Early Recognition and Management of Severe Sepsis and Septic Shock

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Objectives

- Discuss the use of screening tools for early recognition and treatment of severe sepsis and septic shock
- Review the current evidenced based guidelines from the Surviving Sepsis Campaign
- Discuss Early Goal Directed Resuscitation for Severe Sepsis and Septic Shock

No Disclosures
Severe Sepsis is one of the Time Critical Emergencies

Time Critical Emergencies

- Severe Sepsis/Septic Shock – Highest mortality (5x greater than)
- Trauma
- STEMI
- Stroke
Sepsis is the leading cause of death in non-coronary care intensive care units, with a mortality rate between 30% and 50%.

From 2007 to 2009, over 2,047,038 patients were admitted with a sepsis-related illness:
- 52.4% are diagnosed in the ED
- 34.8% on the hospital wards
- 12.8% in the ICU

Definitions

Correct Coding for Sepsis

- Sepsis 995.91
- Severe Sepsis 995.92
- Septic Shock 785.52

There is NO diagnostic code for:
1. "Urosepsis"
2. "Septicemia"
3. "Sepsis syndrome"
4. "Sepsis syndrome in shock"
5. "Septicemia"
6. "Bacteremia"
7. "Gram negative sepsis"
8. "Gram positive sepsis"

Definitions (ACCP/SCCM)

- Systemic Inflammatory Response Syndrome (SIRS): 2 or more of the following
  - Fever or hypothermia (T >100.4 or < 96.8)
  - Tachycardia ( HR > 90)
  - Tachypnea ( RR > 20 or PaCO2 < 32)
  - Leukocytosis, leukopenia or left shift (WBC > 12,000, < 4,000 or > 10% bands)

- Sepsis
  - SIRS as a result of infection

Crit Care Med 1992;20:864-874
Definitions

- **Severe Sepsis**
  - Sepsis associated with organ dysfunction, hypoperfusion, or hypotension.
  - Hypoperfusion and perfusion abnormalities may include: lactic acidosis, oliguria or acute alteration in mental status.

- **Septic shock**
  - A subset of severe sepsis with hypotension (BP < 90 or drop of > 40 from baseline), despite adequate fluid resuscitation.

Sepsis: A Complex Disease

Systemic Inflammatory Response Syndrome to Septic shock: A Continuum
**Sepsis:** The presence (probable or documented) of infection together with systemic manifestations of infection

(More than just SIRS plus infection)

**TABLE 1. Diagnostic Criteria for Sepsis**

<table>
<thead>
<tr>
<th>Infection, documented or suspected, and some of the following:</th>
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<tbody>
<tr>
<td><strong>General variables</strong></td>
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<tr>
<td>Fever (&gt;38°C)</td>
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<tr>
<td>Hypotension (core temperature &lt;38°C)</td>
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<td>Heart rate &gt;100/min or more than two standard deviations above the normal value for age</td>
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<tr>
<td>Tachycardia</td>
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<td>Altered mental status</td>
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<tr>
<td>Significant increase or decrease in body weight (±10% from normal value)</td>
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<tr>
<td>Hypoperfusion (pH &lt;7.30 or &lt;140 mmHg or &gt;7.10 mmHg/L) in the absence of diabetes</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Inflammatory variables</strong></th>
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</thead>
<tbody>
<tr>
<td>Leukocytosis (WBC count &gt;12,000/μL)</td>
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<tr>
<td>Leukopenia (WBC count &lt;3,500/μL)</td>
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<tr>
<td>Normal WBC count with greater than 10% neutrophils</td>
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<tr>
<td>Plasma C reactive protein more than two standard deviations above the normal value</td>
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<tr>
<td>Plasma procalcitonin more than two standard deviations above the normal value</td>
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</tbody>
</table>
Table 1 Continued. Criteria for sepsis

<table>
<thead>
<tr>
<th>Hemodynamic variables</th>
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<tbody>
<tr>
<td>Arterial hypotension (SAP &lt;90 mm Hg, MAP &lt;70 mm Hg, or an SBP decrease &gt; 40 mm Hg)</td>
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<tr>
<td>Organ dysfunction variables</td>
<td></td>
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<tr>
<td>Arterial hypoxemia (PaO2/FiO2 &lt; 300)</td>
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<tr>
<td>Acute oliguria (urine output &lt; 0.5 ml/kg/hr for at least 3 hrs despite adequate fluid resuscitation)</td>
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<tr>
<td>Creatinine increase &gt; 1.5 mg/dL or 442 micromol/L</td>
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<tr>
<td>Coagulation abnormalities (INR &gt; 1.2 or platelet count &lt; 100,000 µL)</td>
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<tr>
<td>Resistant bowel sounds</td>
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<tr>
<td>Thrombocytopenia (platelet count &lt; 100,000 µL)</td>
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<tr>
<td>Hypokalemia (plasma total potassium &lt; 3.5 mmol/L or &lt; 50 mmol/L)</td>
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</table>

