Sepsis

- SEPSIS:
  - SIRS
  - DRG 871
  - death
  - time sensitivity
  - blood chemicals
  - virus
  - severe
  - bacteria
  - infection
  - organ failure
  - toxic response
  - shock
  - inflammation
  - mortality
  - increased LOS
  - parasite
  - 50% unnecessary
  - reimbursement
  - severe
  - No dedicated drug tx
  - difficult
diagnosis

Suma Desai Jain, MD
Ochsner Clinic Foundation
New Orleans, Louisiana
Disclosures

No conflicts of interest to disclose
Updates in Sepsis

- Introduction
- Epidemiology
- Surviving sepsis guidelines 2012
- Updates
  - Resuscitation protocols
  - Map Goals
  - Transfusion
  - Sepsis-3
  - Bundle
- Management
- Questions
What is SEPSIS?

- Sepsis is a systemic, deleterious host response to infection leading to:
  - Severe sepsis and
    - acute organ dysfunction secondary to documented or suspected infection
  - Septic shock
    - severe sepsis plus hypotension not reversed with fluid resuscitation
The Sepsis spectrum

**SIRS**
- A clinical response arising from a nonspecific insult, with ≥2 of the following:
  - $T > 38°C$ or $< 36°C$
  - HR > 90 beats/min
  - RR > 20/min
  - WBC $> 12,000/\text{mm}^3$ or $< 4,000/\text{mm}^3$ or $> 10\%$ bands

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

**Severe Sepsis**
- Sepsis with organ failure

**Septic Shock**
- Refractory hypotension

SIRS = systemic inflammatory response syndrome

Why Focus on Sepsis?

- 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

Why Sepsis?

- Major public health concern
  - The cost to the US healthcare system for sepsis, and pneumonia grew twice as fast as the overall growth in hospital charges
  - $54 billion per year
  - Approximately 180 percent increase from 1997 to 2005
    - Aging, recognition
  - Long-term physical, psychological, and cognitive disabilities

Comparison With Other Major Diseases

Incidence of Severe Sepsis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cases/100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS*</td>
<td>50</td>
</tr>
<tr>
<td>Colon Cancer§</td>
<td>100</td>
</tr>
<tr>
<td>Breast Cancer§</td>
<td>150</td>
</tr>
<tr>
<td>CHF†</td>
<td>200</td>
</tr>
<tr>
<td>Severe Sepsis‡</td>
<td>300</td>
</tr>
</tbody>
</table>

Mortality of Severe Sepsis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Deaths/Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS*</td>
<td>50,000</td>
</tr>
<tr>
<td>Breast Cancer§</td>
<td>100,000</td>
</tr>
<tr>
<td>AMI†</td>
<td>150,000</td>
</tr>
<tr>
<td>Severe Sepsis‡</td>
<td>200,000</td>
</tr>
</tbody>
</table>

Why Sepsis?

Figure 4. Average length of stay for those hospitalized for septicemia or sepsis compared with those hospitalized for other conditions, 2008

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Septicemia or sepsis hospitalizations</th>
<th>Other hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>8.4</td>
<td>4.8</td>
</tr>
<tr>
<td>Under 65 years</td>
<td>9.1</td>
<td>4.3</td>
</tr>
<tr>
<td>65 and over</td>
<td>8.0</td>
<td>5.6</td>
</tr>
</tbody>
</table>

\(^1\) Difference is statistically significant at the 0.05 level.


R. Phillip Dellinger, MD¹; Mitchell M. Levy, MD²; Andrew Rhodes, MB BS³; Djillali Annane, MD⁴; Herwig Gerlach, MD, PhD⁵; Steven M. Opal, MD⁶; Jonathan E. Sevransky, MD⁷; Charles L. Sprung, MD⁸; Ivor S. Douglas, MD⁹; Roman Jaeschke, MD¹⁰; Tiffany M. Osborn, MD, MPH¹¹; Mark E. Nunnally, MD¹²; Sean R. Townsend, MD¹³; Konrad Reinhart, MD¹⁴; Ruth M. Kleinpell, PhD, RN-CS¹⁵; Derek C. Angus, MD, MPH¹⁶; Clifford S. Deutschman, MD, MS¹⁷; Flavia R. Machado, MD, PhD¹⁸; Gordon D. Rubenfeld, MD¹⁹; Steven A. Webb, MB BS, PhD²⁰; Richard J. Beale, MB BS²¹; Jean-Louis Vincent, MD, PhD²²; Rui Moreno, MD, PhD²³; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*
Surviving Sepsis Campaign

