SEVERE SEPSIS: INITIAL RECOGNITION AND RESUSCITATION

Expected Practice:

- Assess all patients and immediately notify physician when a patient presents with clinical findings suggestive of sepsis.
- Clinical findings for severe sepsis include:
  - Documented or suspected infection
  - AND
  - 2 or more of the following systemic inflammatory response syndrome (SIRS) criteria:
    - Heart rate > 90 beats per minute
    - Temperature < 36°C (96.8°F) or > 38.3°C (101°F)
    - Respiratory rate > 20 breaths per minute or PaCO2 < 32 mmHg
    - White blood cell count > 12,000/mm³ or ≤ 4000/mm³ or a left shift in the immaturation of granulocytes (bands) > 10%
  - AND
  - At least one of the following indicators of tissue hypoperfusion or sepsis related acute organ dysfunction:
    - Acute altered mental status
    - Systolic blood pressure < 90 mmHg or mean arterial pressure < 70 mmHg or a SBP decrease of 40 mmHg
    - Blood glucose > 140 mg/dL in patients without diabetes.
    - Arterial hypoxemia (PaO₂/FiO₂ < 300)
    - Acute oliguria (< 0.5 ml/kg per hour for at least 2 hours)
    - Creatinine increase > 0.5 mg/dL above baseline
    - Coagulation abnormalities (INR > 1.5 or a PTT > 60 secs)
    - Ileus
    - Thrombocytopenia (platelet count, < 100,000 µL⁻¹)
    - Hyperbilirubinemia (plasma total bilirubin > 2mg/dL) Lactate > 2 mmol/L
- Obtain serum lactate measurements. Hyperlactatemia is defined as lactic acid level > 4 mmol/L. [Level D]
- Obtain blood cultures as well as cultures from all potential sites of infection prior to initiating broad spectrum antibiotics. Blood cultures should be drawn prior to initiation of antibiotic therapy and within 1 hour of sepsis diagnosis. [Level D]
- Evaluate for and remove potential sources of infection (for example, obviously infected invasive devices). [Level D]
- Maintain the following therapeutic endpoints during resuscitation: mean arterial pressure at > 65 mmHg, central venous pressure (CVP) 8-12 mmHg and central venous or mixed venous oxygen saturation > 70%. [Level D]
  - Administer fluids to attain a CVP of 8-12 mmHg or ≥12 mmHg if on a ventilator [Level D]
  - Administer vasopressors if necessary to achieve a mean arterial pressure of 65 mmHg if fluid replacement is not successful [Level D]
  - If venous oxygen saturation goal not attained consider additional fluids, blood transfusion and/or dobutamine administration [Level D]
- Maintain blood glucose levels at <150mg/dL. [Level D]
- Consider administration of human recombinant activated protein C (drotrecogin alfa activated) for patients at risk for dying and presenting with septic shock, sepsis with multiple organ failure and sepsis-induced acute respiratory distress syndrome. [Level D]
Note: Administration of human recombinant activated protein C (drotrecogin alfa activated) is no longer a recommended. The FDA sent out notification on October 25, 2011 that Eli Lilly has withdrawn this drug from the market. In a recently completed clinical trial (PROWESS-SHOCK trial), the drug failed to show a survival benefit for patients with severe sepsis and septic shock.

Scope and Impact of the Problem:
Severe sepsis is a major healthcare problem that affects millions of people around the world each year with an extremely high mortality rate of 30 to 60 percent. Mortality from sepsis is greater than breast cancer, lung cancer, and colon cancer combined and is the number one cause of death in the non-coronary ICU. The incidence of severe sepsis is expected to double over the next 25 to 30 years.

