Surviving Sepsis Campaign update

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Disclosures

• Received funding from:
  NIH NIGMS, SCCM, AHA, MedicOne, SIS

• Consulting fees from Beckman Coulter, Edwards, Cytovale

• Member, Surviving Sepsis Campaign, ATS representative

• Member, 2016 Third International Sepsis Definitions Task Force

Caveats

• Surviving Sepsis Campaign is sponsored by large professional societies in critical care

• Previously received industry funding, for which I have no conflict of interest
Two days earlier, diving for a basketball, Rory had cut his arm. He arrived at his pediatrician’s office the next day…vomiting, feverish, and with pain in his leg. He was sent to the emergency room at NYU Langone Medical Center. The doctors agreed: he was suffering from an upset stomach and dehydration.

On April 1, three nights after he was sent home from the emergency room, he died in the ICU. The cause was severe septic shock brought on by the infection.

What happened?

- No review of ED vital signs prior to discharge
- No communication between ED staff and pediatrician
- Labs resulted 3 hrs after discharge
- Knowledge and awareness of clinicians and public
- Absence of routine sepsis protocol

What happened next?

- Broad quality improvement initiatives in New York City emergency departments
- Department of Health, New York State
- Leaned on clinical practice guidelines care for pediatric and adult sepsis patients
Future directions
Examine recent studies contributing to new SSC guidelines
Barriers to implementation of the SSC
Future directions

Agenda

• Brief history lesson
• Examine recent studies contributing to new SSC guidelines
• Barriers to implementation of the SSC
• Future directions

Document history

Endorsed by intensive care professionals around the world, the Barcelona Declaration urges governments and healthcare providers to recognize the growing burden of sepsis and to commit to providing adequate resources to combat it. For healthcare professionals, a five-point action plan aims to improve the management of sepsis and save lives by addressing the following:
Diagnosis, Treatment, Referral, Education, Counseling

Barcelona Declaration, 2002
Important benchmarks

• 2003 partnership with Institute for Healthcare Improvement
• 2008 International Sepsis Forum leaves campaign to remove conflict of interest
• 2011 Gordon and Betty Moore Foundation join
• 2014 new leadership for revisions (Evans, Rhodes)
• 2013-4 adoption of SSC bundles as part of regulations in NY, Illinois, and CMS Sep1 bundle

Document history

Why do we have guidelines?

• Evidence is complex and voluminous
• Interpreting the evidence is inherently subjective
• Can clinicians maintain adequate knowledge of evidence base?
Why do we have guidelines?

- Rate the quality of the evidence
- Make a practice recommendation based on
  - The quality of the evidence
  - Preferences and values
- GRADE system

What is GRADE?

<table>
<thead>
<tr>
<th>Strength</th>
<th>Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Separates evidence from recs</td>
<td>Flexibility to incorporate values and preferences, not just evidence</td>
</tr>
<tr>
<td>Systematic</td>
<td>Specific road-map leads to more consistent recommendations</td>
</tr>
<tr>
<td>Transparent</td>
<td>Even if we disagree with the conclusions, we can see how the conclusion was reached</td>
</tr>
</tbody>
</table>

Strength of evidence

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Quality of Evidence</th>
<th>Lower #</th>
<th>Higher #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized trial</td>
<td>High (A)</td>
<td>Risk of bias</td>
<td>Large effect</td>
</tr>
<tr>
<td></td>
<td>Moderate (B)</td>
<td>- Serious</td>
<td>- Large</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Very serious</td>
<td>- Very large</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inconsistency</td>
<td>Low response</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Serious</td>
<td>- Evidence of a gradient</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Very serious</td>
<td>- Evidence of a gradient</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indirectness</td>
<td>No plausible confounding</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Serious</td>
<td>- Would reduce a demonstrated effect or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Very serious</td>
<td>- Would suggest a quantifiable effect when</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Imprecision</td>
<td>results show no effect</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Serious</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Very serious</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Publication bias</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 Likely</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 Very likely</td>
<td>2</td>
</tr>
<tr>
<td>Observational study</td>
<td>Low (C)</td>
<td>1 Serious</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Very low (D)</td>
<td>2 Very serious</td>
<td>2</td>
</tr>
</tbody>
</table>

Guyatt JCE 2011
**Strength of recommendation**

**Factors**
- Quality of evidence
- Balance between desirable and undesirable effects
- Importance of the outcome
- Costs (resources allocation)

**Summary statement in GRADE**

- Strength of recommendation
  - Strong (1-“We recommend”)
  - Weak (2- “We suggest”)
- Quality of evidence
  - High (A)
  - Moderate (B)
  - Low (C)
  - Very low (D)

**30,000 foot view**

Evidence

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>21</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>19</td>
<td>30</td>
<td>5</td>
</tr>
</tbody>
</table>
30,000 foot view

Cardiology ACC/AHA Guidelines
59% of recommendations
80% of strong recommendations
< "A" evidence

Surviving Sepsis
36% of recommendations
80% of strong recommendations
< "A" evidence

Evidence

Confidence

Lots of bundles

- Bundle is a tool to simplify complex decisions
- A collection of tasks “bundled” under a single heading
- Usually 3-5 things

- Without a bundle …
  - An event may trigger numerous separate activities that may or may not be remembered

- Similar to checklists, standard order sets, etc.
  - A “trick” to make sure you do everything correctly

- Typically, constructed from evidence-based guidelines
  - Meant to have been shown to improve outcome
Conceptual advantages

- Bundle several “good things” together
- Simplifies the message
- Reduces the chance something will be forgotten
- By Koontz’ analysis
  - May be able to ‘push’ elements in absence of knowledge or receptiveness
- The word “bundle” may have cachet

Conceptual disadvantages

- Not everything in the bundle may be “good”
- Ineffective, unnecessarily expensive
- Potentially harmful
- Over or undertreatment
  - Mismatch of suite of bundles to suite of patients
- Still requires all the standard elements of implementation science
- Manipulation of knowledge-attitude-behavior pathway
- The word “bundle” may lose cachet

What are the bundles?