- Facilitate early recognition of severe sepsis
  - Provider education
  - Screening tools
  - Treat sepsis as an emergency

- Emphasize timely evidence-based management
  - Assessment of perfusion
  - Early antibiotics
  - Fluid resuscitation
  - Assessment of adequacy of resuscitation
Recommendations: Initial Resuscitation and Infection Issues*

A. Initial Resuscitation

1. Protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hrs of resuscitation:
   a) Central venous pressure 8–12 mm Hg
   b) Mean arterial pressure (MAP) ≥ 65 mm Hg
   c) Urine output ≥ 0.5 mL/kg/hr
   d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).

2. In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C).
EGDT 2001, Single center, 263 patients

Purpose: evaluate efficacy of 6 hrs of EGDT prior to admission to ICU
EGDT algorithm

**EARLY**
Initial 6 hrs of resuscitation in the ED

**GOAL DIRECTED**
- CVP > 8
- MAP > 65
- ScvO2 > 70%

---

**Figure 2. Protocol for Early Goal-Directed Therapy.**
CVP denotes central venous pressure, MAP mean arterial pressure, and ScvO2 central venous oxygen saturation.
<table>
<thead>
<tr>
<th></th>
<th>EGDT</th>
<th>Usual</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF</td>
<td>4.9L</td>
<td>3.5L</td>
</tr>
<tr>
<td>Pressors</td>
<td>27.4%</td>
<td>30.3%</td>
</tr>
<tr>
<td>CVC</td>
<td>Mandatory</td>
<td>Mandatory</td>
</tr>
<tr>
<td>PRBC</td>
<td>64.1%</td>
<td>18.5%</td>
</tr>
</tbody>
</table>
EGDT- results

- Mortality: 30.5% vs 46.5% (p=0.009)
- Significant decrease in 28 day and 60 day mortality
STANDARD of CARE
A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*
ProCESS Trial

- Published in NEJM May 1, 2014
- Multicenter, USA; 1341 patients enrolled
- Is EGDT generalizable and are all aspects necessary?
- 3 groups
  - EGDT
  - Protocol Standard
    - No CVC, inotropes, blood products mandates
  - Usual Care
<table>
<thead>
<tr>
<th></th>
<th>EGDT</th>
<th>Protocol</th>
<th>Usual</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IVF</strong></td>
<td>5.0L</td>
<td>5.5L</td>
<td>4.4L</td>
</tr>
<tr>
<td><strong>Pressors</strong></td>
<td>54%</td>
<td>52%</td>
<td>44%</td>
</tr>
<tr>
<td><strong>CVC</strong></td>
<td>93%</td>
<td>56%</td>
<td>57%</td>
</tr>
<tr>
<td><strong>PRBC</strong></td>
<td>14.4%</td>
<td>8.3%</td>
<td>7.5%</td>
</tr>
</tbody>
</table>
Process

Goals

21%

The Protocol

18.2%

Business As Usual

18.9%
Results:
› No 60 day mortality difference
› No difference in 90 day/ 1 year mortality or need for organ support

Conclusion: “protocol-based resuscitation of ER septic shock patients did not improve outcomes.”
Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*
ARISE Trial

- NEJM October 2014
- 51 ctrs; Australia, New Zealand; 1600 pts
- Purpose: to determine whether EGDT recq from SSC could be generalized to diverse healthcare setting

- 2 groups
  - EGDT
  - Usual Care
<table>
<thead>
<tr>
<th></th>
<th>EGDT</th>
<th>Pragmatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF</td>
<td>1.96L</td>
<td>1.71L</td>
</tr>
<tr>
<td>Pressors</td>
<td>66.6%</td>
<td>57.8%</td>
</tr>
<tr>
<td>A-Lines</td>
<td>91%</td>
<td>76%</td>
</tr>
<tr>
<td>CVC</td>
<td>90%</td>
<td>61.9%</td>
</tr>
<tr>
<td>PRBC</td>
<td>13.6%</td>
<td>7.0%</td>
</tr>
</tbody>
</table>
No difference in 90 day mortality
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 Sadique, 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*
ProMISE Trial

