SEPSIS THROUGH THE YEARS

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Kentucky Sepsis Summit

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Sepsis Through the Years

Maryanne Whitney, RN, CNS, MSN, Cynosure Health
Through the years
It's better everyday
Hippocrates 460-370 B.C.

- Greek Word- *Sipsi*
  - Meaning “make rotten”

- Ibn Sina (979-1037BC)
  - Observed the coincidence of “septicaemia” and fever
Ignaz Semmelweis 1818-1865
A FEW GOOD MEN....

• Louis Pasteur
  – Identified tiny cell “bacteria” that cause putrefaction
  – Also discovered the bacteria could be killed by heat

• Joseph Lister
  – Identify that 50% of patients with amputations died from sepsis
  – Developed instrument sterilization & hands sanitation in the OR

• Hugo Schottmuller- 1914
  – Paved the way for modern definition of sepsis
    • “Sepsis is present if a pathogenic bacteria invades the bloodstream such a way that causes subjective and objective symptoms”
DISCOVERY THROUGH THE YEARS

• Death rate was very high
• WWII
  – Development of antibiotics
  – Death rate declined further
• 1967
  – ARDS was discovered as a complication of sepsis as an inflammatory reaction
• 1989 Roger C Bone
  – Offered a sepsis definition that is still valid today
    • “An invasion of microorganisms and or their toxins into the bloodstream, along with the organisms reaction against this invasion”
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

*N Engl J Med 2001; 345:1368-1377

November 8, 2001

DOI: 10.1056/NEJMo010307
Infection or trauma

SIRS
Systemic Inflammatory Response Syndrome

Sepsis
2 or more SIRS + Infection

Severe Sepsis
Sepsis + s/s of organ dysfunction

Septic Shock
Refractory Hypotension +/- or lactate >= 4

SEPSIS IS A CONTINuum
2012 GUIDELINES

• 2012 Surviving Sepsis Campaign published new guidelines (w/ recommendations)
  – Early screening (any location) and performance improvement program for sepsis
  – IV antibiotics within 1 hr
  – Fluid resuscitation with crystalloids 30mL/kg
• Septic shock – persistent hypotension or lactate >4mmol
  – Vasopressors – 1\textsuperscript{st} Norepinephrine then vasopressin---- after fluid resuscitation
  – Central Venous Access with CVP & ScVO2
  – Normalization of lactate as a goal
• Performance Improvement efforts to improve patient outcomes
CARE CONTINUES TO EVOLVE
ARISE, PROMISE AND PROCESS VS. USUAL CARE

• Requirement of CVP and ScvO2 via a CVC as part of early resuscitation does not change survival benefit in all patients with septic shock who have received timely antibiotics and fluid resuscitation compared with controls.

• Requiring measurement of CVP and ScvO2 in all patients with lactate >4 mmol/L and/or persistent hypotension after initial fluid challenge and timely antibiotics is not supported by available evidence.
2016 “SEPSIS-3”! NOW WHAT!
WHY UPDATE DEFINITIONS?

• We need improved definitions to:
  – Ensure early recognition and management
  – Improve our identification of patients for research

• **1991 – North American consensus definitions**
  – Sepsis = infection + systemic inflammation (SIRS)
  – SIRS: not specific; perhaps not sensitive enough; not accurate

• **2001 – International consensus definitions**
  – Confirmation of SIRS + long list of organ dysfunction criteria
  – Not data-driven; overly inclusive without supporting evidence

• **2014 – A return to ‘older’ definitions of sepsis**
  – Data-driven; quantified organ dysfunction
  – Narrow criteria to enhance early identification of patients
SEPSIS: INCOMPLETELY DEFINED

• Sepsis is an ancient syndrome, yet we still struggle in defining it.
• Definitions are essential for:
  – Public awareness
  – Drug development and clinical trials
  – Epidemiology and surveillance
  – Performance and quality improvement
  – Clinical care
• The major challenges we face in ‘defining’ sepsis is that:
  – We lack a ‘gold standard’ for the diagnosis
  – We have an incomplete understanding of disease pathophysiology
  – We have competing pressures (the ‘good’ vs. the ‘perfect’)
  – We have been facing a rapidly changing landscape
SEPSIS 3: A PRIMER

- Sepsis is: ‘life-threatening organ dysfunction caused by a disregulated host response to infection’

- Sepsis-3 does away with:
  - SIRS criteria (sepsis is pro- and anti-inflammatory)
  - Severe sepsis (sepsis = the old severe sepsis)
  - Antiquated concepts: sepsis syndrome; septicemia

*Singer et al, JAMA 2016. PMID: 26903338*
Sepsis-3 organizes the measurement of organ dysfunction through the SOFA score (Sequential Organ Failure Assessment).

