TPM Vol. 32, No. S1, 2025
ISSN: 1972-6325
https://www.tpmap.org/

SEPTIC SHOCK IN THE EMERGENCY AND CRITICAL CARE SETTING: A REVIEW OF CLINICAL CHALLENGES AND OUTCOMES

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Abstract:
septic shock is a serious syndrome caused by infection, leading to inflammation, low blood pressure, and organ failure. Understanding its mechanisms is vital for better patient care in critical settings. The pathophysiology involves infection-driven events causing low blood pressure, reduced organ perfusion, and cell dysfunction. Septic shock poses a global health issue with varying incidence rates but consistently high mortality, necessitating improved detection and resource allocation in high-burden areas. It results from a complex interaction of infections, immune responses, and personal risk factors, requiring a thorough management and prevention approach. Clinically, it presents with low blood pressure, fever, rapid heart rate, and altered mental state, with diagnosis relying on persistent low blood pressure and high lactate levels. Advanced scoring systems can aid in early detection and improve outcomes. Management has shifted from rigid protocols to flexible, data-driven, patient-focused approaches emphasizing timely diagnosis, proper antibiotics, hemodynamic support, and source control. Advanced analytics and continuous monitoring may enhance future outcomes for these critically ill patients. Septic shock causes complications, mainly organ failure, which significantly heightens the mortality risk.

Keywords: Septic Shock, Pathophysiology, Clinical Presentation, Epidemiology and Incidence

INTRODUCTION:

Septic shock is a severe and life-threatening condition that arises as a complication of sepsis, characterized by a profound systemic inflammatory response to an infection that leads to significant morbidity and mortality. It is defined by the immune system's release of inflammatory mediators, which leads to substantial pathophysiological changes, including vasodilation, hematological abnormalities, and ultimately, organ dysfunction and failure. The condition is characterized by a critical drop in blood pressure, known as hypotension, which can lead to inadequate blood flow to vital organs. This hypotension is primarily due to vasodilation, where blood vessels widen excessively, contributing to decreased systemic vascular resistance and circulatory instability. In septic shock, the body's inflammatory response can become dysregulated, leading to a cascade of events that may culminate in multiple organ failure (MOF). Despite advancements in medical care, including the use of antibiotics and intensive monitoring, mortality rates for septic shock remain alarmingly high, ranging from 20% to 55%, and can escalate to 77% 90% when shock is present. [1-3]

The pathophysiology of septic shock involves a complex interplay of various mechanisms that result in inadequate tissue perfusion and metabolic derangements. At the core of septic shock is an alteration in hemodynamics, primarily manifested as hypotension, a hallmark of the condition. This low blood pressure results from the release of immunologic and vasoactive mediators that disrupt vascular tone, leading to vasodilation. The decrease in arteriovenous pressure gradient is critical, as it directly contributes to tissue hypoperfusion and cellular energy

depletion. This gradient loss is influenced by multiple pathogenic mechanisms, including cardiogenic, vasohypotonic, and hypovolemic factors, all of which converge to exacerbate circulatory failure. As blood flow to organs diminishes, organ hypoperfusion occurs, which is a critical aspect of septic shock. This inadequate blood supply leads to anaerobic metabolism, resulting in lactic acidosis—a metabolic condition that indicates severe tissue hypoperfusion. The accumulation of lactic acid reflects the imbalance between oxygen supply and demand, further complicating the patient's metabolic state. Cellular dysfunction is another significant consequence of the pathophysiological changes in septic shock. The impaired oxygen extraction and increased oxygen needs, coupled with altered myocardial contractility, contribute to organ dysfunction. Prolonged inadequate tissue perfusion can lead to irreversible damage and death if not promptly addressed. The systemic inflammatory response triggered by the invading pathogens plays a pivotal role in the progression from sepsis to septic shock. This response includes the release of various endogenous factors such as cytokines, which can exacerbate the inflammatory state and lead to further organ dysfunction. [4-8]

