A Review of the Revised Sepsis Care Bundles

The rationale behind the new definitions, screening tools, and treatment guidelines.

ABSTRACT: Sepsis is an extreme response to infection that can cause tissue damage, organ failure, and death if not treated promptly and appropriately. Each year in the United States, sepsis affects more than 1.5 million people and kills roughly 250,000. Prompt recognition and treatment of sepsis are essential to saving lives, and nurses play a critical role in the early detection of sepsis, as they are often first to recognize the signs and symptoms of infection. Here, the authors review recent revisions to the sepsis care bundles and discuss screening and assessment tools nurses can use to identify sepsis in the ICU, in the ED, on the medical–surgical unit, and outside the hospital.

Keywords: quick Sequential Organ Failure Assessment (qSOFA), sepsis, sepsis care bundles, sepsis treatment guidelines, septic shock, Sequential Organ Failure Assessment (SOFA), Surviving Sepsis Campaign, Third International Consensus Definitions for Sepsis and Septic Shock

Sepsis, an extreme response to infection that can cause tissue damage and organ failure if not treated promptly and appropriately,[1] is a leading cause of death worldwide.[2] Projections based on hospital data alone suggest that, globally, there are more than 31 million sepsis cases and 5 million deaths from sepsis each year.[2] However, disease burden and death rates may be higher than reported since, in less developed countries where there is a higher prevalence of infectious disease, sepsis epidemiological data are lacking.[2] Each year in the United States, sepsis affects more than 1.5 million people and kills roughly 250,000.[3] According to the Agency for Healthcare Research and Quality, sepsis accounts for more hospital expenditures than acute myocardial infarction and acute cerebrovascular disease combined, and septicemia was the most expensive condition treated in the United States in 2013, consuming a staggering $23.7 billion.[4]

The reported incidence of sepsis continues to rise.[5] Possible explanations include the increase in antibiotic-resistant infections, the growing use of immunosuppressive medications, improved coding of sepsis as a result of automatic calculations of clinical variables in electronic health records (EHRs), improved diagnosis of sepsis because of greater awareness, and the aging of the U.S. population with the subsequent accompanying surge in chronic disease.[6,7] In countries with advanced health care delivery systems, people over age 65 account for 60% of sepsis cases and 75% of sepsis-related deaths.[8] According to the Centers for Disease Control and Prevention, seven in 10 patients with sepsis recently received health care services or had chronic diseases that required frequent medical care.[3]

Prompt recognition and treatment of sepsis are essential to saving lives. Early goal-directed therapy has been shown to improve patient outcomes and decrease

By Donna Lester, DNP, MS, ACNP-BC, CC-CNS, Tonja Hartjes, DNP, ACNP-BC, FNP-BC, CCRN-CSC, FAANP, and Amanda Bennett, DNP, AG-ACNP-BC

mortality by more than 15% compared with standard care.[9,10] In response to the landmark study by Rivers and colleagues, in which in-hospital mortality rates were lower in patients receiving early goal-directed therapy compared with those receiving usual care (30.5% versus 46.5%),[10,11] the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) recommended early goal-directed therapy for sepsis and, in 2002, launched the Surviving Sepsis Campaign (SSC) to improve sepsis care. The SSC guidelines were first published in 2004 and have undergone three revisions, most recently in 2016.[12] (See Table 1 for a summary of the 2016 guidelines.[12]) As the 2016 SSC guidelines were being developed, the SCCM and ESICM also convened a task force to evaluate and update sepsis definitions and clinical criteria based on advances in the understanding of sepsis pathobiology and epidemiology.[5] In February 2016, this task force published the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3),[5] which introduced new screening, assessment, and management strategies.

Nurses play a critical role in the early detection of sepsis, as they are often first to recognize signs and symptoms of infection. As such, nurses can ensure that patients are screened promptly and treated appropriately. This article reviews the revised definitions of sepsis and septic shock; reviews screening and assessment tools used to identify sepsis in the ICU, in the ED, on the medical–surgical unit, and outside the hospital; describes sepsis diagnostic criteria, as well as the care bundles at the center of the SSC treatment guidelines; and discusses the nursing implications associated with sepsis and its management.

