UP A RIVER WITHOUT A PADDLE: DEFINING SEPSIS IN 2016, REVISITING TREATMENT GOALS AND OTHER CHALLENGING TOPICS IN SEPSIS

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DISCLOSURE

- I have no actual or potential conflicts of interests in relation to this presentation
- I will not discuss off label use and/or investigational uses of medications or treatments in my presentation
learning objectives

At the completion of this program, the participant will be able to:

- Restate the basic physiology surrounding sepsis and septic shock
- Define changes to the definition of sepsis and septic shock as defined by Sepsis-3
- Explain the significance of early goal directed therapy (EGDT)
- Identify the recent literature challenging EGDT
- Discuss evolving challenges surrounding sepsis management
Tale as old as time

“Sepsis” is derived from the Greek work “sepo” which literally means “I rot”

Believe to be “biological decay” that occurred in colon and released “dangerous principles” and that could cause “auto-intoxication”

“Inflammation is not itself considered to be a disease but a salutary operation…but when it cannot accomplish that salutary purpose…it dose mischief” - John Hunter, MD (1728-1793)
**SCOPE OF THE PROBLEM**

- One of top 5 diagnoses for ICU admissions in US
- CDC National Center for Health Statistics
  - 621,000 cases in 2000 → 1.41 million cases in 2008
- Increasing age in US population
- Increasing life expectancy
- Inflated reporting

http://www.sccm.org/Communications/Pages/CriticalCareStats.aspx.
SIRS: FROM INSULT TO SHOCK

- Micro capillary leak
- Leads to peripheral vasodilation
- Decreased ability of tissues to take up O2
- Increased heart rate and contractility
- ↑ cardiac output
- Can progress to distributive shock → death

SEPISIS MEDIATED DISTURBANCE OF COAGULATION

**Blood Pressure and Cardiac Output**

- **Arterial Oxygen Saturation**
- **Hemoglobin**
- **Preload (PCWP)**
- **Contractility**
  - (Positive)
  - (Negative)
- **Afterload (SVR)**
- **Heart Rate**
- **Stroke Volume**
- **Oxygen Delivery**
- **Cardiac Output (CO)**
- **Blood Pressure**
THE RISE OF EGDT: RIVERS, ET.AL.

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL 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 PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

Inclusion criteria
2/4 SIRS criteria AND
one of the following: 1) hypotension after fluids
2) Lactate ≥ 4

Groups
1) EGDT
2) Standard treatment

Study performed
9 bed ED unit at a tertiary medical center

Primary outcome
In-hospital mortality (p=0.009)
30.5% EGDT
45.5% standard care

Secondary outcomes
1) Resuscitation end points
2) Organ dysfunction score
3) Coagulation related variables
4) Administered treatments
5) Consumption of health care resources
Early Goal Directed Therapy (EGDT)

- Hemodynamic augmentation
- More “concrete” resuscitation strategy
- Resuscitation end points:
  - Lactate clearance
  - Correction of pH and base deficit
  - Normalization of mixed venous oxygen saturation (ScVO2)

**RIVERS LIMITATIONS**

- Single center study (large medical center)
- n=263
- Support by Edwards Lifesciences and Nova Biomedical
- 9 bed ED with one attending physician, two residents and three nurses

10+ YEARS OF EARLY GOAL DIRECTED THERAPY


2002: Surviving Sepsis Campaign

2004: First guidelines published

2005: Implementing the Surviving Sepsis Campaign (SSC)

2008: 2nd edition of guidelines published

2012: 3rd edition of guidelines

http://www.survivingsepsis.org/About-SSC/Pages/History.aspx.

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*
INITIAL RESUSCITATION: CURRENT GUIDELINES

- CVP
  - 8-12 mmHg
  - 12-15 mmHg in intubated patients
- MAP ≥ 65 mmHg
- Urine output ≥ 0.5 ml/kg/hr
- ScVO₂ 70%
- Normalization of lactate levels

ANTIMICROBIAL THERAPY AND SOURCE CONTROL

- Broad spectrum antibiotics within one hour
- Empiric combination beyond 3-5 days inappropriate
- Source control within 12 hours if possible
  - Least insult in severely septic patients
- Remove lines if possible source
- Oral chlorhexidine

HEMODYNAMIC SUPPORT

- 30 mL/kg of fluids
  - Crystalloids preferred
  - Albumin if needed
- Continued fluid administration as long as needed
- Vasopressors to maintain MAP $\geq$ 65 mmHg
  - Norepinephrine (NE) preferred + low dose vasopressin
  - Epinephrine as needed or in place of NE
  - Dopamine as alternative only in certain patient population
  - Phenylephrine only as salvage therapy

INOTROPIC AGENTS, STEROIDS AND BLOOD

- Trail of dobutamine in selected patients
  - Myocardial dysfunction
  - Hypoperfusion despite volume resuscitation and vasopressor therapy
- Hydrocortisone in those patients refractory to volume resuscitation and vasopressor therapy
  - 200 mg/day as continuous infusion
- Red blood cell transfusion
  - After hypoperfusion resolved
  - Goal 7.0-9.0 g/dL
Testing your knowledge

