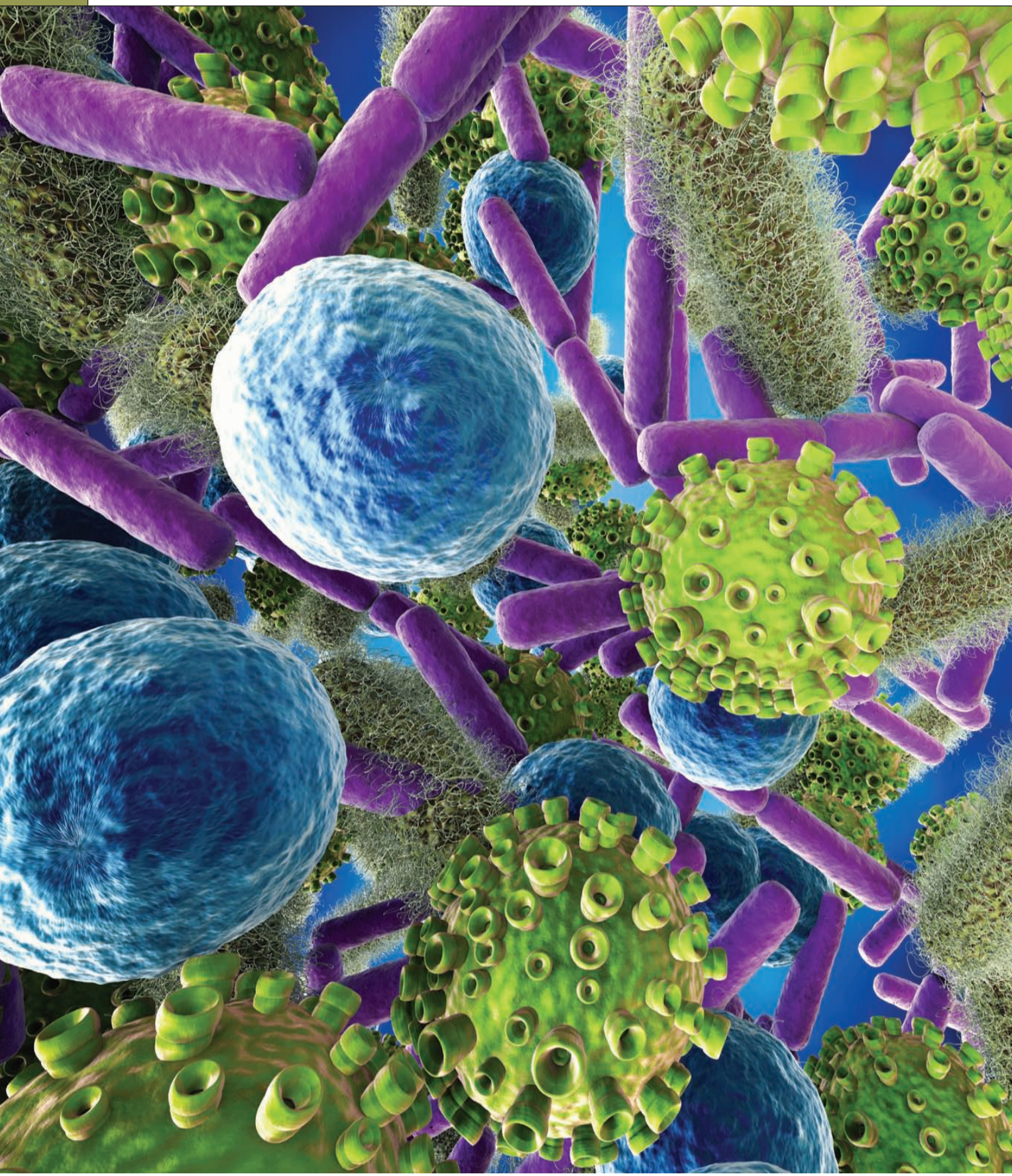

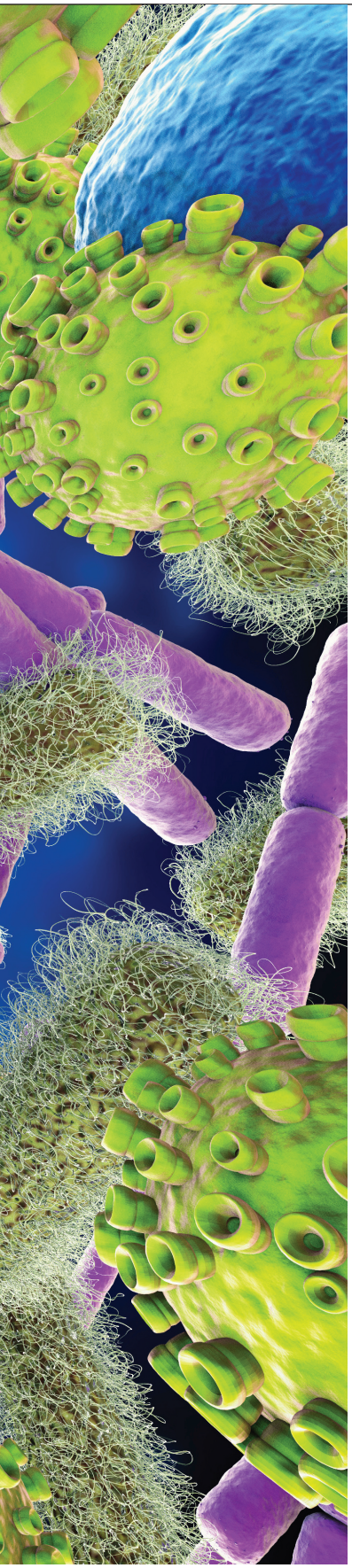

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Evidence-based updates to the 2021 Surviving Sepsis Campaign guidelines

Part 2: Guideline review and clinical application

Abstract: NPs should be prepared to screen for sepsis, initiate treatment, and optimize care for sepsis survivors. The 2021 Surviving Sepsis Campaign guidelines offer best practices for identification and management of sepsis and septic shock. This article, second in a 2-part series, presents evidence updates and discusses implications for NPs.

By Karen D. Lehman, DNP, APRN-BC

Sepsis may be diagnosed in any healthcare setting, and NPs must be prepared to recognize the symptoms and promptly initiate sepsis guidelines. Additionally, NPs often treat postsepsis survivors, and these patients carry their own unique set of complications. In 2021, the Surviving Sepsis Campaign (SSC) published updated sepsis care guidelines.[1] These recommendations were meant to offer guidance for providers caring for acutely ill hospitalized patients with sepsis or septic shock.[1] This article is the second part of a two-article series. The first article reviewed the history of the sepsis guidelines and described new understandings in pathophysiology and diagnostics.[2] This article examines the 2021 SSC guidelines and confers implications for NPs.

