</tr>
<tr>
<td><strong>Primary Outcome</strong></td>
<td>60 Day Mortality</td>
<td>90 Day Mortality</td>
<td>90 Day Mortality</td>
</tr>
<tr>
<td><strong>Primary Outcome Result (relative risk)</strong></td>
<td>EGDT 21% Protocol Based 18.1% Usual Care 18.9%</td>
<td>EGDT 18.6% Usual Care 18.8%</td>
<td>EGDT 30% Usual Care 29%</td>
</tr>
<tr>
<td><strong>Publication Date</strong></td>
<td>May 2014</td>
<td>October 2014</td>
<td>Mar 2014</td>
</tr>
<tr>
<td><strong>Journal</strong></td>
<td>NEJM</td>
<td>NEJM</td>
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</tbody>
</table>

Adapted from:
Protocolized Care for Early Septic Shock Shock Trial
90-day mortality

ProCESS

ARISE

ProMISE
A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit

• In this trial of critically ill patients in the intensive care unit, the use of albumin (4%) and saline resulted in similar outcomes at 28 days.

• Two treatments = equivalent with respect to clinical outcomes.

In patients with severe sepsis, albumin replacement in addition to crystalloids, as compared with crystalloids alone, did not improve the rate of survival at 28 and 90 days.

Despite your intentions, this same 69-year-old woman receives only 2 liters of fluid over 6 hours in the ED while awaiting ICU transfer.

In the ICU, resuscitation is “ramped up” considerably with 8 liters of normal saline, but the patient develops ARDS & oliguric renal failure by the next morning. She remains hypotensive.
In this patient, the next best step includes which of the following:

(A) Start Dopamine gtt for MAP > 60 mmHg
(B) Administer high dose Vasopressin
(C) Start Rosuvastatin (lipid) medication (anti-inflammatory)
(D) Transfuse PRBC for Hb > 10 gm/dL
(E) Start Levophed gtt for MAP > 65 mmHg
Comparison of Dopamine & Norepinephrine in the Treatment of Shock

- **Conclusions:** No significant difference in the rate of death between patients with shock who were treated with dopamine vs. norepinephrine,
- Dopamine $\Rightarrow$ number of adverse events.

Vasopressin vs. Norepinephrine Infusion in Patients with Septic Shock


Table 3. Serious Adverse Events in Patients Who Had Septic Shock.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Norepinephrine Group (N = 382)</th>
<th>Vasopressin Group (N = 396)</th>
<th>P Value&lt;sup&gt;≤&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one serious adverse event</td>
<td>40 (10.5)</td>
<td>41 (10.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Acute myocardial infarction or ischemia</td>
<td>7 (1.8)</td>
<td>8 (2.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>8 (2.1)</td>
<td>3 (0.8)</td>
<td>0.14</td>
</tr>
<tr>
<td>Life-threatening arrhythmia</td>
<td>6 (1.6)</td>
<td>8 (2.0)</td>
<td>0.79</td>
</tr>
<tr>
<td>Acute mesenteric ischemia</td>
<td>13 (3.4)</td>
<td>9 (2.3)</td>
<td>0.39</td>
</tr>
<tr>
<td>Hyponatremia†</td>
<td>1 (0.3)</td>
<td>1 (0.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Digital ischemia</td>
<td>2 (0.5)</td>
<td>8 (2.0)</td>
<td>0.11</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>1 (0.3)</td>
<td>1 (0.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Other‡</td>
<td>2 (0.5)</td>
<td>5 (1.3)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

* Two-sided P values are based on Fisher’s exact test.
† Hyponatremia was defined as a serum sodium level of less than 130 mmol per liter.
‡ Other events include acute hepatitis, agranulocytosis, pulmonary embolism, seizures, drug error, and two cases of drug extravasation from the central venous catheter.
High versus Low Blood-Pressure (MAP >65) Target in Patients with Septic Shock

Targeting a mean arterial pressure of 80 to 85 mm Hg, as compared with 65 to 70 mm Hg

Lipid (anti-inflammatory) Medication in ARDS

- Multicenter trial in which patients with sepsis-associated ARDS were randomly assigned to receive either enteral rosuvastatin or placebo in a double-blind manner.

