Sepsis: Early Recognition and Pre-Hospital Treatment

April 20, 2017

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Disclosures

- No financial relationships with pharmaceutical companies, smart phone applications
- No discussion of off-label use of medication
Audience Query

- Outpatient / office practice
- Urgent care / emergency care
- Skilled nursing facility
- Inpatient / hospital
Educational Objectives

- Update definitions of sepsis and septic shock based on current consensus recommendations
- Review the importance of early recognition of sepsis based on current evidence
- Recognize early warning signs of sepsis and take appropriate next steps
- Highlight changes with the 2016 Surviving Sepsis Campaign recommendations
- Plan pre-hospital treatment, including fluid resuscitation and early antibiotics
Sepsis is...

- A complication of some infections that involves the body’s overwhelming and life-threatening inflammatory response, which can progress to cause tissue damage, organ failure, and death.

- (previously) arbitrarily defined as having an infection accompanied by at least 2 systemic inflammatory response syndrome (SIRS) criteria:
  - Temp > 100.4°F or < 96.8°F
  - HR > 90
  - Respiratory rate > 20 or PaCO₂ < 32 mm Hg or respiratory failure requiring positive pressure ventilation
  - WBC > 12,000 or < 4,000 or >10% bands
Changing the paradigm

- SIRS criteria lack sensitivity and specificity
- SIRS criteria may be positive in normal / physiologic adaptation and normal organ function
- SIRS criteria do a poor job predicting mortality
Sepsis is...

• Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)
  – “Sepsis should be defined as life-threatening organ dysfunction caused by dysregulated host response to infection.”
Sepsis is...

• Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)
  – “Sepsis should be defined as life-threatening organ dysfunction caused by dysregulated host response to infection.”
  – Organ dysfunction represented by an increase in Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more
## SOFA Score

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score\(^a\)

<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
<th>Score</th>
<th>Score</th>
<th>Score</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Respiration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>(\text{Pao}_2/\text{FiO}_2), mm Hg (kPa)</td>
<td>(\geq 400) ((53.3))</td>
<td>(&lt; 400) ((53.3))</td>
<td>(&lt; 300) ((40))</td>
<td>(&lt; 200) ((26.7)) with respiratory support</td>
<td>(&lt; 100) ((13.3)) with respiratory support</td>
</tr>
<tr>
<td><strong>Coagulation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelets, (\times 10^3/\mu)L</td>
<td>(\geq 150)</td>
<td>(&lt; 150)</td>
<td>(&lt; 100)</td>
<td>(&lt; 50)</td>
<td>(&lt; 20)</td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilirubin, mg/dL ((\mu\text{mol/L}))</td>
<td>(&lt; 1.2) ((20))</td>
<td>(1.2-1.9) ((20-32))</td>
<td>(2.0-5.9) ((33-101))</td>
<td>(6.0-11.9) ((102-204))</td>
<td>(&gt; 12.0) ((204))</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MAP (\geq 70) mm Hg</td>
<td></td>
<td></td>
<td>Dopamine (&lt; 5) or dobutamine ((\text{any dose}))(^b)</td>
<td>Dopamine (5.1-15) or epinephrine (\leq 0.1) or norepinephrine (\leq 0.1)(^b)</td>
<td>Dopamine (&gt; 15) or epinephrine (&gt; 0.1) or norepinephrine (&gt; 0.1)(^b)</td>
</tr>
<tr>
<td><strong>Central nervous system</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasgow Coma Scale score(^a)</td>
<td>15</td>
<td>13-14</td>
<td>10-12</td>
<td>6-9</td>
<td>&lt;6</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine, mg/dL ((\mu\text{mol/L}))</td>
<td>(&lt; 1.2) ((110))</td>
<td>(1.2-1.9) ((110-170))</td>
<td>(2.0-3.4) ((171-299))</td>
<td>(3.5-4.9) ((300-440))</td>
<td>(&gt; 5.0) ((440))</td>
</tr>
<tr>
<td>Urine output, mL/d</td>
<td></td>
<td></td>
<td></td>
<td>&lt;500</td>
<td>&lt;200</td>
</tr>
</tbody>
</table>

Abbreviations: \(\text{FiO}_2\), fraction of inspired oxygen; MAP, mean arterial pressure; \(\text{Pao}_2\), partial pressure of oxygen.  
\(^{a}\) Catecholamine doses are given as \(\mu\text{g/kg/min}\) for at least 1 hour.  
\(^{b}\) Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

\(^{a}\) Adapted from Vincent et al.\(^{27}\)
There’s an app for that

MedCalx

Sepsis Clinical Guide

SmartIntern: Sepsis 2016
Septic shock is... 

• Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)
  – “Septic shock should be defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.”
  • Vasopressor requirement to maintain MAP $\geq 65$ mm Hg
  OR
  • Lactate $> 2$ mmol/L despite adequate fluid resuscitation (in the absence of hypovolemia)
Sepsis is Costly

- More US deaths from sepsis than from prostate cancer, breast cancer, and AIDS combined
- According to AHRQ, sepsis is the most expensive condition treated in the US
- Readmission rates for sepsis are 2-3 times higher than readmission rates for heart failure, pneumonia, COPD
- $23.7 billion in health care expenditures in 2013
Good News

• Early recognition and treatment decrease mortality

• Since implementing early diagnosis and treatment with IVF and antibiotics, absolute mortality rates have decreased 16-23%
Risk factors for sepsis

- Type of infection:
  - Lungs (35%)
  - Urinary tract (25%)
  - Skin (11%)
  - Gastrointestinal tract (11%)
Risk factors for sepsis

- Type of infection: lungs, urinary tract, skin, GI tract
- Type of patient:
  - Young (< 1 year old)
  - Older (≥ 65 years old)
  - Immune compromised
  - Co-existing chronic medical conditions (diabetes, AIDS, malignancy, kidney or liver disease, recent burns or trauma)
Prevention of sepsis

- Good management of chronic disease
- Wound care
- Infection prevention
- Smoking cessation
- Educate healthcare workers to think about sepsis
- Educating patients about
  - Vaccination
  - Hand hygiene
  - Wound hygiene
  - Signs and symptoms of sepsis
WHAT CAN YOU DO TO PREVENT SEPSIS?

1. Get vaccinated against the flu, pneumonia, and any other infections that could lead to sepsis. Talk to your doctor for more information.

2. Prevent infections that can lead to sepsis by
   - Cleaning scrapes and wounds
   - Practicing good hygiene (e.g., hand washing)

3. Know that time matters. If you have a severe infection, look for signs like: shivering, fever, or very cold, extreme pain or discomfort, clammy or sweaty skin, confusion or disorientation, short of breath, rapid breathing, and high heart rate.
Rapid Identification of Sepsis

• Known or suggested infection
• Systemic manifestations of sepsis:
  – Hyperthermia or hypothermia
  – Tachycardia
  – Tachypnea
  – Acute mental status change
  – Leukocytosis or leukopenia
  – Hyperglycemia (not explained by diabetes)
• Indications of new or worsened organ dysfunction
Rapid Identification of Sepsis

- Known or suggested infection
- Signs/symptoms of infection:
  - Temp > 38.3°C or < 36°C
  - HR > 90
  - Acutely altered mental status
  - WBC > 12,000 or < 4,000
  - Plasma glucose > 120 mg/dL in the absence of DM

- Criteria for organ dysfunction:
  - SBP < 90 mm Hg (or decrease ≥ 40 mm Hg from baseline), MAP < 65 mm Hg
  - Bilateral pulmonary infiltrates with increasing O₂ requirements to maintain SpO₂ > 90% or PaO₂/FIO₂ ratio < 300
  - Creatinine > 2.0 mg/dL
  - Bilirubin > 2 mg/dL
  - Platelet count < 100,000
  - Coagulopathy
  - Lactate > 2 mmol/L
After diagnosis...

- Prompt treatment is key
- More than 15 years of data have shown that protocols and order "bundles" facilitate more timely resuscitation
- Surviving Sepsis Campaign reviews evidence and publishes recommendations for management ever 4 years
## Implications of the strength of a recommendation

<table>
<thead>
<tr>
<th>Strong Recommendation</th>
<th>Weak Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For patients</strong></td>
<td></td>
</tr>
<tr>
<td>Most individuals would want the recommended course of action. A small proportion would not.</td>
<td>The majority of individuals would want the suggested course of action but many would not.</td>
</tr>
<tr>
<td><strong>For clinicians</strong></td>
<td></td>
</tr>
<tr>
<td>Most individuals should receive the recommended course of action.</td>
<td>Different choices are likely to be appropriate for different patients and therapy should be tailored to the individual patient’s circumstances.</td>
</tr>
<tr>
<td><strong>For policy makers</strong></td>
<td></td>
</tr>
<tr>
<td>The recommendation can be adapted as policy in most situations, including use as performance indicators</td>
<td>Policy-making will require substantial debates and involvement of many stakeholders.</td>
</tr>
</tbody>
</table>
Surviving Sepsis Campaign

- International Guidelines for Management of Sepsis and Septic Shock: 2012
  - “Early goal-directed therapy”
  - Specific goals for central venous pressure (CVP), MAP, central venous oxygen saturation
  - 3 key randomized trials (PROCESS, PROMISE, ARISE) did not show a mortality benefit with EGDT compared with protocols for early fluid resuscitation and antibiotics
Surviving Sepsis Campaign

• International Guidelines for Management of Sepsis and Septic Shock: 2016
  – Sepsis-induced hypoperfusion should be treated with at least 30 ml/kg of crystalloid IVF given in 3 hours or less (strong recommendation, low quality of evidence)
  – Use frequent clinical assessment to measure responsiveness to IVF (best practice statement)
  – Administer broad-spectrum IV antibiotics for all likely pathogens within 1 hour after sepsis recognition (strong recommendation, moderate quality of evidence)
  – Obtain anatomic source control of infection as rapidly as is practical
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K.I.S.S.

