

Evaluation and Management of Suspected Sepsis and Septic Shock in Adult Patients

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ARTICLE INFO

Article history:

Received
14 September 2025

Revised
19 October 2025

Accepted
31 December 2025

Manuscript ID:
JSOCMED-140931-412-3

Checked for Plagiarism: Yes

Language Editor:
Rebecca

Editor-Chief:
Prof. Aznan Lelo, PhD

Keywords

ABSTRACT

Sepsis is a life-threatening clinical syndrome arising from a dysregulated host response to infection, encompassing a continuum of severity ranging from sepsis to septic shock. Despite advances in critical care, sepsis remains a leading cause of morbidity and mortality worldwide, with reported mortality rates exceeding 10% in sepsis and rising beyond 40% when septic shock develops. Contemporary management strategies emphasize early recognition, prompt source control, timely administration of antimicrobial therapy, and hemodynamic optimization of the patient. Current clinical practice largely aligns with the definitions proposed by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine, which focuses on organ dysfunction as a central feature of sepsis. However, these definitions are not universally adopted, as alternative frameworks, including earlier systemic inflammatory response-based criteria, continue to influence clinical and regulatory practices in certain settings. The ongoing debate highlights concerns that the broad application of modern definitions may inadvertently promote overtreatment, particularly unnecessary exposure to broad-spectrum antibiotics in patients with less severe disease. This review summarizes contemporary concepts in the clinical management of sepsis and septic shock, integrating evolving definitions with practical and bedside decision making. Emphasis is placed on balancing rapid, protocolized care for high-risk patients with judicious therapeutic strategies to minimize harm in patients with milder presentations. By synthesizing guideline-based recommendations and ongoing controversies, this review aims to provide a pragmatic framework for clinicians managing sepsis in diverse clinical contexts.

Sepsis, Septic Shock, Early Goal-Directed Therapy, Surviving Sepsis Campaign, Lactate Clearance

How to cite: Tona AI. Evaluation and Management of Suspected Sepsis and Septic Shock in Adult Patients. *Journal of Society Medicine*. 2025; 4 (12): 388-393. DOI: <https://doi.org/10.71197/jsocmed.v4i12.251>

INTRODUCTION

Sepsis is a life-threatening clinical syndrome arising from a dysregulated host response to infection, resulting in acute organ dysfunction and systemic physiological derangements [1]. Clinically, sepsis exists along a continuum of severity, ranging from infection-associated organ dysfunction to septic shock, the most severe manifestation, characterized by profound circulatory, cellular, and metabolic abnormalities and a markedly increased risk of mortality [1,2]. Despite substantial advances in antimicrobial therapy, hemodynamic monitoring, and supportive intensive care, sepsis remains a major global health issue. Mortality rates vary according to patient characteristics, comorbidities, and healthcare system capacity but consistently exceed 10% in sepsis and may surpass 40% once septic shock develops [2,3].

Sepsis is a highly heterogeneous syndrome with high mortality rates. Variability in host immune response, pathogen burden, timing of presentation, and access to timely medical care contributes to the wide differences in clinical manifestations, therapeutic responses, and outcomes across diverse settings. This heterogeneity underscores the need for adaptable, context-sensitive management strategies rather than rigid, one-size-fits-all management approaches. Contemporary sepsis care emphasizes early recognition, rapid

diagnostic evaluation, prompt source control, timely administration of empiric antimicrobial therapy, and individualized hemodynamic resuscitation. This review focuses on the early evaluation and initial management of suspected sepsis and septic shock in adult patients, with particular emphasis on first-hour decision-making in emergency and critical care settings. Detailed discussions of long-term intensive care management, immunomodulatory therapies, and post-sepsis syndromes are beyond the scope of this article. The aim is to integrate evidence-based recommendations from international guidelines with pragmatic bedside decision-making to optimize outcomes while minimizing the potential harm associated with overtreatment [4–6].

Immediate Evaluation and Management

Immediate evaluation and early therapeutic intervention are critical for patients with suspected sepsis or septic shock, as delays in stabilization are strongly associated with increased morbidity and mortality rates. Initial management priorities include securing the airway when clinically indicated, correcting hypoxemia, and establishing venous access to enable the prompt administration of intravenous fluids and empiric antimicrobial therapy [3,4]. These interventions are directed toward stabilizing vital organ function during the early and high-risk phases of illness. The key components of emergency management within the first hour of presentation are summarized in Table 1.

