Understanding the Latest Sepsis Guidelines –
Case Presentation

Presented by:
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• Objectives:
  – Discuss the epidemiology of severe sepsis & its implications.
  – Explain the 2016 Third International consensus definitions for sepsis and septic shock
  – Discuss the sepsis bundles
  – Explore the new phase IV of the surviving sepsis campaign
  – Using a case presentation explain the surviving sepsis campaign guidelines for the management of sepsis and septic shock.

• Leading cause of death in noncoronary ICU in the US
• Estimated more than 1 million cases of severe sepsis in the US annually
• In the US, more than 500 patients die of severe sepsis daily
• High mortality rate of 28 to 50%
• Costs an average of $22,000 per patient with a total cost of $20.3 billion to US hospital
The Response: Surviving Sepsis Campaign

- The Society of Critical Care Medicine (SCCM), European Society of Intensive Care Medicine (ESICM), & International Sepsis Forum (ISF) joined forces to develop a three phase Surviving Sepsis Campaign.

Surviving Sepsis Campaign Guidelines

- A campaign developed by 11 organizations made up of international critical care and infectious disease experts.

Severe Sepsis

- It is a disease of the microcirculation
- Patients in septic shock have persistent microcirculatory alterations which lead to associated organ failure and death
- Therefore, microvascular recruitment and not just global hemodynamic resuscitation should be targeted.

Case Presentation

History of present illness:
• 50 y.o. Caucasian male seen in the ED
• C.C.: several day history of hematemesis & melena.
• Other associated manifestations included weakness, dizziness, & anorexia.
• Three days ago, he saw his PCP with a C.C. of bilateral leg pain. He was given narcotics for presumptive peripheral neuropathy
Medical History

Past Surgical History: Hemorroidectomy
Past Medical History: Right Rib Fracture, Seasonal Allergies, Hepatitis C, Liver Cirrhosis, ETOH Abuse

Medications: Nasarel, Claritin, Roxicet, ASA, Advil, Codeine, Tylenol

Social History: Married with 2 children, Ages 14 & 21

Occupation: Unemployed (recently laid off)

ETOH: a bottle of wine & Several beers

Tobacco: Neg

Drugs: Neg

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Medical History

On admission:

Vital Signs – T 36.5 C, P 104, RR 22, B/P 91/57
General – 71 kg, Moderate distress, A&O x3
HEENT – Scleral icterus
Musculoskeletal – 2+ edema bil. Lower extremities. Sl. Erythema, warm & tender to palpation esp. both feet
Skin – spider angioma, mild jaundice
Abdomen – Mildly distended, nontender, normoactive bowel sounds

Does this patient have an anion gap metabolic acidosis?

Anion gap is the difference between cations and anions.
Normal is 8-16. 132-(97+17) = 18

For every 1 gm decrease of Albumin from normal (4gm), add 2.5 to the anion gap.

4-2.5=1.5 x 2.5 = 3.75 + 18 = 21.75 (actual anion gap)

What are the 2 most common causes of metabolic acidosis in the acute care?
10/12 - 1211
AST 103  A0 66  TP 6.1  Mg 1  Ca 8.1
ALT 96  BT 1.8  Alb 2.5  Amylase 37
Lipase 150  Ammonia 5  Acetaminophen neg
ETOH neg

10/12 - 1211
6.9  9.9  112  Neutrophils 83%
28.7

10/12 - 1616
7.3 ± 19.3/79.2 ± 9.8  BE -14.6
On 3 L NC

Does he have sepsis?

ACCP/SCCM Consensus

Definitions

• Infection
  – Inflammatory response to microorganism, or
  – Invasion of normally sterile tissues
• Systemic Inflammatory Response Syndrome (SIRS)
  – Systemic response to a variety of processes
• Sepsis
  – Infection plus
  – 2 SIRS criteria
• Severe Sepsis
  – Sepsis
  – Organ dysfunction
• Septic shock
  – Sepsis
  – Hypotension despite fluid resuscitation
• Multiple Organ Dysfunction Syndrome (MODS)
  – Altered organ function in an acutely ill patient
  – Homeostasis cannot be maintained without intervention

Sepsis 2.0 vs Sepsis 3.0

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Sepsis 2.0</strong></td>
<td><strong>Sepsis 3.0</strong></td>
</tr>
<tr>
<td>SIRS</td>
<td>Eliminated</td>
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<tr>
<td>Sepsis</td>
<td>New definition</td>
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<tr>
<td>Severe sepsis</td>
<td>Eliminated</td>
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Third International Consensus Definitions for Sepsis and Septic Shock 2016