Supporting Evidence:
- More than 750,000 cases of severe sepsis occurred annually (year 2000) and mortality ranges from 28 to 50 percent with an overall hospital mortality of about 30 percent. Sepsis (infection and 2 of the SIRS criteria) can rapidly progress to severe sepsis (infection + SIRS criteria + organ dysfunction) to septic shock (persistent hypotension and tissue hypoperfusion despite sufficient fluid resuscitation) within 24 hours.
- Treatment should be initiated regardless of where the patient is located within the hospital. A prospective randomized study of 263 emergency department patients diagnosed with severe sepsis or septic shock showed that patients treated aggressively with a goal direction towards tissue oxygenation within the first 6 hours of presentation had a 16 percent improvement in mortality. Another small retrospective study showed a decrease in mortality in patients identified with signs of severe sepsis and treated within the first 6 hours.
- Serum lactate levels can be elevated in the setting of a normal or increased cardiac output. The measurement of serum lactate can reflect occult decreases in global tissue perfusion and as such may be an indicator of organ malperfusion. The presence and the clearance rate of lactate are associated with increases in patient morbidity and mortality.
- Early administration of appropriate antibiotics decreases mortality in patients with Gram- positive and -negative bacteremias. Empiric broad spectrum antibiotics should be initiated when possible after obtaining appropriate cultures but prior to identification of the infecting organism and reassessed after 48 to 72 hours based on culture results and clinical data.
- According to the Surviving Sepsis Campaign guidelines, during the first 6 hours of treatment the goal is to achieve and maintain a CVP of 8-12 mmHg or 12-15 mmHg for patients receiving mechanical ventilation and a MAP of at least 65 mmHg with fluid resuscitation. Dobutamine is identified as the medication of choice to increase cardiac output to normal levels or to improve lactate clearance when cardiac output is not being measured. Two large clinical trials did not show a benefit from increasing cardiac output above physiologic normal levels in order to increase oxygen delivery to the tissues. Available data do not support the use of low dose dopamine for renal protection.
- Colloids have not been shown to be of more benefit than crystalloid for fluid resuscitation. One large randomized controlled trial comparing 4 percent albumin with normal saline in the treatment of patients requiring volume resuscitation found no significant difference in mortality between the groups. Several literature reviews have concluded that choice of fluids does not appear to change outcomes.
- In the setting of hypotension, fluid replacement should be optimized before vasopressors are started. No high-level evidence exists to identify the most appropriate vasopressor to use for the treatment of septic shock and selection is based on multiple clinical parameters. However, in the Surviving Sepsis Campaign Guidelines for the Management of Severe Sepsis and Septic Shock norepinephrine or dopamine are identified as the initial vasopressors of choice to increase vascular tone and blood pressure.
- Two meta analyses concluded that administration of high dose corticosteroids are of no benefit or may be detrimental to patients with septic shock. In vasopressor dependent shock, the addition of low-dose exogenous cortisol has been shown to improve the uptake of the patient’s own and the exogenously administered sympathetic stimulants when serum cortisol levels are low.
- Maintaining glucose levels within normal range (80-110 mg/dL) but at least < 150mg/dL has been shown to decrease morbidity and mortality in a surgical population but did not focus on septic patients. Maintaining glucose levels < 150mg/dL showed reduced morbidity but not mortality in critically ill medical patients with sepsis.
- In a large double blind study, human recombinant activated protein C (drotrecogin alfa activated) decreased mortality by 6 percent in patients with severe sepsis and decreased mortality by 13 percent for patients at high risk for death (i.e., patients having an APACHE II score of 25 or greater).
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AACN Evidence Leveling System

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
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<tbody>
<tr>
<td>Level A</td>
<td>Meta-analysis of quantitative studies or metasynthesis of qualitative studies with results that consistently support a specific action, intervention or treatment.</td>
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<tr>
<td>Level B</td>
<td>Well-designed, controlled studies with results that consistently support a specific action, intervention or treatment.</td>
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<tr>
<td>Level C</td>
<td>Qualitative studies, descriptive or correlational studies, integrative review, systematic reviews, or randomized controlled trials with inconsistent results.</td>
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<tr>
<td>Level D</td>
<td>Peer-reviewed professional organizational standards with clinical studies to support recommendations.</td>
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<tr>
<td>Level E</td>
<td>Multiple case reports, theory-based evidence from expert opinions, or peer-reviewed professional organizational standards without clinical studies to support recommendations.</td>
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<tr>
<td>Level M</td>
<td>Manufacturer’s recommendations only.</td>
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Actions for Nursing Practice:

- Educate all nursing staff on the risk factors and clinical signs of sepsis.
- Create an interdisciplinary team including but not limited to a physician, pharmacist, respiratory care practitioner, nursing and dietitian to develop protocols or guidelines for the initial identification and management of the patient presenting with signs of sepsis and severe sepsis.
- Consider development of a rapid response team to facilitate prompt identification and treatment of patients with sepsis.

Need More Information or Help?
- Go to www.aacn.org and select Practice Resource Network.

References: