

Current approaches to the diagnosis, treatment, and prognosis of sepsis

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ABSTRACT

Sepsis is a critical clinical condition characterized by organ dysfunction resulting from an uncontrolled host response to infection and is associated with a high risk of mortality. Its incidence is increasing due to aging populations, immunosuppression, and resistant pathogens. Although bacteria are the most common causative agents, viral pathogens such as SARS-CoV-2 have also emerged as important contributors. Advanced age, comorbidities, immune deficiencies, and nosocomial infections are the main risk factors. Diagnosis is established through a combined assessment of clinical, laboratory, radiological, and microbiological findings. Early fluid resuscitation, oxygen support, and appropriate empirical antibiotic therapy are crucial in reducing mortality. Timely initiation of appropriate treatment improves survival and plays a life-saving role.

Keywords: Sepsis, septic shock, organ dysfunction, MODS

INTRODUCTION

Sepsis is a life-threatening syndrome characterized by organ dysfunction that arises from dysregulated physiological, biological, and biochemical responses to infection. This condition may progress to multiple organ failure and ultimately death. Septic shock is defined as persistent hypotension requiring vasopressor therapy to maintain a mean arterial pressure of ≥ 65 mmHg despite adequate fluid resuscitation, in conjunction with a serum lactate level > 2 mmol/L.¹ Multiple organ dysfunction syndrome (MODS) refers to progressive organ failure in which homeostasis cannot be sustained without external support.² Contemporary guidelines highlight the pivotal role of early recognition of sepsis in reducing mortality and advocate the application of scoring systems such as qSOFA, SOFA, and NEWS for this purpose.³⁻⁵

INCIDENCE AND CAUSATIVE PATHOGENS IN SEPSIS

The incidence of sepsis has shown a rising trend in recent years, largely attributed to the growth of the elderly population, the increasing prevalence of immunosuppression, and the widespread emergence of multidrug-resistant infections.^{6,7} Racial and seasonal variations have also been observed; the highest incidence rates have been reported among African American men, and a seasonal increase has been noted during winter months in association with a higher frequency of respiratory infections. The majority of cases occur in individuals aged 65 years and older.⁸⁻¹⁰ Among cases with identified pathogens, bacteria remain the predominant

etiological agents, with gram-positive microorganisms being the most prominent. Among viral pathogens, SARS-CoV-2 has emerged as a major cause of sepsis during the pandemic. Nevertheless, in approximately half of the cases, no causative microorganism can be identified.¹¹

RISK FACTORS FOR THE DEVELOPMENT OF SEPSIS

Risk factors for the development of sepsis include intensive care unit (ICU) admission, bacteremia, advanced age (≥ 65 years), immunosuppression, diabetes, obesity, cancer, prior hospitalization, and genetic predisposition. Approximately half of ICU patients develop nosocomial infections, and systemic complications are frequently observed in cases with bacteremia.^{12,13} Advanced age is an independent determinant associated with both increased incidence and mortality of sepsis.¹⁴ Conditions causing immune suppression, the use of immunosuppressive therapies, diabetes, and obesity contribute to sepsis development by impairing immune function and increasing the risk of nosocomial infections.¹⁵ Malignancy is among the most common comorbidities and may increase the risk of sepsis by nearly tenfold.¹⁶ Hospitalization, particularly following antibiotic therapy, poses a risk due to alterations in the microbiota.¹⁷ Furthermore, genetic factors such as antibody production defects, T-cell deficiencies, phagocytic dysfunction, natural killer cell impairment, or complement deficiencies can predispose individuals to infection.¹⁸

CLINICAL, LABORATORY, AND DIAGNOSTIC EVALUATION

Although no single clinical finding is specific for sepsis, patients commonly present with hypotension, tachycardia, fever, and leukocytosis. In septic shock, cold skin, cyanosis, mottling, and evidence of organ dysfunction (e.g., oliguria, altered mental status) may be observed.³ Clinical manifestations may include symptoms attributable to the infectious focus, arterial hypotension, fever or hypothermia, tachycardia, tachypnea, and signs of end-organ hypoperfusion. In the early phase, the skin may appear warm and flushed; however, as shock progresses, patients may develop cool extremities, delayed capillary refill, cyanosis, and mottling (Table).

Laboratory findings in sepsis are nonspecific and may reflect either the underlying cause or alterations related to tissue hypoperfusion.³ Common abnormalities include leukocytosis or leukopenia, increased immature neutrophils, hyperglycemia in the absence of diabetes, elevated C-reactive protein (CRP) and procalcitonin levels, arterial hypoxemia, oliguria, increased creatinine, coagulopathy, thrombocytopenia, hyperbilirubinemia, and hyperlactatemia.¹⁹ In addition, features of adrenal insufficiency (e.g., hyponatremia, hyperkalemia) and the euthyroid sick syndrome may also be observed (Table).

In sepsis, imaging modalities targeting the suspected site of infection (e.g., chest radiography, thoracic or abdominal computed tomography) are utilized. Although positive culture results support the diagnosis, they are not always obtainable and are not mandatory for diagnosis. The diagnosis of sepsis and septic shock is established through an integrated assessment of clinical, laboratory, radiological, physiological, and microbiological findings (Table). To avoid delays in treatment, the diagnosis may be made in the presence of compatible findings once alternative causes have been excluded, without awaiting culture results.

TREATMENT AND MANAGEMENT OF SEPSIS

The cornerstone of therapy in sepsis and septic shock is the prompt initiation of fluid resuscitation and antibiotics in the early phase, with the aim of rapidly restoring

perfusion. Securing the airway, correcting hypoxemia, establishing adequate venous access, and ensuring the timely administration of fluids and antimicrobial therapy constitute the essential components of effective management.³ In the presence of hypoxemia, supplemental oxygen should be administered, and oxygen saturation should be continuously monitored via pulse oximetry, generally maintained within the range of 90–96%. Noninvasive ventilation, high-flow oxygen therapy, or endotracheal intubation may be required to ensure adequate oxygenation or to reduce the increased work of breathing. While peripheral venous access may be sufficient at the initiation of fluid resuscitation, placement of a central venous catheter is recommended as soon as feasible.

Routine use of glucocorticoids in sepsis is not recommended; however, corticosteroid therapy may be considered in cases of refractory hypotension despite adequate fluid resuscitation and vasopressor therapy, particularly when critical illness–related adrenal insufficiency is suspected. In such cases, hydrocortisone is recommended as monotherapy, administered in divided doses, with a total daily dose not exceeding 400 mg.²⁰

ANTIMICROBIAL THERAPY

Early initiation of appropriate antibiotic therapy is one of the most critical prognostic factors in sepsis and may reduce mortality by approximately 50%.²¹ Empirical broad-spectrum antimicrobial therapy should be started as soon as possible, ideally within the first hour after culture collection. The choice of agents should consider recent antibiotic exposure, prior microbiological isolates, comorbidities, immune status, infection site, and local epidemiology. In most cases, empirical coverage for both gram-positive and gram-negative pathogens is recommended, with subsequent de-escalation once the causative organism is identified.

To ensure adequate tissue perfusion, crystalloid fluids should generally be initiated at 30 ml/kg based on actual body weight within the first hour, administered as rapid boluses in the absence of pulmonary edema.²² Clinical status, hemodynamic response, and pulmonary findings should be reassessed after each bolus, and fluid administration discontinued if necessary. During the first three hours, administration of 2–3 liters of fluid is generally sufficient; hemodynamic targets include a central venous pressure (CVP) of 8–12 mmHg,

Table. Diagnostic criteria and supportive findings in sepsis

Assessment domain	Key diagnostic indicators	Clinical interpretation
Clinical findings	Fever or hypothermia, tachycardia, tachypnea, altered mental status, hypotension	Indicates systemic inflammatory and hemodynamic response to infection.
Laboratory markers	Leukocytosis or leukopenia, elevated C-reactive protein and procalcitonin, hyperlactatemia, increased creatinine, thrombocytopenia	Reflects infection, tissue hypoperfusion, and organ dysfunction.
Organ dysfunction parameters (sepsis-3)	Increase in SOFA score ≥ 2 from baseline	Defines sepsis as life-threatening organ dysfunction due to dysregulated host response to infection.
Microbiological findings	Positive blood or site-specific cultures (when available)	Confirms infection source; however, culture negativity does not exclude sepsis.
Hemodynamic parameters	Mean arterial pressure < 65 mmHg despite fluids; serum lactate > 2 mmol/L	Suggests septic shock requiring vasopressor therapy.
Imaging and adjunctive tests	Radiologic evidence (chest X-ray, CT, or ultrasound) identifying infectious focus	Supports localization of infection and guides source control.

