Recognition and Management of Severe Sepsis and Septic Shock
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The Minnesota Medical Association designates this internet activity for a maximum of 1 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Physicians and other licensed health care professionals requesting CME credit must complete the CME Evaluation form provided to them and follow the instructions on the form.

The speaker has no personal financial relationships to disclose.
Recognition and Management of Severe Sepsis and Septic Shock

David M. Larson, MD, FACEP

MHA Web Conference
June 17, 2015
Objectives

- Discuss the use of screening tools for early recognition and treatment of severe sepsis and septic shock.
- Review the current evidence based guidelines from the Surviving Sepsis Campaign.
- Discuss recent randomized controlled trials on Early Goal Directed Therapy for the management of Sepsis patients.
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

Hospitalization rates for septicemia or sepsis more than doubled from 2000 through 2008.

Figure 1. Hospitalizations for and with septicemia or sepsis

NOTE: Significant linear trend from 2000 through 2008 for both categories.
Hospitalization rates for sepsis or septicemia were similar for males and females and increased with age.

Figure 2. Rates of hospitalization for septicemia or sepsis, by sex and age, 2008

NOTES: Rates are significantly higher for males and females in each successive age group.
Protocols and Checklists

Colleagues share the tools they have developed in their own institutions as they implement the Surviving Sepsis Campaign. Here you’ll find locally-created protocols, checklists, policies, and similar documents so you don’t have to start from scratch. If you have items to share based on the 2012 guidelines and revised bundles, please email PDFs to info@survivingsepsis.org. Permissions from your institution may be required. The Campaign is creating new materials and anticipates posting on this site in late June 2013.

Campaign Screening Tool Sample

The Surviving Sepsis Campaign provides a paper screening tool to assist when evaluating patients in the hospital emergency department, medical/surgical/telemetry wards, or in the ICU. The previous version with callouts to indicate the changes from 2008 to 2012 is available.

Community Resources

ICU Severe Sepsis Screening Tool - Saint Joseph Mercy Health System
Patient Units Severe Sepsis Screening Tool - Saint Joseph Mercy Health System
Sepsis Pocket Card - Saint Joseph Mercy Health System
Sepsis Recognition and Treatment Protocols - Stony Brook
Sepsis Pediatric Order Set - Stony Brook
Pediatric ICU Screening Tool - Stony Brook
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 (AIMB)
- 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
- European Society of Pediatric and Neonatal Intensive Care
- 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 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

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Andrew Rhodes, MB BS; Djillali Annane, MD; Herwig Gerlach, MD, PhD; Steven M. Opal, MD; Jonathan E. Sevransky, MD; Charles L. Sprung, MD; Ivor S. Douglas, MD; Roman Jaeschke, MD; Tiffany M. Osborn, MD, MPH; Mark E. Nunnally, MD; Sean R. Townsend, MD; Konrad Reinhart, MD; Ruth M. Kleinpell, PhD, RN-CS; Derek C. Angus, MD, MPH; Clifford S. Deutschman, MD, MS; Flavia R. Machado, MD, PhD; Gordon D. Rubenfeld, MD; Steven A. Webb, MB BS, PhD; Richard J. Beale, MB BS; Jean-Louis Vincent, MD, PhD; Rui Moreno, MD, PhD; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

Definitions

The degree to which a televised image broadcast signal is recorded.

Definition n. l.
The teacher gave definitions of the new words.
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

Crit Care Med 1992;20:864-874
Systemic Inflammatory Response Syndrome to Septic shock: A Continuum

**SIRS** → **Sepsis** → **Severe Sepsis**

**SIRS**
A Clinical response arising from a nonspecific insult with 2 of the following:
- Temp > 100.9 or > 96.8°F
- HR > 90
- RR > 20 or pCO₂ < 32
- WBC > 12 K, < 4 K, > 10% Bands

**Sepsis**
SIRS with a presumed or confirmed infectious process

**Severe Sepsis**
Sepsis induced tissue hypoperfusion or organ dysfunction
- Respiratory
- Renal, GI
- CNS
- Hematologic
- Refractory hypotension

**Septic Shock**
Data from 172 ICUs in Australia/New Zealand

96,385 patients with Infection with organ failure

12.2% did not meet SIRS criteria
SIRS in Severe Sepsis

- Most Common SIRS criteria
  - Elevated HR
  - Elevated RR

- Only 60% had abnormal Temp
  - 30% high
  - 30% low

NEJM April 23, 2015
2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference

