Severe Sepsis
A TIME CRITICAL Diagnosis
Across the Spectrum of Care

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Division of Pulmonary and Critical Care
University of Kansas
21st Century Sepsis Teaching?

“as the physicians say it happens in hectic fever, that in the beginning of the malady it is easy to cure but difficult to detect, but in the course of time, not having been either detected or treated in the beginning, it becomes easy to detect but difficult to cure”

Niccolò Machiavelli
The Prince – 1513 or 1532
What is Sepsis?

Life threatening organ dysfunction due to a dysregulated host response to infection
What is Sepsis?

Life threatening organ dysfunction due to a dysregulated host response to infection
Interesting Case

• 72 y.o. banker; flank pain and fever at nursing home
• Recent admission to hospital for a stroke.
• Aide notes mild confusion while getting him ready for breakfast
• previous L. ureteral stent placement
• Hx of CAD, HTN, Stroke with left leg weakness
• Meds include terazosin, atorvastatin, metoprolol, aspirin
• BP 105/43, P 117, R 22, T 39.1°, SpO₂ 87%
What should NH do now?

A. 3 L bolus of LR
B. Apply oxygen
C. Point of care lactate level
D. IV or PO levofloxacin, 2 L bolus of LR, transfer to hospital for ICU admission
What should NH do now?

A. 3 L bolus of LR
B. Apply oxygen
C. Point of care lactate level
D. IV or PO levofloxacin, 2 L bolus of LR, transfer to hospital for ICU admission

In truth, none of these answers are wrong. But hospital transfer is key, based on the information we have.
What should EMS do when they arrive?

A. Blood cultures
B. Apply oxygen
C. Point of care lactate level
D. IV or PO levofloxacin, 2 L bolus of LR, transport to hospital for ICU admission
What should EMS do when they arrive?

A. Blood cultures
B. Apply oxygen
C. Point of care lactate level
D. IV or PO levofloxacin, 2 L bolus of LR, transport to hospital for ICU admission

Again, any of these could be good. But transfer to the hospital is key.
What should happen on arrival to ER?

A. Blood cultures
B. Apply oxygen
C. Point of care lactate level
D. IV or PO levofloxacin, 2 L bolus of LR, ICU admission
What should happen on arrival to ER?

A. Blood cultures
B. Apply oxygen
C. Point of care lactate level
D. IV or PO levofloxacin, 2 L bolus of LR, ICU admission

All of the above, actually.
At the hospital

- Labs: WBC – 14.7, 33% bands
- Plt – 96,000
- BUN – 47, Cr. – 3.2
- D-dimer – 4.7, fibrinogen – 72, PTT – 39
- Lactate – 2.6
- UA – not available
Severe Sepsis

• THE major cause of morbidity and mortality worldwide
  – Leading cause of death in noncoronary ICU (US)*
  – 11th leading cause of death overall (US) † §

• More than 750,000 cases of severe sepsis in US annually ‡

• In the US, more than 500 patients die of severe sepsis daily ‡

*Sands KE et al. JAMA. 1997;278:234-40;
§ Murphy SL. National Vital Statistics Reports.
Severe Sepsis
How Common – How Deadly?

Incidence of Severe Sepsis

Mortality of Severe Sepsis

Figure 2. Cognitive Impairment Among Survivors of Severe Sepsis at Each Survey Time Point

<table>
<thead>
<tr>
<th>Survey Type</th>
<th>Cognitive Impairment</th>
<th>Time to Sepsis Admission, Median (IQR), y</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Sepsis</td>
<td></td>
<td>-3.1 (-3.7 to -2.7)</td>
<td>484</td>
</tr>
<tr>
<td>After Sepsis</td>
<td></td>
<td>0.9 (0.4 to 1.4)</td>
<td>623</td>
</tr>
<tr>
<td>Before Sepsis</td>
<td>Mild</td>
<td>-1.1 (-1.7 to -0.7)</td>
<td>623</td>
</tr>
<tr>
<td>After Sepsis</td>
<td>Moderate to Severe</td>
<td>2.8 (2.3 to 3.4)</td>
<td>288</td>
</tr>
</tbody>
</table>