- Traditionally: three waves: Surviving Sepsis Campaign bundles
  - Resuscitation
    - Manager
      - Bolus fluid: 3 mL/kg or less in first hour
      - Maintenance: 20-30 mL/kg/m²/hour
      - Monitor central venous pressure (CVP)
      - Measure central venous oxygen saturation (ScvO₂)
      - Target for CVP: 8-12 mmHg
      - Target for ScvO₂: 70-75%
  - Early goals
    - Blood pressure (BP): 90 mmHg (IPPV)
    - CVP: 8-12 mmHg
    - Central venous oxygen saturation (ScvO₂): 70-75%
  - Other
    - Vasoactive medication
    - Nutrition support
  - Manager: 24 h
  - Sticker: Surviving Sepsis Campaing Blue Lives Matter

- Why: 1.3 million Americans die each year from sepsis
  - More deaths than lung cancer
  - More deaths than breast and prostate cancer combined

- How: Clinical pathways
  - Evidence-based and locally validated
  - Developed by a team of experts
  - Updated regularly

- What: Improved survival, reduced hospital stay, reduced costs

- When: National effort
  - Countries: Memorandum of understanding: 30 countries
  - Actions: International guidelines

- Why: Global effort
  - Efficacy: Reduced mortality, reduced hospital stay, reduced costs
  - Resources: Improved quality, improved outcomes

- How: International collaboration
  - Partnerships: National and international organizations
  - Actions: Implementation of guidelines

- What: Improved outcomes, global awareness, global impact

- When: Continuous improvement
  - Objectives: Long-term goals
  - Actions: Ongoing evaluation, adaptation, dissemination

- Why: Continuous improvement, adaptation, dissemination
  - Resources: Ongoing evaluation, adaptation, dissemination
  - Objectives: Long-term goals
Do they work?

Improvement in Process of Care and Outcomes After a Multi-Dimension Severe Sepsis Educational Program in Spain

What is the mechanism?
Looking towards new data

Major advances in diagnosis

- Standard approach to diagnosis of infection is unchanged
- No randomized trials of shock diagnosis
- 2 major guidelines, expert opinion

Major advances in diagnosis

<table>
<thead>
<tr>
<th>Action</th>
<th>Condit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic</td>
<td></td>
</tr>
<tr>
<td>Clinical diagnosis in the criterion</td>
<td>SBP&lt;90</td>
</tr>
<tr>
<td>Lactate value: 4.0 mmol/L or more</td>
<td></td>
</tr>
<tr>
<td>Blood pressure: 130 mmHg &gt; systolic or diastolic</td>
<td></td>
</tr>
<tr>
<td>Perioperative infections, training needs, directed resuscitation, molecular tests</td>
<td></td>
</tr>
</tbody>
</table>

- ESCM states elevated lactate without hypotension may be “shock”
- Broad variability in certain aspects of shock definition
  - SBP threshold
  - “Despite fluid resuscitation”
  - Vasopressor dose
  - Lactate thresholds.
Do we need devices to diagnose sepsis?

- Invasive hemodynamic devices
  - PAC catheter
  - ScrO₂ catheter

- Non invasive hemodynamic devices
  - Focused cardiac ultrasound
  - Pulse contour analysis

Do we need devices?

- Not included in clinical criteria from 2001, 2014
- Can assist in determining the hemodynamic perturbations

Do we need devices?
### Major advances in treatment

- Did not address all aspects of therapy
- We did address prompt treatment of septic shock (rescue and stabilization)
- Avoided strategies for late / persistent shock
- Discuss only selected topics today

### Major advances in fluids

- 5 major trials
- > 12,000 subjects
- Extensively addressed all aspects
- May have hastened prompt treatment of septic shock (rescue and stabilization) of balanced electrolyte solutions
- Avoided strategies for late / persistent shock
- Discuss only selected topics today
Major advances in fluids

- More than 6 potential solutions to test, traditional fixed 1:1 randomization designs may be limited
- May require novel adaptive designs
- Split study
- Will the initial fluid bolus remain mandatory?

Major advances in protocols

- EGDT
- Hgb thresholds
- MAP targets
- Lactate guided resuscitation

Major advances in protocols

- But what is next for the “prompt” resuscitation?
- Major challenge for clinical practice guideline development when “usual care” wins
- Rely on clinical acumen / diffusion of best practice
- Difficult to assess “quality of care”
Proposed algorithm for prompt diagnosis and treatment

Derived from:
- Evidence in systematic review
- Protocolized standard care arm of the ProCESS trial
- NQF 5500 bundle
- Typical practice at the CRISMA Center, University of Pittsburgh

This is not:
- A rigorous protocol to be tested in an RCT
- Meant to standardize care
- The term “consider” is in the algorithm TEN times
Next steps for the SSC

Conclusions

Conclusions
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