- https://kahoot.it/#/
- Launch Kahoot
- Game PIN: 582890
THE PARADIGM SHIFT
Challenging the cornerstone of septic shock management
A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

**Inclusion criteria**
2/4 SIRS criteria AND one of the following: 1) hypotension after fluids 2) Lactate $\geq$ 4

**Study groups**
1) Protocol based EGDT 2) Protocol based PBST 3) Usual care

**Study performed**
31 EDs in the US
Supplemental oxygen ± endotracheal intubation and mechanical ventilation

2 large bore (18 g or larger) IV's (Central line if unable to achieve)¹

Sedation, analgesia, +/- or paralysis (if intubated)

500-1000 ml fluid bolus* (min. initial total fluid² = 2 L*, unless fluid replete/overload³)

SBP*, Shock Index (SI)

SBP < 100 mmHg⁴, or SI ≥ 0.8, or on vasopressors

Fluid replete/overload³??

No  Yes  Yes

Hypoperfusion⁵,⁶??

Reassess q30 min
Monitor for fluid overload³
Consider recheck lactate, HCT

Vasopressors⁴
Isotonic IVF @ 250-500 ml/hour³

<table>
<thead>
<tr>
<th>Time-sensitive target</th>
<th>Time allowed 7</th>
<th>Corrective action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid bolus (500-1000 ml)</td>
<td>20 minutes</td>
<td>3rd IV or central line</td>
</tr>
<tr>
<td>Initial fluid bolus (2 L)</td>
<td>1 hour</td>
<td>3rd IV or central line</td>
</tr>
<tr>
<td>SBP ≥ 100 mmHg</td>
<td>1 hour</td>
<td>Vasopressors</td>
</tr>
</tbody>
</table>

Protocol based "standard care" protocol

ProCESS Investigators, et.al. NEJM. 2014 May 1; 370(18): 1683-93.
Primary outcome
In-hospital all cause mortality at 60 days (p=0.83)*
   21% EGDT
   18.2% PBST
   18.9% usual care

Secondary outcomes
1) All cause mortality at 60 days
2) Cumulative mortality at 90 days and 1 year
3) Duration of CV failure
4) Respiratory failure
5) Acute renal failure
6) Duration of hospital stay
7) Discharge disposition

ProCESS Investigators, et.al. NEJM. 2014 May 1; 370(18): 1683-93.
**ProCESS LIMITATIONS**

- All large academic medical centers
- Extensive care team
- Central line placement
  - 56.5% in PBST
  - 57.9% in the usual care
- Slightly sicker group in Rivers, et. al?

ProCESS Investigators, et.al. *NEJM.* 2014 May 1; 370(18): 1683-93.
ARISE TRIAL

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

Inclusion criteria
2/4 SIRS criteria AND one of the following: 1) hypotension after fluids 2) Lactate ≥ 4

Study groups
1) EGDT
2) Usual care

Study performed
51 centers in variety of sites

ARISE TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

ABSTRACT

Primary outcome
Death from any cause within 90 days ((p=0.90)

18.6% in EGDT
18.8% usual care

Secondary outcomes
1) Survival time at 90 days
2) Mortality in the ICU
3) Mortality at 28 days
4) In-hospital mortality at 60 days
5) Cause specific morality at 90 days
6) **Length of stay in ED, ICU and elsewhere in hospital**
7) Receipt and duration of mechanical ventilation, **vasopressor support** or RRT

ARISE Secondary Outcomes (Cont)

- Destination at the time of discharge
- Limitation of therapy
- Adverse events
- Subgroup analysis a priori for primary outcome
  - Country, age, APACHE II score, mechanical ventilation, refractory hypotension, lactate level and IV fluid administration

### B Subgroup Analyses

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>EGDT</th>
<th>Usual Care</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td>147/792 (18.6)</td>
<td>150/796 (18.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Australia</td>
<td>126/677 (18.6)</td>
<td>132/679 (19.4)</td>
<td>0.95 (0.72–1.24)</td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td>New Zealand</td>
<td>13/67 (19.4)</td>
<td>8/69 (11.6)</td>
<td>1.84 (0.71–4.76)</td>
<td>0.21</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>8/48 (16.7)</td>
<td>10/48 (20.8)</td>
<td>0.76 (0.27–2.13)</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;65 yr</td>
<td>61/393 (15.5)</td>
<td>50/387 (12.9)</td>
<td>1.24 (0.83–1.85)</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>≥65 yr</td>
<td>86/399 (21.6)</td>
<td>100/409 (24.4)</td>
<td>0.85 (0.61–1.18)</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td><strong>APACHE II</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>114/720 (15.8)</td>
<td>114/718 (15.9)</td>
<td>1.00 (0.75–1.32)</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>≥25</td>
<td>33/72 (45.8)</td>
<td>36/78 (46.2)</td>
<td>0.99 (0.52–1.88)</td>
<td>0.97</td>
<td></td>
</tr>
<tr>
<td><strong>Invasive mechanical ventilation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19/71 (26.8)</td>
<td>23/64 (35.9)</td>
<td>0.65 (0.31–1.36)</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>128/721 (17.8)</td>
<td>127/732 (17.3)</td>
<td>1.03 (0.78–1.35)</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td><strong>Refractory hypotension</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>90/554 (16.2)</td>
<td>97/557 (17.4)</td>
<td>0.92 (0.67–1.26)</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>57/238 (23.9)</td>
<td>53/239 (22.2)</td>
<td>1.11 (0.72–1.69)</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td><strong>Hypofusion</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Yes</td>
<td>99/365 (27.1)</td>
<td>93/369 (25.2)</td>
<td>1.10 (0.79–1.54)</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>48/427 (11.2)</td>
<td>57/427 (13.3)</td>
<td>0.82 (0.55–1.24)</td>
<td>0.35</td>
<td></td>
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<tr>
<td><strong>IV fluid volume before randomization</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>≥20 ml/kg</td>
<td>106/574 (18.5)</td>
<td>104/572 (18.2)</td>
<td>1.02 (0.76–1.37)</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td>&lt;20 ml/kg</td>
<td>28/181 (15.5)</td>
<td>35/181 (19.3)</td>
<td>0.76 (0.44–1.32)</td>
<td>0.33</td>
<td></td>
</tr>
</tbody>
</table>
ARISE LIMITATIONS

