Severe Sepsis and Septic Shock

Ensuring Best Practices Through Core Measures

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Objectives

- **Discuss** how sepsis protocols might improve outcomes

- **Summarize** data/documentation requirements
  - Center of Medicare and Medicaid Services (CMS) core measures

- **Examine** an approach to an interdisciplinary sepsis protocol

- **Identify** the limitations and challenges

- **Consider** possible future directions
Background: What and Why

- **Sepsis**: Body’s overwhelming, life threatening response to infection
  - Tissue damage
  - Organ failure
  - Death

- Signs and Symptoms?
  - Combination
  - Streamlined and efficient identification
Background: What and Why

Hospitalizations for and with sepsis

NOTE: Significant linear trend from 2000 through 2008 for both categories.

From 2000 – 2008, hospitalization rate for those with sepsis as principal or secondary diagnosis increased by 70%.

In 2009, accounted for almost $15.4 billion aggregate hospital cost. Most expensive reason for hospitalization.

In 2009, in-hospital mortality rate of sepsis ~16% versus 2% in hospitalizations for other diagnoses.

Sepsis mortality ranges 16 – 49% for all ages. Approximately 25%.

Sepsis CMS Core Measures: SEP-1

Early Management Bundles
- Severe sepsis
- Septic shock

Two time frames
- 3 hour
- 6 hour
SEP-1: Why Bundles?
The Literature

- Multicenter efforts to promote bundles ➔
  - Guideline **compliance, lower hospital mortality** (Ferrer, 2008)

- Compliance of <30% ➔
  - **Mortality reduction of 4-6%** (Ferrer, 2008 and Levy, 2010)

- Compliance of 52% ➔
  - **Mortality reduction >20%** (Levy, 2010)

- All bundle elements complete vs. incomplete ➔
  - **Mortality difference of 14%** (Coba, 2011)

See References section for citations
SEP-1: Definitions

Defining Severe Sepsis and Septic Shock
Sepsis: SIRS + infection source

Any two

- **T**: >38.3 or <36°C
- **HR**: >90
- **RR**: >20
- **WBC**: >12,000 or <4,000 OR Bands >10%
### Severe Sepsis: Sepsis + organ dysfunction

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP/MAP</td>
<td>• SBP &lt;90 mmHg OR drop &gt;40 OR • MAP &lt;65</td>
</tr>
<tr>
<td>SCr/UOP</td>
<td>• SCr &gt;2.0 OR • UOP &lt;0.5 mL/kg/min x 2 hr</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>• &gt;2 mg/dL</td>
</tr>
<tr>
<td>Platelet</td>
<td>• &lt;100,000</td>
</tr>
<tr>
<td>INR/PTT</td>
<td>• INR &gt;1.5 OR • PTT &gt;60 s</td>
</tr>
<tr>
<td>Respiratory</td>
<td>• Mechanical ventilation, bipap mask</td>
</tr>
<tr>
<td>Lactate</td>
<td>• &gt;2 mmol/L</td>
</tr>
</tbody>
</table>
Severe Sepsis: Sepsis + organ dysfunction

- OR documentation of severe sepsis diagnosis by provider
- OR pre-hospital documentation
Septic Shock: Severe sepsis AND ...

Within 1 hr after IVF 30 ml/kg
- MAP <65
- SBP <90
- SBP decrease >40

OR documented in chart!

Lactate >4
SEP-1: Bundles

Treating Severe Sepsis and Shock: All or Nothing
SEP-1: Severe Sepsis Bundle

**Severe Sepsis**
- Serum lactate
- Blood cultures Pre-ABX
- Give ABX
- Repeat lactate if >2

**Septic Shock**
- IVF ≥30 mL/kg
- Repeat volume/perfusion assess
- Pressors if low BP

< 3h
< 6h
Antibiotics (ABX): ASAP!!!
Intravenous Fluids: Crystalloids

- Normal saline OR lactated ringers
- No situation stated in which to forego 30 mL/kg
Repeat Assessment: Volume Status and Tissue Perfusion

Focused Physical Exam
- Vitals
- Cardiopulmonary exam
- Capillary refill
- Peripheral pulse
- Skin exam

Focused Physical Exam
- Central venous pressure
- Central venous oxygen
- Bedside CV ultrasound
- Passive leg raise/ fluid challenge

