Disclosure

- MCE has received grant support from:
  - American Lung Association
  - NIH NHLBI
Objectives

- Identify common presentation of septic shock
- Identify common missed opportunities in septic shock
  - Why do we fear fluid resuscitation
- Understand core measures for CMS for septic shock
- Assessing fluid resuscitation
A bad run at dialysis

- 58 yo history of CAD and ESRD presents from his dialysis unit
- He endorses a 2 day history of URI symptoms
- His dialysis was terminated early for low blood pressure and he was sent to the ED
- Temp 95°F HR 101 RR 22 BP 89/54
- 92% SpO₂ on room air
- CBC reveals a white count of 8,600
Our Patient

- Patient identified as a septic alert in ED.
- Vanco and pip/tazo given
- Resident ordered a 250 cc bolus of 0.9NS
  - “I don’t want to overload him”
  - This is repeated for a total of 750cc
- In ED, he deteriorates from resp standpoint
  - Requires bipap and xfer to ICU
Where do they come from?

- Recognition often focuses on patients from community into ER, but…
Where do they come from?

- Recognition often focuses on patients from community into ER, but…
  - Up to 50% of sepsis is hospital-acquired
Where do they come from?

- Recognition often focuses on patients from community into ER, but...
  - Up to 50% of sepsis is hospital-acquired
  - Up to 25% of sepsis is ICU-acquired

JAMA 1995, 274(12):968
What do we need to achieve in sepsis?

- CMS Mandated Targets for Hospitals
  - Measure lactate
  - Obtain cultures prior to antibiotics
  - Administer antibiotics
  - Administer 30ml/kg fluid for hypotension or elevated lactate
  - Apply vasopressors
  - Assess volume status
  - Repeat lactate
What do we need to achieve in sepsis?

- CMS Mandated Targets for Hospitals
  - Measure lactate
  - Obtain cultures prior to antibiotics
  - Administer antibiotics
  - Administer 30ml/kg fluid for hypotension or elevated lactate
  - Apply vasopressors
  - Assess volume status
  - Repeat lactate
Why did CMS Choose These Targets?

Limitations

- Single center and a single group of investigators
- Is the whole protocol necessary?
- 3 Arms (Rivers, “standard”, usual care)
- N = 1341 patients
- 31 ER departments
- Inclusion:
  - Sepsis suspected
  - >=2 SIRS criteria
  - Shock (BP < 90 after fluids or lactate > 4)
Figure S1. - Protocol for early goal-directed therapy (EGDT)

1. Supplemental oxygen + endotracheal intubation and mechanical ventilation
2. Insert central line with osmotic port
3. Sedation, analgesia, +/or paralysis (if intubated)
4. 500 cc fluid bolus if CVP <8 mmHg
   - CVP: 8-12 mmHg
   - MAP: ≥65 mm Hg and <90 mm Hg
   - ScvO2: <70% if HCT <30%, transfuse PRBCs
   - ≥70% goals achieved?
     - Yes: Reassess q15-30 min
     - No: Vasoactive agents
5. If CVP <8 mmHg, <8 mmHg

Figure S2. - Protocol for Standard Therapy

1. Supplemental oxygen + endotracheal intubation and mechanical ventilation
2. 2 large bore (18 g or larger) IV’s (Central line if unable to achieve)
3. Sedation, analgesia, +/or paralysis (if intubated)
4. 500-1000 mL fluid bolus*
   - SBP* Shock Index (SI)
   - SBP <100 mmHg*, or SI ≥ 0.8, or on vasopressors
   - Field replete/overload?
     - Yes: Vasopressors
     - No: Fluid bolus
5. Hypoperfusion^
   - Reassess q30 min
   - Monitor for fluid overload
   - Consider recheck lactate, HCT

CVP - central venous pressure, MAP - mean arterial pressure, ScvO2 - central venous oxygen saturation, HCT - hematocrit, PRBCs - packed red blood cells

*Time-sensitive target
\[\text{Time allowed} \quad \text{Corrective action}\]
- Fluid bolus (500-1000 mL) 20 minutes 3rd IV or central line
- Initial fluid bolus (2 L) 1 hour 3rd IV or central line
- SBP ≥ 100 mmHg 1 hour Vasopressors
What Did They Actually Do?

