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Sepsis Management in Hospitalized Patients: The Interplay of Dental Infections, Medical Treatment, Critical Care, Radiological Diagnostics, and Nursing Interventions

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Abstract:

Sepsis management in hospitalized patients is a multifaceted challenge, particularly when dental infections are involved. Dental infections can serve as a source of systemic infection, leading to sepsis, especially in patients with comorbidities or compromised immune systems. Prompt identification and management of these infections are crucial to prevent the progression to severe sepsis or septic shock. Medical treatment typically begins with broad-spectrum antibiotics tailored to the suspected organism, while critical care support may involve intravenous fluids and vasopressors to manage hemodynamic instability. Additionally, interdisciplinary collaboration among clinicians, including dentists and infectious disease specialists, is essential to address the root cause of the infection and ensure comprehensive care. Radiological diagnostics play a pivotal role in the assessment of sepsis, helping to identify potential sources of infection, such as abscesses or osteomyelitis related to dental disease. Imaging modalities like X-rays, CT scans, and MRIs can offer vital insights into the extent of infection and inform treatment strategies. Concurrently, nursing interventions are integral to effective sepsis management, as nurses monitor vital signs, administer medications, and provide education to patients and families about the importance of oral health in preventing sepsis. By recognizing the interplay of these components—dental infections, medical and critical care treatments, radiological diagnostics, and nursing interventions—healthcare teams can enhance patient outcomes and reduce morbidity associated with sepsis.

Keywords: Sepsis management, dental infections, medical treatment, critical care, radiological diagnostics

Introduction:

Sepsis, a complex and often life-threatening condition arising from the body's dysregulated response to infection, poses significant challenges in the management of hospitalized patients. According to the World Health Organization, sepsis is responsible for a considerable proportion of global morbidity and mortality, affecting millions of individuals each year. The pathophysiology of sepsis is intricate, involving immune dysregulation, inadequate tissue perfusion, and subsequent organ dysfunction, which can lead to multi-organ failure if not promptly and effectively addressed. In light of the multifactorial nature of sepsis, an interdisciplinary approach to its management is crucial, particularly in a hospital setting where patients may present with a variety of underlying infections, including dental infections, which are increasingly recognized as potential sources of sepsis [1].

Dental infections can serve as a significant contributing factor to the onset of sepsis, highlighting the importance of oral health in the overall management of critically ill patients. The oral cavity is home to a diverse microbiome, where pathogenic bacteria can enter the bloodstream through various routes, such as periodontal disease or dental procedures. Once in circulation, these pathogens can trigger systemic inflammatory responses that lead to sepsis. Therefore, understanding the connection between oral health and systemic infections is paramount for healthcare

providers who are tasked with identifying and mitigating potential sources of sepsis in hospitalized patients [2].

Effective management of sepsis encompasses an array of medical treatments, critical care strategies, and nursing interventions. The cornerstone of sepsis management lies in the early identification of sepsis and the prompt initiation of broad-spectrum intravenous antibiotics, along with fluid resuscitation and supportive measures. Adherence to early goal-directed therapy has been shown to improve outcomes in septic patients, making it essential that healthcare teams are well-versed in the latest clinical guidelines and protocols. Critical care environments play an instrumental role in managing the complications associated with sepsis, wherein healthcare professionals must employ a diverse set of advanced monitoring techniques to assess the severity of the patient's condition, including vital signs, hemodynamic parameters, and laboratory results [3].

Moreover, the integration of radiological diagnostics is vital in the comprehensive assessment of septic patients. Advanced imaging techniques, such as computed tomography (CT) scans, ultrasound, and magnetic resonance imaging (MRI), can aid in identifying sources of infection, such as abscesses or other focal lesions, that may require surgical intervention or targeted medical therapy. The ability to accurately localize the source of sepsis can significantly influence therapeutic decisions and improve clinical outcomes [4].