All OR Any Two
Protocolizing Sepsis Management
Interdisciplinary Sepsis Protocols
Pharmacist involvement in a multidisciplinary initiative to reduce sepsis-related mortality

Background and Baseline

- **Wake Forest Baptist Health**: 885-bed, tertiary care center
- **Sepsis bundle initiated**: 60.9%
- **Bundle initiation <1 hour**: 5%
- **Antibiotics <1 hour**: 5.4%
- **Mean time to antibiotics**: 6.6 hours

Code Sepsis Cascade

1. Bedside RN
2. Rapid Response
3. Rapid Response RN
4. Interdisciplinary Pages
5. Code Sepsis
Individual Care Components

- **Education**: RNs, MDs, PharmDs, hospital awareness
- **Pharmacy Department**: Timely antibiotics

Impact: Time to Antibiotics

Impact: Mortality

Influence of an Institution-Specific Sepsis Protocol on the Adequacy of Empiric Antibiotics

Empiric Antibiotic Protocol

Background: Wake Forest Baptist Health

- Institution-specific sepsis ABX protocol per local antibiogram, guidelines

Design

- Retrospective comparison of pre and post-implementation periods

Exclusions

- Negative or contaminated/colonized cultures
- Non-empiric therapy
- Outside scope of protocol (post-implementation)

Primary endpoint:

- Adequacy of ABX

Secondary endpoints:

- Number of ABX per patient
- 28-day mortality

Results

- **Adequate ABX:**
  - Pre-implementation: 68%
  - Post-implementation: 85%
  - \( P < 0.05 \)

- **Secondary analysis:** If ABX were prescribed per protocol
  - Antibiotics per patient: 2.47 → 2.11
  - \( P = 0.017 \)

- **28-day mortality:**
  - Pre-implementation: 32%
  - Post-implementation: 24%
  - \( P = 0.390 \)
ED Code Sepsis

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SIRS x 2 + Suspect Infection → POC lactate → Evidence of new organ dysfunction

Related to Infection?

Yes/unclear → Internal Sepsis

Initial lactate >2 → Repeat

If persistent hypotension s/p bolus OR lactate ≥4

No → Stop process

Overhead code sepsis + prepare for ICU
Code Sepsis: Pharmacy and Antibiotics

- **Hospital Policy:** Wake Forest pharmacy protocol
  - Code sepsis with page to pharmacy
  - Patient work-up
  - At 15 minutes → Call RN/MD with recommendations
  - Ensure expedient antibiotic deliver (<15 minutes)
  - Document in log

- **Contrast with Wake Forest protocol:** Hand delivery of ABX
Pharmacy: Guideline and Checklist

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RPh ABX Guide

- CNS
- CAP
- HCAP/unknown
- Intra-abd
- Skin/soft tissue
# Code Sepsis: Documentation

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## Pharmacy: Tracer log

<table>
<thead>
<tr>
<th>Date</th>
<th>RPh Initial</th>
<th>Time of Code Sepsis Alert</th>
<th>Time of 1st call to identify source</th>
<th>Time of 2nd call if no info from 1st call</th>
<th>Patient Name</th>
<th>MRN</th>
<th>Name of person you contacted</th>
<th>Time of hand delivery if drug not in Pyxis</th>
<th>RN name/signature</th>
<th>RX Tech Initial</th>
</tr>
</thead>
</table>

**Required to fill out for every code sepsis alert**
Triage: Documentation

Retrospective:
- Bundle compliance → ALL COMPONENTS
- Outcomes
Documentation: Exclusions

- **Age** < 18 years
- **Length of stay (LOS)** > 120 days
- **Transfer** from another acute care facility
  - LTAC, acute rehab, acute care hospital
- Severe sepsis: **Comfort care or death** < 3 hours
- Septic shock: **Comfort care or death** < 6 hours
- **Intravenous ABX** x 24+ hours prior to severe sepsis
- **Refusal** of any bundle component per patient/caregiver
Initiate for all patients being treated for Sepsis/Severe Sepsis/Septic Shock  

**SIRS Criteria**
- [ ] HR > 90
- [ ] RR > 20
- [ ] WBC > 12,000 or < 4,000 or 10% bands
- [ ] Temp > 100.4 (38C) or < 96.8 (36C)