- Extensive care team
- Reduced risk of death
  - Only ~5% of patients LTCF vs ProCESS where 16% of patients were nursing home residents before hospital admission

PROMISE TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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*

ABSTRACT

Inclusion criteria
2/4 SIRS criteria AND one of the following: 1) hypotension after fluids 2) Lactate ≥ 4

Study groups
1) EGDT
2) Usual care

Study performed
56 hospitals in England

Trial of Early, Goal-Directed Resuscitation for Septic Shock

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and Kathryn M. Rowan, Ph.D., for the ProMISe Trial Investigators*

Primary outcome
All cause mortality at 90 days
29.2% usual group
29.3% EGDT

Secondary outcomes
1) SOFA scores at 6 hours
2) Receipt of advanced CV, respiratory or renal support and number of days free from such support (first 28 days)
3) Length of stay in ED, ICU and hospital
4) Duration of survival
PROMISE PRIMARY AND SECONDARY OUTCOMES (CONT.)

- All cause mortality at 28 days and 1 year
- Health related quality of life
- Resource use
- Costs at 90 days and 1 year
- Adverse events
  - Up to 30 days

PROMISE TRIAL LIMITATIONS

- Difficult to enroll patients on nights and weekends
- Lower mortality rate overall
- Less sick at baseline versus Rivers trial
- Antibiotics given earlier versus Rivers trial

SURVIVING SEPSIS CAMPAIGN SPEAKS

The leadership of the Surviving Sepsis Campaign (SSC) has believed since its inception that both the SSC Guidelines and the SSC performance improvement indicators (1) will evolve as new evidence that improves our understanding of how best to care for patients with severe sepsis and septic shock becomes available.

With publication of 3 trials (2,3,4) that do not demonstrate superiority of required use of a central venous catheter (CVC) to monitor central venous pressure (CVP) and central venous oxygen saturation (ScvO₂) in all patients with septic shock who have received timely antibiotics and fluid resuscitation compared with controls or in all patients with lactate ≥4 mmol/L, the SSC Executive Committee has revised the improvement bundles as follows:

**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.

TESTING YOUR KNOWLEDGE

- https://kahoot.it/#/
- Launch Kahoot
- Game PIN: 725495
SEPSIS-3

New definitions for an old problem
Sepsis-3

- The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)
- Task force of 19 experts
- Society of Critical Care Medicine (SCCM) and European Society of Intensive Care (ESICM)
- Attempt to provide uniformity of diagnosis of sepsis and septic shock
E VOLUTION OF SEPSIS DEFINITIONS

1991: ACCP/SCCM Conference

2001: International Sepsis Definitions Conference

2016: Sepsis-3
WHY WAS SEPSIS-3 NEEDED?

- Limitations of previous definitions
- Multiple definitions and terminologies
- 2001 consensus further muddied the waters
- No gold standard diagnostic test
- Clearer definitions
- Improved understanding sepsis pathobiology
PUBLIC PERCEPTION OF SEPSIS

- 90% of public unaware of sepsis
- Poorly understood outside of medical community
- Long term sequela
- Nebulous definitions

PUBLIC PERCEPTION OF SEPSIS
1992 CONSENSUS DEFINITION

Table 1—Definitions

*Infection* = microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms.

*Bacteremia* = the presence of viable bacteria in the blood.

*Systemic inflammatory response syndrome (SIRS)* = the systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions: (1) temperature >38°C or <36°C; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or PaCO$_2$ <32 mm Hg; and (4) white blood cell count >12,000/cu mm, <4,000/cu mm, or >10% immature (band) forms.

*Sepsis* = the systemic response to infection, manifested by two or more of the following conditions as a result of infection: (1) temperature >38°C or <36°C; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or PaCO$_2$ <32 mm Hg; and white blood cell count >12,000/cu mm, <4,000/cu mm, or >10% immature (band) forms.

*Severe sepsis* = sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status.

