Sepsis Management: The Latest Evidence-Based Practice

What is the Surviving Sepsis Campaign (SSC) and why is it sweeping the nation?

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Variation in Care Practices

- As of 2003, there were 1,739 U.S. hospitals in the IHI comparative database that exhibit a 450 percent variation in a patient's chance for dying.

Chain of Survival in Sepsis

Early Detection

Hospital Care

Improved Outcomes
SIRS: Systemic Inflammatory Response Syndrome

- Two or more of the following:
  - Temperature $> 38^\circ C$ (100.4) or $< 36^\circ C$
  - Heart Rate $> 90$ bpm
  - Respiratory Rate $> 20$ breaths/min
  - WBC Count $> 12,000/mm^3$, $< 4,000/mm^3$, or are there $> 10\%$ immature neutrophils (bands)

Global tissue hypoxia *precedes* Hypotension, MODS and death

Serious infection

↓

Sepsis

Infection + SIRS

↓

Severe Sepsis

(Organ Failure)

↓

Septic Shock

“Sepsis”
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The sooner that treatment begins, the better the outcomes, just like….

Code STEMI – “Time is Muscle”
Code Stroke – “Time is Brain”
Code Trauma – “The Golden Hour”

Code Sepsis - “Time is Tissue”
Inquiring Minds Want To Know…

• How does one diagnose sepsis?
• Does the patient have to look deathly ill?
• You cannot treat what you do not diagnose
Putting the pieces of the puzzle together...

- Labs
- Acid/base
- Organ dysfunction
- Current therapies
- Vital Signs
- Co-morbidities
- Perfusion
- Trend
ACUTE ORGAN DYSFUNCTION = SEVERE SEPSIS

- Altered Consciousness
- Confusion
- Tachypnea
  SaO$_2$ <90%
- Tachycardia
- Hypotension
- Acidosis
  ↓ Bicarb
  ↑ Lactate
- Jaundice
  ↑ Total Bili
- Oliguria
- ↑ Creatinine
- ↓ Platelets
  ↑ PT/APTT
  ↑ D-dimer
  ↑ Fibrinogen

SEVERE SEPSIS MORTALITY INCREASES WITH THE NUMBER OF ORGAN DYSFUNCTIONS

Common Sources Seen

- **Chest**
  - Pneumonia
  - Aspiration pneumonia

- **Acute abdomen**
  - Perforation of intestines
  - Abscesses
  - Cholecystitis
  - Pancreatitis

- **Urinary tract**
  - Foley associated UTI
  - Pyelonephritis

- **Skin and tissues**
  - Post surgical wounds
  - Decubitus ulcers
  - Cellulitis
  - Spinal abscess

- **Central line associated blood sepsis infection**

- **Meningitis**

- **Subacute Bacterial Endocarditis**

- **Translocation of bacteria across gut**
The Surviving Sepsis Campaign Bundles

Resuscitation Bundle
(To be accomplished over first 6 hours):
• Lactate
• Blood cultures prior to antibiotics (1C)
• Source control (1C)
• Broad-spectrum antibiotics within 1 hour of diagnosis of septic shock (1B) and severe sepsis without septic shock (1D)
• For hypotension or lactate > 4:
  • Deliver an initial minimum of 20 mL/kg of crystalloid (or colloid equivalent) (1C)
  • Apply vasopressors not responding to fluid resuscitation (1C)
• For persistent hypotension despite fluid resuscitation (septic shock) or lactate > 4 mmol/L (1C)
  • CVP of 8 -12 mmHg & MAP > 65 mmHg & UO >0.5mL/kg/hr
  • ScvO₂ of ≥ 70%
  • Blood or dobutamine (2C)

Management Bundle
(To be accomplished over first 24 hours):
• Low-dose steroids administered for septic shock on vasopressors) (2C)
• Drotrecogin alfa (activated) administered in patients with severe sepsis and clinical assessment of high risk of death (2B, except 2C for postoperative patients)
• Glucose control < 150 mg/dL (2C)
• Vt 6 mL/kg (1B) & Inspiratory plateau pressures <30 cmH₂O for mech ventilated patients (1C)

SEVERE SEPSIS: A HEALTHCARE CHALLENGE

- Clinical definition is not applied at the bedside
- No single test or marker exists…or does it?!!!

