Dr. Stein has declared no conflicts of interest related to the content of her presentation.
HOW TO IMPROVE CARE FOR
THE PATIENT WITH SEPSIS

Susan J. Stein, M.D.
NAMDRC March 21, 2013
Patient Safety Officer
Olive View UCLA Medical Center
Relative Mortality
Acute MI - Look what we’ve done

• Core measures
  • compliance with aspirin at arrival
  • Aspirin at discharge
  • ACE or ARB
  • Smoking cessation
  • Beta blocker at arrival/discharge
  • Time to lysis

• Door to balloon in 90 minutes
AMI

- $T_0$
- Arrive at ED
- EKG and labs
- Cath lab team at home, asleep in their beds

- $T_{90 \text{ minutes}}$
- Patient’s diagnostic angiogram is complete
- Vessel is open
Sepsis

- No core measures specific for sepsis
- Core measures only for CAP
  - Oxygenation assessment
  - Pneumococcal vaccination
  - Blood cultures done
  - Initial antibiotic within 6 hours
  - Antibiotic selection (CAP)
Sepsis

- $T_0$
- Patient arrives in ED
- Temperature taken
- Bloods drawn

- $T_{90\text{ minutes}}$
- ? Antibiotic orders written
- ?Antibiotics infused
- Peripheral IV started
- ?team aware of lactate
- ?Pt. received fluids
Surviving Sepsis

- A campaign led by the Society of Critical Care Medicine to standardize the management of severe sepsis and septic shock.
- Multiple sponsoring agencies **AACN, ACCP, ACEP, ANZICS, ATS, ERS, ESCMID, SIS, ESICM, ISF, SCCM, IHI**, etc. Endorsed by multiple organizations!
GRADE SYSTEM

• Grading of Recommendations
  • 1. Strong
  • 2. Weak

• Grading of Evidence
  • A. High (RCTs)
  • B. Moderate (RCT’s or observational)
  • C. Low (Well done observational)
  • D. Very Low (Expert opinion)

Dellinger et al, Crit Care Med 2012 41:580-637
Why Target Sepsis?

- Major cause of in-hospital mortality
- In our hospitals, 30-50% of the mortalities receive a sepsis code
- Recommendations are not complex
- It may be time to make evidence based treatments the standard of care.
Sepsis Mortalities
Sepsis Overview

- It’s all about maintaining the oxygen supply to the tissues
- No oxygen -> global tissue hypoxemia -> cardiovascular and/or multi-organ failure
- How do you assess organ oxygenation?
- How do you know how much is enough?
  - Loss of organ function may be too late!
  - Lactic acid (lactate) may be helpful.
- How do we meet our oxygen supply goals?
The Evidence

• Randomized 263 patients to “standard” vs. EGDT in ED.
• 16% absolute mortality reduction in EGDT patients.
• Identified the 6 Golden Hours of Sepsis
Shift of Work- Understanding who the Sepsis docs really are

- Workload is moved from the ICU:
- ICU 1:2 or 1:1 nursing
- Elements of care are usual in ICU
- ED- busy, overwhelmed, not used to inserting monitoring devices
- Usually do not give scheduled medications
### Table 4. Treatments Administered. *

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hours after the Start of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–6</td>
</tr>
<tr>
<td><strong>Total fluids (ml)</strong></td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>3499±2438</td>
</tr>
<tr>
<td>EGDT</td>
<td>4981±2984</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Red-cell transfusion (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>18.5</td>
</tr>
<tr>
<td>EGDT</td>
<td>64.1</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Any vasopressor (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>30.3</td>
</tr>
<tr>
<td>EGDT</td>
<td>27.4</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Inotropic agent (dobutamine) (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>0.8</td>
</tr>
<tr>
<td>EGDT</td>
<td>13.7</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Mechanical ventilation (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>53.8</td>
</tr>
<tr>
<td>EGDT</td>
<td>53.0</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>0.90</td>
</tr>
<tr>
<td><strong>Pulmonary-artery catheterization (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>34</td>
</tr>
<tr>
<td>EGDT</td>
<td>0</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>0.12</td>
</tr>
</tbody>
</table>

*Plus–minus values are means ±SD. Because some patients received a specific treatment both during the period from 0 to 6 hours and during the period from 7 to 72 hours, the cumulative totals for those two periods do not necessarily equal the values for the period from 0 to 72 hours. EGDT denotes early goal-directed therapy.

†Administered vasopressors included norepinephrine, epinephrine, dopamine, and phenylephrine hydrochloride.