Figure 3. Functional Trajectories by Baseline Functioning

Limitations at baseline
- Severe
- Mild to moderate
- None

Mean Number of ADL and IADL Limitations

<table>
<thead>
<tr>
<th>Time to sepsis admission, median (IQR), y</th>
<th>Third Survey Before Sepsis</th>
<th>Second Survey Before Sepsis</th>
<th>Last Survey Before Sepsis</th>
<th>First Survey After Sepsis</th>
<th>Second Survey After Sepsis</th>
<th>Third Survey After Sepsis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to sepsis admission, median (IQR), y</td>
<td>-5.2 (-5.6 to -4.7)</td>
<td>-3.1 (-3.7 to -2.7)</td>
<td>-1.1 (-1.7 to -0.7)</td>
<td>0.9 (0.4 to 1.4)</td>
<td>2.8 (2.3 to 3.4)</td>
<td>5.2 (4.5 to 5.5)</td>
</tr>
<tr>
<td>No. of patients, by baseline physical functioning</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe limits</td>
<td>87</td>
<td>127</td>
<td>159</td>
<td>159</td>
<td>42</td>
<td>14</td>
</tr>
<tr>
<td>Mild to moderate limits</td>
<td>105</td>
<td>151</td>
<td>195</td>
<td>195</td>
<td>93</td>
<td>28</td>
</tr>
<tr>
<td>No limits</td>
<td>142</td>
<td>206</td>
<td>269</td>
<td>269</td>
<td>153</td>
<td>56</td>
</tr>
</tbody>
</table>

Age Related Incidence of Severe Sepsis

Sepsis Incidence

Compounding Growth
Doubling time = 8.5 years

Why is this important?

Because ALL previous epidemiological studies have been based on administrative or claims data.
Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014

Health Systems

– HCA
– VA
– Univ of Pittsburgh
– Cerner Health Facts
– Institute for Health Metrics
– Brigham and Women’s
– Emory Healthcare
## Study Hospitals vs. AHA

<table>
<thead>
<tr>
<th>Hospital Characteristic</th>
<th>Study Hospitals (N=409)</th>
<th>AHA Hospitals (N=4,810)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>% of Study Cohort</td>
</tr>
<tr>
<td><strong>Geographic Region</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>56</td>
<td>13.7%</td>
</tr>
<tr>
<td>South</td>
<td>205</td>
<td>50.1%</td>
</tr>
<tr>
<td>Midwest</td>
<td>60</td>
<td>14.7%</td>
</tr>
<tr>
<td>West</td>
<td>88</td>
<td>21.5%</td>
</tr>
<tr>
<td><strong>Teaching Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teaching</td>
<td>152</td>
<td>37.2%</td>
</tr>
<tr>
<td>Nonteaching</td>
<td>257</td>
<td>62.8%</td>
</tr>
<tr>
<td><strong>AHA Hospital Size</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small (&lt;200 beds)</td>
<td>220</td>
<td>53.8%</td>
</tr>
<tr>
<td>Medium (200-499 beds)</td>
<td>155</td>
<td>37.9%</td>
</tr>
<tr>
<td>Large (≥500 beds)</td>
<td>34</td>
<td>8.3%</td>
</tr>
</tbody>
</table>

8.5% of hospitals; ~10% of US admissions
Clinical Criteria: Sepsis-3?

1. Presumed serious infection:
   - Blood culture obtained (regardless of result), AND
   - ≥4 QADs—starting within ±2 days of blood culture day

Sepsis: Presumed serious infection plus ≥1 criteria for acute organ dysfunction

Septic shock: Presumed serious infection plus vasopressor plus serum lactate level ≥2.0 mmol/L

of estimated glomerular filtration rate relative to baseline
(excluding patients with ICD-9-CM code for end-stage kidney disease [585.6])
- Total bilirubin level ≥2.0 mg/dL and doubling from baseline
- Platelet count <100 cells/µL and ≥50% decline from baseline (baseline must be ≥100 cells/µL)
- Serum lactate ≥2.0 mmol/L