<table>
<thead>
<tr>
<th>Tissue perfusion variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperlactatemia (D-1 &gt; 1 mmol/L)</td>
</tr>
<tr>
<td>Decreased capillary refill or mottling</td>
</tr>
</tbody>
</table>

**Definitions**

- **Severe Sepsis:** Sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion
- **Sepsis-induced hypotension:** Systolic Blood pressure <90 mm Hg or MAP <70 mm Hg or SBP decrease > 40 mm Hg
- **Septic Shock:** Sepsis induced hypotension persisting despite adequate fluid resuscitation

**TABLE 2: Severe Sepsis**

- Severe sepsis definition = sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection)
- Lactate above upper limits laboratory normal
- Urine output < 0.5 ml/kg/hr for more than 2 hrs despite adequate fluid resuscitation
- Acute lung injury with PaO2/FiO2 < 200 in the absence of pneumonia as infection source
- Acute lung injury with PaO2/FiO2 < 200 in the presence of pneumonia as infection source
- C-reactive protein > 10 mg/L (71.8 µmol/L)
- Bilirubin > 2 mg/dl (34.2 µmol/L)
- Platelet count < 100,000 µL
- Coagulopathy (international normalized ratio > 1.5)

Manifestations of Organ Dysfunction in Severe Sepsis

- Altered LOC
- Confusion
- Acute Lung injury
- SpO2 < 90
- Bilirubin > 2
- INR > 1.5
- Tachycardia, ↓ CO, hypotension
- Oliguria
- Cr > 2.0
- Ileus, Peritonitis, Pancreatitis
- Platelet count < 100K

Multiple Organ Dysfunction and Mortality

Surviving Sepsis Campaign
Current Surviving Sepsis Campaign Guideline Sponsors

- American Association of Critical-Care Nurses
- American College of Chest Physicians
- American College of Emergency Physicians
- Australian and New Zealand Intensive Care Society
- Asia Pacific Association of Critical Care Medicine
- American Thoracic Society
- Brazilian Society of Critical Care (ABCC)
- Canadian Critical Care Society
- Chinese Society of Critical Care Medicine
- Chinese Society of Critical Care Medicine – Chinese Medical Association
- Emirates Intensive Care Society
- European Respiratory Society
- European Society of Clinical Microbiology and Infectious Diseases
- European Society of Intensive Care Medicine
- Infectious Diseases Society of America
- Indian Society of Critical Care Medicine
- International Pan Arab Critical Care Medicine Society
- Japanese Association for Acute Medicine
- Japanese Society of Intensive Care Medicine
- Pediatric Acute Lung Injury and Sepsis Investigators
- Society for Academic Emergency Medicine
- Society of Critical Care Medicine
- Society of Hospital Medicine
- Surgical Infection Society
- World Federation of Critical Care Nurses
- World Federation of Pediatric Intensive and Critical Care Societies
- World Federation of Societies of Intensive and Critical Care Medicine

2012 SSC Guidelines


Early Recognition and Treatment

- Screening for Sepsis
- Usefulness of Lactate in screening
- Early Antibiotic Treatment
Screening for Sepsis

- **2012 Severe Sepsis Guideline:**
  - "We recommend routine screening of potentially infected seriously ill patients for severe sepsis to increase the early identification of sepsis and allow implementation of early sepsis therapy" (grade 1C)

Routine Screening for Severe Sepsis

- Early recognition of sepsis and implementation of early evidenced based therapies improves outcomes and decreases mortality
- Sepsis screening tools should be utilized in all hospitals (ED, ICU and general medical ward)
Positive Triage Screen for Sepsis

- In a patient with suspected infection and 2 or more of the following: (3-100 rule)
  - Temp >100
  - HR > 100
  - Systolic BP < 100
  - RR > 20/Sp02 < 90
  - Altered LOC
Nurse response to positive Sepsis screen

- Initiate evaluation for Severe Sepsis/Septic Shock
- Order stat Lactate, CBC, Blood culture, UA/UC, metabolic profile
- Cardiac monitor, non-invasive BP monitor, oximetry
- Start IV fluids
- Notify physician immediately

Why lactate?

- When oxygen demand exceeds consumption, anaerobic metabolism results in lactic acidosis.
- Lactate is a surrogate marker for global tissue hypoxia (normal < 2mmol/L, Lactate > 4 = tissue hypoperfusion)
- An elevated lactate may identify a patient in early shock
Every hospital should be able to perform a lactate with results within 30 minutes

In a recent survey by the Minnesota Hospital Association, 24% of Minnesota hospitals are not able to perform a lactate.