*Septic shock* = sepsis-induced with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. Patients who are receiving inotropic or vasoactive agents may not be hypotensive at the time that perfusion abnormalities are measured.

*Sepsis-induced hypotension* = a systolic blood pressure <90 mm Hg or a reduction of ≥40 mm Hg from baseline in the absence of other causes for hypotension.

*Multiple organ dysfunction syndrome (MODS)* = presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.
DEFINING THE DISEASE CONTINUUM OF SEPSIS

From initial insult to shock-traditional views
2001 TASK FORCE: ACCP/SCCM

<table>
<thead>
<tr>
<th>TABLE 1. Diagnostic Criteria for Sepsis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infection, documented or suspected, and some of the following:</strong></td>
</tr>
<tr>
<td><strong>General variables</strong></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 so above the normal value for age</td>
</tr>
<tr>
<td>Tachypnea</td>
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<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><strong>Inflammatory variables</strong></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 so above the normal value</td>
</tr>
<tr>
<td>Plasma procalcitonin more than two so above the normal value</td>
</tr>
<tr>
<td><strong>Hemodynamic variables</strong></td>
</tr>
<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 so below normal for age)</td>
</tr>
<tr>
<td><strong>Organ dysfunction variables</strong></td>
</tr>
<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>
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<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>
<tr>
<td><strong>Tissue perfusion variables</strong></td>
</tr>
<tr>
<td>Hyperlactatemia (&gt; 1 mmol/L)</td>
</tr>
<tr>
<td>Decreased capillary refill or mottling</td>
</tr>
</tbody>
</table>

Variable Definitions: The Problem with SIRS

- Focus on inflammatory excess
- Pathogen factors:
  - Microbe
  - Site of infection
- Host factors:
  - Chronic disease states
  - Immunosuppression at baseline
  - Age, sex, race
  - Genetic characteristics
- Performs poorly in discriminant and construct validity

VARIABLE DEFINITIONS: ORGAN DYSFUNCTION OR FAILURE

- Various scoring systems available
- Predominant score=SOFA
- Limitations of SOFA
  - Labs
  - Cutoffs developed by consensus
  - Unfamiliar in non-critical care areas
VARIABLE DEFINITIONS: SEPTIC SHOCK

- Heterogeneity in mortality across current definitions
- Mixed bag of in clinical variables
- Take home: who’s really sick?

http://petsittersoflasvegas.com/need-puppy-gets-sick/
## 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{Paco}_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>
<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>(&lt; 20)</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 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>MAP &lt; 70 mm Hg</td>
<td>Dopamine (&lt; 5) or dobutamine (any dose)(^{b})</td>
<td>Dopamine (5.1-15) or epinephrine (&lt; 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>
</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>(&lt; 6)</td>
<td></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 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>(&lt; 500)</td>
<td>(&lt; 200)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: \(\text{FiO}_2\), fraction of inspired oxygen; MAP, mean arterial pressure; \(\text{Paco}_2\), 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.
SEPSIS: NEW DEFINITION

- Life threatening organ dysfunction caused by dysregulated host response to infection
- In-hospital mortality >10%
- Shift of SIRS criteria to aid in diagnosis
- Emphasis on life threatening organ dysfunction
- Basically old definition of “severe sepsis”
HOW DO WE DEFINE “DYSREGULATED”

- No current clinical measures
- Best estimate of those most likely to have sepsis
- Interrogation of large data sets iCorrelation with outcomes
- Multivariable regression of 21 bedside and lab values defined 2001 task force criteria
SEPSIS: HOW’D WE ARRIVE HERE

- >140,000 patients with suspected infection
- Outcomes to assess predictive validity:
  - Mortality and ICU stay of ≥ 72 hours
- Inside and outside ICU
- Criteria were analyzed in 4 external US and non-US data sets

SEPSIS: HOW’D WE ARRIVE HERE?

- ICU mortality: SOFA and Logistic Organ Dysfunction System superior to SIRS
  - AUROC=0.74; 95% CI, 0.73-0.76 for SOFA
  - AUROC=0.72, 95% CI, 0.7-0.73 for change in SOFA
  - AUROC=0.75; 95% CI, 0.72-0.76 for LODS
  - AUROC=0.64; 95% CI, 0.62-0.66 for SIRS
SEPSIS: HOW’D WE ARRIVE HERE?

- Outside ICU mortality: SOFA or change in SOFA similar to SIRS
  - AUROC=0.79; 95% CI, 0.78-0.8 for SOFA
  - AUROC=0.79; 95% CI, 0.78-0.79 for change in SOFA
  - AUROC=0.76; 95% CI, 0.75-0.77 for SIRS

LIMITATIONS OF SEPSIS DEFINITION

- Studied only those with documented or suspected infection
- Simple diagnostic criteria
- No measurements distinguish chronic from acute dysfunction
- Two more commonly known outcomes associated with sepsis
- Time course not linear
- Prospective validation needed
**SCREENING FOR SEPSIS**