Septic shock: vasopressor-dependent hypotension + lactate >2

Sepsis-3 includes clinical criteria to predict life-threatening disease.
NEW DIAGNOSTIC TRIGGERS

- quickSOFA, or qSOFA (Sequential (sepsis induced) Organ Failure Assessment)
- The qSOFA assessment directs physicians to look for these warning signs in patients:
  - An alteration in mental status
  - A decrease in systolic blood pressure of less than 100 mm Hg
  - A respiration rate greater than 22 breaths/min

http://qsofa.org/
SEPSIS-3 WORKFLOW

Singer et al, JAMA 2016. PMID: 26903338

Patient with suspected infection

qSOFA ≥2? (see A)
Yes
No

Assess for evidence of organ dysfunction

SOF A ≥2? (see B)
Yes
No

Monitor clinical condition; reevaluate for possible sepsis if clinically indicated

Despite adequate fluid resuscitation, 1. vasopressors required to maintain MAP ≥65 mm Hg AND 2. serum lactate level > 2 mmol/L?
Yes
No

Sepsis

Sepsis still suspected?
Yes
No

Monitor clinical condition; reevaluate for possible sepsis if clinically indicated

qSOFA Variables
- Respiratory rate
- Mental status
- Systolic blood pressure

SOF A Variables
- PaO2/FiO2 ratio
- Glasgow Coma Scale score
- Mean arterial pressure
- Administration of vasopressors with type and dose rate of infusion
- Serum creatinine or urine output
- Bilirubin
- Platelet count
STRENGTHS OF SEPSIS-3

• Provides an opportunity for timely reassessment of definitions
• Criteria are designed within a grounding framework
• Criteria are data-driven and based on large, international datasets
• Use well-validated organ dysfunction criteria (SOFA)
• qSOFA is simple and available without any diagnostic testing
POTENTIAL LIMITATIONS OF SEPSIS-3

- Does not provide any ‘gold standard’ for defining sepsis
- Confusion about the use of lactate in management of sepsis
- Fairly homogeneous representation on consensus committee
- Draws in the nets of sepsis, rather than expanding them
- Exclusive focus (almost) on critical illness and sepsis
- Outlines operational workflows that may be poorly aligned with on-the-ground operations (including CMS measures)
- Has yet to be proven prospectively
WHAT DOES IT MEAN FOR YOU?

• Early treatment of sepsis remains critical to improving outcomes
• Early treatment requires early identification
• Most sepsis patients are presenting through the ED
• Continue to use the processes currently in place
  – early identification and treatment in the ED
  – hospital wards

Consider......

• Do SEPSIS-3 definitions fundamentally alter these processes?
• What are the competing priorities in improving sepsis care that can help put SEPSIS-3 into context with our current strategies?
Definitions are UNCHANGED for CMS
Screening is UNCHANGED
Measurements for HEN & CMS are UNCHANGED
Treatment in UNCHANGED
Today’s Challenges are Different

Healthcare Today:
Complex, Confounding, Challenging...Changing

Governance  Market Share  Private Equity  Supply Chain
Telemedicine  Medicare  Evidence Based Medicine
Primary Care  Managed Care  CPOE
Quality  Medical Education  People
Fraud & Abuse  Medicaid  MSO
Patient Safety  Health Insurance Exchanges

Healthcare Systems
ACO  Patient Satisfaction  Comparative Effectiveness Research
Medical Home  Managed Care  Bundled Payment
Joint Ventures  Group Practice  Health Reform
Health Navigators  Capitation  Accountable Care Organization
Physician Employment  Transparency  Physician Extenders
PHO  Service Line Management  Leadership
Industry Consolidation  Networks  Networks
Regional Health Information Organizations  Population Health Management
Centers of Excellence  EMR  Ambulatory Centers
Clinical Integration  IT  P4P
Mergers  Gainsharing  Revenue Cycle
Readmissions  Volume  Capital Competition
Care Redesign
SEPSIS IS THE KILLER IN OUR MIDST
SEVERE SEPSIS: A SIGNIFICANT HEALTHCARE CHALLENGE

- Hospitalizations have doubled 2000-2008
- Most costly reason for hospitalization in 2011
  - 20 billion in aggregate hospital cost
- 1 out of 23 patients in hospital had septicemia
- Major cause of morbidity and mortality worldwide
  - Leading cause of death in non-coronary ICU
  - 10th leading cause of death overall
- In the US, more than 700 patients die of severe sepsis daily
  - (1.6 million new cases per year)
- 1 DEATH EVERY 2 MINUTES
THE #1 CAUSE OF INPATIENT DEATH

2014 Acute Care Discharges
11% of Patients Have Sepsis DX

2014 Acute Care Deaths
48% of Patients Have Sepsis DX

The same pattern in every hospital
## SEVERE SEPSIS VS. CURRENT TREATMENT PRIORITIES