- April 2015 NEJM
- Multicenter, United Kingdom 1260 pts
- Purpose
- 2 Groups
  - EG DT
  - Usual Care
<table>
<thead>
<tr>
<th></th>
<th>EGDT</th>
<th>Usual</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF</td>
<td>2.23L</td>
<td>2.02L</td>
</tr>
<tr>
<td>Pressors</td>
<td>53.3%</td>
<td>46.6%</td>
</tr>
<tr>
<td>A-Lines</td>
<td>74.2%</td>
<td>62.2%</td>
</tr>
<tr>
<td>CVC</td>
<td>92.1%</td>
<td>50.9%</td>
</tr>
<tr>
<td>PRBC</td>
<td>8.8%</td>
<td>3.8%</td>
</tr>
</tbody>
</table>
ProMISEe

- Increased treatment intensity in the EG DT group
  - More IVF, vasoactive drugs, and PRBC transfusions, more days advanced cardiovascular support, and longer stays in the intensive care unit.

- No difference in 90 day mortality 29.5% EG DT vs 29.2% usual care
After EGDT- What now?

- 2001 – single center, primary investigator trial that changed the standard of care
  - Improved sepsis care since likely due to earlier recognition and early fluids, abx, and pressors
  - EGDT not necessary now, given culture change, but was necessary to change the culture

- Protocols
  - Most agree that entire bundle is unnecessary
  - Concern for a lack of vigilance without protocolized care plan

- All 3 studies, intervention group received more of everything - central lines, dobutamine, pressors, PRBC, but made no difference in outcomes

- Commonality
  - Early antibiotics, fluids and vasopressors, and a high survival rate from severe sepsis and septic shock.
Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg (grade 1C).
Does a Higher MAP Decrease Renal Failure in Sepsis?
High versus Low Blood-Pressure Target in Patients with Septic Shock

Pierre Asfar, M.D., Ph.D., Ferhat Meziani, M.D., Ph.D., Jean-François Hamel, M.D., Fabien Grelon, M.D., Bruno Megarbane, M.D., Ph.D., Nadia Anguel, M.D., Jean-Paul Mira, M.D., Ph.D., Pierre-François Dequin, M.D., Ph.D., Soizic Gergaud, M.D., Nicolas Weiss, M.D., Ph.D., François Legay, M.D., Yves Le Tulzo, M.D., Ph.D., Marie Conrad, M.D., René Robert, M.D., Ph.D., Frédéric Gonzalez, M.D., Christophe Guitton, M.D., Ph.D., Fabienne Tamion, M.D., Ph.D., Jean-Marie Tonnelier, M.D., Pierre Guezennec, M.D., Thierry Van Der Linden, M.D., Antoine Vieillard-Baron, M.D., Ph.D., Eric Mariotte, M.D., Gaël Pradel, M.D., Olivier Lesieur, M.D., Jean-Damien Ricard, M.D., Ph.D., Fabien Hervé, M.D., Damien du Cheyron, M.D., Ph.D., Claude Guerin, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Jean-Louis Teboul, M.D., Ph.D., and Peter Radermacher, M.D., Ph.D., for the SEPSISPAHEM Investigators*
SEPSISPAM

- NEJM 4/2014
- Multicenter, randomized, open label
- 776 patients, France
- 2 groups
  - MAP 65-70mm Hg
  - MAP 80-85mm Hg
SEPSISPAM - Results

- No difference in 28 or 90 day mortality
- No difference in 28 day survival without organ support
- More AFIB in higher MAP group
- Longer pressor duration and dose
- Patients with Chronic Hypertension in the higher MAP group – fewer on RRT, no change in mortality
Surviving Sepsis Campaign