<table>
<thead>
<tr>
<th>Outside of ICU</th>
<th>ICU patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quick SOFA (qSOFA)</td>
<td>SOFA score superior to qSOFA</td>
</tr>
<tr>
<td>2 or more of the</td>
<td>Modifying effects in ICU</td>
</tr>
<tr>
<td>following:</td>
<td></td>
</tr>
<tr>
<td>• Respiratory rate ≥ 22</td>
<td></td>
</tr>
<tr>
<td>• Altered mental status*</td>
<td></td>
</tr>
<tr>
<td>• SBP ≤ 100 mmHg</td>
<td>No role for lactate**</td>
</tr>
</tbody>
</table>

*Glasgow Coma Scale ≤13 but reduced to AMS to reduce calculation burden (AMS represents anything <15)

**Addition of lactate measurement did not meaningfully improve prediction validity but may help identify patients at intermediate risk

SEPTIC SHOCK: NEW DEFINITION

- Persistent hypotension requiring vasopressors to maintain MAP ≥ 65 mm Hg **AND** serum lactate > 2 mmol/L **DESPITE** adequate volume resuscitation
- Certain subset of septic patients
- Increased morality >40%
- Broader view from 2001 task force
**Septic Shock: How'd We Arrive Here?**

- Goal to identify those patients at highest risk of mortality as defined as having “septic shock”
- Systematic review and meta-analysis
  - 44 studies patients reporting septic shock outcomes
  - 92 studies reporting different cutoffs to identify septic shock
  - > 165,000 patients

*JAMA. 2016 Feb 23;315(8):775-87.*
SEPTIC SHOCK: HOW’D WE ARRIVE HERE?

- Delphi process
  - 3 rounds

- Cohort studies
  - Hypotension after fluid resuscitation, vasopressor therapy, lactate >2 mmol/L and lactate ≤ 2 mmol/L
  - 6 groups either alone or in combo
  - 2 logistic regression models to test for:
    - True mortality using above markers AND independent association of the criteria adjusted for covariates

SEPTIC SHOCK: SYSTEMATIC REVIEW AND META-ANALYSIS RESULTS

- Systematic review
  - Wide heterogeneity in shock criteria

- Two meta-analysis
  - Nearly 4-fold difference in septic shock mortality depending upon definitions
  - Separate meta-analysis exploring clinical criteria of septic shock

SEPTIC SHOCK: DELPHI STUDY

- **1st round**
  - Persistent hypotension, vasopressor therapy, hyperlactatemia

- **2nd round**
  - Descriptive analysis of SSC database
  - Predictive validity analyses

- **3rd round**
  - Provided analyses to task force members
  - New definition and clinical criteria for septic shock

Figure 3. Selection of Surviving Sepsis Campaign Database Cohort

28,150 Patients identified from SSC database

4,419 Excluded from full case analysis (missing continuous serum lactate values)\(^a\)

23,731 With serum lactate values

790 Excluded (serum lactate level >4 mmol/L and did not receive fluids or vasopressors)

22,941 Potentially eligible for full analysis set

4,101 Excluded (did not meet septic shock definition by definition groups)

18,840 Met potential septic shock definition groups and included in full case analysis cohort

Group 1
8,520 Patients
Hypotensive after fluids
Requires vasopressors
Serum lactate >2 mmol/L

Group 2
3,985 Patients
Hypotensive after fluids
Requires vasopressors
Serum lactate ≤2 mmol/L

Group 3
223 Patients
Hypotensive after fluids
Requires no vasopressors
Serum lactate >2 mmol/L

Group 4
2,696 Patients
Not hypotensive after fluids
Requires no vasopressors
Serum lactate >2 mmol/L

Group 5
2,696 Patients
Not hypotensive before fluids
Requires vasopressors
Serum lactate >2 mmol/L

Group 6
150 Patients
Hypotensive after fluids
Requires no vasopressors
Serum lactate ≤2 mmol/L
Figure 4. Serum Lactate Level Analysis

Adjusted odds ratio for actual serum lactate levels for the entire septic shock cohort (N = 18,840). The covariates used in the regression model include region (United States and Europe), location where sepsis was suspected (emergency department, ward, or critical care unit), antibiotic administration, steroid use, organ failures (pulmonary, renal, hepatic, and acutely altered mental state), infection source (pneumonia, urinary tract infection, abdominal, meningitis, and other), hyperthermia (>38.3°C), hypothermia (<36°C), chills with rigor, tachypnea (>20/min), leukopenia (<4000 cells/μL), hyperglycemia (plasma glucose >120 mg/dL [6.7 mmol/L]), platelet count <100 ×10^3/μL, and coagulopathy (eMethods 3 in the Supplement). The adjusted odds ratio (OR) for the 6 groups presented in eTable 7 in the Supplement and the adjusted OR for the individual variables (lactate, vasopressor therapy, and fluids) are reported in eTable 8 in the Supplement. To convert serum lactate values to mg/dL, divide by 0.111.
**Delphi Study: Round 2**

Table 4. Characteristics of Serum Lactate Level Cutoff Values for Complete Case Analysis and Imputation Analysis Using Surviving Sepsis Campaign Database