- Early, adequate IVF
- Early, appropriate antibiotics and infection control
- Watch clinical status closely
Surviving Sepsis Campaign

• International Guidelines for Management of Sepsis and Septic Shock: 2016
  – IV steroids are not routinely recommended, but if fluid resuscitation and vasopressors are insufficient to raise MAP ≥ 65, add hydrocortisone IV 200 mg/day (weak recommendation, low quality of evidence)
  – Avoid hypoglycemia and severe hyperglycemia; check blood glucose frequently (every 1-2 hours) and use insulin protocols to target blood glucose 110-180 (strong recommendation, high quality of evidence)
  – Recommend early enteral feeding for patients with sepsis or septic shock who can be fed enterally (strong recommendation, moderate quality of evidence)
Surviving Sepsis Campaign

  - Recommend goals of care be incorporated into treatment and end-of-care planning, using palliative care principles where appropriate (strong recommendation, moderate quality of evidence)
  - Goals of care should be addressed as early as feasible, but no later than within 72 hours of ICU admission (weak recommendation; low quality of evidence)
Clinical vignette

78 year old M brought to office by his daughter for evaluation of leg rash. She is worried that “he is not himself.”

Brief chart review:

PMH: DM, HTN, CKD, A-fib, chronic venous stasis

1 month ago: 82.3 kg, HR 76, BP 148/87
Today: 80.1 kg, HR 104, BP 105/52, T100.4
Clinical vignette

LLE became sore, red 3 days ago
Sleepy yesterday
Didn’t eat much
Chills last night
Confused this am
Clinical vignette
Clinical vignette

• Mental status: knows self, daughter, place
• HEENT: Anicteric, lips dry, no JVD
• CV: Irreg irreg tachycardia, radial and DP pulses palpable but weak, cap refill 3-4 sec
• Resp: Poor effort, but equal and clear
• Abd: Soft, nontender, normal bowel sounds
• Ext: Chronic venous stasis changes bilat, LLE ulcer with surrounding erythema
Is this sepsis?

• Source of infection:
  – Infected LLE venous stasis ulcer

• Signs of organ dysfunction
  – Relative hypotension
  – Altered mental status
  – Tachycardia
  – Poor cap refill and dry mucous membranes
Is this septic shock?

“Septic shock should be defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.”

- Vasopressor requirement to maintain MAP ≥ 65 mm Hg
- Lactate > 2 mmol/L despite adequate fluid resuscitation (in the absence of hypovolemia)
Next steps

• Recognize that this is a medical emergency
• Inform patient and his daughter that you are worried he has sepsis and needs immediate transfer to the hospital
• Have staff arrange transfer by EMS
• Begin IVF (if possible)
• Consider IM or IV antibiotics
• Communicate with ED physician about diagnosis and concerns
Using SOFA score

• Baseline with CKD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
<th>% Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Creatinine 1.2 - 1.9 mg/dL</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>2. Glasgow coma score of 15</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>3. PaO₂:FiO₂ ratio &gt; 400</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>4. MAP ≥ 70 mmHg (without pressors)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>5. Platelets &gt; 150 (x10³/mm³)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>6. Bilirubin &lt; 1.2 mg/dL</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
<td>100%</td>
</tr>
</tbody>
</table>
Using SOFA score

- After initial labs in ED

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
<th>% Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Creatinine 3.5 - 4.9 mg/dL or UOP &lt; 500</td>
<td>3</td>
<td>33.3%</td>
</tr>
<tr>
<td>2. PaO₂:FiO₂ ratio ≤ 300</td>
<td>2</td>
<td>22.2%</td>
</tr>
<tr>
<td>3. Glasgow coma score 13 - 14</td>
<td>1</td>
<td>11.1%</td>
</tr>
<tr>
<td>4. Bilirubin 1.2 - 1.9 mg/dL</td>
<td>1</td>
<td>11.1%</td>
</tr>
<tr>
<td>5. Platelets 101 - 150 (x10³/mm³)</td>
<td>1</td>
<td>11.1%</td>
</tr>
<tr>
<td>6. MAP &lt; 70 mmHg (without pressors)</td>
<td>1</td>
<td>11.1%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>9</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

- Estimated mortality: 15-20%
Next steps

• Crystalloid IVF to restore hemodynamic stability, usually at least 30 ml/kg
• Broad spectrum antibiotics appropriate for suspected source
  – Vancomycin and piperacillin/tazobactam for LE skin/soft tissue infection in diabetic
• Rapid anatomic control of source
  – Surgery to eval for debridement
• Blood glucose targets 110 – 180
• Review goals of care with patient and family
Summary

- In patients with infection – look for signs of organ dysfunction to diagnose sepsis
  - Use SOFA score when labs are available to more formally describe and predict mortality
- Prompt IVF in sepsis with clinical hypoperfusion
  - Anticipate at least 30 ml/kg, given within 3 hour
- Prompt broad spectrum empiric antibiotics for infection source
  - Given within 1 hour
- Use frequent clinical assessment to gauge response to treatment
- After adequate fluid resuscitation, need for vasopressors to maintain MAP ≥ 65 or persistent lactic acidosis is diagnostic of septic shock and confers higher mortality
- Discuss goals of care early and incorporate them in plan
Resources