SIRS criteria x2 *plus* Possible Source of Infection?  
- [ ] Yes
- [ ] No
  
  **Source:** __________

**Draw POC Lactate (call lab 21020)**  
- **Time:** __________
- **Result:** __________

**Does the patient have Evidence of New Organ Dysfunction?**  
- [ ] Yes
- [ ] No

  - Lactate > 2.0 mmol/L
  - Bilirubin > 2 mg/dl
  - Creatinine > 2.0, or Urine Output < 0.5ml/kg/hr for 2 hours
  - SBP < 90, or MAP < 65, SBP ↓ by 40mmHg from baseline
  - Acute Respiratory Failure—Evidenced by NEW Mechanical Ventilation, BiPAP or CPAP

  - INR > 1.5 or PTT > 60 sec
  - Platelet Count <100k
  - Altered Mental Status (unrelated to neuro path)

**Are SIRS Criteria x2 and Evidence of New Organ Dysfunction related to an Infection?**  
- [ ] Yes
- [ ] No

  If Yes or Unclear, Activate an ED Internal Code Sepsis  
  - **Time Activated:** __________

<table>
<thead>
<tr>
<th>Resuscitation Bundle</th>
<th>Result</th>
<th>Time</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood cultures obtained (Prior to ABX initiation)</td>
<td>Order in Meditech</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administer broad spectrum antibiotics (See recommendations in the order set)</td>
<td>Suspected Source</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Administer Fluid Bolus, unless contraindicated  
  **CMS/SSC recommends 30ml/kg crystalloid (NS or LR) on a pressure bag for Initial Lactate > 4.0 or hypotension** | WT in kg:  
  30ml/kg = (__________ ) | Fluid Bolus End Time documented in Meditech | |
<table>
<thead>
<tr>
<th>6 Hour Bundle</th>
<th>Result</th>
<th>Time</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-measure lactate if initial $\geq 2.0$ mmol/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For persistent hypotension after 30ml/kg infusion,</td>
<td>$\square$ Norepinephrine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>initiate Vasopressors;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>After Fluid Bolus, does the pt have persistent hypotension or a Lactate &gt; 4.0, if yes dial &quot;44&quot; and call overhead &quot;Code Sepsis&quot;</strong></td>
<td>$\square$ Hypotension  $\square$ Lactate &gt; 4.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ED MD to notify Intensivist</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Completed by ER MD/LIP or Intensivist</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Required: LIP documented reassessment of volume status and tissue perfusion,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If persistent hypotension after fluid bolus, Initial Lactate &gt; 4.0 or documentation of Septic Shock</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Either:</strong> Focus exam (after fluid resuscitation) including VS, cardiopulmonary, cap refill, pulse &amp; skin findings</td>
<td>$\square$ Focus Exam  or $\square$ Central Line Insertion  Time: $\square$</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Or two of the following:</strong> CVP, ScvO2, Bedside cardiovascular ultrasound, fluid challenge or passive leg raise</td>
<td>$\square$ CVP  $\square$ ScvO2  $\square$ ECHO  $\square$ Fluid Challenge</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Code Sepsis: Reassessment

Septic Shock Reassessment

Reassessment

Date of exam: _
Time of exam: _

Vital Signs:

<table>
<thead>
<tr>
<th>Date Time</th>
<th>Temp</th>
<th>Pulse</th>
<th>Resp</th>
<th>B/P</th>
<th>Pulse Ox</th>
<th>O2 Delivery</th>
<th>O2 Flow Rate</th>
<th>FiO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/11 0000</td>
<td></td>
<td>110</td>
<td>18</td>
<td>102/53</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>03/10 2313</td>
<td>37.2</td>
<td>99</td>
<td>18</td>
<td>88/38</td>
<td>98</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cardiac assessment: normal heart sounds, regular rate & rhythm, no ectopy
Respiratory assessment: clear to auscultation
Capillary refill assess: brisk
Peripheral pulse assess:
  Radial pulse: 3+
  Dorsalis pedis pulse: 3+
  Posterior tibialis pulse: 3+
Skin color: normal color
# Code Sepsis: Monitoring