- The primary outcome was mortality before hospital discharge home or until study day 60.

- Secondary outcomes included the number of ventilator-free days (days that patients were alive and breathing spontaneously) to day 28 and organ-failure–free days to day 14.

In our patients, there is a discussion of placing a pulmonary artery catheter to obtain the PAOP (i.e., wedge pressure), as opposed to management using CVP, if this is done it is most likely to result in which of the following (Single Answer)?

(A) Decreased 28-day mortality
(B) Decreased length of ICU stay
(C) Decreased incidence of congestive heart failure
(D) No identifiable benefit
(E) Decreased incidence of renal dysfunction
Pulmonary-Artery versus Central Venous Catheter to Guide Treatment of Acute Lung Injury

- Hemodynamic monitoring is a common physiological intervention in patients with acute lung injury.

- In this randomized, controlled trial no significant difference in 60-day mortality whether monitoring was performed with a pulmonary-artery catheter or a central venous catheter.

Graph: Kaplan-Meier Estimates of the Probability of Survival and of Survival without the Need for Assisted Ventilation during the First 60 Days after Randomization

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network
Our same 69 year-old woman with septic shock developed diffuse bilateral infiltrates and progressive hypoxemic respiratory failure (Pa/FiO₂<100) consistent with ARDS necessitating mechanical ventilation.

She is 5’3” (160 cm) and weights 198 pounds (90 kg). The RT asks you after intubation what tidal volume you want on the ventilator. Your best response is ?

(A) 314 ml
(B) 430 ml
(C) 540 ml
(D) 665 ml

Females: PBW (kg) = 45.5 + 2.3 (height (in) – 60)
kg = 45.5 + 2.3 (63 – 60)
kg = 45.5 + 6.9
kg = 52.4

52.4 x 6 cc/kg = 314.
Probability of Survival and of Being Discharged Home and Breathing without Assistance in ARDNet

- Acute lung injury & acute respiratory distress syndrome
- A multicenter, randomized trial
- Compared traditional ventilation, initial tidal volume of 12 ml/kg of and an (plateau pressure) of 50 cm of water or less, with ventilation with a lower tidal volume, which involved an initial tidal volume of 6 ml/kg and a plateau pressure of 30 cm of water or less.

Case Presentation - Question

Which of the following statement is TRUE (Single Answer) about the Berlin Definition of ARDS for this patient who had a P/F ratio of ~85 at intubation and also had AKI and shock?

(A) This is categorized as moderate ARDS
(B) Because she had urosepsis, this would not be ARDS
(C) Her predicted hospital mortality would be less than 20%
(D) We need a wedge pressure to determine if ALI is present
(E) None of the above is true
To review salient points about BERLIN Definition of ARDS within the context of this particular patient example.

- **Berlin** = Better defined cohort
  - Validated current studies

- **Mortality**
  - Mild 27%
  - Moderate 32%
  - Severe 45%
**Case Presentation - Question**

The patient’s is currently on 0.70 FiO₂ using assist control with a set rate of 22, Vt of 6 ml/kg, and PEEP of 10 cm H₂O. The blood gas is pH 7.39, PaO₂ of 71, PaCO₂ of 42. The Plateau airway pressure (Pplat) on the ventilator is 41 cm H₂O.

What if anything is needed at this point the patients care to improve survival?

(A) Do nothing things have improved  
(B) Place a chest tube to decrease the pressures  
(C) Call surgery for trach – to lower resistance and pressures  
(D) Adjust the Ventilator
Probability of Survival and of Being Discharged Home and Breathing without Assistance in ARDNet

Case Presentation - Question

It is now day 4, and this same patient with ARDS and sepsis is out of shock and off vasopressors. She remains heavily sedated and on the ventilator. You are not sure of her fluid status, but she is clinically very edematous though oliguric.

