SIRS to Septic Shock: Prevention, Early Detection, Treatment and Prevention of Complications

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Overview

- Definitions
- Risk Factors
- Prognostic factors
- Early Diagnosis, Management and Treatment
- Prevention

Definitions

- Infection: presence of pathogen in sterile space
- Bacteremia: presence of bacteria in blood
- SIRS:
  - Dysregulated inflammatory response to a non-infectious insult
  - Autoimmune conditions, pancreatitis, vasculitis, surgery
- Sepsis
  - Dysregulated inflammatory response to infection

SIRS vs Sepsis

<table>
<thead>
<tr>
<th></th>
<th>SIRS</th>
<th>Sepsis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology</td>
<td>Non-infectious</td>
<td>Infection</td>
</tr>
<tr>
<td>Temperature</td>
<td>&gt;38.3°C or &lt;36°C</td>
<td>&gt;38.3°C or &lt;36°C</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>&gt;90 bpm</td>
<td>&gt;90 bpm</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>&gt;20 or PaCO2&lt;32mmHg</td>
<td>&gt;20 or PaCO2&lt;32mmHg</td>
</tr>
<tr>
<td>WBC</td>
<td>&gt;12K, &lt;4K or &gt;10% bands</td>
<td>&gt;12K, &lt;4K or &gt;10% bands</td>
</tr>
</tbody>
</table>
| Examples       | Pancreatitis, vasculitis | Pneumonia
                | Autoimmune conditions   | Endocarditis
                | Surgery                  | Cholangitis
                |                          | Pyelonephritis          |
**Diagnostic Criteria for Sepsis**

<table>
<thead>
<tr>
<th>General</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Altered Mentation</td>
<td></td>
</tr>
<tr>
<td>Edema or fluid balance</td>
<td>&gt;20mL/kg/24 hours</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Glucose &gt;140 mg/dL No diabetes</td>
</tr>
<tr>
<td>Inflammatory</td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>Leukocytosis (&gt;12K)</td>
</tr>
<tr>
<td>Leukopenia (&lt;4K)</td>
<td></td>
</tr>
<tr>
<td>Hemodynamics</td>
<td></td>
</tr>
<tr>
<td>Plasma CRP</td>
<td>&gt;2 SD above normal</td>
</tr>
<tr>
<td>Arterial Hypotension</td>
<td>SBP &lt;90mmHg MAP &lt;70mm Hg</td>
</tr>
<tr>
<td>Organ Dysfunction</td>
<td></td>
</tr>
<tr>
<td>Arterial hypoxemia</td>
<td>PaO2/FiO2 &lt;300</td>
</tr>
<tr>
<td>Acute Oliguria</td>
<td>UOP &lt; 0.5mL/kg/hr X 2 hours</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>INR &gt;1.5 aPTT &gt;60 seconds</td>
</tr>
<tr>
<td>Ileus</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>&lt;100,000</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>Total bil &gt; 4 mg/dL</td>
</tr>
<tr>
<td>Tissue Perfusion</td>
<td></td>
</tr>
<tr>
<td>Hyperlactatemia</td>
<td>&gt;1 mmol/L</td>
</tr>
<tr>
<td>Mottling</td>
<td>Decr. capillary filling</td>
</tr>
</tbody>
</table>

**Septic Shock**

- Severe sepsis & Mean SBP <60 mmHg or low dose pressors despite adequate fluid resuscitation*
- Refractory: higher doses of pressors to keep mean SBP >60mmHg despite fluid resuscitation*

<table>
<thead>
<tr>
<th></th>
<th>Septic Shock</th>
<th>Refractory Septic Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine</td>
<td>&gt;5mcg/kg/min</td>
<td>&gt;15mcg/kg/min</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>&lt;0.25 mcg/kg/min</td>
<td>&gt;0.25 mcg/kg/min</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>&lt;0.25 mcg/kg/min</td>
<td>&gt;0.25 mcg/kg/min</td>
</tr>
</tbody>
</table>

