American College of Physicians
Sepsis update

By
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Potential Conflicts of Interest

- No direct or indirect potential financial conflict of interest as to any material presented in this presentation

Outline

- Sepsis 3 and the new definition of sepsis
- Sepsis bundle and the Surviving Sepsis Campaign
What is the definition of Sepsis?

A. 2 or more SIRS criteria with a suspected or confirmed infection

B. 2 or more SIRS

C. 2 or more SIRS, suspected or confirmed infection, new onset organ dysfunction/failure

D. 2 or more SIRS, suspected or confirmed infection, new onset organ dysfunction/failure, with hypotension &/or elevated lactate levels
23y/o male pt. presents to ED with c/o severe cramping and diarrhea X 3 days. T 101, P 94, R 18, B/P 100/68 – Initial WBC 18.75. Pt family member reports fatigue, weakness, and lethargy along with decreased urine output X 2 days.

Based on information provided, and defining criteria, which of the following would you suspect and how would you screen this patient?

A. SIRS
B. Sepsis
C. Severe Sepsis
D. Septic Shock
E. None of the above
SEPSIS STEPS

SIRS
T: >100.4 F < 96.8 F
RR: >20
HR: >90
WBC: >12,000 <4,000
>10% bands
PCO2 < 32 mmHg

2 SIRS
Confirmed or suspected infection

SEPSIS
Sepsis +
Signs of End Organ Damage
Hypotension (SBP <90)
Lactate >4 mmol

SEVERE SEPSIS
Sepsis +
Signs of End Organ Damage
Hypotension (SBP <90)
Lactate >4 mmol

SEPTIC SHOCK
Severe Sepsis with persistent:
Signs of End Organ Damage
Hypotension (SBP <90)
Lactate >4 mmol

Slides Courtesy of Curtis Merritt, D.O.
1. Why
Issues with the 1991 and 2001 Definitions

- SIRS – based
- “Severe Sepsis”
- Different criteria yielding different results
SIRS Sensitivity

SIRS is an *appropriate* response to infection – or any other stimulus that activates inflammation.

**Conclusions:** Almost half of patients hospitalized on the wards developed SIRS at least once during their ward stay. Our findings suggest that screening ward patients using SIRS criteria for identifying those with sepsis would be impractical.
Severe Sepsis

- Confusing
  - Most people say “sepsis” when they mean “severe sepsis”
  - Is “severe sepsis” really needed?
Different Criteria, Different Results

Benchmarking the Incidence and Mortality of Severe Sepsis in the United States*

David F. Gaieski MD1; J. Matthew Edwards, MD1; Michael J. Kallan, MS2; Brendan G. Carr, MD, MA, MS1–3

Crit Care Med 2013; 41: 1167-1174

Number of cases

900K – 3.1 Mil

Total mortality

250K – 375K

Four different ways to identify sepsis; four different sets of results
Variable Variables

hypotension (SAP <90, MAP <60 or <70, fall in SAP >40)

AND/OR

.. that persists despite adequate fluid resuscitation (either unspecified or after challenges of either 20 ml/kg OR 1000 ml)

AND/OR

biochemical variables (e.g. lactate >2 or >4, or base deficit >5)

AND/OR

use of inotropes and/or vasopressors [±dose specified]

AND/OR

new onset organ dysfunction (defined variably using APACHE II, APACHE III, or SOFA cardiovascular component)
Increased Understanding of Sepsis Pathobiology

- More than just rampant inflammation
- Key role of immunosuppression
- Contribution of non-immune mechanisms
- Possible adaptive nature of organ dysfunction – hibernation
- Re-appraisal of the nature of septic shock
2. How
SCCM/ESICM Task Force to Re-Define Sepsis

- Co-Chairs – Mervyn Singer, Cliff Deutschman

Derek Angus
Djilali Annane
Michael Bauer
Rinaldo Bellomo
Gordon Bernard
Jean-Daniel Chiche
Craig Coopersmith