Table 1. First-Hour Emergency Management of Suspected Sepsis and Septic Shock

Domain	Intervention	Clinical Rationale
Airway	Assess airway patency; secure airway if indicated	Prevent hypoxia and aspiration in patients with respiratory failure or altered consciousness
Breathing	Administer supplemental oxygen; monitor SpO ₂ continuously	Ensure adequate oxygen delivery and early detection of respiratory deterioration
Circulation	Establish venous access (peripheral or intraosseous initially)	Enable rapid administration of fluids, antibiotics, and vasoactive agents
Fluid resuscitation	Administer crystalloids up to 30 mL/kg in patients with hypotension or hypoperfusion	Restore effective circulating volume and improve tissue perfusion
Antimicrobial therapy	Initiate empiric broad-spectrum antibiotics	Achieve early infection control; delays increase mortality
Lactate measurement	Measure serum lactate	Assess severity of hypoperfusion and guide resuscitation
Hemodynamic monitoring	Monitor blood pressure, heart rate, urine output	Evaluate response to therapy and guide escalation
Vasopressors	Initiate if hypotension persists after fluids	Maintain MAP \geq 65 mmHg to ensure organ perfusion

Respiratory Stabilization

Early stabilization of respiratory function is a cornerstone of the initial management of patients with sepsis. Supplemental oxygen should be administered to patients with hypoxemia, with continuous monitoring using pulse oximetry to facilitate early detection of respiratory deterioration [3,4]. Although optimal peripheral oxygen saturation targets have not been definitively established, most clinical recommendations support maintaining saturation between 90% and 96% to ensure adequate tissue oxygen delivery while avoiding the potential harm associated with hyperoxia. Oxygen targets should be individualized based on the patient's condition, comorbid pulmonary diseases, and response to therapy.

Routine arterial blood gas analysis is not required for all patients during the initial evaluation; however, clinicians should be aware of the limitations of pulse oximetry. Evidence indicates that pulse oximetry may overestimate arterial oxygen saturation in individuals with darker skin pigmentation, including Asian, Black, and Hispanic populations, potentially leading to unrecognized hypoxemia [7-10]. Awareness of this limitation is essential when interpreting the oxygen saturation values in patients with sepsis.

Escalation of respiratory support may be necessary in patients with persistent hypoxemia, increased work of breathing, or evolving respiratory failure despite supplemental oxygen therapy. Depending on the clinical severity, noninvasive ventilation, high-flow nasal oxygen therapy, or endotracheal intubation with invasive mechanical ventilation may be required [3,4]. In addition to respiratory indications, airway protection may be necessary in patients with sepsis-associated encephalopathy or depressed levels of consciousness, which increase the risk of aspiration and airway compromise [8]. Decisions regarding advanced airway management should be individualized and guided by careful clinical assessment.

Establishment of Venous Access

Rapid establishment of venous access is a fundamental component of early sepsis management. Peripheral intravenous or intraosseous access is often sufficient during the initial phase of resuscitation and should be obtained without delay to allow timely administration of fluids and antibiotics. However, central venous access is necessary during the course of treatment in many patients. Importantly, the insertion of a central venous catheter should not delay time-sensitive resuscitation interventions, particularly fluid resuscitation and antimicrobial therapy.

Central venous catheters provide reliable access for the administration of vasoactive agents, other intravenous medications, and blood products, and facilitate frequent blood sampling. Although central venous pressure and central venous oxygen saturation can be measured via a central line, randomized controlled trials have demonstrated limited benefits from the routine use of these parameters to guide resuscitation compared with clinical assessment and dynamic perfusion indicators [11–15]. Accordingly, decisions regarding central venous catheterization should be individualized and driven by clinical necessity rather than being employed solely for hemodynamic monitoring purposes.

Initial Diagnostic Evaluation

Diagnostic evaluation should be performed in parallel with resuscitation efforts and airway stabilization. A focused history and physical examination, combined with early laboratory testing, microbiological sampling, and targeted imaging, are essential for identifying the source of infection, assessing disease severity, and guiding empiric therapy (Table 2). Whenever feasible, these investigations should be performed rapidly—ideally within the first 45 minutes of presentation—but should never delay the initiation of intravenous fluid or antimicrobial therapy.

Table 2. Initial Diagnostic Evaluation in Suspected Sepsis

Evaluation	Clinical Purpose
Focused history and physical examination	Identify infection source and early organ dysfunction
Complete blood count with differential	Assess inflammatory response and cytopenias
Serum electrolytes	Detect metabolic and fluid-related abnormalities
Renal and hepatic function tests	Evaluate sepsis-associated organ dysfunction
Coagulation profile (PT, aPTT, INR)	Identify coagulopathy or DIC
Serum lactate	Assess tissue hypoperfusion and disease severity
Blood cultures (≥2 sets before antibiotics)	Identify causative pathogens and guide targeted therapy
Cultures from suspected infection sites	Improve diagnostic yield and source-directed management
Blood gas analysis (if indicated)	Evaluate acid–base status and oxygenation
Targeted imaging studies	Localize infection source and support source control
Procalcitonin (when available)	Adjunct biomarker to guide antibiotic duration

Baseline laboratory evaluations typically include a complete blood count with differential, serum electrolytes, renal and hepatic function tests, and coagulation study results. Serum lactate measurement is strongly recommended, as elevated lactate levels are associated with increased disease severity and adverse outcomes and may be used to monitor the response to resuscitation [16–18]. Microbiological evaluation should

include peripheral blood cultures obtained from at least two separate venipuncture sites, along with cultures from suspected sources of infection, when readily accessible. Obtaining blood cultures before antimicrobial administration improves pathogen detection and facilitates targeted therapy, underscoring the importance of early sampling without delaying treatment [19]. Blood gas analysis may be performed when clinically indicated to assess acid–base status, oxygenation, or ventilation. Imaging studies directed at the suspected source of infection, including chest radiography and computed tomography, should be promptly performed to support diagnostic and therapeutic decision-making. When available, serum procalcitonin levels may serve as an adjunct to guide the duration of antimicrobial therapy, particularly in patients with respiratory tract infections, as procalcitonin-guided strategies have been shown to reduce antibiotic exposure without increasing mortality [20,21].

