

Sepsis and Septic Shock Strategies

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KEYWORDS

• Sepsis • Septic shock • Resuscitation • Goal-directed therapy • Critical care

KEY POINTS

- Three therapeutic principles most substantially improve organ dysfunction and survival in sepsis: (1) early, appropriate antimicrobial therapy; (2) restoration of adequate cellular perfusion; and (3) timely source control.
- The new definitions of sepsis and septic shock reflect the inadequate sensitivity, specificity, and lack of prognostication of systemic inflammatory response syndrome criteria. Sequential (sepsis-related) organ failure assessment more effectively prognosticates in sepsis and critical illness.
- Inadequate cellular perfusion accelerates injury and reestablishing perfusion limits injury. The best methods to assess perfusion, target therapy, and reestablish adequate perfusion remain controversial.
- Multiple organ systems are affected by sepsis and septic shock and an evidence-based multipronged approach to systems-based therapy in critical illness results in improved outcomes.

INTRODUCTION

Sepsis and septic shock are syndromes of immense clinical importance. Suspected sepsis accounts for more than half a million emergency department visits annually in the United States.¹ Between 2003 and 2007, there was a 71% increase in the number of hospitalizations for sepsis and a 57% increase in hospital costs.² In 2013, sepsis was the most expensive reason for hospitalization, accounting for more than \$23.7 billion (6.2%) of total US hospital costs and was the second most common reason for hospitalization, accounting for 3.6% of stays.³ Of those admitted, 50% are treated in the intensive care unit (ICU) representing 10% of all ICU admissions. Surgical patients in particular account for nearly one-third of sepsis cases in the United States.⁴ The mortality of sepsis has been reported to be declining from 45% in 1993 to 37% in

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2003, 29% in 2007, and to as low as 18.4% in 2012.^{2,5,6} Despite this trend, in another recent examination of 2 large complementary hospital cohorts from 2010 to 2012, sepsis was found to have a mortality range of 34% to 56% and most of those patients were identified to have sepsis at admission.⁷ These data emphasize that sepsis mortality remains significant. Although there has been a vast amount of research directed toward improving outcomes in sepsis, 3 therapeutic principles most substantially improve organ dysfunction and survival in sepsis: (1) early, appropriate antimicrobial therapy; (2) restoration of adequate cellular perfusion; and (3) timely source control. Thus, survival is dependent on early recognition and rapid treatment. In the article to follow, the authors summarize recent changes in defining sepsis, highlight pathophysiologic rationale for current therapeutic strategies, and discuss therapeutic approaches to improve outcome.

DEFINITIONS

For more than 2 decades, sepsis had been defined by a combination of the systemic inflammatory response syndrome (SIRS) and the presence of infection (**Fig. 1**).^{8,9} The inadequate sensitivity and specificity of SIRS combined with the latest information regarding sepsis pathobiology prompted a recent revised data-driven definition of sepsis and septic shock: the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) (**Fig. 2**).¹⁰ Sepsis is now defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction can be identified as an acute change in the total Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score ≥ 2 points consequent to the infection.^{11–13} The term “severe sepsis” was removed from the definitions and deemed redundant. Septic shock is a subset of sepsis in which underlying circulatory,

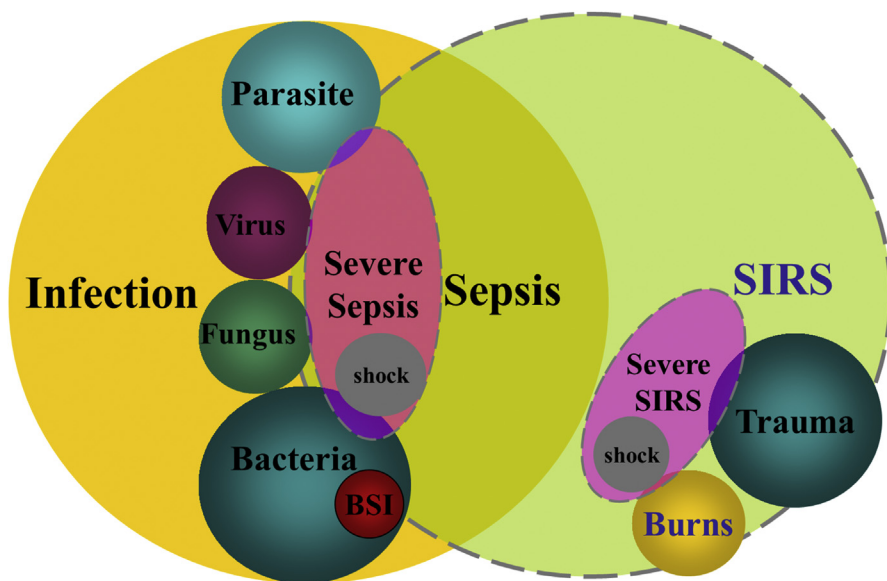


Fig. 1. Early conceptual view of the definition of SIRS, sepsis, severe sepsis, and septic shock whereby infection induces an inflammatory SIRS response. BSI, Blood Stream Infection. (Adapted from Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Chest* 1992;101:1645; with permission.)

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