Severe Sepsis
*Diagnosis and Treatment Across the Care Continuum*

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21st Century Sepsis Teaching?

“as the physicians say it happens in hectic fever, that in the beginning of the malady it is easy to cure but difficult to detect, but in the course of time, not having been either detected or treated in the beginning, it becomes easy to detect but difficult to cure”

Niccolò Machiavelli
The Prince – 1513 or 1532
What is Sepsis?

Life threatening organ dysfunction due to a dysregulated host response to infection
Interesting Case

- 72 y.o. banker; flank pain and fever at nursing home
- Recent admission to hospital for a stroke.
- Aide notes mild confusion while getting him ready for breakfast
- Previous L. ureteral stent placement
- Hx of CAD, HTN, Stroke with left leg weakness
- Meds include terazosin, atorvastatin, metoprolol, aspirin
- BP 105/43, P 117, R 22, T 39.1°, SpO₂ 87%

What should NH do now?

A. 3 L bolus of LR
B. Apply oxygen
C. Point of care lactate level
D. IV or PO levofloxacin, 2 L bolus of LR, transfer to hospital for ICU admission
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B. Apply oxygen  
C. Point of care lactate level  
D. IV or PO levofloxacin, 2 L bolus of LR, transfer to hospital for ICU admission

In truth, none of these answers are wrong. But hospital transfer is key, based on the information we have.

What should EMS do when they arrive?

A. Blood cultures  
B. Apply oxygen  
C. Point of care lactate level  
D. IV or PO levofloxacin, 2 L bolus of LR, transport to hospital for ICU admission
What should EMS do when they arrive?

A. Blood cultures  
B. Apply oxygen  
C. Point of care lactate level  
D. IV or PO levofloxacin, 2 L bolus of LR, transport to hospital for ICU admission

Again, any of these could be good. But transfer to the hospital is key.

What should happen on arrival to ER?

A. Blood cultures  
B. Apply oxygen  
C. Point of care lactate level  
D. IV or PO levofloxacin, 2 L bolus of LR, ICU admission
What should happen on arrival to ER?

A. Blood cultures  
B. Apply oxygen  
C. Point of care lactate level  
D. IV or PO levofloxacin, 2 L bolus of LR, ICU admission

All of the above, actually.

At the hospital

• Labs: WBC – 14.7, 33% bands  
• Plt – 96,000  
• BUN – 47, Cr. – 3.2  
• D-dimer – 4.7, fibrinogen – 72, PTT – 39  
• Lactate – 2.6  
• UA – not available
Severe Sepsis

• THE major cause of morbidity and mortality worldwide
  - Leading cause of death in noncoronary ICU (US)*
  - 11th leading cause of death overall (US) † §

• More than 750,000 cases of severe sepsis in US annually‡

• In the US, more than 500 patients die of severe sepsis daily‡

*Sands KE et al. JAMA. 1997;278:234-40;
§ Murphy SL. National Vital Statistics Reports.

Severe Sepsis
How Common – How Deadly?

Incidence of Severe Sepsis

Mortality of Severe Sepsis

Figure 2. Cognitive Impairment Among Survivors of Severe Sepsis at Each Survey Time Point.


Age Related Incidence of Severe Sepsis

Sepsis Incidence

Compounding Growth
Doubling time = 8.5 years

Sepsis ≠ Hypotension

Sepsis ≠ Bacteremia

ACCP/SCCM Consensus Definitions

• Infection
  – Inflammatory response to microorganisms, or
  – Invasion of normally sterile tissues

• Systemic Inflammatory Response Syndrome (SIRS)
  – Systemic response to a variety of processes
  – ≥2 SIRS criteria

• Sepsis
  – Infection plus
  – ≥2 SIRS criteria

• Severe Sepsis
  – Sepsis
  – Organ dysfunction

• Septic shock
  – Sepsis
  – Hypotension despite fluid resuscitation

SIRS: Systemic Inflammatory Response Syndrome

- SIRS: nonspecific insult
  - 2 of the following:
    - Temperature
      > 38°C or < 36°C
    - HR > 90 beats/min
    - Respirations > 20/min
    - WBC > 12,000/µL or
      - < 4,000/µL or
      - > 10% bands or other