Table S4. – Resuscitation and processes of care from baseline to 72h.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Protocol-based EGDT (N=439)</th>
<th>Protocol-based Standard Therapy (N=446)</th>
<th>Usual care (N=456)</th>
<th>p-value\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-randomization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravenous fluids\textsuperscript{b} – mL</td>
<td>2254 $\pm$ 1472</td>
<td>2226 $\pm$ 1363</td>
<td>2083 $\pm$ 1405</td>
<td>0.15</td>
</tr>
<tr>
<td>Fluids per body weight (mL/kg)</td>
<td>30.5 $\pm$ 22.3</td>
<td>29.2 $\pm$ 19.1</td>
<td>28 $\pm$ 21</td>
<td></td>
</tr>
<tr>
<td>Vasopressor use\textsuperscript{c}</td>
<td>84 (19.1)</td>
<td>75 (16.8)</td>
<td>69 (15.1)</td>
<td>0.28</td>
</tr>
<tr>
<td>Dobutamine use</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>5 (1.1)</td>
<td>7 (1.6)</td>
<td>9 (2.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>60 (13.7)</td>
<td>65 (14.6)</td>
<td>63 (13.8)</td>
<td>0.93</td>
</tr>
<tr>
<td>Intravenous antibiotics</td>
<td>332 (75.6)</td>
<td>343 (76.9)</td>
<td>347 (76.1)</td>
<td>0.91</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>41 (9.3)</td>
<td>42 (9.4)</td>
<td>38 (8.3)</td>
<td>0.82</td>
</tr>
<tr>
<td>Activated protein C</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Randomization to hour 6\textsuperscript{d}</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resuscitation elements</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central venous catheterization</td>
<td>411 (93.6)</td>
<td>252 (56.5)</td>
<td>264 (57.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Central venous oximeter catheterization\textsuperscript{e}</td>
<td>409 (93.2)</td>
<td>18 (4.0)</td>
<td>16 (3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Intravenous fluids – mL</td>
<td>2805 $\pm$ 1957</td>
<td>3285 $\pm$ 1743</td>
<td>2279 $\pm$ 1881</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>241 (54.9)</td>
<td>233 (52.2)</td>
<td>201 (44.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Dobutamine use</td>
<td>35 (8)</td>
<td>5 (1.1)</td>
<td>4 (0.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>63 (14.4)</td>
<td>37 (8.3)</td>
<td>34 (7.5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
### What Did They Actually Do?

#### Table S4. – Resuscitation and processes of care from baseline to 72h.  

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-randomization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravenous fluids b – mL</td>
<td>2254 ± 1472</td>
<td>2226 ± 1363</td>
<td>2083 ± 1405</td>
<td>0.15</td>
</tr>
<tr>
<td>Fluids per body weight (mL/kg)</td>
<td>30.5 ± 22.3</td>
<td>29.2 ± 19.1</td>
<td>28 ± 21</td>
<td></td>
</tr>
<tr>
<td>Vasopressor use c</td>
<td>84 (19.1)</td>
<td>75 (16.8)</td>
<td>69 (15.1)</td>
<td>0.28</td>
</tr>
<tr>
<td>Dobutamine use</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>5 (1.1)</td>
<td>7 (1.6)</td>
<td>9 (2.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>60 (13.7)</td>
<td>65 (14.6)</td>
<td>63 (13.8)</td>
<td>0.93</td>
</tr>
<tr>
<td>Intravenous antibiotics</td>
<td>332 (75.6)</td>
<td>343 (76.9)</td>
<td>347 (76.1)</td>
<td>0.91</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>41 (9.3)</td>
<td>42 (9.4)</td>
<td>38 (8.3)</td>
<td>0.82</td>
</tr>
<tr>
<td>Activated protein C</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Randomization to hour 6d</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resuscitation elements</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central venous catheterization</td>
<td>411 (93.6)</td>
<td>292 (66.5)</td>
<td>264 (57.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Central venous oximeter catheterization c</td>
<td>409 (93.2)</td>
<td>18 (4.0)</td>
<td>16 (3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Intravenous fluids – mL</td>
<td>3905 ± 1957</td>
<td>3285 ± 1743</td>
<td>2279 ± 1581</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>241 (54.9)</td>
<td>233 (52.2)</td>
<td>201 (44.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Dobutamine use</td>
<td>35 (8)</td>
<td>5 (1.1)</td>
<td>4 (0.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>63 (14.4)</td>
<td>37 (8.3)</td>
<td>34 (7.5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Did they help?