Published online September 13, 2017.
### Patient Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients With Sepsis, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N = 173 690)</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>66.5 (15.5)</td>
</tr>
<tr>
<td>20-39</td>
<td>11 475 (6.6)</td>
</tr>
<tr>
<td>40-59</td>
<td>40 975 (23.6)</td>
</tr>
<tr>
<td>60-79</td>
<td>80 857 (46.6)</td>
</tr>
<tr>
<td>≥80</td>
<td>40 383 (23.3)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>100 030 (57.6)</td>
</tr>
<tr>
<td>Women</td>
<td>73 660 (42.4)</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>117 081 (67.4)</td>
</tr>
<tr>
<td>Black</td>
<td>26 564 (15.3)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>18 417 (10.6)</td>
</tr>
<tr>
<td>Asian</td>
<td>3499 (2.0)</td>
</tr>
<tr>
<td>Other</td>
<td>4497 (2.6)</td>
</tr>
</tbody>
</table>

*JAMA. doi:10.1001/jama.2017.13836 Published online September 13, 2017.*
## Patient Comorbidities

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>62,043</td>
<td>35.7</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>53,742</td>
<td>30.9</td>
</tr>
<tr>
<td>Renal disease</td>
<td>46,560</td>
<td>26.8</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>44,168</td>
<td>25.4</td>
</tr>
<tr>
<td>Cancer</td>
<td>34,229</td>
<td>19.7</td>
</tr>
<tr>
<td>Dementia or cerebrovascular disease</td>
<td>17,862</td>
<td>10.3</td>
</tr>
<tr>
<td>Liver disease</td>
<td>17,437</td>
<td>10.0</td>
</tr>
<tr>
<td>HIV or AIDS</td>
<td>1,726</td>
<td>1.0</td>
</tr>
</tbody>
</table>
## Patient Characteristics

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present-on-admission sepsis</td>
<td>150,801</td>
<td>86.8%</td>
</tr>
<tr>
<td>Hospital-onset sepsis</td>
<td>22,889</td>
<td>13.2%</td>
</tr>
<tr>
<td>Positive blood cultures(^b)</td>
<td>24,949</td>
<td>17.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No. of organ dysfunction criteria met</th>
<th>Mean (SD)</th>
<th>Median (range)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>2.1 (1.4)</td>
<td>2 (1-2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Required ICU admission</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required ICU admission</td>
<td>94,956</td>
<td>54.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICU length of stay</th>
<th>Mean (SD)</th>
<th>Median (range)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>6.4 (8.8)</td>
<td>5 (2-6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hospital length of stay</th>
<th>Mean (SD)</th>
<th>Median (range)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>12.0 (12.1)</td>
<td>10 (8-12)</td>
</tr>
</tbody>
</table>
Patient Outcomes

Mortality: Hosp Acquired – 25.5%; POA – 13.4%
Sepsis vs. Septic Shock - ??

<table>
<thead>
<tr>
<th>Discharge dispositiona</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Home</td>
<td>86 301 (49.7)</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>26 061 (15.0)</td>
</tr>
<tr>
<td>Hospice</td>
<td>10 731 (6.2)</td>
</tr>
<tr>
<td>Nonacute care facility</td>
<td>42 127 (24.3)</td>
</tr>
<tr>
<td>Transfer to acute care hospital</td>
<td>4216 (2.4)</td>
</tr>
</tbody>
</table>

\(^a\) Discharge disposition includes the following categories: Home, In-hospital death, Hospice, Nonacute care facility, and Transfer to acute care hospital.