Guideline review and updates

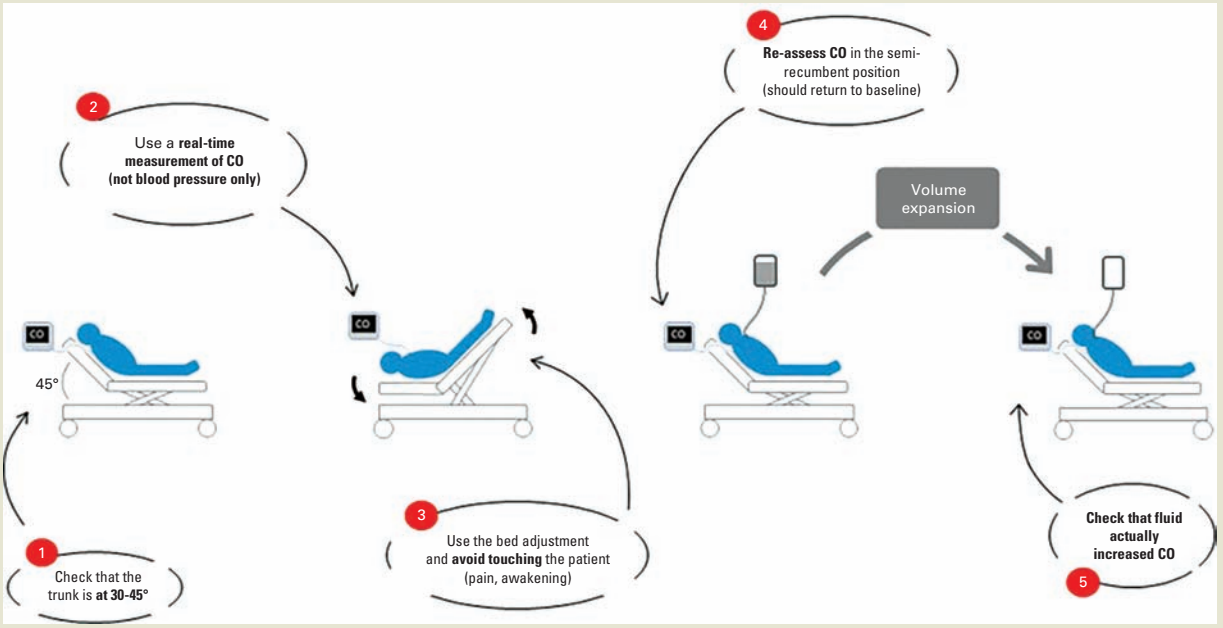
The 2021 SSC guidelines recognize that sepsis remains a highly unique process, and the clinician must consider each individual's characteristics in order to provide patient-centered care.[1] While many of the 2021 recommendations are similar to previous guidelines, there are notable differences in screening, assessment, treatment, and promoting postsepsis care.

Screening. At this time, no single perfect test or screening tool for sepsis exists. The guidelines offer quick Sequential Organ Failure Score (qSOFA) and systemic inflammatory response syndrome (SIRS) criteria as screening examples.[1]

The qSOFA is positive when at least two of the following are present: systolic BP of 100 mm Hg or less, respiratory rate of 22 breaths/minute or greater, and a Glasgow Coma Score less than 15. The

Keywords: sepsis, septic shock, Surviving Sepsis Campaign guidelines

Passive leg raise



Practical rules for performing passive leg raising. Abbreviation: CO, cardiac output.

Source: Monnet X, Shi R, Teboul JL. Prediction of fluid responsiveness. What's new?. *Ann Intensive Care.* 2022;12(1):46. Published 2022 May 28. doi:10.1186/s13613-022-01022-8.

2021 guidelines advise against using qSOFA as a single screening tool due to poor sensitivity.[1]

The SIRS criteria combined with suspected infection should alert the NP to potential sepsis when two or more of the following are present: hyperthermia of greater than 38.0° C (100.4° F) or hypothermia less than 36° C (96.8° F), heart rate greater than 90 beats/minute, leukocytosis greater than 12,000/mcL or leukopenia less than 4,000/mcL, or tachypnea greater than 20 breaths/minute.[3] As discussed in the previous article, SIRS is a common tool but has been criticized for poor specificity.[2]

More than one screening tool may be utilized based on institutional performance improvement efforts, recognizing that these are screening tools rather than diagnostic tests, and a negative result may not rule out sepsis.[1] Hospitals and affiliated clinics should promote a standardized sepsis plan for screening and interdisciplinary actions for consistent and outcome-driven sepsis management.[1,4]

Assessment. The authors of the guideline suggest using hemodynamic monitoring parameters to assess fluid status.[1] Dynamic parameters include response to a passive leg raise or response to a fluid bolus using echocardiography, pulse pressure variation, stroke volume, or stroke volume variation. The passive leg raise simulates a fluid challenge by shifting about 300 mL of venous blood from the lower body toward the right heart, allowing the clinician to challenge preload without administering I.V. fluids (see *Passive leg raise*).[5,6] A positive passive leg raise equals at least 10% increase in stroke volume.[5,6] Using a passive leg raise to assess stroke volume has been found to result in less I.V. fluid resuscitation and reduced risk of respiratory and renal failure.[7]

If hemodynamic monitoring is not offered, the clinician may opt to evaluate capillary refill time (CRT), mottling, and skin temperature, in conjunction with downward trending lactate measurements, to evaluate the efficacy of fluid administration.[1] CRT was noted to be an effective assessment tool in the early hours of septic shock, and normal CRT associated with less organ dysfunction and mortality than abnormal CRT.[8] For these reasons, the SSC guideline suggests using

CRT to guide resuscitation, along with lactate levels.[1] Lactate is the most commonly measured biomarker in sepsis, though many nonsepsis conditions can also cause lactic acidosis. Lactate was discussed in detail in part one of this article series.[2]

Treatment.