CT Brain
Acute Intracranial Bleed

Pathology
Malignancy

Radiology
Fracture

Labs
Troponin, CK’s

What are some reasons that a diagnosis of severe sepsis is a challenge?
What are our options?

**aPTT**
- Biphasic waveform
- 90%/92%
- Chopin, *CCM* 2006

**Procalcitonin**
- Clec’h, *CCM* 2006
- Uzzan, *CCM* 2006

**Endocan**
- Schepereel, *CCM* 2006

What are some reasons that a diagnosis of severe sepsis is a challenge?
Procalcitonin

- The prohormone of the hormone calcitonin
- Produced by several cell types and many organs in response to pro-inflammatory stimuli
  - In particular, bacterial products
- Normal <0.03ng/ml
  - Usually not elevated by viral infections, bacterial colonization, and autoimmune diseases
- PCT increases in 2-12 hours post systemic bacterial infection (12-24 hour ½ life)
  - Trend over 6 days may assist with abx DC date

PCT

- Multiple traumas, major surgery, severe burns, or in neonates can have elevated PCT levels but the return to baseline is usually rapid
- PCT x 2 (6 hours apart) highly specific for bacteremia and has a 95% negative predictive value
- Pancreatitis diagnostic assistance
  - Infectious vs. sterile necrosis
- Plasma levels rapidly fall as the inflammatory activity regresses

Figure 1: PCT increase reflects the continuous development from a healthy condition to the most severe states of disease (severe sepsis and septic shock).

Case Review

30 year old male, 4\textsuperscript{th} year medical student from the east coast doing a clinical rotation at the local medical school
These materials are intended for healthcare professional educational purposes only. PharmacyOneSource.com is not making recommendations on diagnosis or treatment of any particular patient. The judgment of the physician/clinician, based on knowledge of the specific patient, should always be the deciding factor.

The following case represents an individual experience that is specific to this patient and may not reflect the typical course of recovery.
Early Recognition - EMS

- Brought to ED via ambulance after a grand mal seizure in the MD’s office
- Signs:
  - Pale, ill looking male
  - Temp 102.4F, ST 110-118, RR 28, SBP 78 palp
- Symptoms:
  - c/o SOB, heavy chest, malaise
  - 2 weeks history of a productive cough
- Current medications are Advair, Acutane
- No significant history
Differential Diagnosis

Exam:
- Decreased BS’s LLL
- Sats 88% on 100% NRB
- Tachycardia
- Tachypneic
- Hypotensive

Labs/Radiographs:
- Lactate-POC
- BMP, CBC Man dif
- PCT
- Cultures obtained
  - BC, UC, Sputum
- CXR-Infiltrate
While in ED
- Emesis x 3
- Decreased LOC
- Possible Seizure
  - Code blue called
  - Depressed respirations
  - Hypotension

Off to CT
- CT brain without contrast
- CT chest
Labs/Radiographs Resulted

- PCT 26ng/dL
- WBC’s 18 with 25% bandemia
- Bicarb 19
- CT head negative
- CT chest LLL infiltrate
Left Lung Infiltrate
Left Lung Infiltrate
Lung CT without Contrast
Diagnosis: Community Acquired PNA
Treatment in the ED: 6-Hour Bundle

- Lactate screening
  - Q6h x 24h then q day x 2 (normalized)
- PCT repeated next am (2.5ng/dL)
- BC before abx administration
- Broad spectrum antibiotics in 3 hours
  - Vancomycin and Meropenem
- EGDT goals met
  - 4L NS fluid bolus
  - Dopamine infusion
    - CVP >8
    - Scv02 >65
    - MAP >65
    - HCT 38.9
- Source control not required
Treatment in the ICU: 24-Hour Bundle