Mitchell M. Levy, MD, FCCP; Mitchell P. Fink, MD, FCCP; John C. Marshall, MD; Edward Abraham, MD; Derek Angus, MD, MPH, FCCP; Deborah Cook, MD, FCCP; Jonathan Cohen, MD; Steven M. Opal, MD; Jean-Louis Vincent, MD, FCCP, PhD; Graham Ramsay, MD; For the International Sepsis Definitions Conference


R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Andrew Rhodes, MB BS; Djillali Annane, MD; Herwig Gerlach, MD, PhD; Steven M. Opal, MD; Jonathan E. Sevransky, MD; Charles L. Sprung, MD; Ivor S. Douglas, MD; Roman Jaeschke, MD; Tiffany M. Osborn, MD, MPH; Mark E. Nunnally, MD; Sean R. Townsend, MD; Konrad Reinhart, MD; Ruth M. Kleinpell, PhD, RN-CS; Derek C. Angus, MD, MPH; Clifford S. Deutschman, MD, MS; Flavia R. Machado, MD, PhD; Gordon D. Rubenfeld, MD; Steven A. Webb, MB BS, PhD; Richard J. Beale, MB BS; Jean-Louis Vincent, MD, PhD; Rui Moreno, MD, PhD; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup *
Definitions – 2012 Surviving Sepsis Guideline

- **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>
</tr>
</thead>
<tbody>
<tr>
<td>General variables</td>
</tr>
<tr>
<td>- Fever (&gt;38.3°C)</td>
</tr>
<tr>
<td>- Hypothermia (core temperature &lt; 36°C)</td>
</tr>
<tr>
<td>- Heart rate &gt; 90/min⁻¹ or more than two sd above the normal value for age</td>
</tr>
<tr>
<td>- Tachypnea</td>
</tr>
<tr>
<td>- Altered mental status</td>
</tr>
<tr>
<td>- Significant edema or positive fluid balance (&gt; 20 mL/kg over 24 hr)</td>
</tr>
<tr>
<td>- Hyperglycemia (plasma glucose &gt; 140 mg/dL or 7.7 mmol/L) in the absence of diabetes</td>
</tr>
<tr>
<td>Inflammatory variables</td>
</tr>
<tr>
<td>- Leukocytosis (WBC count &gt; 12,000 µL⁻¹)</td>
</tr>
<tr>
<td>- Leukopenia (WBC count &lt; 4000 µL⁻¹)</td>
</tr>
<tr>
<td>- Normal WBC count with greater than 10% immature forms</td>
</tr>
<tr>
<td>- Plasma C-reactive protein more than two sd above the normal value</td>
</tr>
<tr>
<td>- Plasma procalcitonin more than two sd above the normal value</td>
</tr>
</tbody>
</table>
Table 1 Continued. Criteria for sepsis

<table>
<thead>
<tr>
<th>Hemodynamic variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypotension (SBP &lt; 90 mm Hg, MAP &lt; 70 mm Hg, or an SBP decrease &gt; 40 mm Hg in adults or less than two SD below normal for age)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organ dysfunction variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypoxemia (Pao₂/Fio₂ &lt; 300)</td>
</tr>
<tr>
<td>Acute oliguria (urine output &lt; 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)</td>
</tr>
<tr>
<td>Creatinine increase &gt; 0.5 mg/dL or 44.2 μmol/L</td>
</tr>
<tr>
<td>Coagulation abnormalities (INR &gt; 1.5 or aPTT &gt; 60 s)</td>
</tr>
<tr>
<td>Ileus (absent bowel sounds)</td>
</tr>
<tr>
<td>Thrombocytopenia (platelet count &lt; 100,000 μL⁻¹)</td>
</tr>
<tr>
<td>Hyperbilirubinemia (plasma total bilirubin &gt; 4 mg/dL or 70 μmol/L)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tissue perfusion variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperlactatemia (&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 > 40mm 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)

