Sepsis 2015: You say you wanted a revolution

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SEPSIS 2015:
YOU SAY YOU WANT A REVOLUTION

R. Phillip Dellinger MD, MSc, MCCM
Professor and Chair of Medicine
Cooper Medical School of Rowan University
Medical Director Adult Health Institute
Senior Critical Care Attending
Cooper University Hospital
Camden NJ USA
POTENTIAL CONFLICTS OF INTEREST

• Hold leadership position in Surviving Sepsis Campaign

• Cooper University Hospital receives consultant fees and research funding from Spectral Inc. for work with the EUPHRATES trial.
Burden of Severe Sepsis

Sepsis Performance Improvement Revolution

Research: New or Ongoing Clinical Trials
Burden of Severe Sepsis
SEVERE SEPSIS

- Severe Sepsis is the Leading Cause of Hospital Death
- Admissions with severe sepsis 8X > chance of death than other conditions
- Most expensive condition treated in the hospital (23 billion dollars per annum)
- Enormous economic burden that can be lessened with early identification and early appropriate evidence based medicine care

NCHS data brief #62, 2011
US National Lib Med, NIH, 2010
HCUP Statistical Brief #160
Causes of death in New Jersey in 2011, according to the most recent data available.
New Jersey Department of Health posted January 8, 2015
“Houston, we have a problem.”

APOLLO 13
“HEALTHCARE, WE HAVE A PROBLEM.”
CURRENTLY FUNDED WITH A GORDON AND BETTY MOORE FOUNDATION GRANT (INTEL FAMILY).

NO DIRECT OR INDIRECT INDUSTRY SUPPORT FOR GUIDELINES REVISION
CURRENT SURVIVING SEPSIS CAMPAIGN GUIDELINE SPONSORS

- American Association of Critical-Care Nurses
- American College of Chest Physicians
- American College of Emergency Physicians
- Australian and New Zealand Intensive Care Society
- Asia Pacific Association of Critical Care Medicine
- American Thoracic Society
- Brazilian Society of Critical Care (AIMB)
- Canadian Critical Care Society
- Chinese Society of Critical Care Medicine
- Emirates Intensive Care Society
- European Respiratory Society
- European Society of Clinical Microbiology and Infectious Diseases
- European Society of Intensive Care Medicine
- European Society of Pediatric and Neonatal Intensive Care
- Infectious Diseases Society of America
- Indian Society of Critical Care Medicine
- International Pan Arab Critical Care Medicine Society
- Japanese Association for Acute Medicine
- Japanese Society of Intensive Care Medicine
- Pediatric Acute Lung Injury and Sepsis Investigators
- Society Academic Emergency Medicine
- Society of Critical Care Medicine
- Society of Hospital Medicine
- Surgical Infection Society
- World Federation of Critical Care Nurses
- World Federation of Pediatric Intensive and Critical Care Societies
- World Federation of Societies of Intensive and Critical Care Medicine

Participation and endorsement:
- German Sepsis Society
- Latin American Sepsis Institute
GUIDELINES ARE NOT ENOUGH

- Protocols
- Performance Improvement Programs
- Audit and Feedback
Early Screening and a Hospital Based Performance Improvement Program
GUIDELINES TO BUNDLES

Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock

R. Phillip Dellinger, MD; Jean M. Carlet, MD, Henry Sibbitt, MD, David Sevruguin, MD, PhD; Thierry Collard, MD; Jonathan Cohen, MD; Jean-Georges De Marchis, MD, PhD; Diane Kem, MD; John C. Marshall, MD; Margaret M. Parke, MD; Grahamann, MD; Janie L. Zimmerman, MD; John Luice Vincent, MD, PHD; Mitchell W. Levy, MD; for the Surviving Sepsis Campaign Management Guidelines Committee

Sponsoring Organizations: American Association of Critical-Care Nurses, American College of Chest Physicians, American College of Emergency Physicians, American Thoracic Society, Australasian and New Zealand Intensive Care Society, European Society of Critical Care Medicine, European Society of Intensive Care Medicine, European Society of Intensive Care Medicine, Society of Critical Care Medicine, Surgical Intensive Society.