Fluid resuscitation is central to the management of sepsis. Photo © Phanie / Alamy Stock Photo.

EVOLUTION OF SEPSIS DEFINITIONS AND SCREENING TOOLS

The first definitions developed to guide sepsis management were introduced in 1991 and based on the idea that sepsis was a systemic inflammatory response syndrome (SIRS) characterized by two or more of the following[13]:

- temperature above 38°C or below 36°C
- heart rate above 90 beats per minute
- respiratory rate above 20 breaths per minute or partial pressure of arterial carbon dioxide below 32 mmHg
- white blood cell count greater than 12,000/mm^3 or less than 4,000/mm^3, or the presence of immature neutrophils ("bands") exceeding 10%

In the presence of infection, SIRS was identified as *sepsis*, and in the presence of multiple organ dysfunction syndrome, hypoperfusion, or hypotension, the syndrome was described as *severe sepsis*.[13] The SIRS criteria met early opposition, as these same physiologic criteria are often observed in such noninfectious conditions as pancreatitis, burns, ischemia, trauma, and hemorrhagic shock.[13]

Sepsis-3. Over the past 27 years, as more was discovered about sepsis-induced biological changes, sepsis diagnostic criteria were expanded; however, sepsis definitions remained largely unchanged until Sepsis-3.[5] In 2016, the Sepsis-3 task force determined that the term *sepsis* should be defined as "life-threatening organ dysfunction" brought on by a "dysregulated" response to infection, and that the term *septic shock* should be used to describe "a subset of sepsis" in which "circulatory, cellular, and metabolic abnormalities" substantially increase the risk of death over that associated with sepsis alone. Septic shock can be identified in patients who require vasopressor therapy to maintain a mean arterial pressure (MAP) of at least 65 mmHg, or have a serum lactate level greater than 2 mmol/L (18 mg/dL), despite adequate fluid resuscitation.[5] The task force deemed the term *severe sepsis*

Table 1. Surviving Sepsis Campaign 2016 Guidelines: Summary of Recommendations and Best Practices[12]

Aspects of Care	Recommendations
Initial resuscitation goals	• Give 30 mL/kg IV crystalloid fluid within the first 3 hours. • Give additional fluids based on frequent reassessment of hemodynamic status (via a thorough examination and evaluation of temperature, heart rate, respiratory rate, blood pressure, arterial oxygen saturation, and urine output, as well as other available noninvasive or invasive monitoring). • Use dynamic rather than static variables to predict fluid responsiveness, if available.[a] • Use 65 mmHg as an initial target MAP in patients with septic shock who require vasopressors. • Guide resuscitation to normalize lactate, a marker of tissue hypoperfusion, in patients with elevated lactate levels.[a]
Antimicrobial therapy	• Initiate empiric broad-spectrum IV antimicrobial therapy within 1 hour of identifying sepsis or septic shock. • If combination therapy is used for septic shock, discontinue it within the first few days in response to clinical improvement or evidence of infection resolution (7 to 10 days of treatment is adequate for most serious infections associated with sepsis or septic shock[a]). • Narrow therapy selection once culture and sensitivities are established or adequate clinical improvement occurs. • DO NOT use sustained systemic antimicrobial prophylaxis in patients with severe inflammatory, noninfectious conditions (such as severe pancreatitis or burn injury). • Assess patients daily for deescalation of antimicrobial therapy (for example, measure procalcitonin levels to support discontinuing antibiotics in patients who subsequently demonstrate little evidence of infection[a]).
Fluid therapy	• Crystalloids are the fluid of choice for initial resuscitation and subsequent IV volume replacement in patients with sepsis and septic shock. • Use albumin in addition to crystalloids for initial resuscitation and subsequent IV volume replacement when patients require substantial amounts of crystalloids.[a] • DO NOT use hydroxyethyl starches for IV volume replacement.
Vasoactive medications	• Norepinephrine should be the first-choice vasopressor. • Add vasopressin (≤ 0.03 U/min) to norepinephrine to raise MAP to target or to reduce norepinephrine dosage. (Epinephrine may be substituted for norepinephrine to raise MAP to target.[a]) • Consider using dopamine as an alternative to norepinephrine in patients at low risk for tachyarrhythmias or bradycardia.[a] • All patients receiving vasopressors should have an arterial line.[b]
Corticosteroid use	• DO NOT use IV hydrocortisone to treat septic shock if fluid resuscitation and vasopressor therapy restores hemodynamic stability. If hemodynamic stability is not restored, IV hydrocortisone may be delivered at a dose of 200 mg/day.[a]
Blood products	• Transfuse red blood cells only if hemoglobin level is < 7 g/dL in the absence of extenuating circumstances such as myocardial ischemia, severe hypoxemia, or acute hemorrhage. • DO NOT use erythropoietin to treat anemia in sepsis. • Use of fresh frozen plasma is not recommended to correct coagulation issues in the absence of bleeding or planned invasive procedures.[b] • Transfuse platelets prophylactically when counts are < 10,000/mm^3 in the absence of apparent bleeding or < 20,000/mm^3 if the patient is at significant risk for bleeding.[b]
Mechanical ventilation	In adults with sepsis-induced ARDS: • Use a target tidal volume of 6 mL/kg of predicted body weight. • Use an upper limit goal for plateau pressures of 30 cm H_2O over higher plateau pressures in severe cases. • Use higher PEEP over lower PEEP. • Use prone over supine positioning and a PaO_2:FiO_2 of < 150 mmHg. • DO NOT use high-frequency oscillatory ventilation. • There is currently no recommendation regarding the use of noninvasive ventilation. • Use neuromuscular blocking agents for no more than 48 hours with a PaO_2:FiO_2 of < 150 mmHg. • Use a conservative fluid strategy in the absence of hypoperfusion. • DO NOT use β_2-agonists in the absence of bronchospasm.