- Sepsis – life threatening organ dysfunction caused by a dysregulated host response to infection.
  - Lay definition: life threatening condition that arises when the body’s response to an infection injures its own tissues and organs
- Organ dysfunction – an acute change in total SOFA (Sequential sepsis related Organ Failure Assessment) score ≥ 2 points consequent to the infection
  - Estimated SOFA 2 or more had an overall mortality risk of approximately 10% in a patient with presumed infection

Third International Consensus Definitions for Sepsis and Septic Shock 2016

- Septic Shock
  - Subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
  - Patients with persistent hypotension requiring vaspressors to maintain MAP ≥65 mmHg and having a serum lactate > 2 despite adequate volume resuscitation.
  - Mortality is in excess of 40%
Third International Consensus Definitions for Sepsis and Septic Shock 2016

- Eliminated the term severe sepsis—felt to be superfluous
- Current use of the 4 SIRS criteria to identify sepsis was unanimously considered by the task force to be unhelpful
  - SIRS do not necessarily indicated a dysregulated, life threatening response
  - Studies in Australia and New Zealand showed 1 in 8 infected ICU patients with new organ dysfunction did not have 2 SIRS yet had protracted course with significant morbidity, mortality*


Third International Consensus Definitions for Sepsis and Septic Shock 2016

- Controversies and Limitations
  - Neither SOFA or qSOFA are meant to be stand alone definitions of sepsis. Failure to meet 2 or more criteria should not lead to a deferral of investigation or treatment of infection.
  - Because lactate measurement offered no meaningful change in the predictive validity beyond 2 or more qSOFA criteria in the identification of patients likely to be septic, the task force could not justify the added complexity and cost alongside the simple bedside criteria.
  - Should not constrain the monitoring of lactate as a guide to therapeutic response or as an indicator of illness severity.
Diagnosis: Sepsis

What are the interventions?

What unit are you going to admit the patient to?

Unit Admission Orders

Admitted to the Medical Unit at 1700 with UGIB
Orders:
- Normal saline 125ml/hr
- Protonix 40 mg IV daily
- MVI, Thiamine, Folate
- Magnesium sulfate 2 gm
- Ativan
- ETOH withdrawal observation
- US abdomen to R/O ascites
- H&H q4h
- GI Consult

10/12 - 2300

Vitals: T37.4 HR 120 RR 60 B/P 76/32

Patient 's condition begins to deteriorate. Neuro: more confused & disoriented.

Lungs: good breath sounds w/rapid kussmaul breathing

Abdomen: Hypoactive

Extremities: edematous, mottled, only dopplerable post. Tibialis pulses
Interpret the basic metabolic panel.

Does the patient have an anion gap metabolic acidosis?

What is contributing to the metabolic acidosis?

Interpret the blood gases.

Surviving Sepsis
Campaign Recommendations

• Early Recognition & Initial Resuscitation
  – Early goal directed therapy within the 1st 6 hours of diagnosis of severe sepsis

Failure to Identify Severe Sepsis Early

• Delay to initiation of therapy
• Development of organ dysfunction
• ↑ resource utilization, LOS, mortality, cost

Sharr et al. CCM 2007 35:5 1257-1262
Sepsis Mortality

<table>
<thead>
<tr>
<th>Patient location</th>
<th>Subjects (%)</th>
<th>Hospital Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Source</td>
<td>100</td>
<td>34.8</td>
</tr>
<tr>
<td>Emergency</td>
<td>52.4</td>
<td>27.6</td>
</tr>
<tr>
<td>ICU</td>
<td>12.8</td>
<td>41.3</td>
</tr>
<tr>
<td>Med-Surg Units</td>
<td>34.8</td>
<td>46.8</td>
</tr>
</tbody>
</table>

Levy MM. Intensive care medicine 2010 Feb, 36(2), 222-231

Early Identification of Severe Sepsis on the Med-Surg units

Surviving Sepsis Campaign Phase IV

- 4 US based collaborative groups
  - 15-20 sites per collaborative
  - N=1746 patients
- Thesis: Timely recognition & management of sepsis on the wards using protocols will reduce mortality and need for ICU transfer
- Goal: Improve sepsis screening & best practice bundle treatment on the wards
- Study: Impact on bundle compliance & mortality
VALUE OF NURSES AT THE BEDSIDE

- Empower nurses to recognize and report sepsis, severe sepsis and septic shock

PATIENT IDENTIFICATION

Emergency Department ➔ Critical Care Units ➔ Medical Surgical Units

Instructions: The tool is optional to assess patients for severe sepsis in the emergency department, on the ward, or on the ICU.