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Serum Lactate Level, mmol/L</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;2 Died/Total % (95% CI)</td>
<td>&gt;3 Died/Total % (95% CI)</td>
<td>&gt;4 Died/Total % (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete Case Analysis (n = 18 795)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital mortality, %</td>
<td>5757/18 795 30.6 (29.9-31.4)</td>
<td>6101/18 795 32.5 (31.8-33.2)</td>
<td>6456/18 975 34.3 (33.7-35.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>5372/6509 82.5 (81.6-83.4)</td>
<td>3779/6509 58.1 (56.8-59.3)</td>
<td>2811/6509 43.2 (42.0-44.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity, %</td>
<td>2748/12 286 22.4 (21.6-23.1)</td>
<td>6418/12 286 52.2 (51.4-53.1)</td>
<td>8564/12 286 69.7 (68.9-70.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPV, %</td>
<td>5372/14 910 36.0 (35.3-36.8)</td>
<td>3779/9647 39.2 (38.2-40.2)</td>
<td>2811/6533 43.0 (41.8-44.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPV, %</td>
<td>2748/3885 70.7 (69.3-72.2)</td>
<td>6418/9148 70.1 (69.2-71.1)</td>
<td>8564/12 286 69.8 (69.0-70.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imputed Missing Serum Lactate Level (n = 22 182)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital mortality, %</td>
<td>6965/22 182 31.4 (30.8-32.0)</td>
<td>7363/22 182 33.2 (32.6-33.8)</td>
<td>7772/22 182 35.0 (34.4-35.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>6457/7748 83.3 (82.5-84.2)</td>
<td>4461/7748 57.6 (56.5-58.7)</td>
<td>2931/7748 37.8 (36.7-38.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity, %</td>
<td>3341/14 434 23.1 (22.5-23.8)</td>
<td>7833/14 434 54.3 (53.5-55.1)</td>
<td>10 801/14 434 74.8 (74.1-75.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPV, %</td>
<td>6457/17 550 36.8 (36.1-37.5)</td>
<td>4461/11 062 40.3 (39.4-41.2)</td>
<td>2931/6564 44.6 (43.4-45.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPV, %</td>
<td>3341/4634 72.1 (70.8-73.4)</td>
<td>7833/11 120 70.4 (69.6-71.3)</td>
<td>10 801/15 618 69.2 (68.4-69.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.
SI conversion factor: To convert serum lactate values to mg/dL, divide by 0.111.
Cohort studies

Table 5. Crude Mortality in Septic Shock Groups From UPMC and KPNC Data sets

<table>
<thead>
<tr>
<th>Variable&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Highest Serum Lactate Levels 24 h After Infection Identified, mmol/L</th>
<th>UPMC</th>
<th></th>
<th>KPNC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 5984)</td>
<td>No.</td>
<td>% (95% CI)</td>
<td>No.</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n = 54135)</td>
<td></td>
<td>(n = 54135)</td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>&gt;2 (all)</td>
<td>315</td>
<td>(5.3)</td>
<td>8051</td>
<td>(14.9)</td>
</tr>
<tr>
<td></td>
<td>&gt;3</td>
<td>246</td>
<td>(4.1)</td>
<td>6006</td>
<td>(11.1)</td>
</tr>
<tr>
<td></td>
<td>&gt;4</td>
<td>189</td>
<td>(3.2)</td>
<td>4438</td>
<td>(8.2)</td>
</tr>
<tr>
<td>Group 2</td>
<td>≤2</td>
<td>147</td>
<td>(2.5)</td>
<td>3094</td>
<td>(5.7)</td>
</tr>
<tr>
<td></td>
<td>&gt;2 (all)</td>
<td>3544</td>
<td>(59.2)</td>
<td>12781</td>
<td>(23.6)</td>
</tr>
<tr>
<td></td>
<td>&gt;3</td>
<td>2492</td>
<td>(41.6)</td>
<td>6417</td>
<td>(11.9)</td>
</tr>
<tr>
<td></td>
<td>&gt;4</td>
<td>1765</td>
<td>(29.5)</td>
<td>3316</td>
<td>(6.1)</td>
</tr>
<tr>
<td>Group 3</td>
<td>&gt;2 (all)</td>
<td>1978</td>
<td>(33.1)</td>
<td>30209</td>
<td>(55.8)</td>
</tr>
<tr>
<td></td>
<td>&gt;3</td>
<td>1033</td>
<td>(17.3)</td>
<td>12450</td>
<td>(23.0)</td>
</tr>
<tr>
<td>Groups 4 and 5</td>
<td>&gt;2 (all)</td>
<td>566</td>
<td>(9.4)</td>
<td>5394</td>
<td>(9.9)</td>
</tr>
</tbody>
</table>

Abbreviations: KPNC, Kaiser Permanente Northern California; SSC, Surviving Sepsis Campaign; UPMC, University of Pittsburgh Medical Center.

SI conversion factor: To convert serum lactate values to mg/dL, divide by 0.111.