Maintain Hct ≥30%

Hb ≤7g/dL

Level 1B Rec
Once tissue hypoperfusion has resolved and in the absence myocardial ischemia, severe hypoxemia, acute hemorrhage, or ischemic heart disease, we recommend that red blood cell transfusion occur only when hemoglobin concentration decreases to <7.0 g/dL to target a hemoglobin concentration of 7.0 - 9.0 g/dL in adults (grade 1B).
Does a Liberal Transfusion Strategy Improve Mortality in Sepsis?
Lower versus Higher Hemoglobin Threshold for Transfusion in Septic Shock

Lars B. Holst, M.D., Nicolai Haase, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Jan Werner, M.D., Ph.D., Anne B. Guttormsen, M.D., Ph.D., Sari Karlsson, M.D., Ph.D., Pär I. Johansson, M.D., Ph.D., Anders Åneman, M.D., Ph.D., Marianne L. Vang, M.D., Robert Winding, M.D., Lars Nebrich, M.D., Helle L. Nibro, M.D., Ph.D., Bodil S. Rasmussen, M.D., Ph.D., Johnny R.M. Lauridsen, M.D., Jane S. Nielsen, M.D., Anders Oldner, M.D., Ph.D., Ville Pettilä, M.D., Ph.D., Maria B. Cronhjort, M.D., Lasse H. Andersen, M.D., Ulf G. Pedersen M.D., Nanna Reiter, M.D., Jørgen Wiis, M.D., Jonathan O. White, M.D., Lene Russell, M.D., Klaus J. Thornberg, M.D., Peter B. Hjortrup, M.D., Rasmus G. Müller, M.D., Morten H. Møller, M.D., Ph.D., Morten Steensen, M.D., Inga Tjäder, M.D., Ph.D., Kristina Kilsand, R.N., Suzanne Odeberg-Wernerman, M.D., Ph.D., Brit Sjøbø, R.N., Helle Bundgaard, M.D., Ph.D., Maria A. Thyø, M.D., David Lodahl, M.D., Rikke Mærkedahl, M.D., Carsten Albeck, M.D., Dorte Illum, M.D., Mary Kruse, M.D., Per Winkel, M.D., D.M.Sc., and Anders Perner, M.D., Ph.D., for the TRISS Trial Group* and the Scandinavian Critical Care Trials Group.
TRISS

- NEJM 10/2014
- Multicenter, parallel group randomized
- 998 patients, Scandinavia
- Patients with Septic shock, hgb ≤ 9g/dl
  - Lower threshold group - tx when hgb ≤ 7g/dl
  - Higher threshold group - tx when hgb ≤ 9g/dl

- Endpoint 90 day mortality
TRISS- results

- Median transfusion
  - Lower threshold group - 1 unit
  - Higher threshold group - 4 units

- No difference in 90 day mortality
- No difference in adverse events
LESS IS MORE

Association of Blood Transfusion With Increased Mortality in Myocardial Infarction

A Meta-analysis and Diversity-Adjusted Study Sequential Analysis

Saurav Chatterjee, MD; Jørn Wetterslev, MD, PhD; Abhishek Sharma, MD; Edgar Lichstein, MD; Debabrata Mukherjee, MD, MS
Meta-analysis of blood transfusion strategy studies in anemia associated with myocardial infarction

All-cause mortality rates, Pooled effect estimates

Increased all-cause mortality with blood transfusion vs no blood transfusion during myocardial infarction

18.2% vs 10.2%

Blood transfusion significantly associated with a higher risk for subsequent myocardial infarction (risk ratio, 2.04; 95% CI, 1.06-3.93; P = .03).

Conclusions

Liberal blood transfusion strategy compared with a restricted blood transfusion strategy is associated with higher all-cause mortality rates.

Requires investigation in a large trial with low risk for bias.
A task force (n = 19) with expertise in sepsis pathobiology, clinical trials, and epidemiology convened by the SCCM and European Society of Intensive Care Medicine.

Concern of previous definitions of sepsis
- Excessive focus on inflammation
- Misleading model that sepsis follows a continuum through severe sepsis to shock,
- Inadequate specificity and sensitivity of SIRS criteria.