1. Is the patient's history suggestive of a new infection?
   - Pneumonia
   - UTI
   - Axillary/arterial line infection
   - Abscess/intravenous line
   - Wound infection
   - Emphysema or tissue necrosis
   - Endocarditis

2. Are any of the following signs & symptoms of infection? Both present or near to the patient?
   - Temperature > 39°C (102°F)
   - Chills and fever
   - Tachypnea > 40 breaths
   - Tachycardia > 100 beats
   - Hypotension
   - Rash or bullous rash
   - Insensible loss with vital signs

If the answer is yes to either question 1 or 2, suspicion of infection is present:

1. Record the current time, 24-hour clock and date / / .
2. Obtain local acid blood culture, CBC with differential, liver function tests, lactate.
3. All physicians must obtain labs; UA, chest X-ray, urine, lumboc, ABGs, CT scan.

3. Are any of the following organ dysfunction criteria present at the site remote from the site of the infection that are not considered to be chronic conditions?
   - Acute altered mental status
   - SBP ≤ 90 or MAP ≤ 65 mmHg
   - SpO2 ≤ 95% on room air or on supplemental O2
   - Creatinine > 2.0 mg/dl (178.6 mmol/l) or Urine Output < 0.5 ml/kg/hour for > 2 hours
   - Bilirubin > 2 mg/dl (34.2 mmol/l)

If suspicion of infection is present AND organ dysfunction is present, the patient meets the criteria for SEVERE SEPSIS and should be entered into the severe sepsis bundle pathway.
Surviving Sepsis Campaign Recommendations

• Early Recognition & Initial Resuscitation
  – Fluids, fluids, and more fluids
  • Crystalloids vs colloids – which is better?
    – SAFE, CRYSMAS, CHEST trials – none showed a significant difference in mortality

  – Do not use hydroxyethyl starches like hetastarch
Surviving Sepsis Campaign Recommendations

• Early Recognition & Initial Resuscitation
  – Fluids, fluids, and more fluids
    • CVP 8-12 mm Hg or 12-15 mm Hg if on vent
    • MAP ≥ 65 mm Hg
    • UOP ≥ 0.5 mL/kg/hr
    • ScVO₂ ≥ 70% or SVO₂ ≥ 65%
    • If fluid is inadequate, transfuse with PRBCs to a hematocrit of ≥30%
    • administer dobutamine (up to a max. of 20 mcg/kg/min) for low cardiac output

• Diagnosis
  – Appropriate cultures should always be obtained before antimicrobial therapy is initiated.
    • Two blood cultures
    • One from each vascular access device >48 hours
  – Cultures of other sites based on clinical manifestations
    • Urine, sputum, CSF, wounds, other bodily fluids
  – Perform imaging studies promptly to confirm & sample any source of infection

• Antibiotic Therapy
  – Should be started within the first hour of recognition of severe sepsis, after appropriate cultures have been obtained
Surviving Sepsis Campaign Recommendations

- **Antibiotic Therapy**
  - Initial empirical broad spectrum antibiotic therapy
  - Reassess & narrow spectrum
  - Limit duration to 7-10 days
  - Stop antibiotics if not due to infectious source

- **Source Control**

**ICU Orders**

- Femoral CVC and intra-arterial lines were inserted
- D5W with 3 amps NaHCO₃ @ 999ml/hr x 6*
- Normal saline @ 999ml/hr
- Urine & blood cultures were sent
- Pipercillin/Tazobactam and Gentamycin were started
- Magnesium 4 gm IV over 4 hours
- Vasopressor was started

Which vasopressor should be used for septic shock?
Surviving Sepsis Campaign Recommendations

- Vasopressors in Septic Shock
  - **First Line**
    - Norepinephrine
  - **Second Line**
    - Epinephrine
    - Vasopressin (0.01-0.03 u/min)
  - **Niche Drugs**
    - Dopamine (bradycardia)
    - Phenylephrine (high cardiac output)

- Insert arterial line
- Target MAP ≥ 65 mm Hg

ICU Orders

- Intubated and placed on pressure controlled ventilation: Rate 18, ΔP 25, PEEP 5
- Ventilation with lower tidal volumes 6ml/kg predicted body weight
Surviving Sepsis Campaign
Recommendations

• Mechanical Ventilation of Sepsis-Induced Acute Lung Injury (ALI/ARDS).
  - ARDSnet
    - Use of low tidal volume 6 ml/kg of predicted body weight with the goal of maintaining a plateau pressure of <30 cm H₂O
    - Permissive hypercapnia be allowed to minimize plateau pressures & tidal volumes
    - PEEP be set to avoid extensive lung collapse at end expiration
    - Results: ↓ relative mortality by 22%