Objective: In 2004, critical care and infection disease experts representing 11 international organizations developed treatment guidelines for severe sepsis and septic shock that would be of practical use for the intensive care unit, under the auspices of the Surviving Sepsis Campaign, an international effort to increase awareness and improve outcomes in severe sepsis. The process involved a modified Delphi method, a consensus conference, critical incident simulation meetings, subgroups and key stakeholders. Identifications, and electronic-based electronic e-mail registry and using the entire registry process involved defined a survivorship target for the primary treatment guidelines for early goal-directed therapy for severe sepsis and septic shock. In 2004, the guidelines were published as a series of recommendations for early goal-directed therapy. These recommendations included interventions such as early goal-directed therapy for severe sepsis and septic shock, one of the recommendations on early goal-directed therapy for severe sepsis and septic shock. These guidelines were developed by an international panel of experts in critical care medicine, infectious disease, and critical care intensivists.

Guidelines to Bundles

Severe Sepsis Bundles:

Sepsis Resuscitation Bundle
(To be accomplished as soon as possible and scored over first 24 hours):
1._iSodium lactate administered prior to antibiotic administration.
2. Blood cultures obtained prior to antibiotic administration.
3. From the time of presentation, broad-spectrum antibiotics administered within 3 hours for ISS admission and 1 hour for non-ICU admission.
4. In the event of hypotension and/or tachycardia > 140 mmHg, (150 mg/day) a. Defer to initial administration of hydrocortisone to out-of-hospital death.
b. Apply vasopressors for hypertension not responding to initial fluid resuscitation to maintain mean arterial pressure > 65 mmHg.
5. In the event of persistent hypotension despite fluid resuscitation (sepsis shock) and/or lactates > 4 mmol/L, (35 mmol/L):
   a. Achieve central venous pressure (CVP) of 8 mm Hg.
   b. Achieve central venous oxygen saturation (SvO2) of >70%.

Sepsis Management Bundle
(To be accomplished as soon as possible and scored over first 24 hours):
1. Low-dose steroids administered for sepsis shock in accordance with a standardized ICU policy.
2. Procalcitonin (PCT) monitored in accordance with a standardized ICU policy.
3. Oxygen saturation maintained > 98% normal, but < 150 mmHg (8.3 kPa).
4. Inotropic agents pressure maintained > 30 cm H2O for ICU patients without ventilated patients.

*Give the individual's weight measurement to the nearest millimeter.
†Achieving a central venous oxygen saturation (SvO2) of >70% is an acceptable alternative.
CONVERTING GOALS TO MEASURABLE INDICATORS
Severe Sepsis Resuscitation Bundle

Complete tasks within 6 hours of identifying severe sepsis.

1. Measure serum lactate.
2. Obtain blood cultures prior to antibiotic administration.
3. Administer broad-spectrum antibiotic within 3 hours of ED admission and within 1 hour of non-ED admission.
4. In the event of hypotension and/or serum lactate > 4 mmol/L:
   a. Deliver an initial minimum of 20 mL/kg of crystalloid or equivalent.
   b. Begin vasopressors for hypotension not responding to initial fluid resuscitation to maintain MAP > 65 mm Hg.
5. In the event of persistent hypotension despite fluid resuscitation (septic shock) and/or lactate > 4 mmol/L:
   a. Achieve a central venous pressure (CVP) of > 8 mm Hg
   b. Achieve a central venous oxygen saturation (ScvO₂) > 70% or mixed venous oxygen saturation (ScvO₂) > 65%

Implement the 6-hour bundle. Available at: http://ssc.sccm.org/6hr_bundles.
Severe Sepsis Management Bundle

Complete tasks within 24 hours of identifying severe sepsis.

1. Administer low-dose steroids for septic shock in accordance with a standardized hospital policy.
   - If not administered, document why the patient did not qualify for low-dose steroids based upon the standardized protocol.

2. Administer recombinant human activated protein C (rhAPC) in accordance with a standardized hospital policy.
   - If not administered, document why the patient did not qualify for rhAPC.

3. Maintain glucose control 80-150 mg/dL.

4. Maintain a median inspiratory plateau pressure (IPP) ≤30 cm H2O for mechanically ventilated patients.

Implement the 24-hour bundle. Available at: http://ssc.sccm.org/24hr_bundles.
CHANGE IN COMPLIANCE OVER TIME

Levy MM, Dellinger, RP, Townsend SA et al.
CHANGE IN MORTALITY OVER TIME

SSC MORTALITY

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Mortality</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36.6%</td>
<td>35.6% - 37.5%</td>
</tr>
<tr>
<td>4</td>
<td>34.2%</td>
<td>33.6% - 34.8%</td>
</tr>
<tr>
<td>8</td>
<td>31.2%</td>
<td>30.6% - 31.8%</td>
</tr>
<tr>
<td>12</td>
<td>28.3%</td>
<td>27.4% - 29.3%</td>
</tr>
<tr>
<td>16</td>
<td>25.6%</td>
<td>24.3% - 27.0%</td>
</tr>
</tbody>
</table>