Initial Therapy

The initial therapy for sepsis and septic shock is directed toward the rapid restoration of effective tissue perfusion and early control of infection. Timely intervention during the first hours following presentation is critical, as delays in resuscitation and antimicrobial therapy are consistently associated with poor prognosis. Contemporary management emphasizes early physiological stabilization, supported by protocol-informed yet clinically individualized decision-making.

Tissue perfusion restoration is primarily achieved through early intravenous fluid resuscitation. Current guidelines recommend the administration of crystalloids at an initial dose of approximately 30 mL/kg, initiated within the first hour and completed within the first three hours in patients with hypotension or evidence of hypoperfusion [22–26]. However, increasing evidence suggests that excessive fluid administration may contribute to fluid overload and organ dysfunction, highlighting the importance of frequent reassessment and individualized fluid strategies rather than fixed volumes of fluid. Empiric antimicrobial therapy should be initiated as early as possible, preferably within the first hour after sepsis recognition. Antibiotic selection should be guided by the suspected source of infection, likely pathogens, and local resistance patterns. When combination therapy is required, beta-lactam antibiotics are generally prioritized because of their favorable pharmacokinetic and pharmacodynamic properties in severe infections [27]. Early initiation should be coupled with prompt microbiological evaluation and timely reassessment with de-escalation based on culture results and clinical response to minimize antimicrobial resistance and adverse effects.

Early Goal-Directed Therapy and Protocol-Based Resuscitation

Early goal-directed therapy (EGDT) plays a pivotal role in the management of sepsis. Initial randomized trials demonstrated improved outcomes using protocol-based resuscitation strategies that targeted predefined physiological endpoints within the first six hours of presentation [10]. However, subsequent large multicenter trials, including ProCESS, ARISE, and ProMISE, failed to demonstrate additional survival benefits compared to contemporary usual care [11–13]. These findings likely reflect improvements in baseline sepsis care, earlier recognition, and greater clinician expertise, resulting in a convergence between protocolized and non-protocolized management strategies.

Meta-analyses evaluating EGDT have yielded mixed results, with some suggesting benefit from early intervention and timely fluid administration rather than strict adherence to specific hemodynamic targets [28,29]. Importantly, protocolized resuscitation has not consistently demonstrated benefits in resource-limited settings, underscoring the need for context-specific approaches [29]. Emerging evidence suggests that alternative markers of perfusion, such as capillary refill time, may provide complementary information to lactate-guided strategies; however, further validation is required before routine adoption [11–14].

Sepsis Bundles

Sepsis bundles, which group multiple time-sensitive interventions into standardized care pathways, have been widely implemented to promote early and coordinated treatment. Although updated guidelines recommend rapid bundle implementation, the evidence supporting rigid adherence remains inconsistent [35,36].

Observational and interventional studies have demonstrated variable effects on mortality, with substantial heterogeneity and risk of bias [17,28]. Collectively, these findings suggest that sepsis bundles should be viewed as flexible clinical frameworks rather than rigid mandates, with successful implementation dependent on clinician expertise, institutional resources, and patient-specific factors.

CONCLUSION

Sepsis and septic shock remain complex and heterogeneous syndromes associated with substantial morbidity and mortality despite advances in critical care medicine. Improved outcomes depend on early recognition, rapid initiation of resuscitation measures, timely antimicrobial therapy, and continuous reassessment. Contemporary evidence supports an individualized, patient-centered approach that prioritizes early stabilization and infection control while avoiding unnecessary or excessive interventions. Protocol-based strategies and sepsis bundles have enhanced awareness and standardization of care; however, their effectiveness varies across clinical contexts, reinforcing the importance of clinical judgment and adaptability in patient care. Future research should focus on refining personalized resuscitation strategies, improving risk stratification, and integrating dynamic markers of perfusion and immune responses to optimize sepsis management.

DECLARATIONS

None

CONSENT FOR PUBLICATION

The Authors agree to be published in the Journal of Society Medicine.

FUNDING

None

COMPETING INTERESTS

The authors declare no conflicts of interest in this case report.

AUTHORS' CONTRIBUTIONS

made substantial contributions to the conception and design of the study, literature review, data interpretation, and drafting of the manuscript. Author AIT critically revised the manuscript for important intellectual content, approved the final version for publication, and agreed to be accountable for all aspects of the study.

ACKNOWLEDGMENTS

None

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