<table>
<thead>
<tr>
<th>Care Priorities</th>
<th>U.S. Incidence</th>
<th># of Deaths</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI (1)</td>
<td>900,000</td>
<td>225,000</td>
<td>25%</td>
</tr>
<tr>
<td>Stroke (2)</td>
<td>700,000</td>
<td>163,500</td>
<td>23%</td>
</tr>
<tr>
<td>Trauma (3)</td>
<td>2.9 million</td>
<td>42,643</td>
<td>1.5%</td>
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<tr>
<td>(Motor Vehicle)</td>
<td>(injuries)</td>
<td></td>
<td></td>
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<tr>
<td>Severe Sepsis (4)</td>
<td>751,000</td>
<td>215,000</td>
<td>29%</td>
</tr>
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</table>
The Keys to achieving a reduction in mortality from severe sepsis are **Early Recognition & Evidence Based Treatment**. BOTH MUST occur.
TIME SENSITIVE DISEASES
Changing the Paradigm of Practice

AMI
Stroke
Trauma
MORTALITY INCREASES WITH # OF ORGAN FAILURES

<table>
<thead>
<tr>
<th>Mortality Rate</th>
<th># of Organ Dysfunctions</th>
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<tbody>
<tr>
<td>21.2%</td>
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</tr>
<tr>
<td>44.3%</td>
<td>2</td>
</tr>
<tr>
<td>64.5%</td>
<td>3</td>
</tr>
<tr>
<td>76.2%</td>
<td>4</td>
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Sepsis Diagnosis Is Difficult

- No single criteria makes the diagnosis
  - (Unlike New ST Elevation on ECG, or New Onset Focal Neuro Exam)
- Changing patient status during encounter
- Diagnosis not black and white but gray
- Patient may look good and yet crash two hours later
- Many physicians like an observation period before reacting, and they lose the critical window of opportunity

- HUMAN FACTORS
  - Competing priorities, lack of awareness, patient looking good leads physicians to going down another path.
EARLY DETECTION!

• Screen Every Emergency Patient
• Screen All Seriously Ill Adult Inpatients
  – Prioritize infections most frequently associated with sepsis
    • UTI, Pneumonia, Abdominal
  
  • MEWs, early warning score to detect at risk patients for decline will capture more than just sepsis
    – Use the EMR for prompts, and alerts
• Treat all Elderly Patients as “High Risk”
  – May have atypical signs- Altered MS, Afebrile
STRATEGIES TO IMPROVE EARLY RECOGNITION

• Examples of Level Two Reliability Methods:
  – Standardized Recognition Process: Use “screening check list/handoff tool/data collection tool” on all admissions, and shift handoffs.
  – Use redundancy: everyone is responsible to speak up if sepsis is suspected
  – Emphasize early lactate and blood cultures
  – Early feedback regarding compliance and using Real Time Data Collection
• **SIRS:** Systemic Inflammatory Response Syndrome
  ✓ Temp < 36°C or > 38°C,
  ✓ Heart Rate > 90/min,
  ✓ Respiratory Rate > 20/min or PaCO2 32mmHg,
  ✓ WBC < 4,000 or > 12,000 or 10% bands.

• **Sepsis:** presence of infection (suspected or confirmed) with systemic manifestations of infection

• **Severe Sepsis:** Sepsis-induced tissue hypo-perfusion or organ dysfunction
  ✓ Neuro – decreased LOC
  ✓ CV- hypotension
  ✓ Respiratory- hypoxemia
  ✓ Renal- low UO
  ✓ Hematological- Thrombocytopenia
  ✓ Metabolic- Elevated lactate

• **Septic Shock:** Hypotension that persists despite adequate fluid resuscitation
Change Culture

Think SEPSIS!!!
EARLY GOAL DIRECTED THERAPY

NNT to prevent one event (death) = 6-8

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<tr>
<th>In-hospital mortality</th>
<th>28-day mortality</th>
<th>60-day mortality</th>
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<tr>
<td>Standard therapy</td>
<td>EGDT</td>
<td>Standard therapy</td>
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CREATE ACTION: BUNDLE IMPLEMENTATION

- Identify clear and concise action for positive sepsis screen
- Who does what? By when?
- Build in concurrent review
• Mobilize resources
  – What are they?
• Mobilize experts
  – Who are they?
• Consensus in diagnosis
  – Allow for clinical decisions
  – Time sensitive
• Create action
  – Antibiotics
  – Labs
  – Fluids
• RRT
  – Can they be involved?
POSITIVE SEPSIS SCREEN
3HR BUNDLE
*(TO BE COMPLETED WITHIN 3 HOURS OF PRESENTATION)*