Slope = 0.7% drop in mortality/quarter,  p-value < 0.001

WHY?
INITIAL RESUSCITATION OF SEPSIS INDUCED TISSUE HYPOPERFUSION

Recommend
Insertion central venous catheter

Recommended goals:
- **Central venous pressure:** 8–12 mm Hg
  - Higher with altered ventricular compliance or increased intrathoracic pressure
- **ScvO2 saturation (SVC)** $\geq 70$

Grade 1C
The Starling principle relates to the fact that the more a myocardial fibril is stretched the greater the contraction.
EXPECTED RESULT OF VOLUME EXPANSION
CENTRAL VENOUS PRESSURE POORLY PREDICTS CARDIAC PRELOAD AND VOLUME STATUS

INTRAVASCULAR VOLUME STATUS AND PERFUSION PARAMETERS

• Limitation of pressure measurement to predict fluid responsiveness

• There are alternatives to CVP for judging fluid responsiveness that are in general more reliable
ARTERIAL SYSTOLIC PRESSURE VARIATION

EFFECT ON CARDIAC FILLING
EFFECT ON STROKE VOLUME
EFFECT ON STROKE VOLUME
<table>
<thead>
<tr>
<th>To be accomplished as soon as possible and scored over first 3 hrs:</th>
<th>To be accomplished as soon as possible and scored over first 6 hrs:</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Serum lactate measured.</td>
<td>✓ Apply vasopressors for hypotension not responding to initial fluid resuscitation to maintain MAP ≥ 65 mm Hg.</td>
</tr>
<tr>
<td>✓ Blood cultures obtained prior to antibiotics administered.</td>
<td>✓ In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate &gt; 4 mmol/L (36 mg/dL):</td>
</tr>
<tr>
<td>✓ Administer broad-spectrum antibiotics.</td>
<td>✓ Measure CVP*</td>
</tr>
<tr>
<td>✓ For hypotension and/or lactate &gt; 4 mmol/L:</td>
<td>✓ Measure ScvO₂*</td>
</tr>
<tr>
<td>✓ Deliver an initial minimum of 30 ml/kg of crystalloid</td>
<td>✓ Remeasure lactate if initial lactate is elevated*</td>
</tr>
</tbody>
</table>

You say you want a revolution

Revolution

The BEATLES
TO BE COMPLETED WITHIN 3 HOURS OF TIME OF PRESENTATION:

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate $\geq 4$mmol/L
5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation to maintain a mean arterial pressure (MAP) ≥65mmHg)

6. In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4 mmol/L (36mg/dl):
   - Measure central venous pressure (CVP)
   - Measure central venous oxygen saturation (ScvO2)

7. Remeasure lactate if elevated.
A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*


Over 1500 Patients

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*


1600 Patients
Both the ProCESS and ARISE trials demonstrated the lack of necessity of using central venous oxygen saturation and central venous pressure monitoring as resuscitation targets when compared to the usual care group.
A. Measure lactate level
B. Obtain blood cultures prior to antibiotics
C. Administer broad spectrum antibiotics
D. Administer 30 ml/kg crystalloid for hypotension or lactate = 4 mmol/L
E. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation to maintain a mean arterial pressure = 65)
F. In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was = 4 mmol/L, re-assess volume status and tissue perfusion and document findings.

*To meet the requirements, a focused exam† by a licenses independent practitioner (LIP) to include vital signs, cardiopulmonary, capillary refill, pulse and skin findings, or any 2 other items below are required:

- Measure CVP
- Measure ScvO2
- Bedside cardiovascular ultrasound
- Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge

G. Re-measure lactate if initial lactate is elevated
<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A.</td>
<td>Measure lactate level</td>
</tr>
<tr>
<td>B.</td>
<td>Obtain blood cultures prior to antibiotics</td>
</tr>
<tr>
<td>C.</td>
<td>Administer broad spectrum antibiotics</td>
</tr>
<tr>
<td>D.</td>
<td>Administer 30 ml/kg crystalloid for hypotension or lactate = 4 mmol/L</td>
</tr>
<tr>
<td>E.</td>
<td>Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation to maintain a mean arterial pressure = 65)</td>
</tr>
<tr>
<td>F.</td>
<td>In the event of persistent hypotension after initial fluid administration (MAP &lt; 65 mm Hg) or if initial lactate was = 4 mmol/L, re-assess volume status and tissue perfusion and document findings.</td>
</tr>
</tbody>
</table>

*To meet the requirements, a focused exam† by a licenses independent practitioner (LIP) to include vital signs, cardiopulmonary, capillary refill, pulse and skin findings, or any 2 other items below are required:*

- Measure CVP
- Measure ScvO2
- Bedside cardiovascular ultrasound
- Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge

G. Re-measure lactate if initial lactate is elevated
You say you got a real solution
Well, you know
We’d all love to see the plan

Revolution
You ask me for a contribution
Well, you know
We’re all doing what we can

Revolution
You tell me it’s (for) the institution
A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*


Over 1500 Patients

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*


1600 Patients
<table>
<thead>
<tr>
<th></th>
<th>ProCESS</th>
<th>ARISE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrollment</td>
<td>&lt;2 hours from detection of shock</td>
<td>2.8 hours (median) from presentation to ED</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>75% received prior to enrollment</td>
<td>70 minutes (median) from presentation to ED</td>
</tr>
<tr>
<td>Fluids</td>
<td>&gt;2 liters prior to enrollment</td>
<td>2515ml (mean) prior to enrollment</td>
</tr>
</tbody>
</table>
• SSC 2006 six hour bundle
• SSC 2012 three hour bundle
• NQF 0500
• ProCESS/ARISE/PROMISE
• NQF 0500 (revised)
• CMS SEP 1
TO SAVE LIVES.....

- **Early** identification
- **Early** antibiotics
- **Early** fluid resuscitation
Table 2 - NQF 0500(revised)

A. Measure lactate level
B. Obtain blood cultures prior to antibiotics
C. Administer broad spectrum antibiotics
D. Administer 30 ml/kg crystalloid for hypotension or lactate = 4 mmol/L
E. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation to maintain a mean arterial pressure = 65)
F. In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was = 4 mmol/L, re-assess volume status and tissue perfusion and document findings.

*To meet the requirements, a focused exam† by a licensees independent practitioner (LIP) to include vital signs, cardiopulmonary, capillary refill, pulse and skin findings, or any 2 other items below are required:

• Measure CVP
• Measure ScvO2
• Bedside cardiovascular ultrasound
• Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge

G. Re-measure lactate if initial lactate is elevated
IMPORTANCE OF REASSESSMENT
Sepsis is a big problem
Logic of indicators is good
Benchmarked performance
The BEATLES

Don’t you know it’s gonna be alright, alright, alright

Revolution
Research / New or Ongoing Clinical Trials
SELEPRESSIN
The Selective Vasopressin Type 1a Receptor Agonist Selepressin (FE 202158) Blocks Vascular Leak in Ovine Severe Sepsis*

Marc O. Maybauer, MD, PhD, EDIC, FCCP1,2; Dirk M. Maybauer, MD, PhD1,2; Perenlei Enkhbaatar, MD, PhD2; Régent Laporte, DVM, MSc, PhD3; Halina Wiśniewska, MS3; Lillian D. Traber, RN1; ChiiDean Lin, PhD4; Juanjuan Fan, PhD5; Hal K. Hawkins, MD, PhD5; Robert A. Cox, PhD5; Kazimierz Wiśniewski, PhD4; Claudio D. Schteingart, PhD3; Donald W. Landry, MD, PhD6; Pierre J.-M. Rivière, PhD3; Daniel L. Traber, PhD, FCCM1

**Objective:** To determine if the selective vasopressin type 1a receptor agonist selepressin (FE 202158) is as effective as the mixed vasopressin type 1a receptor/vasopressin V2 receptor agonist vasoactive hormone arginine vasopressin when used as a titrated first-line vasopressor therapy in an ovine model of Pseudomonas aeruginosa pneumonia-induced severe sepsis.

*See also p. 1747.

1Investigational Intensive Care Unit, Department of Anesthesiology, University of Texas Medical Branch, Galveston, TX.
2Department of Anaesthesia and Intensive Care, Philipps University of Marburg, Marburg, Germany.
3Ferring Research Institute, San Diego, CA.
4Department of Mathematics and Statistics, San Diego State University, San Diego, CA.
5Department of Pathology, University of Texas Medical Branch, Galveston, TX.
6Department of Medicine, Columbia University, New York City, NY.
†Deceased.