“If a patient is sick enough to order a blood culture, then they are sick enough to order a lactate.” (Scott Davis, MD, Director of ICU SCH)

Link lactate to blood culture order

Early Antibiotics

- 2012 Severe Sepsis Guideline
  - “The administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis (grade 1C) should be the goal of therapy”
In septic shock every hour delay in antibiotic administration was associated with a 7.6% decrease in survival. (Kumar, Crit Care Med 2006; 34:1589)

Early Antibiotics Treatment

- **Empiric initial regimen:**
  - Piperacillin/tazobactam 4.5 gm IV q6h
  - Vancomycin 20mg/kg, max 2gm) IV stat then adjust per pharmacy

  If penicillin allergy, then:
  - Meropenem 1g IV q8hr

  If community acquired pneumonia suspected, add:
  - Levofloxacin 750mg IV q24hr or
  - Azithromycin 500mg IV q24hrs

Severe Sepsis/Septic Shock Protocol

- Every hospital should have a written protocol for the initial resuscitation of severe sepsis
  - Currently only 28% of Minnesota Hospitals have a sepsis protocol in the ED and 25% in the inpatient unit.

- Protocol based on:
  - 2012 Surviving Sepsis Campaign Guideline and Bundles
  - Utilizing Early Goal Directed Therapy for Severe Sepsis
2012 Severe Sepsis Guideline

“We recommend the **protocolized**, quantitative resuscitation of patients with sepsis induced tissue hypoperfusion (defined as hypotension persisting after initial fluid challenge or blood lactate ≥ 4.) This protocol should be initiated as soon as hypoperfusion is recognized and should not be delayed pending ICU admission” (grade 1C)

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**Trigger to implement severe sepsis/septic shock resuscitation protocol**

The patient has all three of the following:

1. Suspected infection
2. Meets SIRS criteria: (at least 2 of 4)
   - Temp > 100.4 or < 96.8F
   - RR > 20
   - HR > 100
   - WBC > 12,000 or < 4,000
3. Systolic BP < 100 after fluid bolus OR Lactate > 4, OR 2 or more organ dysfunctions

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**Early Goal Directed Resuscitation in Severe Sepsis**
Early Goal-Directed Therapy Results

**28-day Mortality**

- **Standard Therapy**
  - n=133
  - 49.2%
  - P = 0.01*

- **EGDT**
  - n=130
  - 33.3%

*Key difference was in sudden CV collapse, not MODS*

**Notes:**
- The trial compared standard therapy (n=133) vs. early goal-directed therapy (n=130).
- The primary outcome was 28-day mortality.
- Standard therapy included fluid resuscitation guided by central venous pressure and urine output targets.
- EGDT included hemodynamic monitoring, fluid resuscitation guided by lactate levels, and inotropic support as needed.

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**References:**
- Early Goal-Directed Therapy Results
Early Goal Directed Resuscitation Protocol

- Goal Directed Resuscitation
  - May start in ED or ICU
  - Recommend placement of a Central Line for monitoring of CVP, ScvO2 and administration of vasopressors if needed.
  - Arterial line recommended in septic shock requiring vasopressors
  - May require transfer to higher level of care if ICU care with invasive monitoring not available

Early Goal Directed Resuscitation

- Goals within 6 hrs:
  - CVP 8-12 mmHg
  - MAP ≥ 65
  - UO ≥ 0.5 ml/kg/hr
  - Superior vena cava oxygen saturation (ScvO2) of 70%
  - Lactate normalization

What is Central Venous Oxygen Saturation (ScvO2)?

- Venous blood gas sample from a central line
- ScvO2 reflects the balance between oxygen delivery (DO2) and oxygen demands

- ScvO2 decreases when DO2 is compromised or demand exceeds supply
- Normal value: 70%
Oxygen Delivery (DO₂)

- Goal in Resuscitation of Shock patients is to Maximize Oxygen Delivery
- \( DO₂ = \text{Cardiac Output} \times \text{Hgb} \times \text{SaO₂} \)

- Cardiac output can be increased by adding an inotrope such as dobutamine in patients with sepsis induced myocardial depression which will optimize oxygen delivery

Hemodynamic Support

- **Vasopressor:**
  - Norepinephrine is the first choice
  - Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed.
  - Vasopressin can be added to NE with intent of decreasing norepinephrine dose.

- **Inotropic Therapy:**
  - A trial of dobutamine up to 20 mcg/kg/min be administered for myocardial dysfunction suggested by elevated cardiac filling pressures or low cardiac output.
**Corticosteroids:**
- Do not use to treat septic shock if adequate fluids and vasopressors are able to restore hemodynamic stability. If not, give intravenous hydrocortisone alone at a dose of 200mg/day (continuous infusion preferred)
- Do not do ACTH stimulation tests

**Mechanical Ventilation**
- Target tidal volume — 6ml/kg to prevent ARDS

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**Resuscitation Bundles**
- Operationalize Guidelines
- Measurement of Quality

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**Surviving Sepsis Campaign/National Quality Forum Bundle**
- TO BE COMPLETED WITHIN 3 HRS*:
  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 mmole/L.