Acute Organ Dysfunction as the Hallmark of Severe Sepsis

- Altered Consciousness
- Confusion
- Psychosis
- Tachypnea
  - PaO2 < 70 mm Hg
  - SaO2 < 90%
  - PaO2/FiO2 < 300
- T. Bilirubin
  - > 4 mg/dL
- Lactic acidosis
- Hypotension
  - SBP < 90
  - MAP < 70
- Oliguria
  - < 20 mL/hr
- Anuria
  - Creatinine
  - (>0.5 mg/dL)
- Platelets (< 100k)
  - (INR>1.5, PTT>60 sec)
  - D-dimer
Severe Sepsis: A Diagnostic Challenge

- Timely and accurate diagnosis remains a challenge
  - 17% of physicians agreed on definition of sepsis, but 83% agreed the dx is often missed
  - Occurs throughout the institution
  - Clinical definition not applied at bedside
  - No single test or marker
- Focus is on supporting underlying organ failure


Diagnostic criteria for severe sepsis include:

A. Positive blood cultures, hypotension
B. Positive blood cultures, tissue hypoxia
C. Positive blood cultures, SIRS, and lactic acidosis
D. Suspected infection, SIRS, and organ dysfunction
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D. Suspected infection, SIRS, and organ dysfunction

Sepsis: What Are We Talking About?

- ICD-9: “septicemia”
- Positive blood cultures
- Multiple positive blood cultures
- Positive blood cultures + hypotension
- Syndrome: how shall we define it?
Role of Biomarkers in Diagnosing Severe Sepsis

- There is none
- Yet
- Procalcitonin – not for diagnosis, but possibly for follow up

Interesting Case

- 72 y.o. man presents with flank pain and fever, mild confusion in E.D.
- previous L. ureteral stent placement
- Hx of CAD, HTN
- Meds include terazosin, atorvastatin, metoprolol
- BP 105/43, P 117, R 22, T 39.1o, SpO2 87%
- Exam: left CVA tenderness, BPH
Interesting Case

- Labs: WBC – 14.7, 33% bands
- Plt – 96,000
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Surviving Sepsis Campaign (SSC) Guidelines for Management of Severe Sepsis and Septic Shock

Crit Care Med 2004;32:858-873
Intensive Care Med 2004;30:536-555


www.survivingsepsis.org
### Table 1. Grading system

<table>
<thead>
<tr>
<th>Grading of recommendations</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Supported by at least two level I investigations</td>
</tr>
<tr>
<td>B</td>
<td>Supported by one level I investigation</td>
</tr>
<tr>
<td>C</td>
<td>Supported by level II investigations only</td>
</tr>
<tr>
<td>D</td>
<td>Supported by at least one level III investigation</td>
</tr>
<tr>
<td>E</td>
<td>Supported by level IV or V evidence</td>
</tr>
</tbody>
</table>

**Grading of evidence**

<table>
<thead>
<tr>
<th>I</th>
<th>Large, randomized trials with clear-cut results; low risk of false-positive (alpha) error of false-negative (beta) error</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>Small, randomized trials with uncertain results; moderate-to-high risk of false-positive (alpha) and/or false-negative (beta) error</td>
</tr>
<tr>
<td>III</td>
<td>Nonrandomized, contemporaneous controls</td>
</tr>
<tr>
<td>IV</td>
<td>Nonrandomized, historical controls and expert opinion</td>
</tr>
<tr>
<td>V</td>
<td>Case series, uncontrolled studies, and expert opinion</td>
</tr>
</tbody>
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**Time Sensitive Interventions**

- **AMI** – “Door to PCI”
  Focus on the timely return of blood flow to the affected areas of the heart.