Hemodynamics. During resuscitation, crystalloid fluids have traditionally been recommended. Since the 2016 SSC guidelines, however, additional studies on choice of crystalloids emerged, supporting use of balanced crystalloids, such as lactated Ringer solution, over 0.9% sodium chloride solution. Possible adverse reactions to 0.9% sodium chloride solution include hyperchloremia and metabolic acidosis, increased cytokine secretion, and renal vasoconstriction.[9] Subsequent studies on balanced solutions support reduced hospital mortality and fewer vasopressor- and ventilator-dependent days compared to patients receiving 0.9% sodium chloride solution.[9,10]

The exact ideal amount of fluids remains unknown, given a lack of prospective trials. However, as referenced in the guidelines, many studies have demonstrated that approximately 30 mL/kg fluid resuscitation is associated with reduced mortality and reduced ICU length of stay.[1] The SSC guideline authors recognize the risk of fluid overload and recommend that dynamic measures of organ perfusion be utilized to avoid both under- and overresuscitation.[1] In addition, excessive I.V. fluids may damage vascular integrity, further compromising organ dysfunction.[11] If a large volume of crystalloids is administered, I.V. albumin administration may be considered.[1]

The mean arterial pressure (MAP) goal during sepsis resuscitation is 65 mm Hg, though more studies are needed to determine the optimal MAP target.[12] Higher MAP achieved with vasopressors was associated with a greater risk of atrial fibrillation without improvement in survival.[1] Another study found that "permissive hypotension" with a MAP target of 60-65 mm Hg did not result in a significant difference in 90-day mortality.[13] While a central line is preferred for vasopressor administration, the 2021 guidelines suggest starting vasopressors peripherally in a vein in or proximal to the antecubital fossa for less than 6 hours if central venous cannulation is delayed.[1]

The 2021 guidelines also offer best practice statements on vasopressor selection. Norepinephrine continues to be the first-line vasopressor choice.[1] If a MAP of 65 mm Hg is not achieved with norepinephrine, vasopressin should be added instead of increasing the norepinephrine dose beyond 0.5 mcg/kg/min.[1] If hypotension persists with dual norepinephrine and vasopressin use, the authors suggest adding epinephrine.[1] Angiotensin II, of which a synthetic human preparation recently became available for clinical use, may have a role as an adjunct vasopressor.[1] For patients with septic shock and ongoing vasopressor requirements, I.V. corticosteroids are suggested.[1] Further studies on optimal combinations of vasopressors in septic shock are needed.

Antibiotic administration. Early initiation of antibiotics (within 1 hour) is an integral part of sepsis care and part of the SSC guidelines. Studies have shown that prompt antibiotic administration reduces mortality, and each hour delay cumulatively increased the odds of in-hospital mortality by 1.04 to 1.16 and of 1-year mortality by 1.10.[1,14-16] The clinician, however, also must consider potential harms, not only for patients with a sepsis mimicker, but also risks associated with antibiotics in general, such as allergic reactions, organ injury, antimicrobial resistance, and *Clostridioides difficile* infection.[1] Previous guidelines recommended to start broad-spectrum antimicrobials to cover all suspected pathogens. The 2021 guidelines specify that if methicillin-resistant *Staphylococcus aureus* is suspected, clinicians should prescribe antibiotics tailored for coverage.[1] Likewise, the authors suggested that antifungals be prescribed for those at high risk for fungal infection, such as patients who are immunocompromised, those with specific genetic mutations, or environmental factors including malnutrition, poor hygiene, environmental conditions, chemical exposure, and use of immunosuppressive agents or antibiotics.[1,17] Viral infections do not typically result in sepsis, though sepsis from a viral etiology has increased secondary to SARS-CoV-2 infection.[18] There are specific COVID-19 guidelines published by the SSC, which may be found on the SSC website at www.sccm.org.[19] There are no recommendations on antiviral use in the 2021 guidelines.[1] Additional situations are addressed in the sepsis guidelines, such as management of those at risk for multidrug-resistant organisms. If an alternate cause of illness other than infection is found or highly suspected, or if the patient is not in shock and has a low likelihood of infection, the authors advise discontinuing or deferring antimicrobials while monitoring the patient closely.[1]

Clinical vignette: vital signs

Vital sign	Measurement
Temperature	39.1° C (102.4° F)
Heart rate	152 bpm
Respiratory rate	36 breaths/minute
BP	102/58 mm Hg
Mean arterial pressure	73 mm Hg
Oxygen saturation	91% on room air

Respiratory care. Many of the remaining guidelines focus on care of the patient with septic shock, including many detailed recommendations on ventilation management. New to the guidelines is that for patients with hypoxia without hypercapnia who do not require invasive ventilator support, high-flow nasal oxygen therapy versus noninvasive ventilation is now suggested, as studies have demonstrated improved survival.[1] The 2021 guidelines also introduce a suggestion for venovenous extracorporeal membrane oxygenation for those with sepsis-induced severe acute respiratory distress syndrome.[1]

Postsepsis care. After sepsis, one third of patients die within the year, half recover, and about 17% contend with long-term impairments.[20-23] Limitations can range from functional decline in activities of daily living, cognitive deterioration, and higher risk of anxiety, posttraumatic stress disorder, or depression.[20-23] Sepsis survivors require hospitalization for recurrent infections more frequently than nonseptic patients.[20-23] Studies have also shown sepsis survivors may have progressive worsening in existing diseases, immunosuppression, and lingering organ injury.[20-23]

Clinical vignette: abnormal ED labs

Lab	Value
White blood cell count	2.8/mcL
Bands	28%
Lactate	4.3 mmol/L
Anion gap	18 mEq/L
Carbon dioxide	12 mEq/L
Creatinine	2.4 mg/dL
Glucose	250 mg/dL
Influenza A H3 PCR	Positive

The 2021 guidelines address postsepsis care in more detail. Postsepsis syndrome and sepsis education is suggested while the patient is in the hospital and in the outpatient setting.[1] Additionally, screening for socioeconomic stressors, which increase sepsis risk, should be conducted, and referrals for appropriate therapies should be made.[24-26] Postsepsis management should emphasize identification of new-onset cognitive, mental, and physical issues with referral to peer support groups and physical, occupational, speech, and/or psychological therapy as indicated; evaluating and adjusting chronic medications in relation to progression of symptoms or organ failure as a result of sepsis; and monitoring for conditions that could be appropriately treated in the outpatient setting, such as organ failure, aspiration, and infection.[1,20] NPs should also be prepared to discuss palliative management with patients and families.[1,20]

The foundation of sepsis treatment includes early identification followed by prompt therapy with fluid resuscitation, early antibiotic use, and source control. The recommendations in the 2021 SSC guidelines encompass more than the individual's pathophysiologic response, taking multiple other factors into account to facilitate thorough care. NPs are well versed in caring for the whole patient and these guidelines may be translated to multiple patient scenarios.[27]