Drs. Marc O. Maybauer, Dirk M. Maybauer, Enkhbaatar, and Laporte contributed equally to this work.

Supported, in part, by Ferring Research Institute, San Diego, CA.

Drs. Marc O. Maybauer, Dirk M. Maybauer, Enkhbaatar, Traber, Hawkins, Cox, and Traber were employees of the University of Texas Medical Branch at Galveston, which was contracted by the Ferring Research Institute to conduct the study reported here. Drs. Lin and Fan are employees of Forestat Consulting Group, which was contracted by the Ferring Research Institute to conduct the statistical analysis of the study reported here. Drs. Laporte, Wiśniewski, Schteingart, and Rivière and Ms. Wiśniewska were employees of the Ferring Research Institute. Dr. Lin consulted for Ferring Research Institute. Drs. Landry and Traber were consultants for Ferring Research Institute.

**Design:** Prospective, randomized, controlled laboratory experiment.

**Setting:** University animal research facility.

**Subjects:** Forty-five chronically instrumented sheep.

**Interventions:** Sheep were anesthetized, insufflated with cooled cotton smoke via tracheostomy, and P. aeruginosa were instilled into their airways. They were then placed on assisted ventilation, awakened, and resuscitated with lactated Ringer’s solution titrated to maintain hematocrit ± 3% from baseline levels. If, despite fluid management, mean arterial pressure fell by more than 10 mm Hg from baseline level, an additional continuous IV infusion of arginine vasopressin or selepressin was titrated to raise and maintain mean arterial pressure within no less than 10 mm Hg from baseline level. Effects of combination treatment of selepressin with the selective vasopressin V2 receptor agonist desmopressin were similarly investigated.

**Measurements and Main Results:** In septic sheep, MAP fell by ~30 mm Hg, systemic vascular resistance index decreased by ~50%, and ~7 L of fluid were retained over 24 hours; this fluid accumulation was partially reduced by arginine vasopressin and almost completely blocked by selepressin; and combined infusion of selepressin and desmopressin increased fluid accumulation to levels similar to arginine vasopressin treatment.

**Conclusions:** Resuscitation with the selective vasopressin type 1a receptor agonist selepressin blocked vascular leak more effectively than the mixed vasopressin type 1a receptor/vasopressin V2 receptor agonist arginine vasopressin because of its lack of agonist activity at the vasopressin V2 receptor. (Crit Care Med 2014; 42:e525–e533)
Gut Integrity in Shock
“SSAIL” TRIAL (TREATMENT OF SEPTIC SHOCK BY INHIBITING AUTODIGESTION AND PRESERVING GUT INTEGRITY WITH ENTERIC LB1148)

• LB1148 – broad-spectrum serine protease inhibitor delivered enterally to gut

• Inhibit the intraluminal pancreatic proteolytic enzymes (proteases) that leak due to loss of gut integrity
SOLUBLE THROMBOMODULIN
ANGIOTENSIN II
Intravenous angiotensin II for the treatment of high-output shock (ATHOS trial): a pilot study

Lakhmir S Chawla1,3*, Laurence Busse2, Ermira Brasha-Mitchell3, Danielle Davison3, Jacqueline Honiq3, Ziyad Alotaibi4 and Michael G Seneff3

Abstract

Introduction: Patients with distributive shock who require high dose vasopressors have a high mortality. Angiotensin II (ATII) may prove useful in patients who remain hypotensive despite catecholamine and vasopressin therapy. The appropriate dose of parenteral angiotensin II for shock is unknown.

Methods: In total, 20 patients with distributive shock and a cardiovascular Sequential Organ Failure Assessment score of 4 were randomized to either ATII infusion (N = 10) or placebo (N = 10) plus standard of care. ATII was started at a dose of 20 ng/kg/min, and titrated for a goal of maintaining a mean arterial pressure (MAP) of 65 mmHg. The infusion (either ATII or placebo) was continued for 6 hours then titrated off. The primary endpoint was the effect of ATII on the standing dose of norepinephrine required to maintain a MAP of 65 mmHg.

Results: ATII resulted in marked reduction in norepinephrine dosing in all patients. The mean hour 1 norepinephrine dose for the placebo cohort was 27.6 ± 29.3 mcg/min versus 7.4 ± 12.4 mcg/min for the ATII cohort (P = 0.06). The most common adverse event attributable to ATII was hypertension, which occurred in 20% of patients receiving ATII. 30-day mortality for the ATII cohort and the placebo cohort was similar (50% versus 60%, P = 1.00).