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis-induced hypotension</td>
</tr>
<tr>
<td>Lactate above upper limits laboratory normal</td>
</tr>
<tr>
<td>Urine output $&lt; 0.5 \text{mL/kg/hr}$ for more than 2 hrs despite adequate fluid resuscitation</td>
</tr>
<tr>
<td>Acute lung injury with $\text{Pac}_2/\text{FiO}_2 &lt; 250$ in the absence of pneumonia as infection source</td>
</tr>
<tr>
<td>Acute lung injury with $\text{Pac}_2/\text{FiO}_2 &lt; 200$ in the presence of pneumonia as infection source</td>
</tr>
<tr>
<td>Creatinine $&gt; 2.0 \text{mg/dL (176.8 , \mu mol/L)}$</td>
</tr>
<tr>
<td>Bilirubin $&gt; 2 \text{mg/dL (34.2 , \mu mol/L)}$</td>
</tr>
<tr>
<td>Platelet count $&lt; 100,000 , \mu \text{L}$</td>
</tr>
<tr>
<td>Coagulopathy (international normalized ratio $&gt; 1.5$)</td>
</tr>
</tbody>
</table>

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
60% of Severe Sepsis/Septic Shock patients have an elevated Troponin
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”
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)
Reminders

Stop Sepsis
3-100s
Recognizing Sepsis Begins in Triage
Screening for Sepsis

- Nurses screen for sepsis on medical floor and ICU every shift on every patient
- Pre-hospital screening by paramedics
- Screening in Nursing Homes
Screening in the ambulance
Emergency Department & General Floor Sepsis Algorithm

Begin at Triage using “Adult ED Sepsis Screening Tool”

Suspected infection and 2 more SIRS criteria?

Yes → Positive screen for sepsis → Proceed with:
- Cardiac monitor
- BP, P, RR, MAP q15 and Temp hourly until stable
- Continuous oximetry
- Oxygen to maintain SpO₂ <90%
- Establish at least 1 large bore IV line
- Obtain BC, UA/UC, CBC w/diff, lactate

Negative screen for sepsis → Triage Level 1 or 2 → Notify physician and begin “Severe Sepsis/Septic Shock Screening Tool”

No → Negative screen for sepsis

SIRS Criteria
- Temperature ≥100 or ≤96.8
- Heart Rate > 100 beats/min
- Respiratory Rate >20/SpO₂<90%
- Altered Mental Status

Nursing Early Detection Tool
100-100-100

3-hr Bundle
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 ≥4mmol/L
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
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 < 96.8°F
   - RR > 20
   - HR > 100
   - WBC > 12,000 or < 4,000
3. Systolic BP < 90 after fluid bolus OR
   - Lactate > 4, OR
   - 2 or more organ dysfunctions
Transfer Trigger Tool

1. **Negative for severe sepsis/septic shock**
   - No
   - Positive for transfer trigger tool criteria?

2. **Positive for transfer trigger tool criteria?**
   - Yes
   - Positive for severe sepsis/septic shock
     - Transfer/admit to ICU or appropriate facility if CAH

3. **Transfer trigger tool**
   - Lactate > 4 mmol/L?
     - OR
   - Unresponsive to 30 mL/kg fluid?
     - OR
   - 2+ organ dysfunction?
     - OR
   - Progression of symptoms despite treatment?
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
Recognizing Sepsis in Older Patients
Difficulties in recognizing Sepsis in older patients

- Fever may be absent
  - 13% in patients > 65yrs vs. 4% in < 65yrs
- Lower incidence of tachycardia and hypoxemia
- Infection may not be apparent
  - More likely to have altered mental status (confusion, delirium)
  - Other non specific complaints such as weakness, falls, anorexia, incontinence
Ask The Question?
“Could this be Sepsis?”

- Patients presenting with:
  - Weakness
  - Syncope
  - Vomiting
  - Confusion
Why lactate?
Why lactate?

- When oxygen demand exceeds consumption, anaerobic metabolism results in lactic acidosis.
Lactate

- Lactate is a marker of “occult” severe sepsis or septic shock before hypotension or altered mental status develops.
- Any lactate elevation above normal is associated with increased mortality
- Lactate ≥ 4 is reported as a Critical Value by RMC lab.
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)
What if my hospital cannot perform a lactate?

- I-Stat Analyzer
- Cost ~ $10,000
- Can also perform blood gas, electrolytes.
- Can be a backup for platform analyzer
Is there a role for Procalcitonin in screening?

