Sepsis-3 definitions. What are they, and how should we use them?

William T. Browne, MD, FCCM

October 28, 2016
ACCP/SCCM Consensus Definitions

• SIRS (Systemic Inflammatory Response Syndrome)
  – Temperature > 38°C or < 36°C
  – Heart rate > 90
  – Respiratory rate > 20 or pCO₂ < 32 mm Hg
  – WBC > 12,000 or < 4,000 or > 10% bands

• Any two of the criteria needed for SIRS diagnosis
ACCP/SCCM Consensus Definitions

• Sepsis
  – Must have diagnosis of SIRS
  – Clinical evidence of infection
    • bacteremia
    • infiltrate on CXR
    • abscess on imaging study
ACCP/SCCM Consensus Definitions

• Severe sepsis
  – must have diagnosis of sepsis
  – evidence of organ dysfunction

• Organ dysfunction
  – increase in BUN/creatinine
  – elevated LFTs
  – hypoxia
  – elevated serum lactate
ACCP/SCCM Consensus Definitions

- Septic shock
  - must have findings of severe sepsis
  - hypotension after adequate fluid resuscitation
  - systolic BP 40 mm Hg below baseline
  - may not have hypotension if receiving pressor agents
Was this a useful bedside tool?
Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

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; Djillali 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
Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
Under these new definitions

Sepsis(new) = Severe Sepsis(old)
Key concepts of sepsis (1)

- Sepsis is the primary cause of death from infection, especially if not recognized and treated promptly. Its recognition mandates urgent attention.
- Sepsis is a syndrome shaped by pathogen factors and host factors (e.g., sex, race and other genetic determinants, age, comorbidities, environment) with characteristics that evolve over time. What differentiates sepsis from infection is an aberrant or dysregulated host response and the presence of organ dysfunction.
Key concepts of sepsis (2)

• Sepsis-induced organ dysfunction may be occult; therefore, its presence should be considered in any patient presenting with infection. Conversely, unrecognized infection may be the cause of new-onset organ dysfunction. Any unexplained organ dysfunction should thus raise the possibility of underlying infection.
Key concepts of sepsis (3)

• The clinical and biological phenotype of sepsis can be modified by preexisting acute illness, long-standing comorbidities, medication, and interventions.

• Specific infections may result in local organ dysfunction without generating a dysregulated systemic host response.
Organ dysfunction

- Organ dysfunction can be identified as an **acute change** in total SOFA score ≥2 points consequent to the infection.
  - The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
  - A SOFA score ≥2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.
Septic shock

- Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
Septic shock

• Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40%.
From: **The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)**  


<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<tbody>
<tr>
<td><strong>Respiration</strong></td>
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<tr>
<td>$P_aO_2/F_iO_2$, mm Hg (kPa)</td>
<td></td>
<td>≥400 (53.3)</td>
<td>&lt;400 (53.3)</td>
<td>&lt;300 (40)</td>
<td>&lt;200 (26.7) with respiratory support</td>
<td>&lt;100 (13.3) with respiratory support</td>
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<td><strong>Coagulation</strong></td>
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<td>Platelets, $\times 10^3/\mu$L</td>
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<td>≥150</td>
<td>&lt;150</td>
<td>&lt;100</td>
<td>&lt;50</td>
<td>&lt;20</td>
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<td><strong>Liver</strong></td>
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<td>Bilirubin, mg/dL (μmol/L)</td>
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<td>&lt;1.2 (20)</td>
<td>1.2-1.9 (20-32)</td>
<td>2.0-5.9 (33-101)</td>
<td>6.0-11.9 (102-204)</td>
<td>&gt;12.0 (204)</td>
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<td><strong>Cardiovascular</strong></td>
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<tr>
<td>MAP ≥70 mm Hg</td>
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<td>MAP &lt;70 mm Hg</td>
<td>Dopamine &lt;5 or dobutamine (any dose)$^b$</td>
<td>Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1$^b$</td>
<td>Dopamine &gt;15 or epinephrine &gt;0.1 or norepinephrine &gt;0.1$^b$</td>
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<tr>
<td><strong>Central nervous system</strong></td>
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<td>Glasgow Coma Scale score$^c$</td>
<td></td>
<td>15</td>
<td>13-14</td>
<td>10-12</td>
<td>6-9</td>
<td>&lt;6</td>
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<td>Creatinine, mg/dL (μmol/L)</td>
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<td>&lt;1.2 (110)</td>
<td>1.2-1.9 (110-170)</td>
<td>2.0-3.4 (171-299)</td>
<td>3.5-4.9 (300-440)</td>
<td>&gt;5.0 (440)</td>
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<td>Urine output, mL/d</td>
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<td></td>
<td>&lt;500</td>
<td>&lt;200</td>
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Abbreviations: $F_iO_2$, fraction of inspired oxygen; MAP, mean arterial pressure; $P_aO_2$, partial pressure of oxygen.  