Table 1. Continued

Glucose control	• Use insulin to manage blood glucose when two consecutive glucose levels are > 180 mg/dL. • Monitor blood glucose every 1–2 hours in patients receiving insulin until glucose levels and insulin infusion rates stabilize, and every 4 hours thereafter.
VTE and stress ulcer prophylaxis	• Use low-molecular-weight heparin rather than unfractionated heparin to treat VTE in patients receiving insulin. • Use both pharmacologic and mechanical VTE prophylaxis, but if pharmacologic VTE prophylaxis is contraindicated, use mechanical VTE prophylaxis alone.[a] • Administer stress ulcer prophylaxis (such as proton pump inhibitors or histamine-2 receptor antagonists[a]) to patients at risk for gastrointestinal bleeding.

ARDS = acute respiratory distress syndrome; FiO_2 = fractional inspired oxygen; MAP = mean arterial pressure; PaO_2 = partial pressure of arterial oxygen; PEEP = positive end-expiratory pressure; VTE = venous thromboembolism.
[a]Weak recommendation, low quality of evidence.
[b]Weak recommendation, very low quality of evidence.

redundant, as it was often used interchangeably with the term *sepsis*, and they unanimously agreed that SIRS screening criteria were unhelpful, being nonspecific and overly sensitive.[5] In earlier studies, SIRS criteria had identified 87% of ICU patients and 50% of medical patients as having sepsis.[14, 15] Sepsis-3 thus no longer supports use of the term *severe sepsis* or use of the SIRS criteria as a screening tool for sepsis.

New screening tools. For ICU sepsis screening, the Sepsis-3 task force recommended use of the Sequential Organ Failure Assessment (SOFA) score, which had been developed to elucidate the progression of multisystem organ failure and evaluate the effects of various therapies on organ dysfunction and failure.[16] For sepsis screening in non-ICU settings, they recommended use of the quick SOFA (qSOFA), an abbreviated version developed in 2016 by Seymour and colleagues.[5] In contrast to the SOFA score, the qSOFA requires no laboratory tests and can be repeated frequently, prompting further assessment of organ function, initiation or escalation of treatment, or transfer to intensive care.[5] (See *The Sequential Organ Failure Assessment (SOFA) Score*[16, 17] and *The Quick Sequential Organ Failure Assessment (qSOFA) Score*.[5, 17])

When Seymour and colleagues retrospectively reviewed data from 148,907 hospital patients with suspected infection (15,768 ICU patients and 133,139 non-ICU patients), they found that the predictive validity for in-hospital mortality of SOFA criteria was significantly greater than both the SIRS and qSOFA criteria when applied to ICU patients. Outside of the ICU, however, qSOFA had significantly greater predictive validity for in-hospital mortality than either the SIRS or SOFA criteria.[18] Likewise, an international prospective cohort study performed in 30 EDs within four European countries found that the qSOFA score was better at predicting in-hospital mortality than the SIRS criteria, supporting Sepsis-3 recommendations.[19]

Nursing assessments for sepsis should consider patients' history, risk factors, and SOFA or qSOFA criteria before determining next steps (see *Nursing Assessment for Sepsis*).