Clinical vignette

MV is a 52-year-old male who is unemployed and uninsured and has a past medical history of type 2 diabetes mellitus, hypertension, hyperlipidemia, depression, and class III obesity. He presented to the ED for a 2-day history of fever and cough (see Clinical vignette: vital signs*). Since he met three SIRS screening criteria, the sepsis order set was initiated, including labs, blood cultures, and alerting the ED NP (see* Clinical vignette: abnormal ED labs*). The ED NP noted that MV had a regular but tachycardic heart rate, tachypnea, crackles in the right upper lobe, trace extremity edema, and a CRT of 5 seconds. A chest X-ray was ordered (see* Clinical vignette: chest X-ray*). Ideal body weight was 80 kg, equating to a recommended I.V. fluid bolus of 2,400 mL. Due to concerns for concomitant heart failure on exam, however, only 1 L of 0.9% sodium chloride solution was prescribed. The ED NP prescribed appropriate time-sensitive oseltamivir for influenza A as well as ceftriaxone and azithromycin for pneumonia.[28] After acetaminophen and I.V. fluids, his heart rate improved to 120 beats per minute, but MAP*

decreased to 62 mm Hg. The remainder of his fluid bolus was prescribed. ICU admission was preferred, though the hospital had no available ICU beds. Numerous attempts were made to transfer the patient to another facility for ICU admission, however, none of the outside hospitals were accepting transfers. He was subsequently admitted to the medical unit at the local hospital. By the time of admission, his MAP had improved to 67 mm Hg.

The hospitalist NP identified ongoing hypotension with MAP of 59 mm Hg. He was diagnosed with septic shock. Due to hospital policy, vasopressors could not be administered to patients outside of the ED or ICU. Therefore, an additional liter of 0.9% sodium chloride solution was prescribed, with resolution of hypotension. Lactate trended down from 4.3 to 2.3 mmol/L. After 12 hours, blood cultures were positive for Streptococcus pneumoniae. *An infectious disease consult was ordered; they recommended continuing current treatments and discharging home on cefdinir to complete a 14-day course and on oseltamivir to complete a 5-day course. Because of the patient's uninsured status, the social worker was consulted and arranged reduced payments. Physical therapy was consulted due to weakness and recommended home health services which MV declined. MV was discharged home after a 4-day hospital stay. Written information on his hospital diagnoses was provided. His primary care NP was apprised of his hospital course, social concerns, and risk for postsepsis syndrome.*

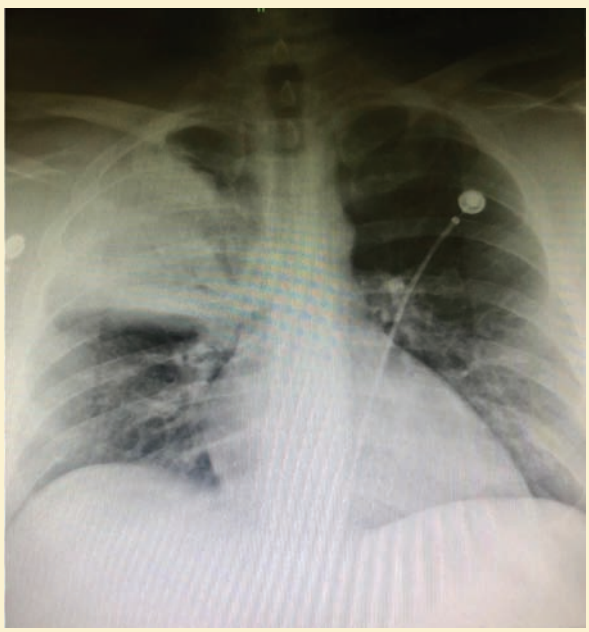
Discussion and follow-up

MV was immediately recognized as a sepsis risk based on SIRS screening criteria while in triage. His care may have been delayed if his qSOFA score of 1 had been the only tool utilized. SSC guidelines call for administration of I.V. antibiotics within 60 minutes; in MV's case, antibiotics were delayed to 90 minutes attributed to temporary, hospital-wide staffing shortages. Prompt antibiotic administration has been shown to reduce mortality; and the longer the delay, the increased odds of mortality.[15,29] An interdisciplinary ED sepsis huddle may have expedited antibiotic administration.[4,30]

