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Evolution of Sepsis Management

From Early Goal-Directed Therapy to Personalized Care

Lyndsay W. Head, MD[a], Craig M. Coopersmith, MD[b,*]

[a]Emory University School of Medicine, 3B South, Emory University Hospital, 1364 Clifton Road, NE, Atlanta, GA 30322, USA; [b]Department of Surgery, Emory Critical Care Center, Emory University School of Medicine, 101 Woodruff Circle, Suite WMB 5105, Atlanta, GA 30322, USA

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Key points

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- A specific protocol termed, ''early goal-directed therapy,'' has not been shown to improve survival in sepsis compared with ''usual care.''
- Although this specific protocol is not beneficial if applied to all patients with sepsis, key tenets of sepsis management, including early fluid resuscitation, cultures, antibiotic therapy, lactate measurement, and vasopressors (if indicated), are indicated in all septic patients.
- Compliance with 3- and 6-hour bundles of sepsis management is associated with improved outcomes in septic patients.

In 1843, pathologist Dr Johann Scherer first noted the presence of lactic acidosis in septic shock. His patient, a 23-year-old woman, became septic following childbirth. She was prescribed a regimen of bloodletting and clystering and died 36 hours later. Her autopsy findings were consistent with severe purulent endometritis, and blood samples revealed an elevated lactic

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*Corresponding author. *E-mail address*: cmcoop3@emory.edu

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acid level [1]. This case was perhaps one of the initial cases to show an association between tissue hypoperfusion and septic shock. Despite many advances in medical technology since this time, the question of how best to manage and prevent the destructive host response of sepsis is still being evaluated today.

DEFINITION OF SEPSIS

In modern critical care, sepsis was first defined by the Society of Critical Care Medicine/American College of Chest Physician consensus conference in 1991 [2]. Sepsis was defined as having at least 2 of 4 components of the systemic inflammatory response syndrome (SIRS) in the setting of a suspected infection. SIRS was defined as (a) temperature greater than 38°C or less than 36°C, (b) heart rate greater than 90 beats per minute, (c) respiratory rate greater than 20 per minute or $PaCO_2$ less than 32 mm Hg, and (d) white blood cell count greater than 12,000/mm^3 or less than 4000/mm^3 or greater than 10% of immature bands. Sepsis in the setting of organ dysfunction was further defined as severe sepsis, and sepsis-induced hypotension persisting despite adequate fluid resuscitation was defined as septic shock. Despite numerous limitations with this definition, a subsequent consensus conference in 2001 expanded the list of diagnostic criteria, but the definition remained unchanged [3].

In 2016, a consensus conference between the Society of Critical Care Medicine and the European Society of Intensive Care Medicine (endorsed by 30 international organizations) proposed a new definition of sepsis. The new definition is that sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection [4]. The clinical criterion used to operationalize organ failure is an increase in the Sequential Organ Failure Assessment (SOFA) score of 2 points or more. Notably, septic shock was defined as a subset of patients with particularly severe circulatory, cellular, and metabolic abnormalities associated with a higher risk of death than sepsis alone. Patients with septic shock at the bedside can be identified as requiring vasopressors to maintain a mean arterial pressure of 65 mm Hg or greater and a serum lactate level of greater than 2 mmol/L. This combination was associated with a mortality of greater than 40% [5].

Notably, the term severe sepsis was eliminated from the new definition. The rationale is that sepsis carries a mortality of approximately 10%–greater than that of myocardial infarction, stroke, or trauma–and the term "severe" is therefore redundant in a syndrome that is potentially life-threatening by definition. In the new paradigm, what was called "sepsis" in earlier definitions is now referred to as "infection" (where the host response may be adaptive) and what was called "severe sepsis" in earlier definitions is now referred to as "sepsis." SIRS continues to be an appropriate method of screening for infection. However, a new screen called quick SOFA (qSOFA) has recently been identified that involves evaluating infected patients for (a) altered mental status, (b) respiratory rate $>$ 22 per minute, and (c) systolic hypotension $<$ 100 mm Hg