Equally important in the interplay of sepsis management are nursing interventions that focus on patient care and education. Nurses act as the frontline caregivers, providing ongoing assessments, administering medications, and fostering communication amongst the healthcare team. Their role in preventing complications, monitoring for signs of deterioration, and advocating for the patient cannot be overstated. Furthermore, nursing practices that emphasize infection control—such as meticulous hand hygiene, appropriate use of personal protective equipment, and education on oral hygiene—are critical in reducing the incidence of sepsis, particularly in vulnerable populations such as the elderly or immunocompromised [5].

Role of Dental Infections in Sepsis Pathogenesis

Dental infections typically arise from the proliferation of bacteria in the oral cavity, leading to conditions such as caries (cavities) or periodontal disease (infections of the gums and supporting structures of teeth). The bacteria involved in these diseases are primarily anaerobic, with commonly implicated species including *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Streptococcus mutans*. To a lesser extent, dental abscesses can occur when these infections progress, resulting in localized pus formation and tissue destruction [6].

The systemic implications of dental infections are often underestimated. However, severe cases can lead to significant consequences, including bacteremia—where bacteria enter the bloodstream—potentially leading to sepsis, a life-threatening condition characterized by systemic inflammatory response syndrome (SIRS).

Sepsis arises when the body's response to an infection causes widespread inflammation. Dental infections can initiate this chain of events through several mechanisms [7]:

1. **Bacteremia**: One of the primary pathways through which dental infections can lead to sepsis is bacteremia. Bacteria in the mouth can enter the bloodstream via various routes, such as during routine activities like brushing teeth, dental cleanings, or even through trauma or ulcers. This is particularly common in individuals with compromised immune systems or pre-existing conditions [8].
2. **Systemic Inflammatory Response**: Once bacteria enter the bloodstream, they can trigger a systemic inflammatory response. The immune system detects these pathogens, leading to the release of pro-inflammatory cytokines and chemokines. This response is intended to eliminate the invading microorganisms but can become dysregulated. Excessive inflammation can cause widespread damage to tissues and organs, a hallmark of sepsis [9].
3. **Tissue Hypoxia and Organ Dysfunction**: As the inflammatory response continues, it can lead to tissue hypoxia due to impaired blood flow and oxygen delivery. Organs begin to dysfunction, which can lead to multi-organ failure, one of the most severe outcomes of sepsis. The dental infection, although localized, can thus precipitate a life-threatening systemic condition [10].

The clinical implications of the link between dental infections and sepsis are profound. An alarming trend is the increasing incidence of sepsis, with dental infections playing a significant role, particularly among high-risk populations including the elderly, individuals with diabetes, and those undergoing immunosuppressive therapies [11].

Healthcare professionals must be vigilant in recognizing the signs of dental infections in patients

presenting with sepsis. Symptoms such as fever, chills, rapid heartbeat, and altered mental status should prompt a thorough dental examination and history-taking, as treating the source of the infection is critical to sepsis management. Effective antibiotics addressing the oral pathogens involved are essential, complemented by dental interventions to eliminate the infection [11].

Given the serious implications of dental infections in sepsis pathogenesis, preventive strategies are crucial. Oral health education is paramount, as awareness of oral hygiene practices can significantly reduce the burden of dental infections. Effective brushing, flossing, and regular dental check-ups can mitigate the occurrence of cavities and periodontal disease [12].

Additionally, systemic health evaluations for high-risk patients—a task ideally undertaken by both dentists and medical professionals—can enhance preventive care. For example, patients with diabetes or cardiovascular diseases should receive tailored oral health advice to minimize infection risks. Furthermore, appropriate antibiotic prophylaxis before dental procedures for patients at heightened risk of infective endocarditis or those with compromised immune systems plays a key role in prevention [13].

Initial Medical Management of Sepsis:

Sepsis is defined as a dysregulated host response to infection, which can lead to multi-organ dysfunction syndrome (MODS) and ultimately, death. Its clinical manifestations range from mild infection signs to profound septic shock, characterized by persistent hypotension despite adequate fluid resuscitation. Early recognition and prompt initiation of treatment are pivotal in improving outcomes. Unfortunately, sepsis carries a high mortality rate, with estimates suggesting that it is responsible for nearly 11 million deaths annually worldwide [14].