<sup>a</sup> Group 1 refers to patients with hypotension + vasopressors + serum lactate levels greater than 2 mmol/L. Group 2 refers to patients with hypotension + vasopressors + serum lactate levels less than 2 mmol/L. Group 3 refers to patients with hypotension and serum lactate levels greater than 2 mmol/L. Groups 4 and 5 refer to isolated serum lactate level greater than 2 mmol/L. Counts within a group are not mutually exclusive, as those with serum lactate levels greater than 2 mmol/L will include those in the higher serum lactate cutoffs.
LIMITATIONS OF SEPTIC SHOCK DEFINITION

- Quality of studies from systematic review
- Observational reports only
- Limited to adult population
- Delphi derived variables only to assess definition
- No gold standard of septic shock currently
- Missing data
- Prospective validation needed
<table>
<thead>
<tr>
<th>Old definitions</th>
<th>New definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis: SIRS + suspected source of infection</td>
<td>Sepsis: Syndrome with dysregulated host response + presence of organ dysfunction</td>
</tr>
<tr>
<td>Severe sepsis: sepsis + end organ damage</td>
<td>Septic shock: subset of patients with circulatory and cellular/metabolic abnormalities that highly increases mortality</td>
</tr>
<tr>
<td>Septic shock: hypotension despite adequate fluid resuscitation</td>
<td></td>
</tr>
</tbody>
</table>
COMPARING AND CONTRASTING: CLINICAL CRITERIA FOR SEPSIS

<table>
<thead>
<tr>
<th>SIRS Criteria (≥ 2 meets SIRS definition)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temp &gt;38°C (100.4°F) or &lt; 36°C (96.8°F)</td>
</tr>
<tr>
<td>Heart Rate &gt; 90</td>
</tr>
<tr>
<td>Respiratory Rate &gt; 20 or PaCO₂ &lt; 32 mm Hg</td>
</tr>
<tr>
<td>WBC &gt; 12,000/mm³, &lt; 4,000/mm³, or &gt; 10% bands</td>
</tr>
</tbody>
</table>

SUSPECTED/DOCUMENTED INFECTION

2 or 3 on qSOFA (HAT):
- Hypotension (SBP ≤100 mmHg)
- AMS (GCS ≤13)
- Tachypnea (≥22/min)

OR
- Rise in SOFA score by 2 or more

https://foamcast.org/2016/02/21/sepsis-redefined/
Comparing and contrasting: Clinical criteria for severe sepsis

Old definitions

New definitions

- NO LONGER EXISTS

Sepsis
+ SBP < 90 mmHg or MAP < 65 mmHg
lactate > 2.0 mmol/L
INR > 1.5 or a PTT > 60 s
Bilirubin > 34 µmol/L
Urine output < 0.5 mL/kg/h for 2 h
Creatinine > 177 µmol/L
Platelets < 100 x 109/L
SpO2 < 90% on room air

https://foamcast.org/2016/02/21/sepsis-redefined/
COMPARING AND CONTRASTING: CLINICAL CRITERIA FOR SEPTIC SHOCK

Old definitions

SEPSIS
+
HYPOTENSION
after adequate fluid resuscitation

New definitions

SEPSIS
+
VASOPRESSORS needed for MAP >65 mmHg
+
LACTATE >2 mmol/L
after adequate fluid resuscitation

https://foamcast.org/2016/02/21/sepsis-redefined/
TESTING YOUR KNOWLEDGE

- https://kahoot.it/#/
- Launch Kahoot
- Game PIN:758192
CURRENT CHALLENGES
SEP-1: EARLY MANAGEMENT BUNDLE, SEVERE/SEPSIS AND SEPTIC SHOCK

- Measure aimed to assess quality of sepsis care
- Follows SSC
- Measure assessing those processes associated with better care
WHY SEPSIS?

- 2009 Agency for Healthcare Research and Quality (AHRQ)
- High mortality for sepsis comparatively
- Rising hospitals stays related to sepsis
- Frequent cause of re-hospitalizations
- Medicare covered 58.1% of sepsis-related hospital stays
GOALS FOR SEP-1

- Efficient, effective and timely high quality sepsis care
- Reduce mortality
- Support of IOM’s aim for quality improvement
- More affordable care
- Provide standard operating procedure

http://www.ahrq.gov/workingforquality/
http://www.nationalacademies.org/hmd/
SEP-1 DESCRIPTION: DART

**DETECT**

1. **DETECT**: Is a systemic infection suspected?
2. Does the patient have 2 or more signs of SIRS?
   - Temperature $>100.9$ ($38.3^\circ$C) $<96.8$ F ($36$ C)
   - WBC $>12000$ $<4000$ or bands $>10\%$
   - Tachycardia $>90$ bpm
   - Tachypnea $>20$ bpm

**SEPSIS = Suspicion of infection + Two or more SIRS**

3. Evaluate for evidence of organ dysfunction AND NOT considered to be chronic or a result of therapy
   - SBP $<90$, MAP $<65$ OR SBP decrease of $>/=40$ points
   - Lactate $>2$ mmol/L
   - Bilirubin $>2$ mg/dL
   - Respiratory Failure (acute failure requiring ventilation or BiPAP)
   - Platelets $<100K$
   - Coagulopathy INR $>1.5$ or a PTT $>60$ sec
   - Cr $>2.0$
   - Urine Output $<.5$ mL/kg/hr for $>2$ hr