Conclusion: Angiotensin II is an effective rescue vasopressor agent in patients with distributive shock requiring multiple vasopressors. The initial dose range of ATII that appears to be appropriate for patients with distributive shock is 2 to 10 ng/kg/min.

**Sources of Endotoxin**

- **Endotoxemia**
  - Endotoxin shed from local bacterial infection

- **Endotoxin translocation from GI tract**
  - Every human has 25-30 grams of Endotoxin in their GI tract
  - Less than 0.001 grams of Endotoxin is enough to kill a person
SEPSIS AND ENDOTOXIN

INTERVENTION

DIRECT HEMOPERFUSION WITH ADSORBENT COLUMN USING POLYMYXIN B IMMOBILIZED FIBER

ANTICOAGULANT

Heparin (3000 U in bolus followed by a continuous infusion of 20 U/kg/h)

FEMORAL or IJ VEIN

BLOOD TUBE

BLOOD PUMP

Duration: 2 hours

Perfusion rate 80-120 ml/min
HEMODYNAMIC EFFECTS OF PMX

Cruz D. et al. Critical Care 2007; 11:R47
Table 1. Baseline Characteristics of the Treatment Groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Polymyxin B Hemoperfusion (n = 34)</th>
<th>Conventional Therapy (n = 30)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>61 (57-66)</td>
<td>67 (61-72)</td>
<td>.09</td>
</tr>
<tr>
<td>Male sex, No. (%)</td>
<td>24 (71)</td>
<td>18 (60)</td>
<td>.53</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>21 (19-23)</td>
<td>20 (18-23)</td>
<td>.86</td>
</tr>
<tr>
<td>SOFA score</td>
<td>11 (10-12)</td>
<td>9 (8-11)</td>
<td>.07</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>76 (72-86)</td>
<td>74 (70-78)</td>
<td>.40</td>
</tr>
<tr>
<td>Noradrenaline, µg/kg/min</td>
<td>0.27 (0.17-0.36)</td>
<td>0.24 (0.13-0.36)</td>
<td>.70</td>
</tr>
<tr>
<td>Dopamine, µg/kg/min</td>
<td>3.1 (1.7-4.4)</td>
<td>4.6 (2.9-5.6)</td>
<td>.13</td>
</tr>
<tr>
<td>Inotropic score</td>
<td>29.9 (20.4-39.4)</td>
<td>28.6 (16.6-40.7)</td>
<td>.85</td>
</tr>
<tr>
<td>Vasopressor dependency index, mm Hg</td>
<td>4.3 (2.7-5.9)</td>
<td>4.1 (2.3-6.0)</td>
<td>.87</td>
</tr>
<tr>
<td>White blood cell count, 1000/µL</td>
<td>13.7 (11.4-16.0)</td>
<td>11.4 (9.0-13.8)</td>
<td>.12</td>
</tr>
<tr>
<td>Paco2/Fio2</td>
<td>235 (206-265)</td>
<td>217 (188-247)</td>
<td>.53</td>
</tr>
<tr>
<td>Diuresis, mL/h</td>
<td>66 (50-90)</td>
<td>87 (59-116)</td>
<td>.22</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>2.3 (1.7-2.9)</td>
<td>1.7 (1.3-2.2)</td>
<td>.18</td>
</tr>
<tr>
<td>Renal replacement therapy, No. (%)</td>
<td>13 (38)</td>
<td>6 (20)</td>
<td>.17</td>
</tr>
</tbody>
</table>

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; Fio2, fraction of inspired oxygen; SOFA, Sequential Organ Failure Assessment.

SI conversion: To convert creatinine to µmol/L, multiply by 88.4.

*Patients in the polymyxin B hemoperfusion group were treated with 2 sessions of direct hemoperfusion with polymyxin B in addition to standard conventional therapy. Range of APACHE II score was 0 to 71, with lower scores indicating better organ function. Range of SOFA score was 0 to 24, with lower scores indicating better organ function. See “Methods” section for formulas for inotropic score and vasopressor dependency index.
Figure 3. Estimation of Survival Rate According to Treatment Group

Patients in the polymyxin B hemoperfusion group were treated with 2 sessions of direct hemoperfusion with polymyxin B in addition to standard conventional therapy.
EUPHRATES
A CLINICAL TRIAL IN ADULTS WITH SEPTIC SHOCK AND ENDOTOXEMIA
The only FDA cleared test for detection of Endotoxin
Thank You