- **Stroke** – “Time is Brain”

**Severe Sepsis – faster treatment improves survival**

- **Trauma** – “The Golden Hour”
  Requires immediate response and medical care “on the scene.”
  Patients typically transferred to a qualified trauma center for care.
Bundles of Care

• Combine multiple elements known to be effective
• Outcome is additive or synergistic
• Framework that leverages change
• Avoids a piecemeal approach

Surviving Sepsis Campaign Bundles

To be completed within 3 hours:
1. Measure serum lactate level
2. Obtain blood cultures prior to administration of antibiotics (1C)
3. Administer broad spectrum antibiotics (1B, 1C)
4. Administer 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L
Surviving Sepsis Campaign Bundles

To be completed within 6 hours

1. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) $\geq 65$ mm Hg

2. In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate $\geq 4$ mmol/L (36 mg/dL)
   
   Measure central venous pressure (CVP)*
   
   Measure central venous oxygen saturation (ScvO2)*

3. Re-measure lactate if initial lactate was elevated*

*Targets are: CVP 8 mm Hg, ScvO2 $> 70\%$, lactate normal

In the early resuscitation of the severe sepsis patient, the MOST important feature is:

A. IV fluid boluses
B. Antibiotics as fast as they can get in
C. Measurement of serum lactate
D. Measurement of ScvO2 within 6 hours
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Septic Shock: Timing of Antibiotics

Only 50% of patients in Septic Shock received antibiotics within 6 hrs.

Kumar Crit Care Med 2006
Studies Using EGDT and/or Bundled Care to Treat Sepsis


CMS Core Measures: Simply Complicated

**Within 3 hours of Presentation of Severe Sepsis**

1. Initial lactate level measurement
2. Broad spectrum antibiotics administered
3. Blood cultures drawn prior to antibiotics
4. Crystalloid fluid initiated

**Did hypotension persist after fluid given?**

- NO
- YES, continue on

**Core Measure goals met, re-measure lactate within 6hrs**

**Within 3 hours of Presentation of Septic Shock**

1. Resuscitation with 30ml/kg crystalloid fluids
2. Evaluate the need for vasopressors

**After fluid resuscitation, but within 6 hours of Presentation of Septic Shock**

Re-assessment of volume status and tissue perfusion
- A focused exam including
  - Vital signs
  - Cardiopulmonary exam
  - Capillary refill evaluation
  - Peripheral pulse evaluation
  - Skin examination
- Must be performed and documented by a Physician, ARNP, or PA

2 out of 4 from the following:

- CVP
- bedside Cardio US
- ScvO2
- Passive Leg Raise or Fluid Challenge
Standard Techniques, Operations, and Procedures for Sepsis

Kansas Delivery System Reform Incentive Payment (DSRIP)

www.kumed.com

www.kansassepsisproject.org

https://coa.kumc.edu/gec/

https://kumcce.ku.edu/
Scope of the Issue

- Nationally, 1 in 4 Americans lives in a rural area
- Approximately 76,000,000 people
- < 10% of physicians work in rural areas
- Rural Americans are:
  - More likely to live below poverty line
  - Older
  - Less likely to have regular medical care
  - More likely to die accidentally

Kansas: Exemplar of Rural America

Data from 2012 STAT Report – Kansas Hospital Association
U.S. States with Similar Population Density

Source: U.S. Census Bureau, 2008 Census.
Looking From the Other Side

Urban Areas
Census Bureau 2010

Trauma Center Locations
Two Different Pictures of Hospitals

Cost/Expenditure


Quality

Severe Sepsis at KU

Mortality Rates – Observed Mortality
Stop Sepsis – What We Do

• Nursing homes, EMS systems, Hospitals
• Training at all levels
  - Workshops and online tools
  - Recognizing sepsis and severe sepsis
  - Early aggressive treatment
  - Quality improvement techniques
• Provision of online data collecting tool
• Continual support from expert faculty

Severe Sepsis: Summary

• Very common disease process
• Evidence supports several treatment modalities
• Early recognition - crucial
• Rapid, aggressive treatment – necessary
• We can ALL do this
Thank you!
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