Richard Hotchkiss
Mitchell Levy
John Marshall
Steve Opal
Gordon Rubenfeld
Tom van der Poll
Jean-Louis Vincent

Greg Martin
Manu Shankar-Hari
Chris Seymour
The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Singer M, Deutschman CS, Seymour CW, Shankar-Hari M et al. Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) JAMA 2016; 315: 801-10
3. What
Task Force Decisions

CONSENSUS

1. Beyond the remit of the task force to define infection
2. Sepsis is not simply infection + two or more SIRS criteria
3. The host response is of key importance
4. Sepsis represents bad infection where
   bad = infection leading to organ dysfunction
5. “Severe sepsis” is not helpful and should be eliminated
Definitions

Per the Merriam – Webster English Dictionary:

- **Definition**
  - “a statement expressing the **essential nature** of something” or, more generically,
  - “a statement that describes **what something is**”

A definition therefore requires an understanding of the pathobiology of the disorder..

.. which, for sepsis, is at best incomplete
The Definition of Sepsis

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection.
The Definition of Sepsis

Key Distinctions

Sepsis is life-threatening *organ dysfunction* caused by a dysregulated host response to infection

So ... “sepsis” now = the old “severe sepsis”
The Definition of Sepsis

Key Distinctions

Sepsis is life-threatening organ dysfunction caused by a *dysregulated host response* to infection

As opposed to the “regulated host response” that characterizes the non-septic response to infection
The Definition of Septic Shock

More problematic
- Is septic shock sepsis where the dysfunctional organ is the cardiovascular system?
  - Task force opinion - NO
    - Also involves cellular/metabolic abnormalities

- What distinguishes septic shock from sepsis?
  - Treatment?
    - NO. Management is the same
  - Pathobiology?
    - Maybe … but at this time not known
The Definition of Septic Shock

- What tangibly differentiates septic shock from sepsis?
  - MORTALITY
  - Septic shock is “really bad” sepsis

Septic shock is a subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.
Sepsis Definitions

- **Advantages**
  - Incorporates most up-to-date thinking on sepsis pathobiology
  - Provides closest approximation possible to describing “what sepsis is”

- **Concerns**
  - Of limited practical utility as they contain elements that cannot be clinically identified
    - “organ dysfunction”
    - “dysregulated host response”
  - Incompatible with ICD-10
29y/o male pt. presents to ED with c/o productive cough and fevers X 3 days. T 102, P 94, R 18, B/P 110/68, 96% on room air– Initial WBC 15.00. Pt reports fatigue, weakness, but preserved appetite and good urine output. Physical exam and imaging is consistent with a RLL pneumonia. Lactate level is normal. He has no other lab abnormalities.

Based on information provided, and defining criteria, which of the following would you suspect and how would you screen this patient?

A. SIRS
B. Sepsis
C. Severe Sepsis
D. Septic Shock
E. None of the above
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 4 mmol/L

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, ScvO2 of 70%, and normalization of lactate
Why measure lactate?
Why measure lactate?

- Diagnose severe sepsis with elevated lactate as a diagnosis of tissue hypoperfusion
- Trigger for quantitative resuscitation if lactate is 4 mg/dL or more
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Blood Cultures
Diagnosis

1. To optimize identification of causative organisms, we recommend at least two blood cultures be obtained before antimicrobial therapy is administered as long as such cultures do not cause significant delay (>45 minutes) in antimicrobial administration, with at least one drawn percutaneously and one drawn through each vascular access device, unless the device was recently (<48 hr.) inserted (Grade 1C).
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Time to Antibiotics Following Onset Septic Shock

Antibiotic Therapy

- We recommend that intravenous antibiotic therapy be started as early as possible and within the first hour of recognition of septic shock (1B) and severe sepsis without septic shock (1C).

