

## **Emergency Department** Antimicrobial **Considerations in Severe Sepsis**

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#### **KEYWORDS**

- Severe sepsis Emergency medicine Timing of antimicrobials
- Antimicrobial pharmacodynamics and pharmacokinetics
  Procalcitonin
- Antimicrobial shortages

### **KEY POINTS**

- The administration of antimicrobials in the emergency department (ED) is of paramount importance for optimal patient outcomes.
- Various factors need to be considered when choosing antimicrobials in the ED, including patient factors, infective microbe factors, and drug-related factors.
- Prompt administration of antimicrobials is a key management strategy.
- Clinicians should use a basic understanding of pharmacokinetic and pharmacodynamic properties when empirically selecting antimicrobials in septic ED patients.
- Antimicrobial shortages are a recurrent threat to the optimal treatment of septic patients. and clinicians should understand how a systems approach can ensure adequate antimicrobial options during these periods.

#### INTRODUCTION

There were more than 3.5 million emergency department (ED) visits in the United States in 2010 associated with a primary diagnosis of infectious and parasitic diseases.<sup>1</sup>

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Sepsis, which is defined as the systemic inflammatory response syndrome (SIRS) accompanied by the probable or documented presence of infection, is an advanced manifestation of infectious diseases and can lead to severe sepsis, septic shock, and multiple organ dysfunction syndrome.<sup>2</sup> Between 1992 and 2001, approximately 2.8 million visits to EDs in the United States were related to sepsis, and more than 10% of these patients required admission to an intensive care unit (ICU).<sup>3</sup> The most prevalent sources of infection leading to sepsis were the lower respiratory tract and the genitourinary tract.<sup>3</sup> Despite recent advances in the understanding and treatment of severe sepsis and septic shock, this syndrome remains a leading cause of death.<sup>4</sup>

Clinical practice guidelines have been developed to aid clinicians in the identification and treatment of patients with severe sepsis and septic shock. Recommended treatment strategies include early goal-directed therapy, obtaining appropriate microbiological specimens before antimicrobial administration (if feasible), identifying and controlling the source of infection in a timely fashion, and administering timely, appropriate empiric intravenous antimicrobial therapy.<sup>2</sup>

Appropriate initial antimicrobial therapy has been defined in numerous ways, and a recent systematic review identified that most studies incorporated in vitro antimicrobial susceptibility test results in the definition of appropriateness; however, timeliness and dosage were rarely included in the definition.<sup>5</sup> Therefore, it is suggested that antimicrobial appropriateness be defined based on the spectrum of activity, route of administration, dosage, and timing.<sup>6–9</sup>

The published literature concerning appropriate antimicrobial utilization in severe infections is rapidly expanding. Accordingly, the aim of this article was to provide a comprehensive, up-to-date review of the key antimicrobial-related considerations in the critically ill patient presenting to the ED.

#### General Approach to Antimicrobial Selection in ED Patients with Sepsis

Emergency medicine (EM) physicians have a critical role in the management of patients with severe sepsis and septic shock. In many cases, the EM physician is the initial point of contact for a patient's medical care. The identification and timely intervention of septic patients in the ED may be the most important phase of care, because delays in therapy are associated with increased morbidity and mortality.<sup>10</sup>

Although guidelines have been published to assist clinicians in the identification and management of patients with severe sepsis/septic shock, optimal antimicrobial administration principles have received relatively little attention.<sup>2,11</sup> Elements that should be considered when administrating antimicrobials include the following: (1) patient-related factors, (2) microorganism-related factors, (3) the importance of the timing of antimicrobial administration, and (4) source control.<sup>12</sup>

EM physicians should primarily consider their patient's age, weight, allergy status, and comorbidities when choosing antimicrobial medication.<sup>13</sup> Renal and hepatic dysfunction may impact the pharmacokinetic properties of antimicrobials, with some medications eliminated primarily by one system or the other.<sup>14</sup> Patients who are pregnant or lactating require special consideration to minimize any potential negative impact on the fetus or newborn. In addition, any recent exposure to antimicrobials is very important to consider, as previous exposure to an antimicrobial may increase the incidence of resistance, therefore leading to treatment failure and increased morbidity and mortality.<sup>15</sup>

Important microorganism factors include the site of infection, intrinsic microbial susceptibility to anti-infectives, and local resistance patterns.<sup>13</sup> Often the site of infection is suspected in EM patients with severe sepsis/septic shock, which provides the clinician valuable information for antimicrobial selection. For instance, infections of the

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