Are New Sepsis Criteria Sufficient for Sepsis Diagnosis?

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Faculty/Presenter Disclosure

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  - **Other:** Surviving Sepsis Campaign Panel Member, ESICM Research Committee Chair

* Fees and honoraria paid to institution
Sepsis, the Equal Opportunity Killer

- 258,000 Americans die from Sepsis each year.
- 5+ million children worldwide die from Sepsis each year.
- 1.6 million cases of Sepsis in the U.S. every year.
- 55% of Americans have ever heard of the word "SEPSIS".

Sepsis is the third leading cause of death in the U.S. after heart disease and cancer.
Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis

THE ACCP/SCCM CONSENSUS CONFERENCE COMMITTEE:
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An American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference was held in Northbrook in August 1991 with the goal of agreeing on a set of definitions that could be applied to patients with sepsis and its sequelae. New definitions were offered for some terms, while others were discarded. Broad definitions of sepsis and the systemic inflammatory response syndrome were proposed, along with detailed physiologic parameters by which a patient may be categorized. Definitions for severe sepsis, septic shock, hypotension, and multiple organ dysfunction syndrome were also offered. The use of severity scoring methods when dealing with septic patients was recommended as an adjunctive tool to assess mortality. Appropriate methods and applications for the use and testing of new therapies were recommended. The use of these terms and techniques should assist clinicians and researchers who deal with sepsis and its sequelae.

(Chest 1992; 101:1644-55)

MODS = multiple organ dysfunction syndrome; SIRS = systemic inflammatory response syndrome
Sepsis is a systemic inflammatory response in the presence of infection.

**SIRS criteria**
- Temperature $> 38°C$ or $< 36°C$
- Heart rate $> 90$/minute
- Respiratory rate $> 20$/minute
- WBC $> 12,000/μL$ or $< 4,000/μL$
SEPSIS

Infection

SIRS
Dear SIRS, I'm sorry to say that I don't like you

Jean-Louis Vincent
2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference

Mitchell M. Levy, MD, FCCP; Mitchell P. Fink, MD, FCCP; John C. Marshall, MD; Edward Abraham, MD; Derek Angus, MD, MPH, FCCP; Deborah Cook, MD, FCCP; Jonathan Cohen, MD; Steven M. Opal, MD; Jean-Louis Vincent, MD, FCCP, PhD; Graham Ramsay, MD; For the International Sepsis Definitions Conference

Objective: In 1991, the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) convened a “Consensus Conference,” the goals of which were “to provide a conceptual and a practical framework to define the systemic inflammatory response to infection, which is a progressive injurious process that falls under the generalized term ‘sepsis’ and includes sepsis-associated organ dysfunction as well.” The general definitions introduced as a result of that conference have been widely used and symptoms of sepsis, cell markers, cytokines, microbiologic data, and coagulation parameters. The subgroups corresponded electronically before the conference and met in person during the conference. A spokesperson for each group presented the deliberation of each group to all conference participants during a plenary session. A writing committee was formed at the conference and developed the current article based on executive summary documents generated by each group and the plenary group.
Table 1. Diagnostic criteria for sepsis

Infection," documented or suspected, and some of the following:"c
General variables
- Fever (core temperature >38.3°C)
- Hypothermia (core temperature <36°C)
- Heart rate >90 min⁻¹ or >2 sd above the normal value for age
- Tachypnea
- Altered mental status
- Significant edema or positive fluid balance (>20 mL/kg over 24 hrs)
- Hyperglycemia (plasma glucose >120 mg/dL or 7.7 mmol/L) in the absence of diabetes

Inflammatory variables
- Leukocytosis (WBC count >12,000 µL⁻¹)
- Leukopenia (WBC count <4000 µL⁻¹)
- Normal WBC count with >10% immature forms
- Plasma C-reactive protein >2 sd above the normal value
- Plasma procalcitonin >2 sd above the normal value

Hemodynamic variables
- Arterial hypotension" (SBP <90 mm Hg, MAP <70, or an SBP decrease >40 mm Hg in adults
  or <2 sd below normal for age)
- S\textsubscript{vO\textsubscript{2} >70%"}
- Cardiac index >3.5 L·min⁻¹·M⁻²³

Organ dysfunction variables
- Arterial hypoxemia (P\textsubscript{a}O\textsubscript{2}/F\textsubscript{IO}\textsubscript{2} <300)
- Acute oliguria (urine output <0.5 mL·kg⁻¹·hr⁻¹ or 45 mmol/L for at least 2 hrs)
- Creatinine increase >0.5 mg/dL
- Coagulation abnormalities (INR >1.5 or aPTT >60 secs)
- Ileus (absent bowel sounds)
- Thrombocytopenia (platelet count <100,000 µL⁻¹)
- Hyperbilirubinemia (plasma total bilirubin >4 mg/dL or 70 mmol/L)

Tissue perfusion variables
- Hyperlactatemia (>1 mmol/L)
- Decreased capillary refill or mottling
Ten big mistakes in intensive care medicine

1. We focus too much on syndromes—prominently the acute respiratory distress syndrome (ARDS), sepsis, and acute kidney injury (AKI)—and we spend much time redefining them. Even though we consider sepsis to be too vaguely defined [1], we did have one sepsis drug that seemed to be effective (activated
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

**IMPORTANCE** Definitions of sepsis and septic shock were last revised in 2001. Considerable advances have since been made into the pathobiology (changes in organ function, morphology, cell biology, biochemistry, immunology, and circulation), management, and epidemiology of sepsis, suggesting the need for reexamination.