- Precursor of calcitonin.
- Rises in response to proinflammatory stimulus especially of bacterial origin.
- Can be used as a marker of severe sepsis caused by bacteria.
- May help differentiate sepsis from non-bacterial causes of SIRS.
- Not a good screening test for bacteremia as sensitivity is 76% and specificity is 70%.
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
In patients with undifferentiated shock, start broad spectrum antibiotics as soon as possible.
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
Source Control
Sites of Infection in Severe Sepsis

Wheeler NEJM 1999
Imaging

- Limited bedside abdominal ultrasound
- CT – chest/abdomen/pelvis
Focused Abdominal Sonography in Sepsis (FASS Exam)
FASS Exam (5 views)

- Right Kidney
- Left Kidney
- Bladder and Pelvis
- Gallbladder
- Subcostal cardiac and IVC
Hydronephrosis
Hydronephrosis
Cholecystitis
Subcostal Cardiac
IVC

Hepatic Vein

RA

IVC
Ridgeview Protocol for Severe Sepsis/Septic Shock
Sepsis Team

• ED physician
• ED RN
• Respiratory Therapist
• Pharmacist
• Lab technician
• Radiology technician
• ICU RN
• ICU MD
Early Goal Directed Therapy in Severe Sepsis
EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUELM RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERTSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

ABSTRACT

Background  Goal-directed therapy has been used for severe sepsis and septic shock in the intensive care unit. This approach involves adjustments of cardiac preload, afterload, and contractility to balance oxygen delivery with oxygen demand. The purpose of this study was to evaluate the efficacy of early goal-directed therapy before admission to the intensive care unit.

Methods  We randomly assigned patients who arrived at an urban emergency department with severe sepsis or septic shock to receive either six hours of early goal-directed therapy or standard therapy (as a control) before admission to the intensive care unit. Clinicians who subsequently assumed the care of the patients were blinded to the treatment assignment. In-hospital mortality (the primary efficacy outcome), end points with respect to resuscitation, and Acute Physiology and Chronic Health Evaluation (APACHE II) scores were obtained serially for 72 hours and compared between the study groups.

Results  Of the 263 enrolled patients, 130 were randomly assigned to early goal-directed therapy and 133 to standard therapy; there were no significant differences between the groups with respect to base-line characteristics. In-hospital mortality was 30.5 percent in the group assigned to early goal-directed therapy, as compared with 46.5 percent in the group assigned to standard therapy (P = 0.009). During the interval from 7 to 72 hours, the patients assigned to early goal-directed therapy had a significantly lower mortality (P = 0.009).

The systemic inflammatory response syndrome can be self-limited or can progress to severe sepsis and septic shock.1 Along this continuum, circulatory abnormalities (intravascular volume depletion, peripheral vasodilatation, myocardial depression, and increased metabolism) lead to an imbalance between systemic oxygen delivery and oxygen demand, resulting in global tissue hypoxia or shock.2 An indicator of serious illness, global tissue hypoxia is a key development preceding multiorgan failure and death.2 The transition to serious illness occurs during the critical “golden hours,” when definitive recognition and treatment provide maximal benefit in terms of outcome. These golden hours may elapse in the emergency department,3 hospital ward,4 or the intensive care unit.5

Early hemodynamic assessment on the basis of physical findings, vital signs, central venous pressure,6 and urinary output7 fails to detect persistent global tissue hypoxia. A more definitive resuscitation strategy involves goal-oriented manipulation of cardiac preload, afterload, and contractility to achieve a balance between systemic oxygen delivery and oxygen demand.2 End points used to confirm the achievement of such a balance (hereafter called resuscitation end points) include normalized values for mixed venous oxygen saturation, arterial lactate concentration, base deficit, and
Dobutamine 2.5 µg/kg/min
Early Goal-Directed Therapy Results

28-day Mortality

Standard Therapy
n=133

EGDT
n=130

49.2%
P = 0.01*

33.3%

*Key difference was in sudden CV collapse, not MODS

Early Goal Directed Therapy 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
Early Goal Directed Therapy

- Goals within 6 hrs:
  - CVP 8-12 mmHg
  - MAP ≥ 65
  - UO ≥ 0.5 ml/kg/hr
  - Superior vena cava oxygen saturation (Scv02) of 70%
  - Lactate normalization
Early Goal Directed Therapy

- Initiate Sepsis Orders
- Supplemental Oxygen OR Mechanical Ventilation with Lung Protective Strategies
- Central Line Placement for CVP, ScvO2 Monitoring
- Initiate Broad Spectrum Antibiotics
- If unable to place central line, obtain lactate clearance. Repeat in 2 hours.