**SEVERE SEPSIS = Sepsis + Evidence of organ dysfunction**

**ACT**

4. **ACT**: To be completed or started within 3 hours from presentation time.
   - Blood Culture(s) – two preferred one is acceptable (prior to antibiotics)
   - IV Antibiotic, broad spectrum (mono or dual therapy)
   - Lactate
   - Initiate or complete 30 mL/kg Fluid Bolus (NS or LR) based on actual body weight
   (for any single SBP $<90$, OR MAP $<65$ OR SBP decrease of 40 points or Lactate $>/=4$)

**SEPTIC SHOCK = Lactate $>/=4$ or Severe Sepsis + persistent hypotension during or after 30 mL/kg fluid bolus e/b two consecutive SBP $<90$ or two consecutive MAP $<65$.

A decrease in SBP $>/=40$ points defines Septic Shock only when LIP documents the drop is r/t infection or sepsis
SEP-1 DESCRIPTION: DART

**REASSESS**

**Step 5. RECOGNIZE AND REASSESS:** To be *completed* within 6 hours from presentation time.

- Repeat Lactate if initial lactate was > 2
- If there is lactate >4 or new or persistent hypotension (shock manifested by two consecutive SBP < 90 or MAP < 65 or decrease of 40 points, after or during 30 mL/kg fluid bolus) **you must:**
  - Perform (within 1 hr) and Document (within 6 hrs) Reassessment of volume status (during/after initial fluid resuscitation) with either:
    1. Repeat focused exam by LIP within one hour of fluid bolus completion
       - VS (Temperature, Pulse, RR, and BP)
       - Capillary refill
       - OR
    2. Complete at least 2 of 5 of the following
       - Administer an additional fluid challenge at rate of at least 500mL over 15 minutes or 1000 mL over 30 min
       - Document a bedside cardiovascular Ultrasound
       - CVP
       - SvO2
       - Passive Leg Raise
       - Start Vasopressor for persistent or recurrent hypoperfusion/hypotension

**TITRATE**

**Step 6. TITRATE**

- Monitor patient response
- Titrating fluids and Vasopressors
HOW IS THIS MEASURE CALCULATED?

- Denominator: inpatients ≥ 18 with ICD-10-CM Principal or other diagnosis code of sepsis, severe sepsis or septic shock
- Numerator: ALL measures must be completed to pass the measure
CONFLICTS WITH SEP-1 AND NEW LITERATURE

- SEP-1 follow current SSC definitions for sepsis, severe sepsis and septic shock
- Role out of SEP-1 initiatives across hospitals
- Clinicians following new guidelines
- Confusion on which guidelines to follow
SEP-1 CHALLENGES

- Very complicated roll out
- Team work required
- Significant impact on patient outcomes
- Large patient population
- Two “time-clocks”
SEP-1 CHALLENGES

- Different requirements for severe sepsis and septic shock
- Multiple exclusion criteria
- Documentation key
- Diagnosis anywhere in the hospital

http://epmonthly.com/article/understanding-the-new-sep-1-sepsis-rollout/
FAQs FOR SEP-1

- Antibiotic administration
  - Combination
  - Timing
- Adequate volume resuscitation
  - Timing of administration
  - Rate of administration
- Who documents what?
- Documentation verbiage

http://www.mhanet.com/mhaimages/Sepsis_FAQ.pdf
PHARMACISTS CONCERNS

- Adverse effects
- Antibiotic exposure
- Protocol development
- Involvement with Code Sepsis


**Pharmacist involvement in a multidisciplinary initiative to reduce sepsis-related mortality.**

Beardsley JR\(^1\), Jones CM\(^2\), Williamson J\(^3\), Chou J\(^4\), Currie-Coyne M\(^3\), Jackson T\(^3\).


**Emergency medicine pharmacists and sepsis management.**

Weant KA\(^1\), Baker SN.
SURVIVING SEPSIS CAMPAIGN SPEAKS

Prepare for Change

As always, hospitals should prepare for major changes that can alter fiscal considerations. Hospitals should develop detailed plans and educate their physician and nursing staff and their coding departments to ensure that their coders accurately capture the sense of the new definitions. In countries that have formally defined national sepsis measures, such as the United Kingdom and the United States, hospitals should also create detailed plans and educate quality department staff to abstract charts and translate the new nomenclature into language compatible with the national quality measure, which typically uses the older terminology.

http://www.survivingsepsis.org/SiteCollectionDocuments/SSC-Statements-Sepsis-Definitions-3-2016.pdf
TAKE HOME MESSAGES

- Sepsis is an evolving disease state
- Sepsis-3 definitions aimed to identify those patients at highest risk morbidity and mortality
- Clinicians are hyperaware of sepsis
- Trio of trials performed to test the external validity of EGDT
- Making a sepsis management “one size fits all” plan is challenging
- Regulatory mandates playing catchup with new definitions
Testing your knowledge

- [https://kahoot.it/#/](https://kahoot.it/#/)
- Game PIN: 47959
- [Launch Kahoot](https://kahoot.it/#/)

Launched Kahoot game.
QUESTIONS