Epidemiology and incidence of septic shock

Global estimates of sepsis incidence in 2017 reached approximately 48.9 million cases, with 11 million sepsis-related deaths, accounting for nearly 20% of all global mortality. Of these, septic shock represents a significant and poorer-prognosis category, with case fatality rates reported between 30% and 50% even in high-income countries and as high as 60% in some contexts. Age-standardized incidence of sepsis overall is approximately 677.5 per 100,000 population, with septic shock constituting 8–10% of sepsis cases in ICU settings and up to 15% in broader hospital samples. Between 500 and 1,000 cases per 100,000 occur annually in North America and Europe, while low- and middle-income countries (LMICs)—notably sub-Saharan Africa, Oceania, and South Asia—often exceed 1,500 cases per 100,000. [9,10] Septic shock, specifically, is estimated to occur in 11 per 100,000 people annually, though data vary widely depending on case definition and setting. [11] For instance, ICU-based studies from Europe and North America report a septic shock frequency of 8.3–10.4% of hospitalized sepsis patients, with ICU mortality around 37% and hospital mortality near 39%. [12] Nationwide studies have reflected a decline in mortality over time, attributed to improved recognition and care. A recent epidemiological study in Japan (2010–2020) showed septic shock incidence rising, but in-hospital mortality declining from 46.7% to 33.2%. Similar regional trends are seen in the U.S., where septic shock mortality was reported as 23.4% at 28 days (2010–2015), and in Korea and Taiwan, with in-hospital mortality rates of 34.3% and reductions from 27.2% to 21.1% over a decade. [13] However, some European data suggest that Sepsis-3-defined septic shock mortality remains high, around 56% in England and 44–46% in France, demonstrating persistent regional disparities. [14] Global meta-analyses estimate that sepsis affects 276–678 per 100,000 annually, with fatality rates varying from 22.5% to 26.7%. Among these, septic shock demonstrates markedly higher mortality. The annual incidence of sepsis may exceed 20 million, accounting for 1–2% of all hospital admissions and 25% of ICU bed usage. [15] Mortality and case fatality rates for septic shock have gradually improved in high-income settings, driven by early recognition, antimicrobial stewardship, and ventilatory support. Nonetheless, the burden remains disproportionately high in LMICs, where systemic limitations, delayed diagnoses, and resource constraints contribute to poorer outcomes. [9] The reported incidence of septic shock is likely underestimated due to variability in diagnostic criteria, underreporting, and data heterogeneity, indicating a need for more standardized epidemiological surveillance.[16]

Causes and risk factors of septic shock

The primary causes of septic shock include bacteremia, which is the presence of pathogenic microbes in the bloodstream, and the by-products of killed bacteria that can trigger cellular injury and activate various immune pathways. [17] Gram-negative bacteria are particularly notorious for causing septic shock due to their outer membrane, which contains lipopolysaccharides (LPS), acting as potent endotoxins.[6] Once in the bloodstream, LPS activates immune responses through recognition molecules, such as CD14 and Toll-like receptors (TLRs), leading to the release of vasoactive mediators that can cause hypotension and organ dysfunction. [6,18] In addition to gram-negative bacteria, other bacterial infections, such as those originating from pneumonia or urinary tract infections, can also precipitate septic shock. [2] The risk of developing septic shock is heightened in individuals with weakened immune systems, such as those with AIDS or undergoing chemotherapy, as their bodies are less capable of mounting an effective response to infections. Age is another significant risk factor; septic shock is most prevalent among the very young and the elderly, who may have less robust immune responses. [2] Understanding these causes and risk factors is crucial for developing effective prevention and treatment strategies, particularly through biotechnological advancements that aim to modulate the immune response and target the pathogens responsible for septic shock.

TPM Vol. 32, No. S1, 2025
ISSN: 1972-6325
https://www.tpmap.org/

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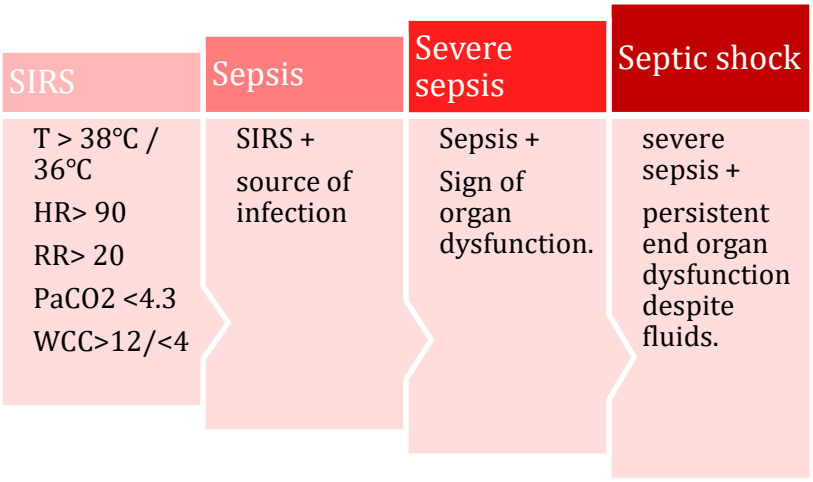
Table [1]: Characteristics of septic shock