CVP 8-12
- CVP 8-12
- CVP < 8
- Crystalloid infusion at 30 ml/kg for a minimum of 2 hours
- Consider addition of albumin 12.5 gm/NaCl to initial fluid resuscitation
- Avoid hydroxyethyl starches

SBP 90-140 (MAP 65-90)
- SBP < 90 (MAP < 65)
- 1. Arterial Line Placement (preferred)
- 2. Norepinephrine is 1st choice pressor
- 3. Epinephrine when additional agent needed
- 4. Vasopressin up to 0.03 units/min if on Norepinephrine & if poor response
- 5. For vasopressor refractory patients, consider Hydrocortisone 200 mg IV per day

ScvO2 70
- ScvO2 < 70
- Transfuse up to 3 units PRBC

Hgb
- Hgb < 9
- 1. Arterial Line Placement (if not in place)
- 2. Dobutamine 2.5 - 20 mcg/kg/min (If HR < 100 and SBP > 100)
- Hgb ≥ 10
- Consider intubation and mechanical ventilation with Lung Protective Strategies

Goals Achieved
- Lactate > 2
- Re-check lactate

The 6 hour SEPSECS Bundle for Severe Sepsis or Septic Shock
### A Randomized Trial of Protocol-Based Care for Early Septic Shock

**March 18, 2014**

#### Table: Cumulative In-Hospital Mortality to 60 Days

<table>
<thead>
<tr>
<th></th>
<th>Protocol-based EGDT</th>
<th>Protocol-based Standard Therapy</th>
<th>Usual Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at Risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protocol-based EGDT</td>
<td>439</td>
<td>373</td>
<td>316</td>
</tr>
<tr>
<td>Protocol-based Standard Therapy</td>
<td>444</td>
<td>370</td>
<td>378</td>
</tr>
<tr>
<td>Usual Care</td>
<td>404</td>
<td>350</td>
<td>371</td>
</tr>
</tbody>
</table>

### Goal-Directed Resuscitation for Patients with Early Septic Shock

*The ARISE Investigators and the ANZICS Clinical Trials Group*

**Oct 1, 2014**

#### Graph: Probability of Survival

- **EGDT** vs **Usual care**

### Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc., David A. Harrison, Ph.D., M. Zia Sadiq, Ph.D., Richard D. Grieve, Ph.D., Rahi Jahan, B.A., Sheila E. Harvey, Ph.D., Derek Bell, M.D., Julian F. Bion, M.D., Timothy J. Coats, M.D., Mervyn Singer, M.D., J. Duncan Young, D.M., and Kathryn M. Rowan, Ph.D., for the ProMiSe Trial Investigators

**April 2, 2015**

#### Graph: Kaplan-Meier Survival Estimates

- **Adjusted hazard ratio, 0.94 (0.79–1.11); P=0.46**
- **P=0.63 by log-rank test**

- **EGDT** vs **Usual care**

- **No. at Risk**
  - EGDT: 623, 492, 470, 461, 449, 445, 440
  - Usual care: 623, 492, 470, 461, 449, 445, 439
<table>
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<tr>
<th></th>
<th>Rivers</th>
<th>PROCESS</th>
<th>ARISE</th>
<th>PROMISE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td>US</td>
<td>US</td>
<td>Australia</td>
<td>United Kingdom</td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>263</td>
<td>1,351</td>
<td>1,600</td>
<td>1,260</td>
</tr>
<tr>
<td><strong>Fluids before Randomization</strong></td>
<td>20-30cc/kg</td>
<td>20-30cc/kg</td>
<td>1,000cc</td>
<td>1,000cc</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>EGDT 6 hrs</td>
<td>EGDT 6 hrs</td>
<td>EGDT 6 hrs</td>
<td>EGDT 6 hrs</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>Usual care</td>
<td>Protocol Rx</td>
<td>Usual care</td>
<td>Usual care</td>
</tr>
<tr>
<td><strong>Primary endpoint</strong></td>
<td>In hosp mortality</td>
<td>60 day mortality</td>
<td>90 day mortality</td>
<td>90 day mortality</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>30.5%</td>
<td>21% (EGDT)</td>
<td>18.6%</td>
<td>29.2%</td>
</tr>
<tr>
<td><strong>Usual Care</strong></td>
<td>46.5%</td>
<td>18.9%</td>
<td>18.8%</td>
<td>29.2%</td>
</tr>
</tbody>
</table>
## Interventions in Usual Care

