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SPECIAL EDITORIAL

The Surviving Sepsis Campaign Bundle: 2018 update

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Introduction

The "sepsis bundle" has been central to the implementation of the Surviving Sepsis Campaign (SSC) from the first publication of its evidence-based guidelines in 2004 through subsequent editions [1–6]. Developed separately from the guidelines publication by the SSC, the bundles have been the cornerstone of sepsis quality improvement since 2005 [7–11]. As noted when they were introduced, the bundle elements were designed to be updated as indicated by new evidence and have evolved accordingly. In response to the publication of "Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016" [12, 13], a revised "hour-1 bundle" has been developed and is presented below (Fig. 1).

The compelling nature of the evidence in the literature, which has demonstrated an association between compliance with bundles and improved survival in patients with sepsis and septic shock, led to the adoption of the SSC measures by the National Quality Forum (NQF) and subsequently both by the New York State (NYS) Department of Health [14] and the Centers for Medicare and Medicaid Services (CMS) [15] in the USA for mandated public reporting. The important relationship between the bundles and survival was confirmed in a publication from this NYS initiative [16].

Paramount in the management of patients with sepsis is the concept that sepsis is a medical emergency. As with polytrauma, acute myocardial infarction, and stroke, early identification and appropriate immediate management in the initial hours after development of sepsis improves outcomes [7–11, 14, 16–21]. The guidelines state that these patients need urgent assessment and treatment, including initial fluid resuscitation while pursuing source control, obtaining further laboratory results, and attaining more precise measurements of hemodynamic status. A guiding principle is that these complex patients need a detailed initial assessment and then ongoing re-evaluation of their response to treatment. The elements of the 2018 bundle, intended to be initiated within the first hour, are listed in Table 1 and presented in the following. Consistent with previous iterations of the SSC sepsis bundles, "time zero" or "time of presentation" is defined as the time of triage in the emergency department or, if referred from another care location, from the earliest chart annotation consistent with all elements of sepsis (formerly severe sepsis) or septic shock ascertained through chart review. Because this new bundle is based on the 2016 Guidelines publication, the guidelines themselves should be referred to for further discussion and evidence related to each element and to sepsis management as a whole.

Hour-1 bundle

The most important change in the revision of the SSC bundles is that the 3-h and 6-h bundles have been combined into a single "hour-1 bundle" with the explicit intention of beginning resuscitation and management immediately. We believe this reflects the clinical reality at the bedside of these seriously ill patients with sepsis and septic shock—that clinicians begin treatment immediately, especially in patients with hypotension, rather than waiting or extending resuscitation measures over a longer period. More than 1 h may be required for resuscitation to be completed, but initiation of resuscitation and treatment, such as obtaining blood for measuring lactate and blood cultures, administration of fluids and antibiotics, and in the case of life-threatening hypotension, initiation of vasopressor therapy, are all begun immediately.

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- Measure lactate level. Remeasure if initial lactate is >2 mmol/L.
- Obtain blood cultures prior to administration of antibiotics.
- Administer broad-spectrum antibiotics.
- Begin rapid administration of 30ml/kg crystalloid for hypotension or lactate ≥4 mmol/L.
- Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥65 mm Hg.

**"Time zero" or "time of presentation" is defined as the time of triage in the Emergency Department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of sepsis (formerly severe sepsis) or septic shock ascertained through chart review.*

Fig. 1 Hour-1 Surviving Sepsis Campaign Bundle of Care

Table 1 Bundle elements with strength of recommendations and under-pinning quality of evidence [12, 13]

Bundle element	Grade of recommendation and level of evidence
Measure lactate level. Re-measure if initial lactate is > 2 mmol/L	Weak recommendation, low quality of evidence
Obtain blood cultures prior to administration of antibiotics	Best practice statement
Administer broad-spectrum antibiotics	Strong recommendation, moderate quality of evidence
Rapidly administer 30 ml/kg crystalloid for hypotension or lactate ≥ 4 mmol/L	Strong recommendation, low quality of evidence
Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥ 65 mm Hg	Strong recommendation, moderate quality of evidence

It is also important to note that there are no published studies that have evaluated the efficacy in important subgroups, including burns and immunocompromised patients. This knowledge gap needs to be addressed in future studies specifically targeting these subgroups. The elements included in the revised bundle are taken from the Surviving Sepsis Campaign Guidelines, and the level of evidence in support of each element can be seen in Table 1 [12, 13]. We believe the new bundle is an accurate reflection of actual clinical care.