‡All pulmonary-artery catheters were inserted while patients were in the intensive care unit.
SIRS criteria and systolic blood pressure ≤90 mm Hg or lactate >4 mmol/liter

Assessment and consent

Standard therapy in emergency department (n=133)

Randomization (n=263)

Early goal-directed therapy (n=130)

Vital signs, laboratory data, cardiac monitoring, pulse oximetry, urinary catheterization, arterial and central venous catheterization

CVP ≥8–12 mm Hg

MAP ≥65 mm Hg

Urine output ≥0.5 ml/kg/hr

Standard care

Hospital admission

Vital signs and laboratory data obtained every 12 hr for 72 hr

CVP ≥8–12 mm Hg

MAP ≥65 mm Hg

Urine output ≥0.5 ml/kg/hr

ScvO₂ ≥70%

SaO₂ ≥93%

Hematocrit ≥30%

Cardiac index

VO₂

Did not complete 6 hr (n=14)

Follow-up

Did not complete 6 hr (n=13)
Understanding Tissue Resuscitation

- $\text{MvO}_2 = \text{Mixed venous oxygen saturation}$
- $\text{ScvO}_2 = \text{Central venous oxygen saturation}$
Goal is ScvO2 ≥ 70 %

- ↑ Hb (supply)

- ↑ PaO2 (supply)

- ↑ O2 extraction  (demand e.g., Sepsis, shivering, spiking, struggling or seizing)

- ↑ Cardiac Output (supply)

- ↑ ScvO2

- ↑ ScvO2

- ↓ ScvO2

- ↑ Scv02
Goal Based Guidelines

- Identify the patient
- Provide timely antibiotics
- Fluid Resuscitate
- Use vasopressors to raise MAP
- Maximize oxygen delivery to the tissues
- Check your work! (Scv0₂, lactate)
Identify the patient AND deliver the proper care

• “Performance improvement efforts in severe sepsis should be used to improve patient outcomes” UG
Performance Improvement Sepsis Teams

- Meet regularly
- Have the support of the institution
- Multidisciplinary involvement (MD’s and RN’s from ICU, ED, floor, pharmacy, and admin)
- Create protocols- orders, standardized procedures,
- Fix time sinks (delay in antibiotic arrival, lactate draws etc.)
Performance Improvement Sepsis Team

• Collect data
  • Can review administrative data using sepsis codes (995.91, 995.92, 785.52)
  • Can collect real time
  • Must collect bundle elements
• Share data with stakeholders
• Feedback mortality, LOS and bundle compliance
Performance Improvement Sepsis Response

- ED vs. Inpatient response
- RRT or non-RRT response
- Expectations of care (everybody involved must have a shared vision, everyone at every level needs to know their role, and what comes next)
- Care plan is agreed upon prior to the 40/40/40 phone call (T, RR, MAP)
Performance Improvement Sepsis Team

- Roll out with leadership support
- Create education
- Let staff know importance/mandate
- Understand the need to train as well as educate
Surviving Sepsis Campaign Bundles

- Resuscitation bundle broken down into two parts
  - 3 hour bundle
  - 6 hour bundle
Education Vs. Training

Education

Training
Education Vs. Training

Education

How to Clean My Own Poop

Training
Getting to Goals
GOAL: Early Identification of the Septic Patient

If only they came in with a sign that said...
I wonder if this is the patient with severe sepsis?
Screening

- 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).
# Sepsis Identification

<table>
<thead>
<tr>
<th>SIRS</th>
<th>Sepsis</th>
<th>Severe Sepsis</th>
<th>Septic Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>T&lt;36 or &gt;38. (3)</td>
<td>+ All abnormal vitals due to infection</td>
<td>+ Organ Dysfunction</td>
<td>Hypotension</td>
</tr>
<tr>
<td>HR &gt;90</td>
<td>+Lactate &lt;4.0 but &gt; ULN</td>
<td>MAP &lt;65</td>
<td></td>
</tr>
<tr>
<td>RR&gt;20</td>
<td>Lactate &gt;4.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC &gt;12K or &lt;4K or &gt;10%bands</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Guide to organ dysfunction

CNS: Altered consciousness, Confusion

Respiratory: Tachypnea
  \( \downarrow \) PaO\(_2\)
  \( \downarrow \) PaO\(_2\)/FiO\(_2\) ratio

Hepatic: Jaundice,
  \( \uparrow \) Liver enzymes
  \( \downarrow \) Albumin

Metabolic: Metabolic Acidosis
  \( \uparrow \) Lactate level
  \( \downarrow \) Lactate Clearance

Cardiovascular: Tachycardia
  Hypotension
  Altered CVP & PAOP

Renal: Oliguria
  Anuria
  \( \uparrow \) Creatinine

Hematologic:
  \( \downarrow \) Platelets
  \( \uparrow \) PT/INR, \( \uparrow \) aPTT
  \( \downarrow \) Protein C
  \( \uparrow \) D-dimer

