SEPSIS PROTOCOL DESIGN

Management

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Disclosures

- Received funding from:
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- Consulting fees from Beckman Coulter, Edwards, Cytovale

- Member, Surviving Sepsis Campaign, ATS representative
Caveats

• I use sepsis protocols in my clinical care in a mixed medical-neuro ICU

• We will discuss elements of management, not whether they should individually be regulated

• Prompt consideration of what your local hospital is or is not already doing for sepsis
• Review where to find evidence for elements of a sepsis protocols

• Some elements of state-of-the-art management

• Illustrative example
Where do we look?

Policy mandates

Systematic reviews

Primary research

Clinical guideline statements
Where do we look?
Sense of time across sources

- Surviving Sepsis Campaign 2012
- SEP1 bundle from CMS
- JAMA algorithm, 2015
- RCTs
Sense of time across sources

3 to 48 hours

Stabilization and management

SSC 2012

SEP1

Systematic reviews

RCT

RCT

RCT
Primary elements of management (after recognition and risk stratification)

- Identification and control of sepsis source
- Timely administration of antibiotics
- Hemodynamic support for shock with appropriate monitoring
- Explicit use of serum lactate
All those physical measures used to control a focus of invasive infection and to restore the optimal function of the affected area.

John Marshall

- Drainage of closed space infection, liquid
- Debridement or physical removal of infected tissue/device
- Abdomen, chest, skin, soft tissue
99 Medical – surgical ICUs
3,663 patients severe sepsis, septic shock
2011 – 2013

OR for source control: 0.81
(95%CI: 0.65, 0.99, p=0.04)
E. Source Control

1. A specific anatomical diagnosis of infection requiring consideration for emergent source control be sought and diagnosed or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hr after the diagnosis is made, if feasible (grade 1C).

2. When infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred (grade 2B).

3. When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (e.g., percutaneous rather than surgical drainage of an abscess) (UG).

4. If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established (UG).
Timely administration of antibiotics

- General concept:
  Shorter time to appropriate antibiotic therapy saves lives

- Varying data about what time cutoffs for what patients
Timely administration of antibiotics

- Early Antibiotics
- Standard Antibiotics
- 4 Hour Delay
Timely administration of antibiotics

Meta analysis of >6 studies
18,000 patients

OR for in hospital mortality if more than 3 hrs =
1.16 (95% CI:0.92, 1.46)

### Recommendations

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Severe Sepsis</th>
<th>Septic shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surviving Sepsis Campaign, 2012 *</td>
<td>1 hr of recognition</td>
<td>1 hr of recognition</td>
</tr>
<tr>
<td>CMS SEP1 bundle</td>
<td>3 hr of recognition</td>
<td>3 hr of recognition</td>
</tr>
</tbody>
</table>

* Strong recommendation, moderate quality of evidence
Hemodynamic support (vasopressors for shock)

- SOAP II trial
- 1,044 septic shock
- More arrhythmias in dopamine vs. norepinephrine

Hemodynamic support

- Not specified in CMS SEP1 bundle
- Appropriate for patients with septic shock (defined?) who are not responsive to initial fluid challenge

## Recommendations

<table>
<thead>
<tr>
<th>Vasopressor choice</th>
<th>Role</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>Primary</td>
<td>Moderate</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Secondary</td>
<td>Low</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>Adjunct, norepi sparing</td>
<td>Moderate</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Primary if bradycardia</td>
<td>Low</td>
</tr>
</tbody>
</table>

Serum lactate measurement

- Prognostic marker for low organ / tissue perfusion
- Robust association in more than > 100 cohorts
- Not a diagnostic marker
- Unclear role in management protocols

Seymour et al. JAMA, 2016
Serum lactate measurement

**Sepsis CMS Core Measure (SEP-1)**

- Measure within 3 hrs
- Repeat within 6 hrs
- Measure every 2 hrs during guided resuscitation protocol
- 49% reduction in odds of death

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**Early Lactate-Guided Therapy in Intensive Care Unit Patients**

A Multicenter, Open-Label, Randomized Controlled Trial

Tim C. Jensen¹, Jaap van Bommel², F. Jeroen Schoonhoven³, Steven J. Slooff Visser⁴, Johan J. van der Weerd⁵, Alex P. Limo³, Mark P. Willemse⁶, and Jan Brand⁷, for the LACAT study group⁸

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**STOPPING SEPSIS**

*Saving Lives in Pennsylvania*
### Recommendations

<table>
<thead>
<tr>
<th>Lactate measurement</th>
<th>Purpose</th>
<th>Timing</th>
<th>Recommended by..</th>
</tr>
</thead>
<tbody>
<tr>
<td>First measurement</td>
<td>Help determine if shock present or not</td>
<td>Triage or immediate at sepsis recognition</td>
<td>SSC – dx criteria SEP1, mandated</td>
</tr>
<tr>
<td>Repeat measure</td>
<td>Response to initial resuscitation</td>
<td>Minimum- 2 hrs Max – 6 hrs</td>
<td>SSC, low quality SEP1, mandated RCTs, improve mortality</td>
</tr>
</tbody>
</table>
Reassessment after a change

Turn the dial → Check the water temp

Intervene on sepsis → Check on the patient

STOPPING SEPSIS
Saving Lives in Pennsylvania

pennsylvania
DEPARTMENT OF HEALTH
## Reassessment after a change

<table>
<thead>
<tr>
<th>Source</th>
<th>Recommendation</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMS SEP1 bundle</td>
<td>Assessment of volume status, tissue perfusion</td>
<td>“Best practice”</td>
</tr>
</tbody>
</table>

**Focused physical exam must include:**
- Vital signs
- Cardiopulmonary exam
- Capillary refill
- Peripheral pulse evaluation
- Skin exam

**OR any two of the following:**
- Central venous pressure
- Central venous oxygen
- Bedside cardiovascular ultrasound
- Passive leg raise or fluid challenge
What have we not covered

<table>
<thead>
<tr>
<th>Hemodynamic monitoring</th>
<th>Static</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Non-invasive</td>
<td>measures</td>
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<table>
<thead>
<tr>
<th>Adjuncts</th>
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<tbody>
<tr>
<td>Corticosteroids</td>
<td>IVIG</td>
</tr>
<tr>
<td>Sedation</td>
<td>Nutrition</td>
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<tr>
<td>Ventilator support</td>
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<table>
<thead>
<tr>
<th>Intravenous fluids</th>
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<tbody>
<tr>
<td>Type</td>
<td>Denouement</td>
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<tr>
<td>Dose</td>
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Wrapping up

• Many steps to state of the art sepsis care

• Core elements include:
  • Initial recognition, risk stratification
  • Source control
  • Antibiotics
  • Lactate measurement
  • Fluids
  • Hemodynamic support
  • Re-assessment

Seymour et al. JAMA, 2015