*Defined as 30mL/kg of crystalloid

**Severe Sepsis**

- Sepsis-induced tissue hypoperfusion or organ dysfunction

<table>
<thead>
<tr>
<th>Clinical parameters</th>
<th>Lab Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>UOP &lt;5mL/kg/hr for &gt;2hrs</td>
<td>Creatinine &gt;2.0 mg/dL</td>
</tr>
<tr>
<td>ALI with PaO2/FiO2 &lt;250 in the absence of pneumonia</td>
<td>Lactate &gt;ULN</td>
</tr>
<tr>
<td>ALI with PaO2/FiO2 &lt;200 in presence of pneumonia</td>
<td>Platelets &lt;100K</td>
</tr>
<tr>
<td></td>
<td>Coagulopathy (INR &gt;1.5)</td>
</tr>
<tr>
<td></td>
<td>Total Bil &gt;2 mg/dL</td>
</tr>
</tbody>
</table>

**MODS**

- End result of SIRS or sepsis
  - Primary: organ dysfunction as a result of direct injury
  - Secondary: result of host response to injury
- Measures: Increased ICU mortality
  - PaO2/FiO2 ratio
  - Serum Cr (or UOP)
  - Serum bilirubin
  - Platelet count
  - Glasgow coma score
  - Hypotension
Incidence of Sepsis

Risk factors
- ICU Patients: Proportionate to prevalence of infection (up to 50%)
- Bacteremia
- Age >65 years: Increased incidence of Sepsis, independent predictor of mortality due to sepsis
- Immunosuppression: Medical Conditions: malignancy, renal failure, liver failure, AIDS
- Medications: steroids, cytotoxic drugs, immunomodulators
- Diabetes and Cancer
- Community-acquired Pneumonia: 48% developed severe sepsis, 5% septic shock
- Genetic Factors
  - Impaired antibody production
  - Impaired cellular immunity
  - Impaired recognition of pathogens

Pathogens

Prognostic Factors
- Host Response
  - Hypothermia, leukopenia in non-survivors (17% vs 5%)
  - Comorbidities, Age >40 and new-onset A. fibrillation
- Site of Infection
  - Urosepsis: 30% mortality
  - GI, Pulmonary or unknown: 50-55% mortality
- Type of Infection
  - Nosocomial pathogens vs Community-acquired
  - MRSA, non-candida fungus, Candida, MSSA, P. aeruginosa
- Antimicrobial therapy
- Delay in restoration of perfusion
Early Detection

• Distinguishing between SIRS and Sepsis
• Recognition of sepsis-induced tissue hypoperfusion
  — Persistent hypotension after initial fluid challenge
  — Lactate >4 mmol/L
• “Routine screening of potentially infected seriously ill patients for severe sepsis to increase the early identification of sepsis and allow implementation of early sepsis therapy”

Screening for Sepsis

Is the patient’s history suggestive of a new infection?
- Pneumonia, sepsis
- Urinary tract infection
- Acute abdominal infection
- Meningitis
- Gastrointestinal infection

Are any of the following signs & symptoms of infection both present and new to the patient? Note: laboratory values may have been obtained for inpatients but may not be available for outpatients.
- Temperature >38.1°C
- Temperature <36°C
- Tachycardia >90 bpm
- Tachypnea >20 bpm
- Anorexia, altered mental status
- Leukocytosis (WBC count >12,000 µL⁻¹)

If the answer is yes to both eliter question 1 & 2, suspicion of infection is present:
- Obtain lactic acid, blood cultures, CBC with differential, basic chemistry labs, bilirubin.
- At the physician’s discretion obtain: UA, chest x-ray, amylase, lipase, ABG, CRP, CT scan.

Early Management

• Stabilize respiration
• Assess Perfusion
• Establish central venous access
• Administer antimicrobials
Treatment: Initial Resuscitation

- Early goal-directed therapy
  - Quantitative resuscitation of patients in the first 6 hrs
  - Goals (grade 1C):
    - CVP 8-12mm Hg
    - MAP ≥ 65 mmHg
    - UOP>0.5ml/kg/hour
    - Central venous or mixed venous Oxygen saturation of 70%, 65%
  - Normalization of lactate as marker of tissue perfusion (grade 2C)
  - Associated with 15.9% absolute reduction in 28-day mortality rate

Diagnosis

- Obtain culture data PRIOR to antimicrobial therapy (45min)
  - Blood cultures x 2 sets (aerobic/anaerobic)
  - Urine, Sputum, CSF or other body fluids
  - DNA Microarray for rapid identification of (most) organisms within 4 hours of a positive blood culture
- Gram stain: PMNs, Organisms
- Imaging