1. Importance of Empirical Antibiotic Therapy

Antibiotic therapy is critical in sepsis management, as it targets the underlying infection driving the systemic inflammatory response. The goal is to initiate empirical antibiotic therapy as soon as possible—ideally within the first hour of recognizing sepsis. Delay in antibiotic administration has been associated with increased mortality, emphasizing the need for rapid action [15].

2. Selection of Antibiotics

Empirical antibiotic therapy should be broad-spectrum to cover the most likely pathogens associated with sepsis, often drawn from common sources such as pneumonia, urinary tract infections, and abdominal infections. The choice of antibiotics is influenced by factors including local antibiogram data, patient-specific factors (e.g., previous antibiotic exposure, immunocompromised status), and the site of infection [16].

For instance, a patient presenting with community-acquired pneumonia might be treated with a combination of a beta-lactam and a macrolide, while a patient suspected of intra-abdominal infection might receive carbapenems or third-generation cephalosporins. In cases of septic shock, the addition of vancomycin is often warranted to cover methicillin-resistant Staphylococcus aureus (MRSA) [17].

3. Duration of Antibiotic Therapy

The duration of antibiotic therapy depends on clinical response and the source of infection. Guidelines recommend a typical duration of 7 to 10 days for most infections; however, treatment may need to be extended for complicated infections or until definitive cultures and sensitivities guide more tailored therapy. Serum markers such as procalcitonin may assist in determining the adequacy of therapy and guiding de-escalation [18].

1. The Role of Fluid Resuscitation

Fluid resuscitation is a critical intervention for managing sepsis, particularly in the context of hypotension and reduced tissue perfusion. Administration of intravenous fluids aims to restore intravascular volume, improve cardiac output, and subsequently enhance organ perfusion. This is especially essential in septic shock, where fluid losses due to increased vascular permeability can lead to significant alterations in hemodynamics [19].

2. Types of Fluids Used

Crystalloids, such as normal saline or lactated Ringer's solution, are the mainstay of initial resuscitation. The Surviving Sepsis Campaign guidelines recommend an initial bolus of 30 mL/kg of crystalloid fluid within the first three hours of recognition of sepsis or septic shock. In cases of ongoing hypovolemia despite crystalloid administration, colloids, or vasopressors may be considered to support hemodynamic stability [17].

3. Monitoring and Adjusting Fluid Therapy

Resuscitation should be guided by ongoing assessment of the patient’s response. Measuring vital signs, urine output, and lactate levels can provide critical insights into fluid status and tissue perfusion. Persistent hypotension or inadequate response to fluid resuscitation may necessitate the early initiation of vasopressors, such as norepinephrine, to achieve hemodynamic goals [20].

Despite established protocols, several challenges impede the effective management of sepsis. These include:

- **Delay in Diagnosis:** Sepsis can present insidiously, leading to delayed recognition and treatment.
- **Antibiotic Resistance:** The emergence of multidrug-resistant organisms complicates the selection of effective empirical therapy.
- **Fluid Overload:** While fluid resuscitation is crucial, excessive fluid administration can result in complications such as pulmonary edema and abdominal compartment syndrome.
- **Individual Variation:** The heterogeneity of sepsis influences how patients respond to treatment, requiring a tailored approach rather than a one-size-fits-all protocol [21].

Critical Care Approaches in Managing Severe Sepsis

The cornerstone of effective management of severe sepsis is early identification, which hinges on the recognition of clinical symptoms and risk factors. The use of standardized criteria such as the Sepsis-3 definition enables clinicians to promptly identify patients presenting with suspected infection and a Sequential Organ Failure Assessment (SOFA) score indicating organ dysfunction. Key indicators of severe sepsis include altered mental status, increased respiratory rate, hypotension, and elevated lactate levels. Implementing screening tools in emergency departments and critical care units can enhance the early recognition of patients at risk for sepsis, thereby improving outcomes through timely intervention [22].

