Sepsis
Key Points

- Sepsis is the combination of a known or suspected infection and an accompanying systemic inflammatory response (SIRS)
- Severe sepsis is sepsis with acute dysfunction of one or more organ systems; septic shock is a subset of severe sepsis
- Severe sepsis is common, frequently fatal, and expensive. More than 750,000 cases occur annually in the United States
- Effective management of patients with severe sepsis requires early identification, cardiopulmonary support, antibiotics, source control, and general supportive care
- The prognosis of the patient with severe sepsis is related to the number of dysfunctional organs
- Cardiopulmonary support consists of early and aggressive fluid resuscitation, maintenance of mean arterial pressure at 65 mm Hg or higher, and measures to maximize and maintain tissue oxygenation
  - Judging the adequacy of tissue oxygenation is informed by measurement of the mixed venous oxygen saturation, and supportive therapy is most effective and beneficial when provided in the first hours of presentation

Patients should receive early intravenous empiric antibiotics directed at all possible sources of infection. Appropriate antibiotics decrease the mortality rate by 10% to 15% in patients with severe sepsis.

Source control can be surgical or nonsurgical and is intended to remove or lessen the burden from the primary focus of infection.

Despite appropriate antibiotics, source control, and organ support, the mortality rate in patients with severe sepsis remains at 28% to 50%.

Specific antisepsis interventions have recently been introduced that target multiple pathophysiologic aspects of the sepsis cascade and can improve outcomes.

To maximize outcomes, supportive measures must be introduced to:
- Ensure proper nutrition
- Maintain fluid, glucose, and electrolyte homeostasis
- Promote tissue oxygenation
- Prevent complications
Impact

- Annual incidence of severe sepsis in the United States is estimated at 240 to 300 cases / 100,000 population
- In Europe, the incidence of severe sepsis exceeds 200,000 annually
- Thus, in the United States and Europe, at least 700 to 1300 patients die daily from severe sepsis
- Patients with severe sepsis account for annual health care expenditures in excess of $16 billion in the United States and £5.2 billion in Europe

Epidemiologic Trends

- The incidence of severe sepsis peaks in children younger than 12 months, remains low until midlife, and then progressively increases
  - Approximately 2/3 of patients with sepsis are >65 yo
  - Elderly account for more than 75% of the overall health care costs of the disease

Epidemiologic Trends

- The incidence of severe sepsis is anticipated to increase approximately 1.5% per year until at least 2050 resulting from
  - Age shifts in the population
  - Prevalence of more critically ill patients (e.g., transplant recipients)
  - Increases in the numbers of invasive diagnostic procedures and monitoring techniques
  - Predicted increase has significant implications for the critical care community because it has been estimated that by 2020 there will be a 22% shortfall of available intensivists' hours to meet this demand
### ACCP/SCCM Consensus Criteria for Sepsis and Related Disorders

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Infection</td>
<td>Microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms</td>
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<tr>
<td>Bacteremia</td>
<td>The presence of viable bacteria in the blood</td>
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<tr>
<td>Sepsis</td>
<td>Systemic response to infection, manifested by two or more SIRS criteria developing as the result of infection</td>
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<tr>
<td>Severe sepsis</td>
<td>Sepsis associated with acute organ dysfunction, hypoperfusion, or hypotension; hypoperfusion and perfusion abnormalities may include, but are not limited to, lactic acidosis, oliguria, or acute alterations in mental status</td>
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<tr>
<td>Septic shock</td>
<td>Sepsis-induced hypotension despite fluid resuscitation in addition to the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis; oliguria, or an acute alteration in mental status; patients receiving inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured</td>
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<tr>
<td>Sepsis-induced hypotension</td>
<td>Systolic blood pressure &lt;90 mm Hg or a reduction 40 mm Hg from baseline without other causes for hypotension</td>
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<tr>
<td>Multiple organ dysfunction syndrome</td>
<td>Altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention</td>
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Systemic Inflammatory Response Syndrome

Systemic response to several clinical insults; it is manifested by at least two of the following:

- Temperature >38°C or <36°C
- Heart rate >90 beats/minute
- Resp rate >20 or partial CO₂ pressure <32 mm Hg
- WBC >12,000/L, <4000/L, or >10% band forms
Death Rate by Entity

Host Factors That May Contribute to an Increased Risk for Sepsis

- Break in membrane integrity
  - Surgery
  - Toxic injury to epithelium
- Age
  - Very young
  - Elderly
- Gender
  - Men > women
- Race
  - Nonwhite > white
- Genetic polymorphisms
  - Tumor necrosis factor promoter gene
  - Toll-like receptors
- Comorbidities
  - Diabetes mellitus
  - Immunosuppression
Patients can be considered febrile when they have a temperature of at least 38°C (100.4°F) or hypothermic with a temperature no higher than 35°C (95°F).

Fewer than 50% of febrile episodes are infectious in origin, and almost 50% of septic patients are normothermic or hypothermic.

Temperatures higher than 41.1°C are most probably noninfectious (e.g., drug fever or thyroid storm).

Fever with a relative bradycardia and a rash may be drug induced or indicate *Salmonella typhi* or *S. paratyphi* infection.

Vital signs can also provide a wealth of information about the patient's prognosis:
- In a study of community-acquired pneumonia (CAP), a temperature below 35°C or 40°C or higher, a pulse 125 beats/min or faster, a respiratory rate of at least 30 breaths/min, and a systolic BP lower than 90 mm Hg were independently associated with increased mortality rate.

Physical Exam

- Altered mental status of the patient is an important clue to the presence of organ dysfunction. Delirium is an acute disorder of attention and cognition
  - It develops in 60% of older hospitalized patients and in more than 80% of mechanically ventilated patients
  - Delirium may be hyperactive (agitated) or hypoactive. Whereas health care workers commonly recognize the former, hypoactive delirium is commonly missed
  - Delirium is often an important early indication of sepsis, and it can be very hazardous and prolonged in the elderly
  - Delirium is associated with prolonged hospital stays, institutionalization, and death

- Photophobia, nuchal rigidity, papilledema, or cranial nerve palsies should direct attention to a focus of infection, such as meningitis, within the CNS

- Orbital pain, periorbital erythema, proptosis, or unilateral rhinorrhea may be seen in a patient with bacterial or fungal sinusitis
  - Although this may be the presenting illness in an immunocompromised patient, it can also be a secondary infection resulting from the obstruction of sinus ostia by nasotracheal or nasogastric tubes

Management

- Severe sepsis is a medical emergency
- The first priority should be to assess and address abnormalities in the airway, breathing, and circulation
- In many instances, the clinical assessment of tissue perfusion and response to therapy can be aided by monitoring devices and laboratory measurements
- Once immediate stabilization has been accomplished, the source of the infection should be established and controlled, and specific antimicrobial agents should be administered
- After stabilization, source control, initiation of appropriate antimicrobial agents, and further support for dysfunctional organs, disease-specific interventions should be considered
Fluid Resuscitation

- The initial therapeutic intervention in patients with severe sepsis is to reverse organ hypoperfusion.

- Large amounts of fluids may be required to restore tissue perfusion and oxygen delivery. In some instances, correction of large fluid deficits may require at least 6 to 10 L of crystalloids.
  - In approximately 50% of patients with severe sepsis who present with hypotension, fluid resuscitation alone will normalize BP and restore hemodynamic stability.

- There has been an ongoing debate as to whether fluid resuscitation is best accomplished with crystalloids or colloids.

Progression of Sepsis

- Infection
  - HR/RR ↑

- Fluids

- Supplemental O₂

- Sepsis
  - Oxygenation ↓

- Severe Sepsis
  - MAP ≤ 70 mm Hg despite fluids

- Vasopressors

- Mechanical Ventilation

- MODS
  - RR < 30,
  - PaO₂ < 55 despite supplemental oxygen

- 30-50% increased mortality
The Key is Early Recognition

- Mental Status
  - Early to be altered in the elderly

- Vital Signs
  - Early Tachycardia
    ✓ “Beware the resting tachycardia”
  - Widening pulse pressure

- Physical Exam
Suspicion of Sepsis

- Sound the Alarm!