mean arterial pressure ≥ 65 mmHg, and urine output ≥ 0.5 ml/kg/hour.²³ As no mortality benefit has been demonstrated with albumin compared to crystalloids, crystalloids remain the preferred resuscitation fluid.²⁴ In patients with persistent hypotension despite adequate fluid replacement, intravenous vasopressors should be initiated, with norepinephrine as the first-line agent.²⁵

The duration of antimicrobial therapy is typically 7–10 days but may be extended in cases of slow clinical response, immunosuppression, undrainable infectious foci, or *Staphylococcus aureus* bacteremia.²⁶

PROGNOSIS IN SEPSIS

Sepsis is a life-threatening emergency with high mortality; while mortality rates are lower in younger patients without comorbidities, they increase markedly with advancing age. Overall mortality exceeds 10% in sepsis and surpasses 40% in septic shock.¹ Prognostic factors can be broadly categorized into host-related and disease-related determinants. Host-related adverse factors include advanced age (>40 years),²⁷ multiple comorbidities,²⁸ immunocompromising conditions (e.g., AIDS, immunosuppression), chronic liver disease, malignancy, alcohol dependence, heart failure, newly developed atrial fibrillation,²⁹ malnutrition, presence of indwelling catheters, prior hospitalization, as well as persistent thrombocytopenia, hyperchloremia, hyperglycemia, hypercoagulability, and elevated procalcitonin levels. The source of infection is also a critical determinant of prognosis; urinary tract–derived sepsis carries the lowest mortality, whereas infections of unknown origin or cases of pneumosepsis may reach mortality rates as high as 50–55%.³⁰ Moreover, sepsis caused by nosocomial pathogens is associated with higher mortality compared to community-acquired infections.³¹

MORBIDITY IN SEPSIS

Among survivors of sepsis, an increased risk of mortality within the first six months after hospital discharge has been reported, along with a higher frequency of recurrent hospitalizations.³² Compared with patients hospitalized for non-sepsis causes, these individuals are at greater risk of major cardiovascular and cerebrovascular events.

In addition to early mortality and rehospitalization risk, the post-sepsis period is frequently associated with a constellation of long-term complications collectively referred to as post-sepsis syndrome. The pathophysiology involves persistent inflammation, immune dysregulation, microvascular injury, and metabolic derangements that may continue long after the initial infection has resolved. Survivors may develop sepsis-associated encephalopathy, manifesting as memory impairment, attention deficits, and reduced executive function. Psychiatric sequelae such as depression, anxiety, and post-traumatic stress disorder are also common, particularly among patients who required prolonged intensive care or mechanical ventilation.

Beyond neurocognitive and psychological outcomes, neuromuscular weakness, exercise intolerance, and chronic

fatigue are frequently observed, contributing to a decline in physical performance and quality of life. Functional dependency, impaired mobility, and loss of employment are additional long-term consequences that may persist for months or even years.

Furthermore, the critical illness period in the intensive care setting may result in long-term cognitive, psychiatric, and physical complications. Early multidisciplinary rehabilitation, nutritional support, and long-term follow-up are therefore crucial to mitigate these effects and enhance recovery in sepsis survivors.

CONCLUSION

Sepsis is a syndrome with high mortality and morbidity that necessitates urgent diagnosis and management. Early recognition, prompt fluid resuscitation, oxygen supplementation, and appropriate antibiotic therapy are of paramount importance in improving patient outcomes.

In recent years, there has been growing interest in the use of advanced technologies and precision medicine approaches to improve sepsis care. Artificial intelligence–based models and machine learning algorithms are being explored to facilitate earlier recognition, risk stratification, and individualized treatment strategies. Integration of clinical, laboratory, and hemodynamic data through predictive analytics may allow for real-time decision support and more accurate prognostic assessment.

Furthermore, ongoing research into host–pathogen interactions, immunomodulatory therapies, and biomarkers holds promise for more personalized interventions in the future. A multidisciplinary approach involving critical care, infectious disease, and rehabilitation teams will remain essential to optimize both short-term survival and long-term quality of life in sepsis survivors.

ETHICAL DECLARATIONS

Peer Review Process

This review was externally peer-reviewed.

Conflict of Interest

The author declare no conflicts of interest.

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Author Contributions

The author confirms sole responsibility for the study conception, design, data collection, analysis, interpretation, and manuscript preparation. All aspects of the work were carried out by the author.

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