Published online September 13, 2017.
US Sepsis Statistics - 2014

- 5.9% of hospitalizations involve sepsis
- Hospital mortality 15.6%
- 35% of hospital deaths
- 1.7 million adult hospitalizations
- 270,000 deaths
- Remember – this is only adults
Sepsis Incidence: 2009 - 2014

![Graph showing the incidence of sepsis from 2009 to 2014, with different methods of detection ( Implicit or explicit sepsis codes, Clinical criteria, Clinical criteria without lactate level, Explicit sepsis codes ).]
Sepsis Mortality Rates: 2009 - 2014

Adjusted in-hospital sepsis mortality or discharge to hospice

Death or Discharge to Hospice, %

Year

Explicit sepsis codes
Clinical criteria without lactate level
Clinical criteria
Implicit or explicit sepsis codes

Published online September 13, 2017.
Important study using clinical findings
Would like an actual comparison of severe sepsis with Sepsis-3
Did not use vital signs data
Would like to see septic shock mortality broken out
571,000 ED visits per year for severe sepsis

Table 3. Patient characteristics of emergency department (ED) visits for suspected severe sepsis, adults (age ≥18 yrs) only

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Raw Observations</th>
<th>Estimated No. of Suspected Severe Sepsis ED Visits (2001–2004) (1000s)</th>
<th>Estimated Annual No. of Suspected Severe Sepsis ED Visits (1000s)</th>
<th>Percentage of Suspected Severe Sepsis ED Visits (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–24</td>
<td>59</td>
<td>173</td>
<td>43</td>
<td>7.6 (5.6–10.2)</td>
</tr>
<tr>
<td>25–44</td>
<td>135</td>
<td>384</td>
<td>96</td>
<td>16.8 (13.7–20.6)</td>
</tr>
<tr>
<td>45–64</td>
<td>176</td>
<td>346</td>
<td>137</td>
<td>24.0 (19.3–28.7)</td>
</tr>
<tr>
<td>65–74</td>
<td>144</td>
<td>452</td>
<td>113</td>
<td>19.8 (16.6–23.4)</td>
</tr>
<tr>
<td>≥75</td>
<td>252</td>
<td>724</td>
<td>181</td>
<td>31.8 (27.8–36.0)</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>133</td>
<td>384</td>
<td>96</td>
<td>16.8 (13.8–20.5)</td>
</tr>
<tr>
<td>No</td>
<td>572</td>
<td>1,701</td>
<td>425</td>
<td>74.6 (70.5–78.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>63</td>
<td>196</td>
<td>49</td>
<td>8.6 (6.5–11.3)</td>
</tr>
<tr>
<td>Mode of arrival (data for 2003–2004 only)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambulance</td>
<td>187</td>
<td>555</td>
<td>278</td>
<td>51.7 (45.0–58.4)</td>
</tr>
<tr>
<td>Walk-in</td>
<td>176</td>
<td>448</td>
<td>224</td>
<td>41.8 (35.5–48.3)</td>
</tr>
<tr>
<td>Public service or unknown</td>
<td>26c</td>
<td>70c</td>
<td>35c</td>
<td>6.5 (3.7–11.1)c</td>
</tr>
</tbody>
</table>

(Crit Care Med 2007; 35:1928–1936)
Impact of older age and nursing home residence on clinical outcomes of US emergency department visits for severe sepsis

Adit A. Ginde MD, MPH\textsuperscript{a,∗}, Marc Moss MD\textsuperscript{b}, Nathan I. Shapiro MD, MPH\textsuperscript{d}, Robert S. Schwartz MD\textsuperscript{c}

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Severe sepsis, % (95% CI)</th>
<th>Infection without severe sepsis, % (95% CI)</th>
<th>No infection, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-79</td>
<td>28% (23-34)</td>
<td>11% (11-12)</td>
<td>11% (11-12)</td>
</tr>
<tr>
<td>≥ 80</td>
<td>29% (24-34)</td>
<td>9.2% (8.6-9.8)</td>
<td>7.5% (7.2-7.9)</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>25% (20-31)</td>
<td>3.9% (3.4-4.4)</td>
<td>2.3% (2.1-2.5)</td>
</tr>
<tr>
<td>Ambulance arrival</td>
<td>57% (50-63)</td>
<td>14% (13-15)</td>
<td>19% (18-20)</td>
</tr>
</tbody>
</table>

Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Severe sepsis, h, median (IQR)</th>
<th>Infection without severe sepsis, % (95% CI)</th>
<th>No infection, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED LOS, h, median (IQR)</td>
<td>4.4 (2.9-6.0)</td>
<td>1.6 (2.9-4.6)</td>
<td>2.7 (1.6-4.5)</td>
</tr>
<tr>
<td>ED disposition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admitted, intensive care</td>
<td>25% (20-30)</td>
<td>3.0% (2.7-3.4)</td>
<td>2.6% (2.4-2.9)</td>
</tr>
<tr>
<td>Admitted, nonintensive care</td>
<td>49% (42-56)</td>
<td>18% (17-19)</td>
<td>13% (12-14)</td>
</tr>
<tr>
<td>Not admitted</td>
<td>26% (20-34)</td>
<td>79% (78-80)</td>
<td>84% (83-85)</td>
</tr>
<tr>
<td>Hospital LOS, d, median (IQR)</td>
<td>6 (4-8)</td>
<td>3 (5-7)</td>
<td>4 (3-6)</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>21% (15-28)</td>
<td>3.0% (2.4-3.8)</td>
<td>4.1% (3.8-4.5)</td>
</tr>
</tbody>
</table>
Impact of older age and nursing home residence on clinical outcomes of US emergency department visits for severe sepsis

Adit A. Ginde MD, MPH\textsuperscript{a,*}, Marc Moss MD\textsuperscript{b}, Nathan I. Shapiro MD, MPH\textsuperscript{d}, Robert S. Schwartz MD\textsuperscript{c}

Table 2  Age and nursing home residence among US ED visits for severe sepsis resulting in hospital death vs discharged alive and ICU vs non-ICU admission

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>In-hospital death, % (95% CI)</th>
<th>Discharged alive, % (95% CI)</th>
<th>ICU admission, % (95% CI)</th>
<th>Non-ICU admission, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (IQR)</td>
<td>76 (64-82)</td>
<td>66 (47-80)</td>
<td>71 (61-83)</td>
<td>70 (54-82)</td>
</tr>
<tr>
<td>18-44</td>
<td>5% (NC)</td>
<td>18% (15-23)</td>
<td>4.3% (NC)</td>
<td>14% (9.1-20)</td>
</tr>
<tr>
<td>45-64</td>
<td>24% (NC)</td>
<td>28% (22-34)</td>
<td>32% (22-46)</td>
<td>25% (19-33)</td>
</tr>
<tr>
<td>65-79</td>
<td>31% (17-50)</td>
<td>28% (23-34)</td>
<td>32% (23-42)</td>
<td>32% (24-40)</td>
</tr>
<tr>
<td>≥ 80</td>
<td>39% (25-55)</td>
<td>26% (20-32)</td>
<td>28% (22-35)</td>
<td>29% (23-36)</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>48% (31-64)</td>
<td>20% (15-26)</td>
<td>39% (27-52)</td>
<td>21% (16-29)</td>
</tr>
</tbody>
</table>
The impact of emergency medical services on the ED care of severe sepsis

146 vs 111 minutes

The impact of emergency medical services on the ED care of severe sepsis

Reduced by 29 minutes
Diagnosis

Everything is vague to a degree you do not realize till you have tried to make it precise.

Bertrand Russell (1872 – 1970)
Sepsis ≠ Hypotension
Sepsis ≠ Bacteremia
ACCP/SCCM Consensus Definitions

- **Infection**
  - Inflammatory response to microorganisms, or
  - Invasion of normally sterile tissues

- **Systemic Inflammatory Response Syndrome (SIRS)**
  - Systemic response to a variety of processes
  - 2 SIRS criteria

- **Sepsis**
  - Infection plus
  \( \geq 2 \) SIRS criteria

- **Severe Sepsis**
  - Sepsis
  - Organ dysfunction

- **Septic shock**
  - Sepsis
  - Hypotension despite fluid resuscitation

SIRS: Systemic Inflammatory Response Syndrome

- SIRS: nonspecific insult 2 of the following:
  - Temperature
    - > 38° C or < 36° C
  - HR > 90 beats/min
  - Respirations > 20/min
  - WBC > 12,000/µL or
    - < 4,000/µL or
    - > 10% bands or other