New definitions and clinical criteria generated
SEPSIS-3: SIRS criteria

- 2 or more SIRS criteria to identify sepsis considered unhelpful.
  - Changes in WBC, temperature, and HR reflect inflammation, or the host response to infection or other insults.
    - Not necessarily a dysregulated, life-threatening response.
  - SIRS criteria present in many hospitalized patients, including those without infection, who never incur adverse outcomes (poor discriminant validity).
Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis

Kirsi-Maija Kaukonen, M.D., Ph.D., Michael Bailey, Ph.D., David Pilcher, F.C.I.C.M., D. Jamie Cooper, M.D., Ph.D., and Rinaldo Bellomo, M.D., Ph.D.
Systemic Inflammatory Response Syndrome
Criteria in Defining Severe Sepsis

- NEJM 4/2015
- 172 ICUs in Australia/New Zealand
- Patients with infection and organ failure
  - SIRS-positive severe sepsis
    - >2 SIRS criteria, an APACHE III diagnosis of infection at admission with at least one organ failure, or an APACHE III diagnosis of severe sepsis or septic shock at admission.
  - SIRS-negative severe sepsis
    - <2 SIRS criteria, and an APACHE III diagnosis of infection at admission with at least one organ failure or an APACHE III diagnosis of severe sepsis or septic shock at admission.
1,171,797 patients
  > 96,385 patients (87.9%) had SIRS-positive severe sepsis
  > 13,278 (12.1%) had SIRS-negative severe sepsis.

Over 14 years
  > Similar characteristics and changes in mortality
  > SIRS-positive group: from 36.1% to 18.3%
  > SIRS-negative group: from 27.7% to 9.3%
  > Mortality increased linearly with each additional SIRS criterion
    • Without any transitional increase in risk at a threshold of two SIRS criteria.
Figure 1. Mortality among Patients with Severe Sepsis, According to Status with Respect to Criteria for the Systemic Inflammatory Response Syndrome (SIRS).

Patients were categorized according to whether they had symptoms meeting two or more SIRS criteria (SIRS-positive sepsis) or symptoms meeting less than two SIRS criteria (SIRS-negative sepsis). Panel A shows the unadjusted annual mortality among patients in the two groups from 2000 through 2013, and Panel B shows the adjusted annual odds of death. The bars represent 95% confidence intervals.
Figure 2. Mortality among Patients with Severe Sepsis, According to Number of SIRS Criteria Met.
The bars represent 95% confidence intervals.
Using 2 or more SIRS criteria to define severe sepsis excluded one in eight (12%) otherwise similar patients with infection, organ failure, and substantial mortality.

- Failed to define a transition point in the risk of death.
Numerous scoring systems to assess severity of organ dysfunction

Sequential Organ Failure Assessment (SOFA)
  - Higher score associated with increased probability of mortality.
  - Grades abnormality by organ system and accounts for clinical interventions.

Limitations
  - Full labs are needed for computation
  - Not well known outside the critical care community.
# SOFA Score

## Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score

<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{Pao}_2/\text{Fi}_2$ (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>
<td></td>
</tr>
<tr>
<td><strong>Coagulation</strong></td>
<td></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></td>
<td></td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td></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>
<td></td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP $\geq 70$ mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP $&lt; 70$ mm Hg</td>
<td>Dopamine $&lt; 5$ or dobutamine (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>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Central nervous system</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasgow Coma Scale score$^c$</td>
<td>$15$</td>
<td>$13-14$</td>
<td>$10-12$</td>
<td>$6-9$</td>
<td></td>
<td>$&lt; 6$</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td></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>
<td></td>
</tr>
<tr>
<td>Urine output, mL/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$&lt; 500$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$&lt; 200$</td>
</tr>
</tbody>
</table>

Abbreviations: $\text{Fi}_2$, fraction of inspired oxygen; MAP, mean arterial pressure; $\text{Pao}_2$, partial pressure of oxygen.

$^a$ Adapted from Vincent et al.$^{27}$  

$^b$ Catecholamine doses are given as $\mu$g/kg/min for at least 1 hour.