A Cumulative In-Hospital Mortality to 60 Days

- Protocol-based EGDT
- Protocol-based standard therapy
- Usual care

No. at Risk
- Protocol-based EGDT: 439, 373, 356, 348, 347, 347, 347
- Protocol-based standard therapy: 446, 389, 376, 368, 366, 366, 365
- Usual care: 456, 396, 376, 371, 371, 371, 370

P = 0.52 by log-rank test
Are we sure EGDT doesn’t work?

Pretty sure…
Really sure?

- PROMISE
- 1260 pts with septic shock in UK
- 90-day mortality
  - EGDT 29.5%
  - Usual Care 29.2%
- EGDT increased cost
So EGDT Doesn’t Work?

- Recent studies didn’t demonstrate harm from EGDT, just a failure to demonstrate an improvement compared to our usual care.
- Our usual care in 2015 reflects most of the principles demonstrated in the Rivers trial in 2000.
- Resuscitation bundles for sepsis are essential, but likely clinician assessment of resuscitation can substitute for EGDT.
  - CMS has now relaxed the requirement for CVP / ScvO2 from septic shock bundle.
How are we going to maximize sepsis care?

- Focus on the patients, not the CMS bundle
- Identification is key
- Default to the best practice
  - Make it easy to do the right thing
- Guidance for clinicians
  - Order sets
  - Note template for sepsis
1st we need to recognize sepsis

- Early signs of sepsis
  - Fever or chills
  - Mental status changes (dizziness, confusion, or reduced consciousness)
  - Tachycardia
  - Tachypnea or short of breath
  - Reduction in urine output
  - Changes in blood pressure (high or low)

- Clock starts at the 1st signs of sepsis
How to find sepsis outside of hospital?

**PRESEP Score**

<table>
<thead>
<tr>
<th>Sign</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>4</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>1</td>
</tr>
<tr>
<td>HR &gt; 90</td>
<td>2</td>
</tr>
<tr>
<td>RR &gt; 22</td>
<td>1</td>
</tr>
<tr>
<td>SaO2 &lt; 92</td>
<td>2</td>
</tr>
<tr>
<td>SBP &lt; 90</td>
<td>2</td>
</tr>
</tbody>
</table>

≥ 4 points has high likelihood of sepsis
How to find sepsis outside of ER?

Criteria:
- HR > 90
- RR > 20
- SBP < 110

Table 7
Final Predictive Model

<table>
<thead>
<tr>
<th>Predictor Variable</th>
<th>Odds Ratio</th>
<th>95% CL</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y), tertiles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>Reference</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>50-59</td>
<td>4.28</td>
<td>1.20-15.38</td>
<td>.03</td>
</tr>
<tr>
<td>≥60</td>
<td>2.19</td>
<td>0.56-8.66</td>
<td>.26</td>
</tr>
<tr>
<td>Nursing home transport (Y/N)</td>
<td>4.73</td>
<td>2.01-11.13</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>EMD complaint: sick person (Y/N)</td>
<td>3.04</td>
<td>1.45-6.37</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Hot tactile temperature (Y/N)</td>
<td>2.90</td>
<td>1.35-6.23</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>SBP, per 1-mm-Hg increase</td>
<td>0.96</td>
<td>0.93-0.99</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>O₂ saturation, per 1% increase</td>
<td>0.95</td>
<td>0.91-0.99</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence limit; Y/N, yes/no.
Can EMR Help Us?

- Sepsis Alert from EPIC
- Prompts treatment for infection and initial lactate
Why is measuring lactate so important?

- Septic Shock Defined as Hypotension or Lactate > 4 mmol/L
How does lactate help?