- Glycemic control
- No intubation
- Xigris administration began within 8 hours
  - > 2 organ dysfunctions
  - Vasopressors post fluid resuscitation
    - 96 hour infusion
    - No side effects noted
- Steroid administration x 7 days
  - No ACTH stim test
  - Pressor-dependent

100% Compliance
Discharged on Hosp Day #6

- PCT trended q AM
  - Reduction to baseline in 2 days
  - Indicates efficacy of therapeutic modalities
  - No bump up (infectious complication)

- Date of discharge:
  - Ambulating well with mild weakness
  - QOL maintained

- Discharged with
  - Levaquin 500mg PO QDx8 days
  - Regular diet
  - Activity as tolerated
  - CXR PA/Lat in 3 weeks
  - F/U physician for appt
Organizational Consensus that Severe Sepsis Must be Managed Early and Aggressively

Call to Action: 4-Tier Process for Severe Sepsis Program Implementation

- Measuring Success
- Implementation of the Sepsis Bundle
- Early Screening with Tools and Triggers
- Organizational Consensus that Severe Sepsis Must be Managed Early and Aggressively
Program Deliverables for a Comprehensive SSC

- ECU
  - Triage for Sepsis
  - EGDT
  - Throughput
- Education (RN/MD)
- Lactate, PCT, Manual differential
- Sepsis Panel
- EMR High Alert Report
- P&P, Guideline
- ECU and CC Order Sets

- Data Collection, Monitoring and Analysis
  - Local & Regional
  - Dellinger “Bundle effectiveness” Testing
- Rapid Response Team integration (proactive)
- Empiric Abx Recommendations
got sepsis?

POSITIVE SEPSIS SCREEN

call RRT
Information Technology
Track and Trigger Systems

- Web-based platforms pull information in real-time from your disparate hospital information systems, stores, and analyzes it to assist in making decisions.
- You can use preconfigured clinical rules or set up your own that notify healthcare personnel about intervention opportunities.
- Improve outcomes and reduce costs.
Information Technology
Track and Trigger Systems

Examples

- Identify patients with heparin-induced thrombocytopenia
- Alerted to any patients with positive cultures for MDRO (MRSA, C. diff, VRE), SSI, CLABSI or other possible hospital-acquired infections
- Identify culture results that indicate a particular antibiotic would be resistant in a patient
Mission Quality Data Shows Efficacy

- Median ICU LOS reduced by 1.5 days
- Median Hosp LOS reduced by 1 day
- Mortality reduction from 30% to 16% \( p=<0.05 \)
- Acute renal failure rate reduced from 18% to 12%
- Acute respiratory failure rate reduced from 58% to 35% \( p=<0.05 \)

2007 \( n=57 \) vs. 2008-2010 \( n=275 \)
CHEST 2006
Summary of Centers

- N=1,298
  - 671 (44.8%) ± 7.8 [95% CI 0.41-0.49]
  - 627 (24.5%) ± 5.5 [95% CI 0.21-0.28]
- RR 0.54
- OR 0.39
- RRR 45%
- ARR 20.3%
- NNT 5

Loma Linda University
Birmingham Hartlands
Henry Ford
Friedrich-Schiller
Redding Medical Center
Beth Isreal Deconess
Univ of Med/Den NJ, Camden
Univ of Pennsylvania
Hoag Hospital
Hahnemann University
Good Samaritan
Barnes Jewish Hospital
St. Pauls Hospital, Vancouver

Rivers, et al. Early goal directed therapy in severe sepsis and septic shock revisited: concepts, controversies, and contemporary findings. CHEST 2006; 130; 1579-1395.
Other SSC Core Reference Articles