<table>
<thead>
<tr>
<th></th>
<th>PROCESS</th>
<th>ARISE</th>
<th>PROMISE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CVP line</strong></td>
<td>56.5%</td>
<td>62%</td>
<td>50.9%</td>
</tr>
<tr>
<td></td>
<td>57.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Art line</strong></td>
<td>?</td>
<td>76%</td>
<td>62.2%</td>
</tr>
<tr>
<td><strong>Vasopressors</strong></td>
<td>52.2%</td>
<td>58%</td>
<td>46.6%</td>
</tr>
<tr>
<td></td>
<td>44.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fluids in 1st 6 hrs</strong></td>
<td>3,300cc, 1,200cc</td>
<td>1,713cc</td>
<td>1,750cc</td>
</tr>
</tbody>
</table>
How do we apply this recent new data?

- Early diagnosis of septic shock is essential
- Lactate still useful for screening
- Early fluid resuscitation still important (all groups in Process received more that 2 liters prior to randomization)
- Early Antibiotics (75% received antibiotics before randomization)
- Having a protocol is important (70% of hospitals had some form of sepsis protocol)
- Central lines used in 50-60% of control groups
Who needs a central line?

- IV access issues
- Patients needing vasopressors
- Unable to assess fluid responsiveness with ultrasound
Resuscitation Bundles

- Operationalize Guidelines
- Measurement of Quality
- Hospitals will begin reporting on Sepsis measures Oct 1, 2015
- Pay for Performance - 2017
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 after initial fluid administration (MAP < 65 mm Hg) or if the initial lactate was ≥ 4mmol/L, re-assess volume status and tissue perfusion and document findings according to Table 1.

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

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥8 mm Hg, ScvO2 of ≥70% and lactate normalization.
DOCUMENT REASSESSMENT OF VOLUME STATUS AND TISSUE PERFUSION WITH:

EITHER

- Repeat focused exam (after initial fluid resuscitation) by licensed independent practitioner including vital signs, cardiopulmonary, capillary refill, pulse and skin findings

OR TWO OF THE FOLLOWING:

- Measure CVP
- Measure Scv02
- Bedside cardiovascular ultrasound
- Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge
How Can We Implement a Sepsis Protocol at our Hospital?

- Organize a Multidisciplinary Team
- Use Process Improvement Techniques
- Make use of Resources
  - Surviving Sepsis Campaign
  - Minnesota Hospital Association
Sepsis Care at Ridgeview Medical
Ridgeview Sepsis Initiative

- 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
  - Primary Care Providers
  - Critical Care Nursing
  - Pharmacy
  - Quality Improvement
  - Hospitalist
  - ED Nursing
  - Laboratory
  - Respiratory Care
Ridgeview Sepsis Protocol

- Adult Severe Sepsis/Septic Shock order set
- Hospital wide colored pictorial Stop Sepsis algorithm
- Sepsis Scorecard
- *ED Severe Sepsis/Septic Shock*
  Screening tool and checklist
- RRT protocol includes screening for severe sepsis
- Sepsis Response Team
Ridgeview Sepsis Mortality

SEP-Historical Sepsis Mortality by Year

- Target: 20.0%
- Yearly Mortality Rates:
  - 2007: 38.0%
  - 2008: 36.0%
  - 2009: 34.0%
  - 2010: 32.0%
  - 2011: 36.0%
  - 2012: 20.0%
  - 2013: 30.6%
  - 2014: 10.0%
Ridgeview Lives Saved

![Bar Chart: SEP-Sepsis Lives Saved]
Financial Impact

- Reduced LOS

- Reduced Cost of care:
  - $213,068 savings: Jan 2013 - June 2014
## Ridgeview Sepsis Scorecard