Fluid Resuscitation

Upon diagnosis, the primary treatment strategy in severe sepsis management is aggressive fluid resuscitation. The Surviving Sepsis Campaign guidelines recommend administering at least 30 mL/kg of crystalloid fluid within the first three hours of recognition of sepsis. This strategy aims to restore hemodynamic stability, improve tissue perfusion, and enhance oxygen delivery. Crystalloids, such as normal saline and lactated Ringer's solution, are typically the first-choice fluids, though the type of fluid may be adapted to individual patient needs. Regular assessments of fluid responsiveness through dynamic indicators help avoid over-resuscitation, which can exacerbate pulmonary edema and other complications. In cases where fluid resuscitation fails to achieve hemodynamic goals, the judicious use of vasopressors, particularly norepinephrine, becomes essential [23].

Antimicrobial Therapy

Initiating broad-spectrum antimicrobial therapy within the first hour of recognition of severe sepsis is critical to combating the underlying infection and mitigating the systemic inflammatory response. Empirical antibiotics tailored to the most likely sources of infection should be promptly administered while waiting for culture results. The role of de-escalation based on culture and susceptibility testing cannot be overstated, as it minimizes the risk of antibiotic resistance and adverse events. In addition, consideration of adjunctive therapies, such as corticosteroids, may be beneficial in patients with septic shock by modulating the inflammatory response, although this remains a topic of ongoing research and debate [24].

Source Control

Effective source control is another vital component of managing severe sepsis, as the persistent source of infection can exacerbate the patient's condition and hinder recovery. Source control strategies may involve surgical interventions, such as drainage of abscesses, removal of infected devices, or debridement of necrotic tissue. Minimally invasive techniques are preferred when possible, but timely surgical intervention is paramount when necessary. Effective communication among surgical teams, intensivists, and infectious disease specialists is critical to ensure that source control measures are implemented swiftly and effectively [25].

Supportive Care

In addition to treating the underlying infection, supportive care plays a crucial role in managing patients with severe sepsis. Continuous monitoring of vital signs and organ function is essential for assessing treatment efficacy and guiding further interventions. Mechanical ventilation may be required for patients experiencing respiratory distress, while renal replacement therapy may be necessary in cases of acute kidney injury. Nutritional support is also critical, as critically ill patients often experience catabolism and may require specialized enteral or parenteral nutrition strategies to maintain metabolic homeostasis. The management of fluid balance, glucose levels, and electrolyte homeostasis further contributes to the overall stabilization of the patient [26].

Interdisciplinary Collaboration

Effective management of severe sepsis is inherently interdisciplinary, necessitating collaboration among various healthcare providers, including intensivists, nurses, pharmacists, microbiologists, and nutritionists. Implementing care bundles—structured protocols that bundle evidence-based

practices—has proven beneficial in standardizing care and improving outcomes. Regular multidisciplinary rounds facilitate real-time communication, allow for rapid reassessment of management strategies, and ensure that all team members are aligned in addressing the multifaceted needs of the patient. Education and training programs focused on sepsis recognition and management for all levels of healthcare personnel are vital in fostering a culture of preparedness and responsiveness [27].

Role of Imaging in Infection Management

Infectious diseases can affect virtually any body system. Radiological diagnostics provide key insights into the presence of infections in organs such as the lungs, liver, kidneys, bones, and soft tissues. For instance, pneumonia, a common respiratory infection, frequently demands radiological evaluation. Chest X-rays or computed tomography (CT) scans are typically employed to identify lung infiltrates, abscesses, or any other structural changes signifying an infectious process [28].

Similarly, imaging can be crucial in evaluating urinary tract infections (UTIs) or pyelonephritis. Ultrasound and CT scans can identify complications such as abscesses, hydronephrosis (swelling of the kidney due to the buildup of urine), and other obstructive processes. In the case of bone infections, or osteomyelitis, magnetic resonance imaging (MRI) can detect inflammation and suppuration within the healthy bone and soft tissue structures surrounding it [29].