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<table>
<thead>
<tr>
<th></th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>Jun</th>
<th>Jul</th>
<th>Aug</th>
<th>Sep</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door to Antibiotics</td>
<td>2:34</td>
<td>2:05</td>
<td>1:57</td>
<td>1:50</td>
<td>1:58</td>
<td>1:58</td>
<td>1:56</td>
<td>1:54</td>
<td>1:35</td>
<td>1:26</td>
<td>1:25</td>
<td>1:16</td>
</tr>
<tr>
<td>Door to Fluid</td>
<td>1:13</td>
<td>1:09</td>
<td>1:04</td>
<td>1:01</td>
<td>0:55</td>
<td>0:50</td>
<td>0:43</td>
<td>0:40</td>
<td>0:38</td>
<td>0:38</td>
<td>0:38</td>
<td>0:40</td>
</tr>
<tr>
<td>Door to Lactate</td>
<td>0:34</td>
<td>0:34</td>
<td>0:32</td>
<td>0:29</td>
<td>1:29</td>
<td>0:26</td>
<td>0:26</td>
<td>0:24</td>
<td>0:22</td>
<td>0:22</td>
<td>0:24</td>
<td>0:24</td>
</tr>
<tr>
<td>Door to Blood Culture</td>
<td>0:30</td>
<td>0:29</td>
<td>0:27</td>
<td>0:28</td>
<td>0:26</td>
<td>0:25</td>
<td>0:26</td>
<td>0:24</td>
<td>0:22</td>
<td>0:22</td>
<td>0:22</td>
<td>0:24</td>
</tr>
</tbody>
</table>

Pharmacy implemented into code sepsis: March 2015
Protocol: Limitations and Challenges

- Determining \( t = 0 \)
- Severe sepsis actually related to infection
- Time from **door to identification**
  - Thus time from **door to antibiotic**
- Lactate!
- Antimicrobial stewardship after stabilization
The Third International Consensus Definitions for Sepsis and Septic Shock: The end of SIRS?
SEP-3: New Definitions

- February 2016

- Purpose:
  - Replace previous definitions
  - Greater consistency for research
  - Earlier recognition and more timely recognition

**SEP-3: Sepsis**

**LIFE-THREATENING ORGAN DYSFUNCTION**

- ARDS
- Sys 80 Dys 40 Map 56
- AKI

**CAUSED BY**

- BCx
- UTI

**DYSREGULATED HOST RESPONSE TO INFECTION**
SEP-3: New Definitions of Sepsis

**Sepsis I-II:**  
Sepsis = [Suspected infection] + [SIRS]

**Sepsis-III:**  
Sepsis = [Suspected infection] + [qSOFA] + [SOFA]

- Infection indicator
- Mortality indicators

qSOFA: The New SIRS Criteria?

SEP-3: Septic Shock

SEPSIS + NOT hypovolemic

VASOPRESSORS TO MAINTAIN MAP ≥65 mmHg

AND

SERUM LACTATE LEVEL ≥18 mg/dL

SEP-3: Implications

- New algorithms
- Potentially quicker identification?
- Less lactate problems
- New pool of limitations
- CMS revisions to requirements

Infection + qSOFA ≥2 → SOFA ≥2 → Sepsis → Adequate IVF → Pressors AND lactate ≥2 → Septic shock

Antimicrobial Stewardship

Managing antibiotics after the fact
Antimicrobial Stewardship: Persistent Reassessment

- Risk of aggressive antibiotic use:
  - Overuse
  - Inappropriate use

- Should be an interdisciplinary effort
  - **MD**: Consistent re-evaluation of diagnosis
  - **RN**: Communication of antibiotic durations, clinical status
  - **PharmD**: Stewardship should be part of workflow!
    - Clinical, de-centralized pharmacists
    - **Infectious disease pharmacists**
Antibiotic Stewardship: Strategies

- **De-escalation** based on culture results
  - Consider contamination/colonization
  - Consider negative cultures despite polymorphonuclear leukocytes (PMNs)
  - MRSA screen, urinalysis

- **Consider other causes** of presentation
  - **Respiratory distress:** Fluid overload
    - CHF, liver cirrhosis, CKD/ESRD
  - **Shock:** Cardiogenic/hypovolemic/hemorrhagic
  - **Reactive leukocytosis:** Work of breathing, trauma, seizures, ACLS, steroids


Questions?