Acute Organ Dysfunction as the Hallmark of Severe Sepsis

- Hypotension: SBP < 90, MAP < 70
- Oliguria - < 20 mL/hr
- Anuria
- Δ Creatinine (>0.5 mg/dL)
- Platelets (< 100k)
- INR>1.5, PTT>60 sec
- D-dimer

- Altered Consciousness
- Confusion
- Psychosis
- Tachypnea
- PaO2 <70 mm Hg
- SaO2 <90%
- PaO2/FiO2 < 300
- T. Bilirubin > 4 mg/dL

Lactic acidosis
The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; D Jillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Definition:
Sepsis is life threatening organ dysfunction caused by a dysregulated host response to infection

Drops the term “severe sepsis”
Drops the use of SIRS and infection + SIRS

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sepsis-2</th>
<th>Sepsis-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>Infection + SIRS</td>
<td>Infection + (\Delta) SOFA (\geq 2)</td>
</tr>
<tr>
<td>Severe Sepsis</td>
<td>Infection + SIRS + organ dysfunction</td>
<td>NON-EXISTENT</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>Infection + Unresponsive Hypotension*</td>
<td>Infection + Unresponsive Hypotension* + Serum Lactate (&gt; 2) mmol/L</td>
</tr>
</tbody>
</table>

*Hypotension that does not respond to volume infusion and requires vasopressor administration
<table>
<thead>
<tr>
<th>SOFA Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaO₂/FiO₂</td>
<td>&lt; 400</td>
<td>&lt; 300</td>
<td>&lt; 200 with respiratory support</td>
<td>&lt; 100 with respiratory support</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>MAP &lt; 70 mm Hg</td>
<td>Dopamine ≤ 5 or dobutamine, any dose</td>
<td>Dopamine &gt; 5 or epinephrine or norepinephrine ≤ 0.1</td>
<td>Dopamine &gt; 15 or epinephrine or norepinephrine &gt; 0.1</td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>1.2 – 1.9</td>
<td>2.0 – 5.9</td>
<td>6.0 – 11.9</td>
<td>&gt; 12.0</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL) or urine output</td>
<td>1.2 – 1.9</td>
<td>2.0 – 3.4</td>
<td>3.5 – 4.9 or &lt; 500 mL/24 hr</td>
<td>≥ 5.0 or &lt; 200 mL/24 hr</td>
</tr>
<tr>
<td><strong>Coagulation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelets x 10³/mm³</td>
<td>&lt; 150</td>
<td>&lt; 100</td>
<td>&lt; 50</td>
<td>&lt; 25</td>
</tr>
<tr>
<td><strong>CNS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasgow Coma Scale</td>
<td>13 - 14</td>
<td>10 - 12</td>
<td>6 - 9</td>
<td>&lt; 6</td>
</tr>
<tr>
<td>Response</td>
<td>Scale</td>
<td>Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------------------------------------------------------</td>
<td>--------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Opening Response</td>
<td>Eyes open spontaneously</td>
<td>4 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eyes open to verbal command, speech, or shout</td>
<td>3 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eyes open to pain (not applied to face)</td>
<td>2 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No eye opening</td>
<td>1 Point</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal Response</td>
<td>Oriented</td>
<td>5 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Confused conversation, but able to answer questions</td>
<td>4 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inappropriate responses, words discernible</td>
<td>3 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Incomprehensible sounds or speech</td>
<td>2 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No verbal response</td>
<td>1 Point</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor Response</td>
<td>Obeys commands for movement</td>
<td>6 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Purposeful movement to painful stimulus</td>
<td>5 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Withdraws from pain</td>
<td>4 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abnormal (spastic) flexion, decorticate posture</td>
<td>3 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extensor (rigid) response, decerebrate posture</td>
<td>2 Points</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No motor response</td>
<td>1 Point</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Minor Brain Injury = 13-15 points; Moderate Brain Injury = 9-12 points; Severe Brain Injury = 3-8 points
Quick SOFA

- Also known as qSOFA
- Any two of:
  - Glasgow Coma Scale < 15
  - Respiratory rate ≥ 22/min
  - Systolic blood pressure ≤ 100 mm Hg
New Sepsis Criteria
A Change We Should Not Make

