

Defining and Diagnosing Sepsis



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KEYWORDS

• Sepsis • Severe sepsis • Septic shock • SOFA • qSOFA

KEY POINTS

- Sepsis is a heterogeneous clinical syndrome that has defied attempts to create an exact definition or develop specific clinical diagnostic criteria.
- Sepsis is characterized by the immune response to an infection that creates harmful effects beyond the local site of the infection.
- The difficulty in defining sepsis has created significant challenges in the determination of reliable epidemiologic data for the disease.
- Despite an increased incidence, the mortality for sepsis has decreased over the past several decades.
- According to the most recent publication on the definitions for sepsis and septic shock, sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection.

INTRODUCTION

The syndrome of sepsis includes an incredibly wide variety of infections and clinical presentations, from the 85-year-old patient with a urinary tract infection with mild confusion to the 18-year-old patient with multiorgan failure from meningitis. Any attempt to define sepsis must incorporate these disparate and heterogeneous manifestations under 1 syndromic banner. The incredible difficulty of this task is reflected in the interplay between conceptual, diagnostic, and research definitions of sepsis.

It is generally accepted that worldwide sepsis represents a large burden of illness, morbidity, and mortality. In 2011, it was estimated that sepsis represented the most expensive single condition treated in US hospitals and accounted for more than \$20 billion dollars in health care costs (5.2% of aggregate US hospital costs).¹ A 2009 study estimated that more than 3 million cases of sepsis occur annually in the United States and result in more than 200,000 deaths.² It is clear that the incidence of sepsis has increased. It is believed that increases in the aging population along with an

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increase in patients that have select comorbidities, such as immunosuppressive conditions, may account for the increased incidence of disease. In addition to the increased elderly population and patients with complex comorbidities, it is also postulated that increased awareness of the condition has contributed to the increase in the incidence of sepsis.³ Despite an increased incidence of sepsis, mortality has decreased. In fact, mortality rates in the 3 most recent studies comparing the use of an early goal-directed therapy protocol with current usual care ranged from 19% to 29%. This is markedly reduced from the mortality rate of greater than 46% in the original 2001 early goal-directed therapy study.⁴⁻⁷

This article discusses the evolution of sepsis definitions that have been published over the past several decades, with attention to the most recent publication by Singer and colleagues.

SEPSIS 1: AN INITIAL DEFINITION

Sepsis is generally accepted to be an advanced, life-threatening infection that produces organ dysfunction and increases morbidity and mortality. The first formal definition of sepsis came in 1992, when a consensus conference defined sepsis as “the systemic response to infection.”⁸ The conference committee believed that much of the harm and damage to the body in sepsis is not the result of the microorganism causing infection, but rather the damage to various organs that are distant from the actual site of infection. Importantly, this is not necessarily owing to a systemic infection itself (ie, bacteremia), but rather to the patient’s immune system response to the infection. An example of this process is the development of the acute respiratory distress syndrome in a patient with a foot abscess. One would not be expected to detect bacteria in sputum cultures that match those in wound cultures from the abscess itself.

Based on the understanding of sepsis at that time, the 1992 conference committee felt that this systemic response to infection was the result of overwhelming inflammation. They named this response the systemic inflammatory response syndrome (SIRS). SIRS is the presence of at least 2 of the 4 criteria listed in **Box 1**.⁸ Importantly, the committee emphasized that the SIRS criteria needed to be both (1) a change from the patient’s baseline and (2) part of the systemic response to the presence of an infectious process.⁸ This highlighted that the presence of SIRS was not unique to sepsis, but

Box 1

Systemic inflammatory response syndrome

Defined as the presence of at least 2 of the following 4 criteria:

Body temperature greater than 38°C or less than 36°C

Heart rate greater than 90 bpm

Tachypnea: RR >20 breaths per minute; or

Hyperventilation: PaCO₂ less than 32 mm Hg

WBC greater than 12,000/mm³ or less than 4000/mm³ or greater than 10% immature neutrophils

Abbreviations: bpm, beats per minute; PaCO₂, partial pressure CO₂ in arterial blood gas sample; RR, respiratory rate; WBC, white blood cell count.

Data 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. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest 1992;101(6):1644–55.

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