Measure lactate level

While serum lactate is not a direct measure of tissue perfusion [22], it can serve as a surrogate, as increases may represent tissue hypoxia, accelerated aerobic glycolysis driven by excess beta-adrenergic stimulation, or other causes associated with worse outcomes [23]. Randomized controlled trials have demonstrated a significant reduction in mortality with lactate-guided resuscitation [24–28].

If initial lactate is elevated (>2 mmol/L), it should be remeasured within 2–4 h to guide resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion [24].

Obtain blood cultures prior to antibiotics

Sterilization of cultures can occur within minutes of the first dose of an appropriate antimicrobial [29, 30], so cultures must be obtained before antibiotic administration to optimize the identification of pathogens and improve outcomes [31, 32]. Appropriate blood cultures include at least two sets (aerobic and anaerobic). Administration of appropriate antibiotic therapy should not be delayed in order to obtain blood cultures.

Administer broad-spectrum antibiotics

Empiric broad-spectrum therapy with one or more intravenous antimicrobials to cover all likely pathogens should be started immediately [21] for patients presenting with sepsis or septic shock. Empiric antimicrobial therapy should be narrowed once pathogen identification and sensitivities are established, or discontinued if a decision is made that the patient does not have infection. The link between early administration of antibiotics for suspected infection and antibiotic stewardship remains an essential aspect of high-quality sepsis management. If infection is subsequently proven not to exist, then antimicrobials should be discontinued.

Administer intravenous fluid

Early effective fluid resuscitation is crucial for the stabilization of sepsis-induced tissue hypoperfusion or septic shock. Given the urgent nature of this medical emergency, initial fluid resuscitation should begin immediately upon recognizing a patient with sepsis and/or hypotension and elevated lactate, and completed within 3 h of recognition. The guidelines recommend this should comprise a minimum of 30 ml/kg of intravenous crystalloid fluid. Although little literature includes controlled data to support this volume, recent interventional studies have described this as usual practice in the early stages of resuscitation, and observational evidence is supportive [7, 8]. The absence of any clear benefit following the administration of colloid compared with crystalloid solutions in the combined subgroups of sepsis, in conjunction with the expense of albumin, supports a strong recommendation for the use of crystalloid solutions in the initial resuscitation of patients with sepsis and septic shock. Because some evidence indicates that a sustained positive fluid balance during ICU stay is harmful [33–37], fluid administration beyond initial resuscitation requires careful assessment of the likelihood that the patient remains fluid responsive.

Apply vasopressors

Urgent restoration of an adequate perfusion pressure to the vital organs is a key part of resuscitation. This should not be delayed. If blood pressure is not restored after initial fluid resuscitation, then vasopressors should be commenced within the first hour to achieve mean arterial pressure (MAP) of $\geq$ 65 mm Hg. The physiologic effects of vasopressors and combined inotrope/vasopressor selection in septic shock are outlined in a large number of literature reviews [38–47].

Summary

Previous iterations of the sepsis bundle were introduced as a means of providing education and improvement related to sepsis management. The literature supports the use of sepsis bundles for improving outcomes in patients with sepsis and septic shock. This new sepsis "hour-1 bundle," based on the 2016 guidelines, should be introduced to emergency department, floor, and ICU staff as the next iteration of ever-improving tools in the care of patients with sepsis and septic shock as we all work to lessen the global burden of sepsis.

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Compliance with ethical standards

Conflicts of interest

Dr. Levy is a Member of the Surviving Sepsis Campaign Executive Committee and is a Surviving Sepsis Campaign Guidelines Author. Dr. Evans is a Member of the Surviving Sepsis Campaign Steering Committee and is a Surviving Sepsis Campaign Guidelines Co-Chair. Dr. Rhodes is a Member of the Surviving Sepsis Campaign Executive Committee and is a Surviving Sepsis Campaign Guidelines Co-Chair.

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