CLINICAL DECISION SUPPORT TOOLS

Clinical decision support (CDS) encompasses a variety of tools that can be integrated into the EHR to assist health care providers in making timely evidence-based decisions. Because of the need for prompt recognition and treatment of sepsis to prevent life-threatening complications, the integration of sepsis CDS into EHRs is invaluable. When coupled with protocol-driven staff response, the implementation of electronic screening tools has been shown to reduce door-to-bolus and door-to-antibiotics times by 31 and 59 minutes, respectively, in ED patients with suspected sepsis.[20] EHR sepsis screening tools have a sensitivity of 93%, a specificity of 98%, and a negative predictive value of up to 100%.[21, 22] Like that of other sepsis screening methods, however, the positive predictive value of EHR sepsis screening tools is low, ranging from 21% to 45%, highlighting the importance of clinical judgment in identifying patients with sepsis.[21, 22]

EARLY GOAL-DIRECTED THERAPY: THE SEPSIS BUNDLES

Bundles are a structured set of interventions that have consistently been shown to improve patient outcomes when performed collectively.[23] In 2004, the SSC introduced a six-hour resuscitation bundle and a 24-hour management bundle.[24] Data collected on 29,470 patients in 218 hospitals in the United States, South America, and Europe between January 2005 and June 2012 indicated that adherence to the 2004 bundles was associated with a 25% relative risk reduction in sepsis mortality rates.[25] In 2012, the SSC revised the 2004 sepsis care bundles, dropping the management bundle and dividing the resuscitation

bundle into three- and six-hour time periods to improve adherence to the SSC guidelines.[9,24] In 2015, the SSC revised the bundles again in accordance with new evidence.[26] This year, in order to treat sepsis as a medical emergency with the same degree of urgency as trauma and stroke, the SSC combined the three- and six-hour bundles into a one-hour bundle.[27] Developed "with the explicit intention of beginning resuscitation and management immediately," the one-hour bundle comprises the following[27]:

- Measure lactate level. Remeasure if initial lactate is > 2 mmol/L.
- Obtain blood cultures prior to administration of antibiotics.
- Administer broad-spectrum antibiotics.
- Begin rapid administration of 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L.
- Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥ 65 mmHg.

THE ONE-HOUR SEPSIS BUNDLE

Serum lactate is measured to assess for tissue hypoperfusion in patients who are not yet hypotensive but who are at risk for septic shock (those with tachypnea and altered mentation in the presence of suspected infection, for example). Lactate levels of 4 mmol/L or higher are associated with a mortality rate of 30%.[9] Either arterial or venous lactate samples may be used.

Blood cultures. To increase the probability of identifying the causative organism and the specific site of infection, two or more blood cultures, one drawn percutaneously and another through the current vascular access device, and any other indicated cultures (such as urine, cerebrospinal fluid, wound, or sputum) should be collected before broad-spectrum antibiotics are administered, provided it does not delay antibiotic administration by more than 45 minutes.[9] It should be noted that cultures are negative in more than half of patients with sepsis who are receiving empiric antimicrobial therapy when blood is drawn.[9]

Broad-spectrum antimicrobials. Appropriate broad-spectrum antimicrobial therapy has been shown to reduce mortality in patients with gram-positive and gram-negative bacteremia, as well as in those with fungal and viral infections.[9]

When the causative organism is identified, antimicrobial therapy should be narrowed to reduce the risk of resistant pathogens, toxicity, and costs.[9] The Infectious Diseases Society of America (IDSA) recommends that facilities develop clinical practice guidelines that standardize antimicrobial prescribing practices based on local epidemiology.[28] Procalcitonin levels can also be used to guide the duration of antibiotic therapy to avoid antimicrobial resistance, reduce length of stay, and lower costs.[29]