<table>
<thead>
<tr>
<th>Quality</th>
<th>Metric Description</th>
<th>Target</th>
<th>实现</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>▲</td>
<td>SEP-Percent of Patients identified in ICU</td>
<td>100.0%</td>
<td>n/a</td>
<td>Jun 2014</td>
</tr>
<tr>
<td>▼</td>
<td>SEP-Percent of Patients identified in ED</td>
<td>0.0%</td>
<td>n/a</td>
<td>Jun 2014</td>
</tr>
<tr>
<td>—</td>
<td>SEP-Percent of Comfort Care/palliative care/AD contradicting sepsis Rx</td>
<td>0.0%</td>
<td>n/a</td>
<td>Jun 2014</td>
</tr>
<tr>
<td>—</td>
<td>SEP-Percent of ED or IP sepsis screening tool used</td>
<td>100.0%</td>
<td>n/a</td>
<td>Jun 2014</td>
</tr>
<tr>
<td>▼</td>
<td>SEP-Percent of Serum lactate measured within 3 hrs of Time Zero</td>
<td>100.0%</td>
<td>95.0%</td>
<td>Jun 2014</td>
</tr>
<tr>
<td>▼</td>
<td>SEP-Percent of broad spectrum antibiotics administered w_in 3 hrs from TZ</td>
<td>100.0%</td>
<td>95.0%</td>
<td>May 2014</td>
</tr>
<tr>
<td>▼</td>
<td>SEP-Percent of blood cultures obtained prior to antibiotic administration</td>
<td>100.0%</td>
<td>95.0%</td>
<td>Jun 2014</td>
</tr>
<tr>
<td>▼</td>
<td>SEP-Percent of initial minimum of 30ml_kg of crystalloid started within 3 hrs of TZ</td>
<td>n/a</td>
<td>95.0%</td>
<td>Jul 2014</td>
</tr>
<tr>
<td>▼</td>
<td>SEP-Percent of Vasopressors administered for a MAP less than 65 w_in 6 hrs of TZ</td>
<td>n/a</td>
<td>n/a</td>
<td>Jul 2014</td>
</tr>
<tr>
<td>▲</td>
<td>SEP-Percent of central line placed within 6 hrs of Time Zero</td>
<td>0.0%</td>
<td>50.0%</td>
<td>Jun 2014</td>
</tr>
<tr>
<td>▼</td>
<td>SEP-Percent of CVP measured within 6 hrs of Time Zero</td>
<td>n/a</td>
<td>95.0%</td>
<td>Jul 2014</td>
</tr>
<tr>
<td>▼</td>
<td>SEP-Percent of ScvO2 measured within 6 hrs of Time Zero</td>
<td>n/a</td>
<td>95.0%</td>
<td>Jul 2014</td>
</tr>
<tr>
<td>▼</td>
<td>SEP-Percent of serum lacate re-measured within 6 hrs of Time Zero</td>
<td>0.0%</td>
<td>95.0%</td>
<td>Jun 2014</td>
</tr>
</tbody>
</table>
CMS LEAPT
Leading Edge Advance Practice Topics

- LEAPT created by CMS
- Partnering with MHA HEN (Hospital Engagement Network)
- Embed evidence based interventions of the Surviving Sepsis Campaign into care processes in hospitals across the state and beyond
SEEING SEPSIS: EARLY IDENTIFICATION SAVES LIVES

Severe sepsis can be associated with a mortality rate of up to 50 percent in hospitals that do not utilize an early detection and treatment bundle. The Minnesota Hospital Association, funded by the CMS' Leading Edge Advanced Practice Topics (LEAPT), has coordinated the development of this Seeing Sepsis Tool Kit to facilitate the adoption of severe sepsis early detection tools and the Surviving Sepsis Campaign three- and six-hour care bundles by hospitals of all sizes.

For more information, contact Karen Olson, MHA HEN patient safety/quality coordinator, 651-603-3521.

SEEING SEPSIS VIDEO GALLERY

Sepsis Physician Simulcast
View a rebroadcast of the Sepsis Physician Simulcast and learn how St. Cloud Hospital decreased mortality due to severe sepsis/septic shock by 49 percent, saving more than 400 lives. Also see how Ridgeview Medical Center in Waconia made early identification of sepsis in the E.D. a priority and decreased mortality due to severe sepsis/septic shock by 60 percent.

Seeing sepsis part 1: Definitions
Learn background definitions and basic pathophysiology for the sepsis continuum.

Seeing sepsis part 2: Early detection
Learn tips and tools to help front line staff detect sepsis early.
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 hydrenephrosis
- 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 pressor support with Norepinephrine
  - 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
Key Points

- Recognize severe sepsis/septic shock as a time critical emergency
- Screen for Sepsis – in the ED, Medical Floor and ICU
- Utilize lactates if screen positive for sepsis
- Aggressive fluid resuscitation (30/kg initial bolus)
- Early broad spectrum antibiotics and source control
- Repeat lactates to monitor resuscitation
Thank you