Early Identification and Management of Patients with Severe Sepsis and Septic Shock in the Emergency Department

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KEYWORDS

• Sepsis • Shock • Early goal-directed therapy • Organ dysfunction • Sepsis bundles

KEY POINTS

- Severe sepsis and septic shock have high prevalence and mortality.
- Treatment is time-sensitive and depends on early identification and risk-stratification.
- Treatment must include antibiotics and targeted therapies designed to optimize oxygen delivery.
- Adherence to a treatment algorithm decreases mortality.

EPIDEMIOLOGY

Severe sepsis and septic shock have great relevance to Emergency Medicine physicians because of their high prevalence, morbidity, and mortality. In some series, these conditions account for 10% of all intensive care unit (ICU) admissions and 750,000 patients yearly[1,2]; the most common source for these admissions is the Emergency Department (ED).[3] Septic shock is the most common cause of death in the ICU,[4] and the frequency of hospitalization for severe sepsis is climbing rapidly, having doubled between 1993 and 2003.[5] Despite significant advances in treating this common condition, mortality for severe sepsis remains at 15% to 40%,[6–8] with over one-third of patients discharged to a long-term care facility.[8] Outcomes are predictably worse for septic shock, with a mortality of 20% to 72%.[7,9,10] Overall, sepsis is

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responsible for 9% of the deaths in the United States,[11] ranking it third after heart disease and cancer among leading causes of death.[2] Twenty percent of this critically ill patient population remains in the ED for longer than 6 hours.[12]

DEFINITIONS

Definitions from the surviving sepsis campaign were modified and expanded in 2013.[13] Sepsis is defined as the suspected or documented presence of infection with evidence of a systemic inflammatory state.[14] This definition may prove challenging in the ED, as the culture results required to confirm infection are often unavailable, and laboratory evidence of a systemic inflammatory state may take hours to obtain. Nevertheless, in the proximal phase of presentation, ED providers are able to determine if a patient with suspected infection exhibits an abnormal physiologic response to a likely infectious insult. Traditionally, this has been defined by the vital sign criteria for the systemic inflammatory response syndrome (SIRS), although this has changed with the updated guidelines. Moving further along the severity spectrum, severe sepsis is defined as sepsis plus organ dysfunction or tissue hypoperfusion, and septic shock is defined as persistent sepsis-induced hypotension despite adequate volume resuscitation. Although more comprehensive than the SIRS criteria, the strict definitions include variables unavailable at presentation, such as urine output and fluid balance; adapted criteria more appropriate for use in the ED can be found in **Box 1**.

PATHOPHYSIOLOGY

Although the inciting event for severe sepsis is infectious, the pathophysiology is driven as much by a susceptible host's immune response as by the infection itself[15]; this is particularly apparent when considering the similarity of host responses to noninfectious severe illnesses such as burns and trauma.[14] Classically, this immune response has been considered an overly aggressive pro-inflammatory state causing collateral damage to the host via a variety of mechanisms. However, recent studies have found increasing evidence for a balance of pro-inflammatory and anti-inflammatory mechanisms,[16] with depletion of dendritic cells,[17] prolonged lymphopenic states, and high levels of immunosuppressive T cells,[18] causing increased susceptibility to secondary infections, difficulty clearing existing infections, and reactivation of latent viral infections.[19,20]

In the context of this systemic immune response, a variety of mechanisms are responsible for the end-organ dysfunction that is the hallmark of severe sepsis. The most important is a mismatch between tissue oxygen demand and delivery whereby the cellular need for oxygen exceeds its availability. Oxygen delivery depends on adequate cardiac output (dependent on preload and contractility), afterload, oxygenation, and oxygen-carrying capacity. The inadequate oxygen delivery resulting from septic shock is classically considered distributive from the vasodilatory effects of bacterial endotoxin,[21,22] endogenous vasopressin deficiency,[23] and central downregulation of vasomotor tone.[24] However, a cardiogenic component secondary to cytokine-mediated myocardial suppression and impaired sarcoplasmic reticulum calcium release[25] has been elucidated; reversible, isolated systolic and diastolic dysfunction have both been described.[26] The contributory effects at initial presentation of inadequate preload due to loss of endothelial integrity,[27] increased insensible losses, and impaired access to hydration in elderly or debilitated hosts should not be overlooked. Last, impaired oxygen delivery is possible despite normal or high blood pressure,[28] and failure of oxygen uptake at a cellular level can occur despite adequate delivery.[29] There are also mechanisms for end-organ dysfunction independent of