Modified from criteria published in:
Goal: Identification/ Screening

• Successful Screening = Nurse Driven
• Suspect Infection?
• Abnormal Vitals?
• Lactate, lactate, lactate
• How are your lactates run? POC TAT Criticals? Nursing protocol?
Screening- SUPO*

**ED**

- Vitals at triage
- Computer or manual screen
- SIRS, tachycardia and fever, hx of fever or chills, hx of cancer
- Allow triage RN to draw lactate

**Inpatient**

- Routine vitals
- Issues with Nursing Attendant VS
- Early warning systems
- Allow RN to draw lactate and blood cultures
- Script language for MD notification “Doctor your patient is SUPO, we need orders for fluids and antibiotics”

*Sepsis Until Proven Otherwise*
Three Hour Bundle

1) Measure lactate level
2) Obtain blood cultures prior to antibiotics
3) Administer broad spectrum antibiotics
4) Administer 30 cc/kg crystalloid for hypotension or lactate ≥ 4.0
Elements of 3 hour Bundle

- Measure **lactate** level
- 1 lactate is often not enough
- Lactates must be easy to get
  - nurse driven protocols
  - POC w/ABG or VBG or TAT <1 hour
  - Phlebotomy dispatched immediately
  - Venous draws are acceptable
  - Abnormals $\geq 4.0$ should be critical (called to unit)
  - Lactates $> \text{ULN}$ should be perceived as abnormal
  - Extra phlebotomies will occur
Lactates

• May be the only indicator or hypoperfusion
• Patient may have nl BP and elevated lactates
• Most etiologies of elevated lactates are concerning
Obtain Blood Cultures prior to antibx

- Standard is blood cultures, 2 sets or 4 bottles prior to antibiotics
- If line is present, one set may/should be drawn from line
- 2 separate sticks- general consensus is no delay necessary between sticks
- Consider all blood cultures drawn are bundled with lactate
- Does it save lives? Maybe
Administer Broad Spectrum Antibiotics

- The administration of effective intravenous anti-microbials within the first hour of recognition of septic shock (grade 1B) and severe sepsis (grade 1C) should be the goal of therapy.
First Hour = 80% survival. Survival decreases 7.6% for each hour antibiotics are delayed.
“Anchor Antibiotic”

• The anchor antibx is the one doing the lions share of the work
• The anchor antibx has gram negative and pneumococcal coverage, the organisms likely to result in rapid demise if not covered
• Anchor ideally has a long half-life and low incidence of allergies
• Identify your anchor antibiotics and ensure immediate availability
Anchor Antibiotic

- Infuse first, ideally capable of rapid infusion
- Stock in ED and local pyxis
- Ideally low incidence of allergies
- Examples of anchors: ceftiazone, pip/tazo, cefepime, quinolones
- Broaden coverage after anchor infused
Our Rules for Antibx in ED

- All antibiotics ordered in the ED must be hung in the ED
- All antibx ordered in the ED must be in the Pyxis
  - Pre-mixed
  - Easy mix
  - Not weight based (e.g. gent)
- Vancomycin is not infused first
- No renal dosing in ED
Pre-choose Antibiotics

- Team to steward antibiotic choices
- Empiric antibiotic menu
  - ID physicians, ED physicians, pharmacist
- Choose based on suspected site of infection
- When in doubt, get an anchor on board, then fine-tune the ideal antibiotics (generic vs. designer)
Administer 30 cc/kg crystalloid for hypotension or lactate ≥ 4.0

- Crystalloid over hydroxyethyl starches (1B)
- “We suggest the use of albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloid (2C)”
- Consider a fluid challenge strategy- Keep giving fluid as long as there is hemodynamic improvement (SVV, stroke volume, BP or pulse pressure) (UG)
What if they are volume overloaded?

• The 2012 guidelines do not address this
• Consider repeating small aliquots
• Assess volume status and fluid responsiveness using ultrasound and/or other non-invasive techniques
• Patients may be more volume tolerant when they are septic
• Concept of “volume responsive” and “volume tolerant”
WARNING:

ALL ROADS LEAD TO DIALYSIS

Too Much Fluid

Too Little Fluid
IVC Assessment

Volume Overload

Hypovolemia

Volume Overload

Hypovolemia
Non-Invasive Stroke Volume

- Key Hemodynamic Parameters:
  Stroke Volume (SV) • Cardiac Output (CO) • Heart Rate (HR) • Stroke Volume Variation (SVV) • Noninvasive Blood Pressure (NIBP) • Total Peripheral Resistance (TPR) • O₂ Saturation (SPO₂) • Oxygen Delivery Index (DO₂I) • Stroke Volume Index (SVI) • Cardiac Index (CI) • Total Peripheral Resistance Index (TPRI) • Thoracic Fluid Content trend (dTFC)

- Continuous Non-Invasive Hemodynamic Insight

- Tailored Fluid management to Optimize Resuscitation

- Validated Accuracy¹⁻⁵

- Predicated Against Swan-Ganz
Passive Leg Raise Maneuver

Patient position: Lying in a semi-recumbent position

Patient position: Passive leg raise (about 45 degrees)
Reversible Fluid Bolus - PLR
**Volume Responsive**

### Bolus Test - Report

<table>
<thead>
<tr>
<th></th>
<th>CI</th>
<th>HR</th>
<th>MAP</th>
<th>TPRI</th>
<th>SVI</th>
<th>DO2I</th>
<th>TFC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>2.6</td>
<td>95</td>
<td>--</td>
<td>--</td>
<td>30</td>
<td>--</td>
<td>45.1</td>
</tr>
<tr>
<td>Challenge</td>
<td>4.2</td>
<td>97</td>
<td>man101</td>
<td>3172</td>
<td>45</td>
<td>358</td>
<td>48.0</td>
</tr>
<tr>
<td>Δ [%]</td>
<td>47.8%</td>
<td>2%</td>
<td>--</td>
<td>--</td>
<td>51.1%</td>
<td>--</td>
<td>6.5%</td>
</tr>
</tbody>
</table>

**SpO2** % (man) 92
**DO2I** mL/min/m² 358
**Hgb** g/dL (man) 14.9
6 Hour Bundle

• Apply vasopressors for hypotension which does not respond to initial fluid resuscitation

• To maintain a MAP ≥ 65

• In the event of persistent arterial hypotension despite volume resuscitation (shock) or initial lactate ≥ 4.0
  • Measure CVP
  • Measure Scv0₂

• Remeasure lactate if initial lactate was elevated
The New Guidelines!


- Adult Guidelines A to W!
Surviving Sepsis 2012 Guidelines
A to W

- A. Initial resuscitation
- B. Screening for sepsis and performance improvement
- C. Diagnosis
- D. Antimicrobial therapy
- E. Source control
- F. Infection prevention
- G. Fluid therapy for severe sepsis and septic shock
- H. Vasopressors
- I. Inotropic therapy
- J. Corticosteroids
- K. Blood product administration
- L. Immunoglobulins
- M. Selenium
- N. Recombinant activated protein C
- O. Mechanical ventilation (ARDS)
- P. Sedation, analgesia and neuromuscular blockade
- Q. Glucose control
- R. Renal replacement therapy
- S. Bicarbonate therapy
- T. DVT prophylaxis
- U. Stress ulcer prophylaxis
- V. Nutrition
- W. Setting goals of care
Top 10- Start or Continue

- 10) Use oral chlorhexidine to reduce the risk of VAP in ventilated patients (grade 2B)
- 9) Target a 6cc/kg TV for ARDS (grade 1A)
- 8) Identify and obtain source control within 12 hours (grade 1C)
- 7) Protocolized approach to keep blood glucose <180 (grade 1A)
- 6) Epinephrine as second line pressor (grade 2B) or fixed dose vasopressin 0.03 units/minute (UG)
Start or Continue- Top 10

• 5) Norepinephrine as first choice vasopressor (grade 1C)
• 4) Check your work-ScvO\(_2\) (grade 1C) or Lactate clearance (grade 2C)
• 3) Create a PI team and process for screening and treating (UG and grade 1C)
• 2) Administer (anchor) antibiotics within 1 hour of recognition of severe sepsis and septic shock (grade 1C and 1B)
• 1) Follow the 3 hour Bundle
Stop or Don’t start- Top 10

10) Activated protein C
9) Renal dose or any dose dopamine (grade 2C)
8) ACTH Stimulation test to determine who should receive hydrocortisone (grade 2B)
7) Phenylephrine (salvage or arrhythmia OK) (grade 1C)
6) Hydroxyethyl starches for fluid resuscitation (grade 1B)
Stop or Don’t Start – Top 10

• 5) Transfusing when Hb $\geq$ 7.0 unless tissue hypoperfusion is not resolved, myocardial ischemia, severe hypoxemia, active bleeding etc.. (grade 1B)
• 4) Laying patients on mechanical ventilation flat or HOB $<$ 35-40 degrees. (grade 1B)
• 3) Using a PA catheter routinely for sepsis induced ARDS (grade 1A)
• 2) Overfeeding, underfeeding, or parenterally feeding (enteral tolerant) (grade 2C, 2C, 2B)
• 1) Building delays into your care (waiting for a bed, bringing back, pharmacy, mixing, completing infusions, getting access…)
Lastly: Recognize when acute episode has resolved and start “wellification”

- Extubate the patient as soon as they are ready (grade 1A)
- Keep things moving
- Get the patient moving
- Remove excess fluid (diuresis)*
- Systematically ensure prophylaxis
- Remove lines and tubes
- Create a shared vision of where the patient is going. (Home.)