For this patient who is now stabilized and out of shock, with the ventilator being gradually reduced, which of the following steps in management have been shown to be helpful in reducing ventilator days, ICU days and improved oxygenation. (Single Answer):

(A) Avoid diuretics and keep CVP >12 due to oliguria
(B) Give diuretics and minimize fluids to goal CVP < 4
(C) Transfuse the patient to maintain Hgb levels of 10
(D) Start steroids for late phase ARDS
(E) Once the patient passes an SBT, discontinue sedation
Comparison of Two Fluid-Management Strategies in Acute Lung Injury

Conservative strategy improved:

- Improved oxygenation
- ↓ duration of Mech. Vent.
- ↓ intensive care days
- **Without** increasing nonpulmonary-organ failures

No significant difference in 60-day mortality

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network

In accordance with the 2013 SCCM Sepsis Guidelines for management of patients such as this, the literature supports which of the following statements as **GRADE 1** (highest level) **(Single Answer)**?

(A) Plateau Pressure should be maintained <30 cm H2O  
(B) Ventilator weaning protocols with SBTs  
(C) Sedation protocols and minimization of sedation  
(D) All of the above  
(E) None of the above
Case Presentation - Question

Which of the following statements regarding management of this patient with severe ARDS is **TRUE (Single Answer)**?

(A) Neuromuscular blockade should be used for mild & moderate ARDS.
(B) HFO is an early choice as established by recent RCTs.
(C) Prone positioning is an management strategy for severe ARDS
(D) Corticosteroids should be started early and often in ARDS
(E) Early tracheostomy is a proven way to reduce LOS and mortality.
Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome.

- Multicenter, double-blind trial, with onset of severe ARDS within the previous 48 hours were randomly assigned to receive, for 48 hours, either cisatracurium besylate (178 patients) or placebo (162 patients).

- Severe ARDS was defined as a ratio $\frac{\text{PaO}_2}{\text{FiO}_2}$ of less than 150, with a PEEP of $\geq 5$ cm and a tidal volume of 6 to 8 ml/Kg predicted body weight.

- In severe ARDS, early administration of a neuromuscular blocking agent improved the adjusted 90-day survival and increased the time off the ventilator without increasing muscle weakness.

Prone Positioning in ARDS

- Guerin Study in the NEJM (2013) used a P/F <150 (slightly different than the more strict Berlin cutoff of 100) and 60% or more FiO$_2$ to demonstrate a large survival advantage (HR 0.4 for 90-day mortality).

- The proning was used for at least 16 hours/day and was stopped when P/F >150 on PEEP <10 and FiO$_2$ <60%.

Video Video

Which of the following states is true regarding post ICU recovery?

A. Most sepsis survivors are back to work in 6 months
B. There is cognitive impairment post sepsis, even in mild disease
C. There is nothing that can be done to improve post ICU recovery
D. Daily interruption of sedation has the least impact on post ICU recovery
The Effects of Critical Illness

• A prospective cohort involving 1194 patients with 1520 hospitalizations for severe sepsis drawn from the Health and Retirement Study, a nationally representative survey of US residents (1998-2006).

• A total of 9223 respondents had a baseline cognitive and functional assessment; 516 survived severe sepsis and 4517 survived a non-sepsis hospitalization to at least 1 follow-up survey and are included in the analysis.

Time to sepsis admission
Median (IQR) y # of patient

Iwashyna T JAMA 2010; 304: 1787 - 1794
Board Keys to ICU Medicine
Conclusions

• Volume resuscitation with saline (30 cc/kg)

• No CVP or PAOP needed, Protocols are not needed!

• After shock resolves then start diuresis (conservative fluids)

• ARDS is still a syndrome: Berlin Criteria is the scoring system

• Treatment Criteria changes with severity, however 6 cc/kg (ideal)

• Keep the Plat Pressure < 30 in ARDS

• SBT, Sedation vacation reduce ICU LOS & cognitive impairment