$^a$ Adapted from Vincent et al.  

$^b$ Catecholamine doses are given as μg/kg/min for at least 1 hour.  

$^c$ Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.
Sequential organ failure assessment (SOFA) calculator
Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock

The baseline Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score should be assumed to be zero unless the patient is known to have preexisting (acute or chronic) organ dysfunction before the onset of infection. qSOFA indicates quick SOFA; MAP, mean arterial pressure.
Quick SOFA (qSOFA)

- Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with qSOFA, ie, alteration in mental status, systolic blood pressure ≤100 mm Hg, or respiratory rate ≥22/min.
Quick SOFA criteria

- Respiratory rate ≥22/min
- Altered mentation
- Systolic blood pressure ≤100 mm Hg
Why is qSOFA useful?

While only 1 in 4 infected patients have 2+ qSOFA POINTS, they account for 3 out of 4 deaths.
Risk of death correlated with qSOFA score
qSOFA calculator
qSOFA does not define sepsis (but the presence of two qSOFA criteria is a predictor of both increased mortality and ICU stays of more than three days in non-ICU patients)
The new definitions recommend using a change in baseline of the total SOFA score of two or more points to represent organ dysfunction.
Stick to the basics!

"Don't get stuck on stupid."

LTG (Ret) Russel Honore
Surviving Sepsis Campaign Bundles

TO BE COMPLETED WITHIN 3 HOURS:

1) Measure lactate level
2) Obtain blood cultures prior to administration of antibiotics
3) Administer broad spectrum antibiotics
4) Administer 30 ml/kg crystalloid for hypotension or lactate $\geq 4\text{mmol/L}$
Surviving Sepsis Campaign Bundles

TO BE COMPLETED WITHIN 6 HOURS:

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

6) 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)*

7) Remeasure lactate if initial lactate was elevated*.

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥8 mm Hg; ScvOs of ≥70%, and normalization of lactate.
What does Surviving Sepsis Campaign say to do with these new definitions?
Step 1: Screening and Management of Infection

The appropriate first step in screening should be identification of infection. Hospitals should continue to use signs and symptoms of infection to promote the early identification of patients with suspected or confirmed infection.

In those patients identified as having infection, management should begin by obtaining blood and other cultures as indicated, administering tailored antibiotics as appropriate, and simultaneously obtaining laboratory results to evaluate the patient for infection-related organ dysfunction.
Step 2: Screening for Organ Dysfunction and Management of Sepsis (formerly called Severe Sepsis)

Patients with sepsis (formerly called severe sepsis) should still be identified by the same organ dysfunction criteria (including lactate level greater than 2 mmol/L). Organ dysfunction may also be identified in the future using the quick Sepsis-Related Organ Failure Assessment (qSOFA)
POWERFUL INFLUENCE OF PROMPT APPROPRIATE ANTIBIOTIC THERAPY ON MORTALITY IN SEPTIC SHOCK

Kumar et al. Crit Care Med 2006
EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D.,
FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*
The Importance of Early Goal-Directed Therapy for Sepsis Induced Hypoperfusion


- In-hospital mortality (all patients)
  - Standard therapy: 40%
  - EGDT: 30%

- 28-day mortality
  - Standard therapy: 50%
  - EGDT: 40%

- 60-day mortality
  - Standard therapy: 55%
  - EGDT: 45%

NNT to prevent 1 event (death) = 6-8
Original Article

Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc., David A. Harrison, Ph.D., M. Zia Sadique, Ph.D., Richard D. Grieve, Ph.D., Rahi Jahan, B.A., Sheila E. Harvey, Ph.D., Derek Bell, M.D., Julian F. Bion, M.D., Timothy J. Coats, M.D., Mervyn Singer, M.D., J. Duncan Young, D.M., Kathryn M. Rowan, Ph.D., for the ProMISE Trial Investigators

N Engl J Med
Volume 372(14):1301-1311
April 2, 2015
Kaplan–Meier Survival Estimates.

Adjusted hazard ratio, 0.94 (0.79–1.11); P=0.46
P=0.63 by log-rank test

No. at Risk

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<td>90</td>
<td>440</td>
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The bottom line

• Have a high index of suspicion
  – Train everyone to recognize early
  – Keep it simple
• Give antibiotics immediately, if not sooner!
• Resuscitate aggressively
• Transfer to ICU if not clinically improving quickly