<table>
<thead>
<tr>
<th>Lactate Group (mmol/L)</th>
<th>Compliant Lactate Measured ≤ 6 hr</th>
<th>Noncompliant Lactate Measured &gt; 6 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Hypotension</td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td>Total, n (Died n/%)</td>
<td>OR* (95% CI) [p]</td>
</tr>
<tr>
<td>≤ 2 (referent)</td>
<td>1,302 (301/23.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt; 2 to ≤ 3</td>
<td>1,009 (242/24.0)</td>
<td>1.04 (0.87–1.24) [0.661]</td>
</tr>
<tr>
<td>&gt; 3 to ≤ 4</td>
<td>693 (158/22.8)</td>
<td>0.99 (0.80–1.21) [0.891]</td>
</tr>
<tr>
<td>&gt; 4</td>
<td>996 (289/29.0)</td>
<td>1.38 (1.16–1.65) [≤0.001]</td>
</tr>
</tbody>
</table>

**OR** = odds ratio.

*Odds ratio based on generalized estimating equation population-averaged logistic regression model.*
How does lactate help?

<table>
<thead>
<tr>
<th>Lactate Group (mmol/L)</th>
<th>Compliant Lactate Measured ≤ 6 hr</th>
<th></th>
<th>Noncompliant Lactate Measured &gt; 6 hr</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Hypotension</td>
<td>Hypotension</td>
<td>No Hypotension</td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td>Total, n (Died n/%)</td>
<td>OR(^a) (95% CI) [p]</td>
<td>Total, n (Died n/%)</td>
<td>OR(^a) (95% CI) [p]</td>
</tr>
<tr>
<td>≤ 2 (referent)</td>
<td>1,302 (301/23.1)</td>
<td>1.00</td>
<td>5,158 (1,423/27.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt; 2 to ≤ 3</td>
<td>1,009 (242/24.0)</td>
<td>1.04 (0.87–1.24) [0.661]</td>
<td>3,241 (991/30.6)</td>
<td>1.16 (1.05–1.27) [0.002]</td>
</tr>
<tr>
<td>&gt; 3 to ≤ 4</td>
<td>693 (158/22.8)</td>
<td>0.99 (0.80–1.21) [0.891]</td>
<td>2,274 (718/31.6)</td>
<td>1.21 (1.09–1.35) [≤0.001]</td>
</tr>
<tr>
<td>&gt; 4</td>
<td>996 (289/29.0)</td>
<td>1.38 (1.16–1.65) [≤0.001]</td>
<td>5,272 (2,344/44.5)</td>
<td>2.10 (1.93–2.27) [≤0.001]</td>
</tr>
</tbody>
</table>

OR = odds ratio.
\(^a\)Odds ratio based on generalized estimating equation population-averaged logistic regression model.
What do we need to do when we find Severe Sepsis?

- **Within 3 hours**
  - Initial lactate
  - Blood cultures
  - Broad spectrum antibiotics

- **Within 6 hours**
  - Repeat lactate (if initial was elevated)
What do we need to do when we find Septic Shock?

- Within 3 hours
  - 30 cc/kg INITIAL FLUID bolus
- Within 6 hours (if hypotension / lactate elevated)
  - Start vasopressors
  - Repeat volume status / tissue perfusion check
### IHIS Sepsis Order Set

#### Order Sets

##### Adult Sepsis Focused

**General**
- **Vital signs every 15 minutes**
  - Routine, Every 15 min First occurrence Today at 1506 Until Specified
- **Pulse oximetry, continuous**
  - Routine, Once First occurrence Today at 1506
- **Cardiac monitoring**
  - Routine, Until discontinued starting Today at 1506 Until Specified

**Labs**

**Imaging**
- **Chest**
  - 0 of 2 selected
- **Abdomen and Pelvis**
  - 0 of 6 selected

**Other Tests**
- **Cardiac Tests - ECG**
  - 0 of 1 selected

**IV Fluids**
- **sodium chloride 0.9% (NS) infusion**
  - 100 mL/hr, Intravenous, Continuous, Starting Today at 1515

**Disease-Specific Medications**
- **DOBUTamine (DOBUTREX) infusion 2000 mcg/mL**
  - 2.5 mcg/kg/min, Intravenous, Continuous, Starting Today at 1515
  - Titrated as needed to a maximum of 20 mcg/kg/day

**General-Purpose Medications**

**Ventilator Management**
- **Ventilator-Associated Pneumonia Prevention**
  - 0 of 7 selected
- **Chest X-Rays**
  - 0 of 2 selected

**Empiric Antibacterial Therapy**
- **cefTRIAXone (ROCEPHIN) injection 2 g**
  - 2 g, Intravenous, Every 24 hours, First Dose Today at 1515
- **azithromycin (ZITHROMAX) injection 500 mg**
  - 500 mg, Intravenous, Every 24 hours, First Dose Today at 1515
Give the Right Amount of Volume

240 ml

350 ml

591 ml

1000 ml

2645 ml

My Septic Need!!!
What Fluids Should I Give?