**OBJECTIVE** To evaluate and, as needed, update definitions for sepsis and septic shock.

**PROCESS** A task force (n = 19) with expertise in sepsis pathobiology, clinical trials, and epidemiology was convened to review the existing literature and to make recommendations for revised definitions.
Sepsis-3 definitions

**SEPSIS**

- Life-threatening organ dysfunction caused by a *dysregulated host response* to infection
- Acute change in total **SOFA** score ≥2 points consequent to the infection

*Singer, M. JAMA 2016 8:801-810*
<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiration</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>
</tr>
<tr>
<td><strong>Pao2/FiO2, mm Hg (kPa)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulation</td>
<td></td>
<td>≥150</td>
<td>&lt;150</td>
<td>&lt;100</td>
<td>&lt;50</td>
<td>&lt;20</td>
</tr>
<tr>
<td><strong>Platelets, x10^3/µL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<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>
</tr>
<tr>
<td><strong>Bilirubin, mg/dL (µmol/L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>MAP ≥70 mm Hg</td>
<td>MAP &lt;70 mm Hg</td>
<td>Dopamine &lt;5 or dobutamine (any dose)</td>
<td>Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1</td>
<td>Dopamine &gt;15 or epinephrine &gt;0.1 or norepinephrine &gt;0.1</td>
<td></td>
</tr>
<tr>
<td>Central nervous system</td>
<td>Glasgow Coma Scale score</td>
<td>15</td>
<td>13-14</td>
<td>10-12</td>
<td>6-9</td>
<td>&lt;6</td>
</tr>
<tr>
<td>Renal</td>
<td>Creatinine, mg/dL (µmol/L)</td>
<td>&gt;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>
</tr>
<tr>
<td></td>
<td>Urine output, mL/d</td>
<td></td>
<td></td>
<td>&lt;500</td>
<td>&lt;200</td>
<td></td>
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</tbody>
</table>
**SEPTIC SHOCK**

Subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality

Persisting hypotension requiring vasopressors to maintain MAP 65mmHg and having a serum lactate level >2 mmol/L (18mg/dL) despite adequate volume resuscitation

Singer, M. JAMA 2016 8:801-810
Sepsis diagnosis

Box 4. qSOFA (Quick SOFA) Criteria

- Respiratory rate ≥22/min
- Altered mentation
- Systolic blood pressure ≤100 mm Hg

• Identifies patients at highest risk of bad outcome (prolonged ICU stay and mortality)

Singer, M. JAMA 2016 8:801-810
Figure. Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock

Patient with suspected infection
Sepsis

Suspected infection

SIRS

Sepsis-1/2
Sepsis

Suspected infection

Organ dysfunction

Sepsis-3
Sepsis vs. infection diagnosis

**Diagnosing infection**
- Local signs and symptoms
- Contextual approach

**Diagnosing sepsis**
- Focus on host response
- Organ dysfunction
Infection diagnosis and Sepsis-3

allowed discussion of biological concepts that are currently incompletely understood, such as genetic influences and cellular abnormalities. The sepsis illness concept is predicated on infection as its trigger, acknowledging the current challenges in the microbiological identification of infection. It was not, however, within the task force brief to examine definitions of infection.

The task force recognized that sepsis is a syndrome without, at present, a validated criterion standard diagnostic test. There is currently no process to operationalize the definitions of sepsis and septic shock, a key deficit that has led to major variations in treatment.
Infection and sepsis

Infection definition

• “Pathologic process induced by a micro-organism”
• Research context: “Combination of body fluid culture order and antibiotic therapy”
• Sepsis-3 Suspected infection: “concomitant orders for blood cultures and antibiotics in a specific period”
Infection and sepsis

Infection = “suspected infection”

- Difficult to exclude in the ICU
- Infection to be considered in all patients with organ dysfunction
- Organ dysfunction may be occult and should be considered in every patient with infection
How good are we at diagnosing infection?

Plausibility of infection – clinical diagnosis at ICU admission versus post hoc evaluation
Houston, we have a problem
SOFA and qSOFA are the new SIRS
What about SIRS?
Any role for SIRS?

Infection is first suspected in association with an in-hospital mortality in excess of 10%. Recognition of this condition thus merits a prompt and appropriate response.

**Nonspecific SIRS criteria such as pyrexia or neutrophilia will continue to aid in the general diagnosis of infection.** These findings complement features of specific infections (e.g., rash, lung consolidation, dysuria, peritonitis) that focus attention toward the likely ana-
Sepsis

SIRS + local symptoms

Suspected infection

Organ dysfunction
Awareness among lay public

Education inexperienced MDs

Recognition of high-risk patients

Broad patient selection in clinical trials

Antibiotic overuse
Infection diagnosis critical

Excludes alternative diagnosis

- Organ dysfunction may have multiple causes

Better sepsis research

- Confirmed infection

Allows targeted infection treatment

- Antibiotics
  - Choice, dose and route
  - Source control
In conclusion

• Defining sepsis is necessary
• Focus on organ dysfunction logical step
• Usefulness in the ICU questionable
• Not a tool to diagnose infection
• Lack of infection diagnosis problematic
• Danger of overuse of interventions including antibiotics