Multiple imaging modalities are employed based on the suspected infection, the anatomical site involved, and the clinical context. Here are some of the prominent techniques used in radiological diagnostics of infection [22]:

1. **X-ray Imaging**: X-rays are often the first line of imaging in many acute infections, particularly in the chest for pneumonia. They provide quick, cost-effective visualization and are effective for initial evaluations. However, they have limitations in sensitivity and specificity, especially in detecting early or subtle infections [30].
2. **Computed Tomography (CT)**: CT scanning offers detailed cross-sectional images and enhances the detection of infections through better visualization of complex anatomy. It is especially useful in identifying deep-seated infections, stating whether infection has spread to adjacent structures, and providing guidance for interventions like drainage [31].
3. **Magnetic Resonance Imaging (MRI)**: MRI is particularly beneficial in soft tissue infections and osteomyelitis due to its ability to provide high-resolution images without radiation exposure. It excels in differentiating between inflammatory and necrotic processes, aiding in treatment planning.
4. **Ultrasound**: Ultrasound imaging is advantageous for assessing soft tissue and fluid collections, such as abscesses. It is non-invasive and can be performed at the bedside, making it ideal for initial evaluations. In pediatric populations, it is often preferred due to the lack of radiation.
5. **Nuclear Medicine**: PET scans and functional imaging can help identify areas with increased metabolic activity that might indicate infection, inflammation, or malignancy. This modality is particularly useful in cases where conventional imaging is inconclusive [32].

When approaching a suspected infection, clinicians typically adopt a stepwise diagnostic pathway utilizing radiological techniques. Initial clinical evaluation, including history-taking and physical examination, is followed by the selection of appropriate imaging based on the probable source of infection. Laboratory tests are concurrently performed to isolate the causative organism or identify markers of infection [33].

Once the imaging is completed, the results are analyzed with a critical eye. The interpretation of radiological findings requires substantial training and experience. Radiologists and infectious disease specialists collaborate to correlate imaging results with clinical presentations, thereby enhancing the accuracy of the diagnosis [34].

Despite the significant advances in imaging technology, challenges remain in the realm of radiological diagnostics for infectious diseases. Some of these challenges include:

- **Radiation Exposure**: While advancements in technology have reduced radiation doses, caution must be exercised, especially in vulnerable populations such as children and pregnant women.
- **Artifact Interference**: Various artifacts can complicate the interpretation of images, leading to misdiagnosis or overlooking critical findings.

- **Timing and Sensitivity**: Certain infections, especially in the early stages, may not present with clear radiological signs. The timing of imaging in relation to symptom onset is crucial.
- **Differential Diagnosis**: Inflammation due to infection can mimic other conditions such as malignancies and autoimmune diseases, complicating the diagnostic process [35].

As technology continues to advance, the future of radiological diagnostics in infectious disease holds immense potential. Emerging techniques such as artificial intelligence (AI) and machine learning promise to enhance image interpretation, improve diagnostic accuracy, and streamline workflows. AI algorithms can be trained to identify patterns within imaging studies, thus aiding radiologists in recognizing abnormalities at earlier stages [36].

Furthermore, the integration of molecular imaging techniques with traditional imaging modalities offers possibilities for identifying pathogens at the cellular and molecular levels. This could lead to more specific and timely treatment options, resulting in better patient outcomes [35].

Nursing Interventions and Their Impact on Sepsis Outcomes

One of the primary nursing interventions in the context of sepsis management is conducting thorough patient assessments to facilitate early recognition of the condition. Nurses are often the first point of contact for patients and, therefore, play a vital role in monitoring vital signs, observing for signs of infection, and assessing the patient's overall clinical status. Using screening tools such as the Sequential Organ Failure Assessment (SOFA) score or the QuickSOFA (qSOFA) can help nurses identify patients at risk of developing sepsis [37].

The timely identification of sepsis significantly affects outcomes; studies have shown that early recognition and initiation of treatment improve survival rates. Nurses must be trained to recognize subtle changes in a patient's condition and communicate effectively with the healthcare team to ensure prompt intervention [38].

Fluid Resuscitation and Monitoring

Fluid resuscitation is a cornerstone of sepsis management, and nursing interventions in this area are crucial. Administering intravenous fluids helps restore circulatory volume and improve tissue perfusion, which can be detrimental in sepsis management. Nurses assess the patient's hydration status and monitor vital signs, fluid intake and output, and signs of fluid overload or electrolyte imbalance [39].