- Change Cl⁻-rich to Cl⁻-poor fluid
- Reduced AKI, ARF, and RRT
- No change to mortality or LOS improvement

\[ \text{Cl}^-\text{-rich: 0.9\% saline, succinylated gelatin solution, or 4\% albumin} \]

\[ \text{Cl}^-\text{-poor: lactated solution, Plasma-Lyte 148, or Cl}^-\text{-poor 20\% albumin} \]
What Fluids Should I Give? UPDATE!

Normal Saline 0.9%

versus

Plasma-Lyte 148 (Buffered crystalloid)

- No difference in AKI or need for RRT

JAMA 2015
What do I do if my patient is still in Shock?

- Reassess Volume Status
- What are you missing?
  - Reassess Antibiotics
  - Look for Source of Infection
    - Lines
    - Abscess
- Start Vasopressors

I feel shocked
How do I assess volume?
The CMS Way

Exam by MD / APP with:
- VS
- Cardiopulm exam
- Cap refill
- Peripheral pulse eval
- Skin Exam

Documentation of 2 of the following:
- CVP
- Central venous oxygen
- Bedside CV ultrasound
- Passive Leg Raise or Fluid Challenge

Must be done within 6 hours if hypotension persists
What should I do if they are volume up?
Start Pressors (6 hours)

- Less tachycardia versus dopamine
- May be better tolerated in cardiac patients

Figure 2. Kaplan–Meier Curves for 28-Day Survival in the Intention-to-Treat Population.
So why do we use Norepinephrine?

**TABLE 7. Norepinephrine Compared With Dopamine in Severe Sepsis Summary of Evidence**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative Comparative Risks* (95% CI)</th>
<th>Relative Effect (95% CI)</th>
<th>No. of Participants (Studies)</th>
<th>Quality of the Evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Assumed Risk</td>
<td>Corresponding Risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-term mortality</td>
<td>Dopamine</td>
<td>Study population</td>
<td>RR 0.91 (0.83 to 0.99)</td>
<td>2043 (6 studies)</td>
<td>moderate</td>
</tr>
<tr>
<td></td>
<td>Norepinephrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>530 per 1000</td>
<td>482 per 1000 (440 to 524)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>Dopamine</td>
<td>Study population</td>
<td>RR 0.47 (0.38 to 0.58)</td>
<td>1931 (2 studies)</td>
<td>moderate</td>
</tr>
<tr>
<td>— Supraventricular arrhythmias</td>
<td>Norepinephrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>229 per 1000</td>
<td>82 per 1000 (34 to 195)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>Dopamine</td>
<td>Study population</td>
<td>RR 0.35 (0.19 to 0.66)</td>
<td>1931 (2 studies)</td>
<td>moderate</td>
</tr>
<tr>
<td>— Ventricular arrhythmias</td>
<td>Norepinephrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>39 per 1000</td>
<td>15 per 1000 (8 to 27)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The assumed risk is the control group risk across studies. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI = confidence interval, RR = risk ratio.

*Strong heterogeneity in the results (I² = 85%), however this reflects degree of effect, not direction of effect. We have decided not to lower the evidence quality.

*Effect results in part from hypovolemic and cardiogenic shock patients in De Backer, *N Engl J Med* 2010. We have lowered the quality of evidence one level for indirectness.
Is it safe to give pressors through IV?
Sepsis Six and the Severe Sepsis Resuscitation Bundle
Daniels et. Al.

- Prospective observational cohort study-500 bed acute general hospital
- Assess the impact of the Surviving Sepsis Campaign resuscitation bundle (SSCRB) and the “sepsis six”
- Sepsis six (1hr of onset of severe sepsis)
  1. Deliver high flow oxygen
  2. Blood cultures
  3. Administer empiric antibiotics
  4. Start resuscitation fluids
  5. Measure serum lactate & complete blood count
  6. Accurate urine output measurement
Sepsis Six and the Severe Sepsis Resuscitation Bundle
Daniels et. Al.