Surviving Sepsis Campaign
Recommendations

• Mechanical Ventilation of Sepsis-Induced Acute Lung Injury (ALI/ARDS).
  - Prone positioning in patients with severe ARDS with P/F ratio <100 despite recruitment maneuvers
  - HOB elevated 30-45°
  - Noninvasive ventilation be considered only in patients with mild-moderate hypoxemia

Surviving Sepsis Campaign
Recommendations

• Mechanical Ventilation of Sepsis-Induced Acute Lung Injury (ALI/ARDS).
  - Weaning protocols
  - Against the routine use of pulmonary artery catheters
  - Use a conservative fluid strategy for patients with established ALI who do not have evidence of tissue hypoperfusion
ICU Orders

• He was sedated with Diprivan and Fentanyl

Surviving Sepsis Campaign Recommendations

• Sedation and Analgesia in Sepsis.
  – Use sedation protocols
  – Bolus or continuous. If continuous, do daily interruption or lightening

• Neuromuscular Blockade in Sepsis.
  – Avoided if possible in the septic patient without ARDS
  • Short course of Cisatracurium of not greater than 48 hours with early sepsis induced ARDS and a P/F ratio of < 150 mm Hg
  – Use train of four to monitor depth of block

ICU Orders

• Also placed on Heparin subcutaneous and Pantoprazole IV
Surviving Sepsis Campaign Recommendations

• Deep Venous Thrombosis Prophylaxis.
  – Recommend LMWH vs low dose unfractionated heparin
  – Combination of pharmacologic & intermittent pneumatic compression devices

• Stress Ulcer Prophylaxis
  – H₂ receptor or proton pump inhibitor

10/13 - 0600
Sedated. VSS T38.6 HR 120 MAP 65-75 Minimal UOP
Norepinephrine 18 mcg/min
D5W with 3 amps NaHCO₃ @ 999cc/hr
Fentanyl @ 50 mcg/h
Diprivan @ 18 mcg/kg/min

10/13 - 0600
Neutrophil 11% ↓
Bands 13% ↓
PT/INR 22.5/3.8 ↑
AST 132 ↑
ALT 63
Lactate 12.4

Interpret the basic metabolic panel.
Interpret the CBC and differential.
Interpret the Coagulation Panel.
What does the lactate of 12.4 indicate?
Interpret the ABG.
ICU Orders

- Transfuse 4 units of PRBCs & 4 units of leukopenic Fresh Frozen Plasma
- Stop the NaHCO₃
- Started Insulin Protocol

Surviving Sepsis Campaign Recommendations

- Blood Product Administration.
  - Target hemoglobin of 7 to 9 g/dl.
  - Use of fresh frozen plasma to correct clotting abnormalities in the absence of bleeding or planned invasive procedures is not recommended.
  - Do not administer antithrombin for the treatment of severe sepsis & septic shock
  - Platelets should be administered if <5,000, between 5,000-30,000 & significant risk of bleeding, or ≤ 50,000 for surgery or invasive procedure

Surviving Sepsis Campaign Recommendations

- Bicarbonate Therapy.
  - Bicarbonate use for the purpose of improving hemodynamics or reducing vasopressor requirements is not recommended for treatment of hypoperfusion induced lactic acidemia with pH ≥ 7.15
Surviving Sepsis Campaign
Recommendations

• Glucose Control.
  – Use protocols to maintain glucose ≤ 180mg/dl
  • Start insulin when 2 consecutive glucose > 180mg/dl
  – When using IV insulin patients should receive a glucose calorie source & blood glucose be monitored q1-2 hrs until stable & then q 4 hrs
  – Low glucose levels obtained with point of care testing be interpreted with caution

Physical Exam

• CXR: bilateral interstitial infiltrates
• Extremities: pitting edema, mottled, cold below knees, hot around thighs, only dopplerable pulses, small bullous skin lesions bilaterally.

Photos taken by Sophia Rodgers
10/13 - 0900
Blood cultures came back positive for gram negative rods in all 4 bottles
Urinalysis had a few bacteria & WBC but nonspecific

What is the significance when the blood cultures come back positive so quickly?

• Dr. DeFlice, the Gastroenterologist, came in. He was told of the patient physical findings and deteriorating condition.

Did the patient eat any raw oysters recently?