- Measure lactate level – not a send out
- Obtain blood cultures prior to administration of antibiotics
- Administer broad spectrum antibiotics
- Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/L
MAKE EARLY EASY

• Automatic
  – Order sets
  – Protocols for fluid, antibiotics and labs
  – Bundle blood cultures with lactate
HYPOTENSION OR LACTATE > OR = 4
6HR BUNDLE
(TO BE COMPLETED WITHIN 6 HOURS OF SEPTIC SHOCK PRESENTATION TIME)

• Apply vasopressors
  – for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65mmHg

• Re-assess volume status and tissue perfusion and document findings
  – In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was ≥4 mmol/L,

• Re-measure lactate if initial lactate elevated.
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 ScVO2
• Bedside cardiovascular ultrasound
• Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge
MAJOR SURPRISES IN MANAGEMENT

• Highest Mortality
  – Sepsis diagnosed on the floors
  – Lactate >2 mmol/l but < 4 mmol/l

• Bundle Compliance
  – Worst on the floor

• Hospitals with RRT/Sepsis Alert as resource saves most lives
Tips for Inpatient Sepsis Detection

• Screen for sepsis every shift and at transfers
• Use the EMR
• Develop Alerts
• Optimize Rapid Response Team involvement
Time Zero

- Will always be when chart annotations suggest all signs and symptoms are present
- May be documented in nursing or physician notes, lab flow sheets, anything with a time stamp
- Equals triage time if all signs & symptoms are present at triage
LEVERAGE TECHNOLOGY

• Use EMR for inpatient screening
• Best Practice Alerts
• Prompts for Interventions
  – Contact MD or RRT
    • Request lactate because one has not been drawn in 4 hours
    • Request blood culture because they have not been drawn
    • N/A pt. does not have suspected or known infection
BEST PRACTICE ALERTS

Consider evaluating for sepsis. A lactate level may be useful.

Open order: Lacto Acid, Plasma
Sepsis Screen Notes

1) 2 or more new SIRS Criteria met?

- Temp over 100.4 F (38 C) or under 96.8 F (36 C).
- Resp Rate over 20.
- Pulse over 90 bpm.
- Change in mental status.
- Blood glucose greater than 120.
- WBC greater than 12000 or less than 4000 or Bands (immature neutrophils) greater than 10%.

2) Actual/Potential source(s) of infection identified?

- Yes, confirmed source identified
- Pending more information
- Potential infection suspected, source not ide ...

- Medical History for Endocarditis, Immunosuppression, Chronic Infection, Indwelling Devices, etc.
- Positive culture results.

3) 1 or more new signs of severe sepsis

- SBP less than 90 mmHg or 40 mmHg below baseline or MAP less than 65 mmHg
- Vasopressor Support to maintain adequate blood pressure
- Respiratory Indicators: new or increased O2 requirements to maintain SpO2 greater than 90% or PaO2/FiO2 ratio less than 300
- Low Urine Output less than 0.5 ml/kg/hour for greater than 2 hours or Creatinine greater than 2.0 mg/dl
- Lactate greater than 4.0 mmol/L
- Platelet Count less than 100000 or Coagulopathy: INR greater than 1.5 or aPTT greater than 60 secs
- Elevated Total Bilirubin greater than 2 mmol/L
3. Select the applicable Signs & Symptoms of Sepsis.

4. If patient has known or suspected infection, complete the following actions:

- **Contacted MD**
  - Requested lactate because it was NOT done within last 4 hours
  - Requested blood cultures because it was NOT already done
  - NA (because there is NO known or suspected infection on Question #1)

- [Sepsis RN: 137221]
SO....PUTTING IT ALL TOGETHER

Stay the course.....for now

Screen every patient in ED @ triage or evaluation.

Screen inpatients every shift.

Bundle blood cultures with lactate.

Administer antibiotics within an hour.

Clear and consistent actions after a positive sepsis screen.

Use Alerts & EMR

Outcomes will follow.
STRATEGIES FOR KEEPING SEPSIS FRONT AND CENTER

• Align team with clinical and quality structures in organization
• Sepsis program/goals part of hospital quality plan
• Reporting progress and data quarterly to executive leadership
• Report to hospital board annually
• Standing agenda item on department meetings
• Communication plan---includes flyers, newsletters, postings in units etc.
• Code sepsis
• Real time data measurement and feedback
Questions & Discussion
### Ideas to Test:

**Top Ten**

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RESOURCES

Surviving Sepsis Campaign
http://www.survivingsepsis.org
• Guidelines
• Bundles
• Protocols & Checklist
• Sample sepsis screen
• Educational videos
• http://www.sccm.org/Research/Quality/Pages/Sepsis-Definitions.aspx
mwhitney@cynosurehealth.org