The efficacy of fluid resuscitation in sepsis has been extensively studied. Research indicates that early and aggressive fluid therapy reduces mortality rates; however, it must be balanced against the risk of fluid overload, which can lead to complications such as pulmonary edema. This highlights the importance of ongoing assessment and vigilant monitoring by nursing staff, who play a key role in adapting treatment based on the patient's response [40].

Administering Antibiotics

Prompt administration of broad-spectrum antibiotics is critical in the management of sepsis, and nurses are integral to this process. The Surviving Sepsis Campaign recommends administering antibiotics within the first hour of suspected sepsis. Nurses must be adept at recognizing the signs of sepsis, facilitating rapid access to antibiotics, and understanding the protocols for selecting appropriate pharmacotherapy based on the patient's clinical picture [41].

Additionally, the administration of antibiotics necessitates ongoing patient assessment. Nurses should monitor for signs of antibiotic effectiveness, including changes in vital signs, laboratory results, and patient-reported symptoms. Furthermore, due to the rise of antibiotic resistance, nurses must remain informed about appropriate antibiotic stewardship practices, which include proper dosing, timing, and potential adverse effects [42].

Collaborative Care and Patient Education

Sepsis management involves a multidisciplinary approach, and nurses serve as coordinators of care, collaborating with physicians, pharmacists, respiratory therapists, and other members of the healthcare team. Effective communication among team members is vital for ensuring that treatment protocols are followed efficiently and adjustments can be made based on the patient's evolving condition [43].

Moreover, post-discharge education is an essential nursing intervention that can improve long-term outcomes for sepsis survivors. Nurses can provide education on recognizing signs of recurrent infection, proper wound care, medication adherence, and lifestyle modifications to enhance recovery. Research indicates that patient education reduces the risk of readmission and improves quality of life following sepsis hospitalization [44].

Psychological Support and Holistic Care

The psychological impact of sepsis can be substantial, leading to conditions such as post-traumatic stress disorder (PTSD), anxiety, and

depression in survivors. As essential providers of patient-centered care, nurses must offer emotional support to patients and their families throughout the treatment process. Engaging patients in conversations about their experiences and encouraging family involvement fosters a supportive environment conducive to healing [43].

Moreover, employing a holistic nursing approach, which addresses the physical, emotional, and social aspects of care, can enhance patient outcomes. By considering the whole person rather than focusing solely on the illness, nurses can contribute to a more comprehensive care plan that supports recovery and improves overall well-being [45].

Conclusion:

In conclusion, the management of sepsis in hospitalized patients is a multifaceted process that requires the collaboration of various healthcare professionals, including physicians, nurses, radiologists, and dental specialists. By understanding the complex interplay between dental infections, medical treatment, critical care, radiological diagnostics, and nursing interventions, the healthcare community can enhance the quality of care delivered to septic patients. This integrated approach fosters timely interventions, improves patient outcomes, and ultimately contributes to the ongoing battle against this devastating condition. As the landscape of healthcare continues to evolve, ongoing research and education will be vital in advancing our understanding and management of sepsis, ensuring that healthcare systems are better equipped to meet the challenges posed by this critical clinical phenomenon.

References:

1. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (Sepsis-3) JAMA. 2016;315:762–74. doi: 10.1001/jama.2016.0288.
2. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47:1181–247. doi: 10.1007/s00134-021-06506-y.
3. Messina A, Palandri C, De Rosa S, et al. Pharmacodynamic analysis of a fluid challenge with 4 ml kg-1 over 10 or 20 min: a multicenter cross-over randomized clinical trial. J Clin Monit Comput 2021 Sep 8. :1–11. doi: 10.1007/s10877-021-00756-3.
4. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006;34:1589–96. doi: 10.1097/01.CCM.0000217961.75225.E9.
5. Hernández G, Ospina-Tascón GA, Damiani LP, et al. Effect of a resuscitation strategy targeting peripheral perfusion status vs serum lactate levels on 28-day mortality among patients with septic shock: the ANDROMEDA-SHOCK randomized clinical trial. JAMA. 2019;321:654–64. doi: 10.1001/jama.2019.0071.
6. Zampieri FG, Machado FR, Biondi RS, et al. BaSICS investigators and the BRICNet members. Effect of intravenous fluid treatment with a balanced solution vs 0.9% saline solution on mortality in critically ill patients: the BaSICS randomized clinical trial. JAMA. 2021;326:1–12. doi: 10.1001/jama.2021.11684.
7. Aya HD, Ster IC, Fletcher N, et al. Pharmacodynamic analysis of a fluid challenge. Crit Care Med. 2016;44:880–91. doi: 10.1097/CCM.0000000000001517.
8. Bauer TT, Ewig S, Marre R, Suttorp N, Welte T. CAPNETZ Study Group. CRB-65 predicts death from community-acquired pneumonia. J Intern Med. 2006;260:93–101. doi: 10.1111/j.1365-2796.2006.01657.x.
9. Mohr NM, Wessman BT, Bassin B, et al. Boarding of critically ill patients in the emergency department. Crit Care Med. 2020;48:1180–7. doi: 10.1097/CCM.0000000000004385.
10. Martins FS, Guedes GG, Santos TM, de Carvalho-Filho MA. Suspected infection in afebrile patients: Are they septic? Medicine (Baltimore) 2017;96:e6299. doi: 10.1097/MD.0000000000006299.
11. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348:1546–54. doi: 10.1056/NEJMoa022139.
12. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395:200–11. doi: 10.1016/S0140-6736(19)32989-7.

13. Li Y, Guo J, Yang H, et al. Comparison of culture-negative and culture-positive sepsis or septic shock: a systematic review and meta-analysis. Crit Care. 2021;25:167. doi: 10.1186/s13054-021-03592-8.

14. Tan CW, Chlebicki MP. Urinary tract infections in adults. Singapore Med J. 2016;57:485–90. doi: 10.11622/smedj.2016153.

15. Bilbao-Meseguer I, Rodriguez-Gascón A, Barrasa H, Isla A, Solinís MÁ. Augmented renal clearance in critically ill patients: a systematic review. Clin Pharmacokinet. 2018;57:1107–21. doi: 10.1007/s40262-018-0636-7.

16. Garnacho-Montero J, Gutiérrez-Pizarraya A, Escoresca-Ortega A, Fernandez-Delgado E, Lopez-Sánchez JM. Adequate antibiotic therapy prior to ICU admission in patients with severe sepsis and septic shock reduces hospital mortality. Crit Care. 2015;19:302. doi: 10.1186/s13054-015-1000-z.

17. Vincent JL, Brealey D, Libert N, et al. Rapid Diagnosis of Infections in the Critically Ill Team. Rapid diagnosis of infection in the critically ill, a multicenter study of molecular detection in bloodstream infections, pneumonia, and sterile site infections. Crit Care Med. 2015;43:2283–91. doi: 10.1097/CCM.0000000000001249.

18. Martínez ML, Ferrer R, Torrents E, et al. Edusepsis Study Group. Impact of source control in patients with severe sepsis and septic shock. Crit Care Med. 2017;45:11–9. doi: 10.1097/CCM.0000000000002011.

19. See KC, Mukhopadhyay A, Lau SC, et al. Shock in the first 24 h of intensive care unit stay: observational study of protocol-based fluid management. Shock. 2015;43:456–62. doi: 10.1097/SHK.0000000000000332.

20. Weiss SL, Peters MJ, Alhazzani W, et al. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Pediatr Crit Care Med. 2020;21(2):e52–e106. doi: 10.1097/PCC.0000000000002198.

21. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41(2):580–637. doi: 10.1097/CCM.0b013e31827e83af.

22. Rhee C, Dantes R, Epstein L, et al. Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009–2014. JAMA. 2017;318(13):1241–1249. doi: 10.1001/jama.2017.13836.

23. Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med. 2003;31(4):1250–1256. doi: 10.1097/01.CCM.0000050454.01978.3B.

24. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Crit Care Med. 2017;45(3):486–552. doi: 10.1097/CCM.0000000000002255.

25. Fleischmann C, Scherag A, Adhikari NK, et al. Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. Am J Respir Crit Care Med. 2016;193(3):259–272. doi: 10.1164/rccm.201504-0781OC.