Vibrio Vulnificus

Vibrio Vulnificus

• Epidemiology
  – First identified in late 1970s, is a gm. Neg bacterium
  – It exists as a free living bacterium inhabiting marine environment.
  – Filter feeding shellfish, such as oysters, concentrate the bacteria.
Epidemiology
- Certain populations are at highest risk for serious infection.
  - Alcoholic cirrhosis – 31 to 43%
  - Underlying liver disease including cirrhosis & chronic hepatitis – 24 to 31%
  - Alcohol abuse without documented liver disease – 12 to 27%
  - Hereditary hemochromatosis – 12%
  - Chronic diseases such as diabetes mellitus, rheumatoid arthritis, thalassemia major, chronic renal failure, preleukemia, lymphoma – 7 to 8%

Clinical Manifestations
- Most serious are wound infections and bacteremia
  - Wound infections
    - *V. vulnificus* may contaminate wounds exposed to estuarine waters or shellfish

Clinical Manifestations
- Primary bacteremia – Associated with ingestion of raw or undercooked shellfish, particularly raw oysters. Generally occurs with patients who are high risk.
  - One-third will present in shock or become hypotensive within 12 hours of hospital admissions.
  - Three-fourths will have distinctive bullous skin lesions
  - Thrombocytopenia is common with evidence of DIC
  - Leukopenia rather than leukocytosis will occur
  - GI bleed
Vibrio Vulnificus

• Mortality
  – More than 50% overall with primary bacteremia and more than 90% in those who become hypotensive.
  – Persons who survive the acute shock often require prolonged hospitalization in the ICU with complications resulting from multiorgan system failure.

Vibrio Vulnificus

• Diagnosis
  – Blood or stool cultures

• Treatment
  – No definitive trials of therapy
  – Tetracycline and Ciprofloxacin (based on clinical observations & limited animal studies)

Vibrio Vulnificus

• Prevention
  – Persons in high risk groups should avoid eating raw or undercooked shellfish, esp. raw oysters and should avoid situations in which estuarine associated wounds are likely to occur.
ID consult was obtained. Pipercillin/Tazbactam & Gentamycin were d/c’d. Changed to Levofloxacin, Ceftazidime, Doxycycline, Metronidazole

Wife arrived with son. She confirmed patient had eaten raw oysters at a local restaurant one week ago. After discussing patient’s extremely grave condition and poor prognosis, wife decided to make him a DNR.

Surviving Sepsis Campaign Recommendations

- Goals of care & communication of prognosis
  - Advanced directives, end of life care planning
  - Goals should be addressed as early as feasible but no later than 72 hours

Chem. BG ↓ 54. Insulin off. 1 amp glucose given. UOP ↓

Bullous skin lesions worsen (see photos)
10/13 - 1800

- Becomes oliguric
- 7.06/58/56
- Hypotensive despite increasing norepinephrine to 25 mcg/min
- Vasopressin added
- Steroids considered

Surviving Sepsis Campaign Recommendations

- Relative Adrenal Insufficiency
  - Steroids
    - Consider for adult septic shock when hypotension responds poorly to adequate fluid resuscitation & vasopressors
    - ACTH stimulation test not be used to identify the subset of adults with septic shock
    - Intravenous corticosteroids (hydrocortisone) 200-300 mg/day in 3 to 4 divided doses for 7 days
    - Wean steroids when vasopressors no longer required
10/13 - 2107
SpO2 ↓ 64%

10/13 - 2200
Daughter arrived from out of town

10/13 - 2400
Peak inspiratory pressures ↑ suddenly 77
SpO2 35%

What contributed to the sudden increase in peak pressure and hypoxia?

10/14 - 0115
Family made decision to withdraw life support. Expired at 0120

**Final blood cultures**

**VIBRIO VULNIFICUS**
Sepsis Bundles - Resuscitation

- Serum lactate measured
  - All patients with elevated lactate >4 mmol/L should be treated with the sepsis bundles regardless of blood pressure
- Blood cultures obtained prior to antibiotics
- Broad spectrum antibiotics within 3 hours of ED or 1 hour for non ER ICU admissions

Sepsis Bundles - Resuscitation

- Hypotension and/or lactate > 4
  - Deliver an initial minimum of 30 ml/kg of crystalloid or colloid equivalent
  - Apply vasopressors for hypotension not responding to initial fluid resuscitation to maintain MAP ≥ 65 mm Hg

Sepsis Bundles - Resuscitation

- In the event of persistent hypotension despite fluid resuscitation and/or lactate >4
- Initial fluid
  - Achieve CVP > 8 mm Hg or 12 to 15 mm Hg for ventilator patients
  - Achieve ScVO₂ >70%
  - If patient is both hypovolemic and the hematocrit is <30%, it is appropriate to transfuse PRBCs provided fluid resuscitation has achieved a CVP ≥8
  - If cardiac output is diminished, consider Dobutamine
References