Onset of Severe Sepsis “Time 0”

Sepsis Six with 1hr & Referral to Sepsis Team (2-Critical Care nurses)

Signs of hypoperfusion (20ml/kg of fluid)

Hypoperfusion

Yes

EGDT

No

Resuscitation Complete

Wexner Medical Center
567 patients – eligible for Sepsis Six and SSCRB

- Median modified early warning score (MEWS): 6 (0-15)
- 71.7% (303/423) hypoperfused patients received fluid challenge
  - Shock reversed 65% of cases
- Shock mortality 64.5% vs. 17.1%
Sepsis Six and the Severe Sepsis Resuscitation Bundle
Daniels et. al.

- Sepsis team
  - Resuscitation bundle (72.9% vs. 23.4%, p<0.001)
  - Mortality (25.5% vs. 38.4%, p<0.001)

### No Shock Cohort

<table>
<thead>
<tr>
<th>Cohort</th>
<th>N (%)</th>
<th>Mortality day 28 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No intervention</td>
<td>192 (34)</td>
<td>23.3</td>
</tr>
<tr>
<td>Resuscitation Bundle (RB) only</td>
<td>18 (3.2)</td>
<td>11.1</td>
</tr>
<tr>
<td>Sepsis Six + RB</td>
<td>143 (25.3)</td>
<td>4.2</td>
</tr>
</tbody>
</table>

Emerg Med J 2011; 507-512
Sepsis Six and the Severe Sepsis Resuscitation Bundle
Daniels et al.

Shock Cohort

<table>
<thead>
<tr>
<th></th>
<th>Usual Care</th>
<th>Sepsis 6 / EGDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>4.2</td>
<td>23.3</td>
</tr>
<tr>
<td>Shock</td>
<td>4.7</td>
<td>79.3</td>
</tr>
</tbody>
</table>

Mortality (%)
The Sepsis Six

- Prospective observational cohort
- Assess the impact of the Surviving Sepsis Campaign resuscitation bundle (SSCRB) and the “sepsis six”
- Sepsis six (1hr of onset of severe sepsis)

Table 5: Individual sepsis six interventions and outcomes

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Mortality when not achieved (%)</th>
<th>Mortality when achieved (%)</th>
<th>Frequency achieved (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High flow oxygen</td>
<td>43.1</td>
<td>31.8</td>
<td>74.3</td>
<td>0.014</td>
</tr>
<tr>
<td>Blood cultures</td>
<td>49.1</td>
<td>26.3</td>
<td>63.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>45.4</td>
<td>28.1</td>
<td>61.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fluids</td>
<td>44.8</td>
<td>30.0</td>
<td>67.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lactate</td>
<td>43.4</td>
<td>30.9</td>
<td>69.1</td>
<td>0.004</td>
</tr>
<tr>
<td>Urine output</td>
<td>42.9</td>
<td>31.0</td>
<td>68.8</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Emerg Med J 2011; 507-512
What can be done prior to ER?
Our Patient

- Worsening mental status and respiratory status
- Eventually weaned off non-invasive after 2 days
Could we do it better?

Next Day

- 64 yo status post K-P transplant presents with 1 day history of nausea / vomiting
- VS AF 123 80/40 22 SpO2 90% on room air
- Abdomen was distended and tender without rebound
What did we do?

- Initial lab work revealed acute kidney injury
- Patient identified as a suspected infection
  - Antibiotics given within 1 hour of presentation
  - Lactate checked (2.2)
  - Blood cultures obtained
  - Surgery evaluated in ED (dx with partial SBO)
- Persistent given 2 liter initial bolus (close)
- Repeat lactate 2.4 (done for shock)
- Started on norepinephrine drip
How’d it turn out?

- Despite concern about his volume status, a total of 7 liters given in first 12 hours
- Clinical exam remained unchanged
- He never required more than 4 LPM of oxygen
- He was off pressors with improved renal function by the morning!
“Everything you need to know about the treatment of sepsis you learned in 1928.”
fake quote Alexander Fleming