Clinical presentation and diagnostic criteria

The clinical presentation of septic shock typically includes symptoms such as fever, tachycardia, hypotension, and altered mental status, which are indicative of a systemic response to infection [Table1]. The diagnosis of septic shock relies on specific criteria, including persistent hypotension despite adequate fluid resuscitation, which is defined as the administration of at least 500 ml of saline or Ringer's lactate solution. In addition to hypotension, elevated serum lactate levels greater than 2 mmol/L are also a critical diagnostic marker, as they indicate tissue hypoperfusion. The presence of these elevated lactate levels, combined with the need for vasopressor support to maintain blood pressure, further solidifies the diagnosis of septic shock. [19,20] The Modified Early Warning Score (MEWS) [Table 2] has been utilized in clinical settings to predict septic shock. Still, it has shown limited effectiveness with an area under the curve (AUC) of 0.73. In contrast, the targeted real-time early warning score (TREWScore) [Table 3] has demonstrated superior predictive capabilities, identifying patients at risk for septic shock with an AUC of 0.83, allowing for earlier intervention. This early identification is crucial, as patients who develop septic shock have a mortality rate ranging from 70% to 90%. [4,20] The diagnostic criteria for septic shock emphasize the importance of recognizing the clinical signs of infection and the physiological responses that accompany it. Clinicians must be vigilant in monitoring patients for signs of sepsis, particularly those who exhibit hypotension and elevated lactate levels, as these indicators are essential for timely and effective management.

Table [2]: Modified Early Warning Score (MEWS)

	3	2	1	0	1	2	3
Respiratory rate		<9		9-14	15-20	21-30	>30
Saturation rate	<90						
Heart rate		<40	40-50	51-100	101-110	111-130	>130
Systolic blood pressure	<70	70-80	81-100	101-200			
Temperature		< 35.1	35.2 -36.5	36.5 – 37.5	>37.5		
Consciousness				A	V	P	U
Urine output	< 75 ml in the last 4 hours						
Nurse being worried	1 point						
A=Alert V=Response to verbal stimulation P=Response to painful stimulation U=Unresponsive							
RIT protocol							
1. Determine MEWS → MEWS >3 contact clinician on duty							
2. Clinician on duty assesses patient <30 min and drafts a plan for treatment							
3. The effect of treatment is analyzed <60 min							

4.	If no effect of treatment →→ doctor on duty contacts RIT
5.	If not complied with 2,3,4 →→ doctor on duty or nurse contacts RIT
6.	Document aberrant parameters in the patient's charts

Table [4]: targeted real-time early warning score (TREWScore)

Category	Variables Used	Description
Vital Signs	Heart rate, respiratory rate, blood pressure (SBP/DBP), temperature, oxygen saturation (SpO_2)	Continuously updated to detect early physiological deterioration.
Laboratory Tests	White blood cell count, lactate, creatinine, bilirubin, platelets, hematocrit, hemoglobin, BUN, glucose	Tracks organ function, perfusion, inflammation, and metabolic status
Organ Function	Urine output, serum creatinine, and liver function tests	Identifies early signs of kidney and liver dysfunction
Fluid Balance	Net fluid balance, input/output volume	Helps detect fluid-responsive hypotension
Clinical Interventions	Vasopressors were initiated, mechanical ventilation was started, and antibiotics were ordered.	Incorporates the timing and frequency of critical interventions
Comorbidities	History of chronic diseases (e.g., diabetes, CHF, COPD, CKD)	Adjusts risk prediction based on baseline patient vulnerability
Demographics	Age, gender	Included as baseline risk modifiers
Admission Type	Emergency vs. elective, surgical vs. medical	Accounts for differing baseline risks
Temporal Patterns	Time trends of the above variables (e.g., rising lactate, falling BP)	Captures subtle changes over time; the model uses these dynamics for prediction
Data Source	Electronic Health Records (EHR) from ICU (e.g., MIMIC-III database)	Structured and unstructured data used for real-time modeling
Modeling Method	Gradient boosting (machine learning)	Combines multiple weak learners to improve accuracy and detect nonlinear relationships

Management strategies:

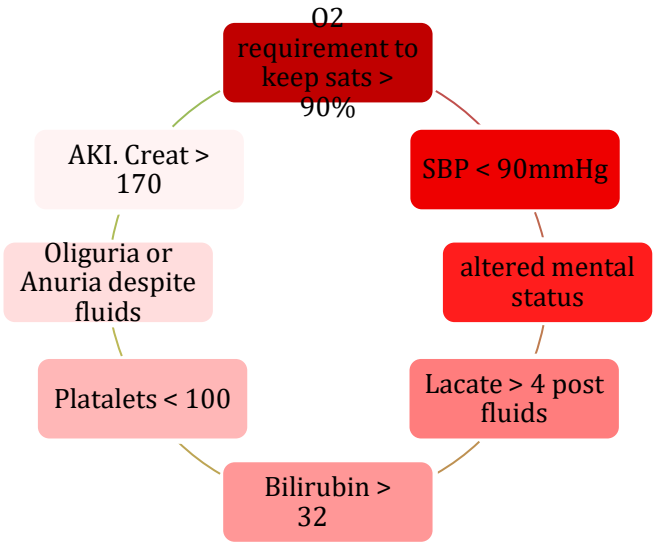
Management of septic shock requires rapid, multifaceted intervention strategies to improve survival and minimize complications. The cornerstone of treatment begins with early recognition and the prompt implementation of protocolized care. The 2021 Surviving Sepsis Campaign (SSC) recommends initiating the "hour-1 bundle," which includes measuring serum lactate, obtaining blood cultures before antibiotic administration, administering broad-spectrum antibiotics, and beginning fluid resuscitation with at least 30 mL/kg of crystalloid fluid to maintain a mean arterial pressure (MAP) of ≥65 mmHg. Empiric broad-spectrum antibiotics should be administered within the first hour after blood cultures are obtained, as delays in antibiotic therapy are linked to a significant increase in mortality, estimated at 7.6% per hour of delay. Once culture results are available, therapy should be narrowed to target identified pathogens, reducing the risk of resistance and toxicity. Fluid resuscitation remains vital to reversing hypotension and ensuring adequate organ perfusion. The SSC recommends using dynamic measures, such as passive leg raises and stroke volume variation, to assess fluid responsiveness. Notably, the ANDROMEDA-SHOCK trial found that guiding fluid resuscitation by capillary refill time was associated with better recovery of organ function compared to lactate-guided resuscitation. When fluid administration fails to restore MAP, vasopressors are indicated. Norepinephrine is the recommended first-line agent due to its efficacy and safety profile, while vasopressin may be added in cases of catecholamine-resistant shock. Epinephrine and dopamine are used selectively, while angiotensin II has emerged as a promising adjunct for patients with refractory hypotension, as demonstrated in the ATHOS-3 trial. Corticosteroids, particularly intravenous hydrocortisone at 200 mg/day, may be considered in septic shock patients who remain hypotensive despite adequate fluid resuscitation and vasopressor therapy. Evidence from the ADRENAL and APROCCHSS trials indicates that while steroids may not significantly reduce mortality, they accelerate shock reversal and reduce ICU stay. Supportive care for complications, such as mechanical ventilation for ARDS, should follow lung-protective strategies with low tidal volumes (6 mL/kg predicted body weight) and limiting plateau pressures below 30 cm H_2O, as supported by the ARDSNet study. Infection source control—such as surgical drainage, abscess debridement, or removal of infected devices—should occur within 6–12 hours of diagnosis, as delayed source control

significantly worsens outcomes. Additionally, thromboprophylaxis using low-molecular-weight heparin and gastrointestinal ulcer prophylaxis using proton pump inhibitors should be part of routine care in high-risk ICU patients. Current strategies prioritize personalized, dynamic resuscitation guided by bedside assessments and clinician judgment. Emerging research is investigating the use of biomarkers, such as procalcitonin and lactate clearance, to refine prognosis and guide the de-escalation of antibiotics. [21-26]

Complications of septic shock

One of the most critical complications is organ dysfunction, which can manifest as single-organ failure or multiple-organ failure [Table5]. Multiple-organ failure is particularly concerning, as it involves the failure of two or more organ systems, often resulting in increased mortality rates, which can range from 20% to 80% depending on various factors. Also, Common complications associated with septic shock include acute respiratory distress syndrome (ARDS) and renal failure. ARDS is characterized by acute lung injury and respiratory failure, complicating the clinical picture and requiring intensive management. [6] Renal failure, or acute kidney injury, is another frequent complication, often necessitating dialysis in severe cases. [4] These complications arise due to the systemic effects of sepsis, which can lead to significant derangements in host physiology, including systemic hypotension and impaired oxygen extraction. The interplay between metabolic and cardiovascular responses in septic shock further complicates the clinical management of affected patients, as they may present with symptoms such as leukocytosis, fever, tachycardia, and tachypnea. The mortality associated with septic shock remains alarmingly high, underscoring the need for effective therapeutic strategies. Current research in biotechnology aims to develop therapies that can prevent the overstimulation of the immune system and systematically eliminate pathogens, potentially helping to mitigate the severe complications associated with septic shock. [6] Understanding these complications is crucial for improving patient management and outcomes in septic shock cases.

Table [1]: Signs of End Organ Dysfunction



CONCLUSION:

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