$^c$ Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.
Clinical Criteria to Identify Patients With Sepsis

- No current clinical measures reflect dysregulated host response.
- Many clinical criteria that best identified infected patients most likely to have sepsis.
- Interrogation of large data sets of hospitalized patients with presumed infection
  - SIRS, SOFA scores, correlation to outcomes
Clinical Criteria to Identify Patients With Sepsis

- Reviewed health record data of 1.3 million patients within U of Pittsburgh health system
- 148,907 with suspected infection, culture, abx
- Hospital mortality and mortality and ICU stay of 3 days or longer, or both—used to assess predictive validity
ICU patients with suspected infection
- SOFA score discrimination for hospital mortality was superior to SIRS
  - (AUROC = 0.74; 95% CI, 0.73-0.76); SIRS (AUROC = 0.64; 95% CI, 0.62-0.66).
- Change in SOFA score of >2 similar to SOFA score
  - (AUROC = 0.72; 95% CI, 0.70-0.73).

Patients outside ICU- discrimination of hospital mortality with SOFA or change in SOFA score was similar to SIRS

Task force recommends
- Using a change in baseline SOFA score of 2 points or more to represent organ dysfunction
- SOFA score of 2 or more had an overall mortality risk of approximately 10%
- SOFA score of 2 or greater identified a 2- to 25-fold increased risk of dying compared with patients with a SOFA score less than 2.
2 of 3 clinical variables offered predictive validity similar to that of the full SOFA score outside the ICU.

- GCS <13
- SBP <100 mm Hg
- RR >22/min

(AUROC = 0.81; 95% CI, 0.80-0.82)

qSOFA (quick SOFA)

- Simple bedside criteria to identify adult patients with suspected infection who are likely to have poor outcomes.
- Should be used to prompt further investigation, to initiate or escalate therapy and to consider referral to critical care or increase monitoring.
Septic shock

- Same process to evaluate Septic shock
  - Hypotension, elevated lactate level, and a sustained need for vasopressor therapy to test in cohort studies,
  - Interrogation of Surviving Sepsis Campaign database, and reproducible in 2 others

- The combination of hypotension, vasopressor use, and lactate level greater than 2 mmol/L (18 mg/dL) identified patients with mortality rates of 35-54%
  - Greater than any of the 3 individually
Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

Organ dysfunction is represented by an increase in the SOFA score of 2 points or more, associated with an in-hospital mortality greater than 10%.

Septic shock
- Subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.
- Clinically identified by a
  - Vasopressor requirement to maintain MAP > 65 mm Hg and
  - Serum lactate > than 2 mmol/L in the absence of hypovolemia
- Hospital mortality > than 40%.

In non-ICU settings, adult patients with suspected infection can be rapidly identified as being more likely to have poor outcomes if they have at least 2 of the following clinical criteria:

- (qSOFA):
  - Respiratory rate of 22/min or greater
  - Altered mentation
  - Systolic blood pressure of 100 mm Hg or less.
Early Management

Revised Bundles in response to 3 prior resuscitation trials

TO BE COMPLETED WITHIN 3 HOURS OF TIME OF PRESENTATION*:

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/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 of severe sepsis or septic shock ascertained through chart review.

TO BE COMPLETED WITHIN 6 HOURS OF TIME OF PRESENTATION:

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65mmHg
6. In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was ≥4 mmol/L, re-assess volume status and tissue perfusion and document findings according to Table 1.
7. Re-measure lactate if initial lactate elevated.
Sepsis Management Goals

- Early Identification
  - qSofa Criteria

- Early Diagnosis
  - SOFA score
  - Or > 2 increase in SOFA score

- Early Evaluation
  - Blood Urine Sputum cultures prior to ABX
  - Imaging Studies
Early Antibiotics

- Early Administration of Empiric Antibiotics
  - Within the first hour of sepsis recognition

Gaieski DF, Mikkelsen ME, Band RA, et al. Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department*. Critical Care Medicine 2010;38(4):1045–53.

Expert opinion supports identifying the source of infection and aggressively managing it when possible.


Chronic Phase

- Monitor for and prevent recurrence of sepsis
  > VAP, CLABSI, UTI. Infection Control Practices.
- Lung Protective Ventilator Strategies
- Protocolized Sedation, Daily Awakenings
- Nutritional Support
- Early Mobilization
- Multi-disciplinary approach.
System-based strategies are effective for improving sepsis care

- Identify patients early and identify the severity of sepsis
- Quickly administer appropriate antibiotics and source control
- Establish institutional goals for physiologic resuscitation
- Multidisciplinary chronic phase of care to ensure compliance