The ED NP hesitated on initially prescribing the full 30 mL/kg I.V. fluid bolus, based on concerns for heart failure. This is not uncommon: patients with chronic conditions such as heart failure are less likely to receive the full fluid bolus.[31] However, no differences in renal, hemodynamic, or respiratory functions were seen between conservative versus usual care fluid management in patients with sepsis.[32] Recent studies demonstrate that 30 mL/kg fluid resuscitation does not increase the odds of intubation or mortality, even among patients with liver, heart, or renal failure.[33,34] The SSC guidelines recommend administering the 30 mL/kg fluid bolus within the first 3 hours.[1] Given MV's hypotension, the ED NP was correct in prescribing the rest of the bolus, which subsequently was given within 3 hours of recognition. With a body mass index over 30, it is acceptable to prescribe crystalloids based on ideal body weight, and studies to date have not shown any significant difference in mortality in patients who receive an adjusted fluid bolus.[35-38] However, the selection of crystalloid did not reflect the updated guidelines.[1] Rather, the ED NP prescribed 0.9% sodium chloride solution, which echoed the hospital culture norms. Given his acidotic state, a balanced crystalloid solution would have been preferred. A change in practice was recommended by the treating NP to the hospital sepsis committee based on current SSC guidelines.

At the time of MV's hospitalization, other hospitals were on diversion for admissions due to COVID-19. This negatively affected the available care for the patient. With persistent hypotension after fluid resuscitation, the hospitalist NP recognized that norepinephrine was indicated. However, given the transfer dilemma,

Clinical vignette: chest X-ray



Portable chest X-ray showing a right upper lobe infiltrate.
Used with permission of NMC Health.

the hospitalist NP was unable to prescribe vasopressors, as the patient was on the medical unit. With fluid resuscitation, his lactate decreased from 4.3 to 2.3 mmol/L and goal MAP was attained. The NP recognized, however, that with I.V. fluids, there were additional risks, such as fluid overload. If MV remained hypotensive, the hospitalist NP was prepared to take the matter to the administrator on call and recommend an exception to the policy. While hemodynamic monitoring was unlikely outside of the ICU, the hospitalist NP knew that vasopressors could be temporarily administered through a peripheral I.V. site. Unfortunately, placement in the medical unit rather than the ICU prevented measurement of stroke volume to assess fluid responsiveness and perfusion status.

MV had increased risk of poorer outcomes and recurrent sepsis given his uninsured status.[39,40] Social work was consulted, and they investigated insurance options and secured funding to cover the cost of oseltamivir and cefdinir. The patient's underlying chronic medical conditions placed him at higher risk of postsepsis syndrome and hospital readmission. His primary care NP should provide ongoing education about his health conditions and recovery process and consider referral to physical therapy if his weakness persists.

Application to practice

Regardless of practice setting—clinic, community, ED, or hospital—it behooves all NPs to apply institutionally approved sepsis screening tools and be prepared to implement emergent treatment. Sepsis occurs in both the outpatient and inpatient setting. Ten percent of patients with sepsis requiring hospitalization were seen in clinic within 1 day of admission, signifying the importance and potential for early treatment.[41] For home health patients, a sepsis-screening protocol increased communication with the patient's primary care provider, which promotes early intervention and admission avoidance.[42] In the ED, working as part of an interdisciplinary team reduces sepsis mortality.[4,30] NPs often bridge the gap between several healthcare disciplines and administrative personnel, which allows opportunities to provide guidance and influence policy change. Of note, the new guidelines contain other recommendations not covered in this article, such as recommendations about the use of steroids, glucose control, nutrition, and so on. Providers are encouraged to review the new sepsis guidelines in its entirety.[1]

Conclusion

Despite updated evidence and knowledge surrounding the pathophysiology of sepsis, the treatment cornerstones remain the same: early recognition, fluid resuscitation, and prompt administration of antibiotics. The 2021 SSC guidelines provide best practice recommendations for sepsis management, and while the emphasis is placed on emergent and acute care, sepsis survivors may also benefit from improved follow-up. NPs have the opportunity and are well suited to improve patient outcomes through prompt detection, early intervention, appropriate posthospitalization care, and dissemination of knowledge. NP

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Karen D. Lehman is a hospitalist NP and PRN ED NP at NMC Health in Newton, Kan., an ED NP with Docs Who Care based in Olathe, Kan., and a hospice NP with Harry Hynes Memorial Hospice in Wichita, Kan.

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