Remark: Although the weight of evidence supports prompt administration of antibiotics following the recognition of severe sepsis and septic shock, the feasibility with which clinicians may achieve this ideal state has not been scientifically validated.
Antibiotic Therapy

- Initial empiric anti-infective therapy – activity against all likely pathogens and adequate concentrations into suspected or potential sources of infection (1B)

- Reassess antibiotic regimen daily for de-escalation (1B)
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Fluid therapy

1. Crystalloids (1B)
2. Albumin (2C)
3. Avoid HES (1B)
Meta-Analysis

Fluid therapy

4. Initial fluid challenge in sepsis-induced tissue hypoperfusion (hypotension or elevated lactate) with suspicion of hypovolemia to be a minimum of 30ml/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid, may be needed in some patients (1B)
SURVIVING SEPSIS
CAMPAIGN BUNDLES

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Resuscitation of Sepsis Induced Tissue Hypoperfusion

- Recommend MAP 65 mm Hg
  Grade 1C
Vasopressors
Meta-analysis – NE versus dopamine

<table>
<thead>
<tr>
<th>Study</th>
<th>Norepinephrine</th>
<th>Dopamine</th>
<th>RR [95% CI]</th>
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<td></td>
<td>Event</td>
<td>Total</td>
<td>Event</td>
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<td>De Backer et al.</td>
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<td>Patel et al.</td>
<td>51</td>
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<tr>
<td>Overall</td>
<td>330</td>
<td>676</td>
<td>396</td>
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Vasopressors

Front line:

(1) Norepinephrine (1B).

(2) Epinephrine (2B)

  Vasopressin .03 units/min (UG)
Vasopressors

- In general **avoid**
  - **Dopamine**, unless
    - Relative or absolute bradycardia and low risk of tachyarrhythmias
    (2C)
  - **Phenylephrine**, unless
    - Norepinephrine associated with serious arrhythmias
    - Cardiac output is known to be high and blood pressure target difficult to achieve
    - As salvage therapy
    (1C)
Sepsis Induced Tissue Hypoperfusion

- Requirement for vasopressors after fluid challenge
- Lactate $\geq 4$ mg/dL
Protocolized Care

SEPSIS-INDUCED HYPOPERFUSION
(Clinical picture of sepsis plus one or both of the following criteria)
1) Hypotension AFTER initial fluid bolus
   OR
2) Lactate ≥ 4 mmol/L with any BP
   With hypotension defined as:
   SBP ≤ 90 mmHg or MAP ≤ 65 mmHg

Supplemental O2 ± ETI with mechanical ventilation (if necessary)

Continue crystalloid resuscitation 250-1000 ml boluses

Critical care consultation (if not already consulted)

CVP ≤ 8 mmHg

CVP < 8 mmHg

CVP 8-12 mmHg

MAP < 65 mmHg

MAP ≥ 65 mmHg

ScvO2 ≤ 70%

ScvO2 ≥ 70%

Transfuse if HCT less than 30

HCT < 70%

HCT ≥ 70%

Inotrope (If PA catheter inserted, keep cardiac index ≥ 3.0 L/min/m²)

Resuscitation complete. Establish re-evaluation intervals.

YES

Achieve ALL Goals?

NO
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SURVIVING SEPSIS CAMPAIGN BUNDLES 2015 UPDATE

DOCUMENT REASSESSMENT OF VOLUME STATUS AND TISSUE PERFUSION WITH:

EITHER

• Repeat focused exam (after initial fluid resuscitation) by licensed independent practitioner including vital signs, cardiopulmonary, capillary refill, pulse, and skin findings.

OR

TWO OF THE FOLLOWING:

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

❖ Of note, the 6-hour bundle has been updated; the 3-hour SSC bundle is not affected.
❖ While no suggestion of harm was indicated with use of a central line in any trial, and published evidence shows significant mortality reduction using the original SSC bundles, the committee has taken a prudent look at all current data and, despite weaknesses as in all studies, determined the above bundles to be the appropriate approach at this time.
Lactate Clearance

In patients with elevated lactate levels as a marker of tissue hypoperfusion we suggest targeting resuscitation to normalize lactate as rapidly as possible (grade 2C).
www.survivingsepsis.org
Questions?