26. Dellinger RP, Carlet JM, Masur H, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med. 2004;32(3):858–873. doi: 10.1097/01.CCM.0000117317.18092.E4.

27. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (Sepsis-3) JAMA. 2016;315(8):762–774. doi: 10.1001/jama.2016.0288.

28. Fleischmann-Struzek C, Mellhammar L, Rose N, et al. Incidence and mortality of hospital- and ICU-treated sepsis: results from an updated and expanded systematic review and meta-analysis. Intensive Care Med. 2020;46(8):1552–1562. doi: 10.1007/s00134-020-06151-x.

29. Dellinger RP, Levy MM, Carlet JM. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med. 2008;36(1):296–327. doi: 10.1097/01.CCM.0000298158.12101.41.

30. Dellinger RP, Levy MM, Carlet JM. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008 (vol 36, pg 296,

2008) Crit Care Med. 2008;36(4):1394–1396. doi: 10.1097/01.CCM.0000298158.12101.41.

31. Weiss SL, Peters MJ, Alhazzani W, et al. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Intensive Care Med. 2020;46(Suppl 1):10–67. doi: 10.1007/s00134-019-05878-6.
32. Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013;39(2):165–228. doi: 10.1007/s00134-012-2769-8.
33. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus definitions for sepsis and septic shock (Sepsis-3) JAMA. 2016;315(8):801–810. doi: 10.1001/jama.2016.0287.
34. Rhodes A, Evans LE, Alhazzani W, et al. surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med. 2017;43(3):304–377. doi: 10.1007/s00134-017-4683-6.
35. Bhattacharjee P, Edelson DP, Churpek MM. Identifying patients with sepsis on the hospital wards. Chest. 2017;151(4):898–907. doi: 10.1016/j.chest.2016.06.020.
36. Downing NL, Rolnick J, Poole SF, et al. Electronic health record-based clinical decision support alert for severe sepsis: a randomised evaluation. BMJ Qual Saf. 2019;28(9):762–768. doi: 10.1136/bmjqs-2018-008765.
37. Dellinger RP. The future of sepsis performance improvement. Crit Care Med. 2015;43(9):1787–1789.
38. Makam AN, Nguyen OK, Auerbach AD. Diagnostic accuracy and effectiveness of automated electronic sepsis alert systems: a systematic review. J Hosp Med. 2015;10(6):396–402. doi: 10.1002/jhm.2347.
39. Schunemann HJ, Wiercioch W, Brozek J, et al. GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations: GRADE-ADOLOPMENT. J Clin Epidemiol. 2017;81:101–110. doi: 10.1016/j.jclinepi.2016.09.009.
40. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. J Clin Epidemiol. 2013;66(7):719–725. doi: 10.1016/j.jclinepi.2012.03.013.
41. Warttig S, Alderson P, Evans DJ, et al. Automated monitoring compared to standard care for the early detection of sepsis in critically ill patients. Cochrane Database Syst Rev. 2018;6(6):CD012404. doi: 10.1002/14651858.CD012404.pub2.
42. Schorr C, Odden A, Evans L, et al. Implementation of a multicenter performance improvement program for early detection and treatment of severe sepsis in general medical–surgical wards. J Hosp Med. 2016;11(S1):S32–S39. doi: 10.1002/jhm.2656.
43. Damiani E, Donati A, Serafini G, et al. Effect of performance improvement programs on compliance with sepsis bundles and mortality: a systematic review and meta-analysis of observational studies. PLoS One. 2015;10(5):e0125827. doi: 10.1371/journal.pone.0125827.
44. Islam MM, Nasrin T, Walther BA, et al. Prediction of sepsis patients using machine learning approach: a meta-analysis. Comput Methods Programs Biomed. 2019;170:1–9. doi: 10.1016/j.cmpb.2018.12.027.
45. Guyatt GH, Oxman AD, Santesso N, et al. GRADE guidelines: 12. Preparing summary of findings tables-binary outcomes. J Clin Epidemiol. 2013;66(2):158–172. doi: 10.1016/j.jclinepi.2012.01.012.