Steven Q. Simpson, MD, FCCP
Kansas City, KS

Opening the Debate on the New Sepsis Definition
Change Is Not Necessarily Progress: Revision of the Sepsis Definition Should Be Based on New Scientific Insights

American Journal of Respiratory and Critical Care Medicine Volume 194 Number 1 | July 1 2016

qSOFA does not replace SIRS in the definition of sepsis

Jean-Louis Vincent¹*, Greg S. Martin² and Mitchell M. Levy³

Vincent et al. Critical Care (2016) 20:210
**SIRS, qSOFA, Severe Sepsis Sensitivity and Specificity**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Source</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIRS ≥2</td>
<td>Sepsis-3</td>
<td>64.0</td>
<td>65.0</td>
</tr>
<tr>
<td></td>
<td>U of C</td>
<td>93.8</td>
<td>12.3</td>
</tr>
<tr>
<td>qSOFA ≥2</td>
<td>Sepsis-3</td>
<td>55.0</td>
<td>84.0</td>
</tr>
<tr>
<td></td>
<td>U of C</td>
<td>68.7</td>
<td>63.5</td>
</tr>
<tr>
<td>NEWS ≥7</td>
<td>U of C</td>
<td>86.6</td>
<td>47.5</td>
</tr>
<tr>
<td>MEWS ≥5</td>
<td>U of C</td>
<td>71.4</td>
<td>65.0</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>Kaukonen et al.</td>
<td>92.0</td>
<td>84.0</td>
</tr>
</tbody>
</table>
Severe Sepsis: A Diagnostic Challenge

- Timely and accurate diagnosis remains a challenge
  - 17% of physicians agreed on definition of sepsis, but 83% agreed the dx is often missed
  - Occurs throughout the institution
  - Clinical definition not applied at bedside
  - No single test or marker

- Focus is on supporting underlying organ failure

Diagnostic criteria for severe sepsis include:

A. Positive blood cultures, hypotension
B. Positive blood cultures, tissue hypoxia
C. Positive blood cultures, SIRS, and lactic acidosis
D. Suspected infection, SIRS, and organ dysfunction
Diagnostic criteria for severe sepsis include:

A. Positive blood cultures, hypotension
B. Positive blood cultures, tissue hypoxia
C. Positive blood cultures, SIRS, and lactic acidosis
D. Suspected infection, SIRS, and organ dysfunction
Sepsis: What Are We Talking About?

- ICD-9: “septicemia”
- Positive blood cultures
- Multiple positive blood cultures
- Positive blood cultures + hypotension
- Syndrome: how shall we define it?
Role of Biomarkers in Diagnosing Severe Sepsis

• There is none
• Yet
• Procalcitonin – not for diagnosis, but possibly for follow up
Interesting Case

- 72 y.o. man presents with flank pain and fever, mild confusion in E.D.
- previous L. ureteral stent placement
- Hx of CAD, HTN
- Meds include terazosin, atorvastatin, metoprolol
- BP 105/43, P 117, R 22, T 39.1o, SpO2 87%
- Exam: left CVA tenderness, BPH
Interesting Case

- Labs: WBC – 14.7, 33% bands
- Plt – 96,000
- BUN – 47, Cr. – 3.2
- D-dimer – 4.7, fibrinogen – 72, PTT – 39
- Lactate – 2.6
- UA – not available
Surviving Sepsis Campaign (SSC) Guidelines for Management of Severe Sepsis and Septic Shock


Crit Care Med 2004;32:858-873
Intensive Care Med 2004;30:536-555


www.survivingsepsis.org
Table 1. Grading system

Grading of recommendations
A. Supported by at least two level I investigations
B. Supported by one level I investigation
C. Supported by level II investigations only
D. Supported by at least one level III investigation
E. Supported by level IV or V evidence

Grading of evidence
I. Large, randomized trials with clear-cut results; low risk of false-positive (alpha) error of
false-negative (beta) error
II. Small, randomized trials with uncertain results; moderate-to-high risk of false-positive
(alpha) and/or false-negative (beta) error
III. Nonrandomized, contemporaneous controls
IV. Nonrandomized, historical controls and expert opinion
V. Case series, uncontrolled studies, and expert opinion

Sackett DL. Chest 1989; 95:2S–4S
Sprung CL, Bernard GR, Dellinger RP. Intensive Care Medicine 2001; 27(Suppl):S1-S2
Time Sensitive Interventions

• AMI – “Door to PCI”
  Focus on the timely return of blood flow to the affected areas of the heart.