*"Time of presentation" is defined as the time of triage in the Emergency Department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements severe sepsis or septic shock ascertained through chart review.
Surviving Sepsis Campaign/National Quality Forum Bundle

- TO BE COMPLETED WITHIN 6 HRS*

5. Apply vasopressors (for hypotension that does not respond to fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mmHg.

6. In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥ 4 mmole/L:
   - 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 mmHg, ScvO2 of ≥70% and lactate normalization.

How to Implement a Sepsis Protocol

- Organize a Team
- Process Improvement
- Useful Resources
  - Surviving Sepsis Campaign
  - Minnesota Hospital Association

Sepsis Care at Ridgeview Medical Center
Sepsis Chronicle

- Participants in the IHI "Improving Outcomes for the High Risk and Critically Ill Patient" Collaborative
- Inaugural multidisciplinary Sepsis Huddle Team 2008

Sepsis Huddle Team

- 2008 began weekly 30 minute huddles
- Membership
  - ED Physician
  - Hospitalist
  - Primary Care Providers
  - ED Nursing
  - Critical Care Nursing
  - Laboratory
  - Pharmacy
  - Respiratory Care
  - Quality Improvement
- Rapid cycle tests of change
- Frequent analysis of metrics

Pearls of Success

- Hospital wide colored pictorial Stop Sepsis algorithm
- Adult Severe Sepsis/Septic Shock order set
- ED Severe Sepsis/Septic Shock Screening tool and checklist
- RRT protocol includes screening for severe sepsis on the inpatient units
- Sepsis Response Team
Sepsis Team

- ED physician
- ED RN
- Respiratory Therapist
- Pharmacist
- Lab technician
- Radiology technician
- ICU RN
- ICU MD

Sepsis scorecard (by month)

Measures of Success

<table>
<thead>
<tr>
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<th>2007 (Baseline)</th>
<th>2013</th>
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<tbody>
<tr>
<td>Mortality - Total</td>
<td>39%</td>
<td>24.3%</td>
</tr>
<tr>
<td>Mortality excluding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>palliative care pts</td>
<td>5.8%</td>
<td></td>
</tr>
</tbody>
</table>
72 yr old female

- Presented to the ED with a complaint of 36 hrs of low back pain and “flu like” symptoms with vomiting and diarrhea.
- Initial Vitals: (2:49am) BP 138/62, HR 93, T 98.6 R 20
- Repeat Vitals: (4:03am) T 103, BP 143/56, HR 108, R 22
- Lab: WBC 12.2 with 93% PMNs, Lactate 3.4, UA positive nitrites.
- Blood cultures, broad spectrum antibiotics and IV fluids started in the ED.
- Abd/Pelvic NC CT scan: 3mm stone distal left ureter with mild to mod hydronephrosis

Urology was consulted and the patient was admitted to a monitored bed at 5:00am

- At 7:41am she became abruptly hypotensive with systolic BP in the 70s.
- Crystalloid volume resuscitation was initiated and was taken to the OR promptly for urethral stenting.
- Intraoperatively, CVP and arterial lines placed
  - Initial CVP 6, MAP 50, ScvO2 82%
  - CVP improved with fluid resuscitation
  - Required Norepinephrine to maintain a MAP > 65
  - Lactate 6 hrs later 1.9 mmole/L
- She developed acute kidney injury and a mild coagulopathy. Blood and Urine cultures: positive for E.coli.

Bundle goals achieved?

- 3 hr:
  - Lactate drawn – yes
  - Blood cultures prior to antibiotics - yes
  - Broad spectrum antibiotics – yes
  - Fluids: 30ml/kg for hypotension – yes
- 6 hr
  - Apply vasopressors for hypotension – yes
  - Measure CVP – yes
  - Measure ScvO2 – yes
  - Remeasure Lactate if elevated - yes
Summary

Key Points

- Recognize severe sepsis/septic shock as a time critical emergency
- Start screening for Sepsis – in the ED, Medical Floor and ICU
- Utilize lactates if screen positive for sepsis
- Implement a severe sepsis/septic shock protocol in your hospital (in the ED and inpatient units)
- Organize a team, identify champions
- Measure your results and work to continually improve
Resources

- Surviving Sepsis Campaign
  - http://www.survivingsepsis.org
- Minnesota Hospital Association
  - Sepsis Physician Education Simulcast – March 13th
  - Sepsis Seminar – April 2nd
  - http://www.mnhospitals.org

Thank you