Antimicrobial Therapy

- Broad spectrum antimicrobials within 1 hour of septic shock or severe sepsis without septic shock
  - Activity against all likely pathogens
  - Adequate penetration for source of infection
- Neutropenic/Immunosuppressed patients
- Most common pathogens are Gram positive, then Gram-negative or mixed infections
  - Fungal or viral infections not as common
Antimicrobial Therapy

- Daily assessment for de-escalation
  - Reduce development of resistance, toxicity, cost
- Combination therapy for neutropenic patients and those with MDR organisms
  - “superior clinical outcome in severely ill, septic patients with high risk of death”
- Duration of therapy may vary depending on source/type of infection and pathogen
  - Typically 7-10 days once source control achieved
  - Exceptions: Staph bacteremia, no source control

Other Adjunctive Therapies

- Glucocorticoids
  - Hydrocortisone 200mg qd for patients in **septic shock** with hemodynamic instability despite fluids and pressors (not severe sepsis)
  - Should be weaned when pressors are discontinued
- Nutrition
  - Enteral vs parenteral vs fasting
- Glucose control
  - Initiation of insulin when 2 consecutive BS > 180

Source Control

- The 2 most important words in this talk!
- Intervention within 12 hours
  - Intra-abdominal abscess/GI perforation, cholangitis, pyelonephritis, necrotizing soft tissue infection, deep space infection (empyema, septic arthritis)
  - Exception: delayed intervention in infected peripancreatic necrosis for demarcation of viable & nonviable tissue
Infection Prevention

- SOD/SDD (Grade 2B)
  - Reduce VAP
- Oral Chlorhexidine gluconate
  - Decreases risk of nosocomial infection

Prevention of complications

- Early Recognition
- Early Goal Directed Therapy
- Appropriate antimicrobial therapy
- Source Control

Complications

- Death
- Irreversible/long-term organ damage
  - Renal failure
  - Ventilatory dependent respiratory failure
- Increased risk of developing sepsis as well as impaired immunity/response to future infections

Case 1

- 57 year old male with history of HCV admitted with a 4 day history of progressive dyspnea, productive sputum and fevers. He called EMS, was hypoxic to 82% on RA. Started on CPAP → ED BIPAP then intubated for ongoing hypoxemia, increased work of breathing.
- CXR revealed RML, RLL infiltrates; CT with bilateral pulmonary consolidation with regions of central necrosis and/or cystic bronchiectasis
- Labs: WBC 16K (11% immature), Lactate 2.5
- Received Cefepime, Vancomycin and transferred to the MICU
Rapid progression to ARDS
- Hypotension despite 6L IVF, reinitiation of norepinephrine due to CVP=4
- AKI with Cr of 1.2 (up from baseline 0.6); however UOP =72ml/hr
- Initial Antibiotics: Vancomycin + cefepime + azithro + clindamycin

Case 2
- 43 year old female with HIV, HCV, DM, HTN, recently treated for diarrhea due to C. difficile and cryptosporidium admitted with progressive cough, dyspnea and respiratory failure. She had ongoing diarrhea.
- Two days after admission, lactate was 4.0, she had AKI (was on CVVHD), was re-intubated and 10 days after admission, underwent total abdominal colectomy with an open abdomen.

Microbiology:
- Influenza B positive via shell-vial Culture
- Sputum cultures with MRSA.
- Blood cultures + MRSA
- Treatment:
  - Oseltamivir
  - Vancomycin \rightarrow\ Linezolid for cavitary pneumonia
  - Cefepime/azithro/clinda discontinued
- Outcome: Patient treated for VAP (Enterobacter), self-extubated, doing well.

At that time, lactate was 25, pH was 6.97 and her WBC was 67K.
- Surgical pathology revealed boggy, distended colon with adhesions to the liver.
- She improved briefly and was off pressors but later developed rise in lactate again, liver failure, respiratory failure, ongoing renal failure and care was withdrawn
- Autopsy revealed intra-abdominal hemorrhage, hemorrhage at the ostomy site, b/l LL pneumonia
References

• Annane D, Bellissant E, Cavaillon JM. Septic Shock. Lancet 2005;365(9453):63