• Stroke – “Time is Brain”

Severe Sepsis – faster treatment improves survival

• Trauma – “The Golden Hour”
  Requires immediate response and medical care “on the scene.”
  Patients typically transferred to a qualified trauma center for care.
Surviving Sepsis Campaign Bundles

To be completed within 3 hours:

1. Measure serum lactate level
2. Obtain blood cultures prior to administration of antibiotics (1C)
3. Administer broad spectrum antibiotics (1B, 1C)
4. Administer 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L
Surviving Sepsis Campaign Bundles

To be completed within 6 hours

1. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg

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

3. Re-measure lactate if initial lactate was elevated*

*Targets are: CVP 8 mm Hg, ScvO2 > 70%, lactate normal
CMS Core Measures: Simply Complicated

Within 3 hours of Presentation of Severe Sepsis

1. Initial lactate level measurement
2. Broad spectrum antibiotics administered
3. Blood cultures drawn prior to antibiotics
4. Crystalloid fluid initiated

Did hypotension persist after fluid given?

YES, continue on

Core Measure goals met, re-measure lactate within 6hrs

Within 3 hours of Presentation of Septic Shock

1. Resuscitation with 30ml/kg crystalloid fluids
2. Evaluate the need for vasopressors

After fluid resuscitation, but within 6 hours of Presentation of Septic Shock

Re-assessment of volume status and tissue perfusion
A focused exam including
- Vital signs
- Cardiopulmonary exam
- Capillary refill evaluation
- Peripheral pulse evaluation
- Skin examination

Must be performed and documented by a Physician, ARNP, or PA

2 out of 4 from the following:
- CVP
- Bedside Cardio US
- ScvO₂
- Passive Leg Raise or Fluid Challenge
In the early resuscitation of the severe sepsis patient, the MOST important feature is:

A. IV fluid boluses
B. Antibiotics as fast as they can get in
C. Measurement of serum lactate
D. Measurement of ScvO2 within 6 hours
In the early resuscitation of the severe sepsis patient, the MOST important feature is:

A. IV fluid boluses
B. Antibiotics as fast as they can get in
C. Measurement of serum lactate
D. Measurement of ScvO2 within 6 hours
Septic Shock: Timing of Antibiotics

Only 50% of patients in Septic Shock received antibiotics within 6 hours.
Antibiotics and Sepsis Progression

3,929 severe sepsis
984 progressed to septic shock
8.0%/hour until antibiotics
Standard Techniques, Operations, and Procedures for Sepsis

Kansas Delivery System Reform Incentive Payment (DSRIP)
Scope of the Issue

- Nationally, 1 in 4 Americans lives in a rural area
- Approximately 76,000,000 people
- < 10% of physicians work in rural areas
- Rural Americans are:
  - More likely to live below poverty line
  - Older
  - Less likely to have regular medical care
  - More likely to die accidentally
Kansas: Exemplar of Rural America

Data from 2012 STAT Report – Kansas Hospital Association
State Designated Rural Health Networks
February 2013

- Red circles = Supporting Hospital
- Black triangles = Critical Access Hospital
U.S. States with Similar Population Density

US Census Bureau 2008
Looking From the Other Side

Urban Areas
Census Bureau 2010
Two Different Pictures of Hospitals

Cost/Expenditure

Quality

Stop Sepsis – What We Do

• Nursing homes, EMS systems, Hospitals
• Training at all levels
  - Workshops and online tools
  - Recognizing sepsis and severe sepsis
  - Early aggressive treatment
  - Quality improvement techniques
• Provision of online data collecting tool
• Continual support from expert faculty
Thank you!

ssimpson3@kumc.edu