Crystalloid administration. A 30 mL/kg bolus of crystalloid IV fluids should be administered for hypotension (a systolic blood pressure below 90 mmHg) or for a lactate level of 4 mmol/L or higher.[9] Patients with sepsis may have ineffective arterial circulation due to vasodilation, resulting in poor tissue perfusion and tissue hypoxia. Administering 30 mL/kg of IV fluids will expand circulating volume and promote adequate perfusion pressure.

The Sequential Organ Failure Assessment (SOFA) Score

A clinical evaluation of the patient that includes laboratory values (bilirubin, creatinine, coagulation studies, and arterial blood gases) is needed to calculate a SOFA score. The SOFA score is most commonly used in the ICU practice setting.

The following are the abnormal physiologic SOFA parameters, each of which receives a score of 2 or higher:

- PaO_2:FiO_2, < 300 mmHg
- platelets, $< 100 \times 10^3/mm^3$
- bilirubin, ≥ 2 mg/dL
- hypotension requiring vasopressor support
- Glasgow Coma Scale score, ≤ 12
- creatinine, ≥ 2 mg/dL, or urine output < 500 mL/day

Physiologic parameters are scored from 0 (normal function) to 4 (organ failure). Each parameter is scored individually, after which a total score is derived to suggest severity of illness. The higher the cumulative score, the greater the patient's risk. A score of 2 or higher in any system indicates an elevated risk of organ dysfunction, poor outcome, or death.

An online SOFA calculator can be found at www.mdcalc.com/sequential-organ-failure-assessment-sofa-score.

FiO_2 = fractional inspired oxygen; PaO_2 = partial pressure of arterial oxygen.
Reprinted from Makic MBF, Bridges E. *Am J Nurs* 2018;118(2):34-9, based on data from Vincent JL, et al. *Intensive Care Med* 1996:22(7):707-10.[16,17]

The Quick Sequential Organ Failure Assessment (qSOFA) Score

The following are the abnormal physiologic qSOFA parameters:

- systolic blood pressure, ≤ 100 mmHg
- respiratory rate, ≥ 22 breaths per minute
- any change in mental status

Patients are assigned one point for each abnormal parameter. Non-ICU patients with a total score of 2 or 3 are considered at elevated risk for an extended ICU stay or death and should be assessed for evidence of organ dysfunction using the SOFA. An online qSOFA calculator can be found at www.mdcalc.com/qsofa-quick-sofa-score-sepsis.

Reprinted from Makic MBF, Bridges E. *Am J Nurs* 2018;118(2):34-9, based on data from Singer M, et al. *JAMA* 2016;315(8):801-10.[5, 17]

Controversy over volume resuscitation. Some have raised concerns that following SSC resuscitation recommendations may result in volume overload, especially in patients with congestive heart failure, end-stage renal disease, or acute respiratory distress syndrome. In one study of more than 400 adult ICU patients receiving treatment for sepsis or septic shock, 67% showed evidence of volume overload on day 1 following initial fluid resuscitation and 48% had persistent fluid overload into day 3.[30] The importance of fluid administration, however, is underscored by the fact that the mortality rate of patients with sepsis and hypotension is nearly 37% and increases to more than 46% if combined with a lactate level of 4 mmol/L or higher.[31]

New York State has mandated public reporting of sepsis survival and bundle compliance since 2013, and the subsequent reductions in in-hospital mortality should lead other states to follow suit.

Vasopressors should be administered to patients with persistent hypotension that does not respond to fluid resuscitation (those who are unable to maintain a MAP of at least 65 mmHg after receiving 30 mL/kg of crystalloid IV fluids).[9] If the patient has life-threatening hypotension, vasopressor therapy should not be withheld until delivery of the 30 mL/kg bolus is completed. Norepinephrine is the first-line vasopressor for septic shock. Epinephrine is the second-choice vasopressor and may be used in addition to or instead of norepinephrine at the discretion of the provider.[9] Phenylephrine has been found to reduce splanchnic blood flow,[32] and therefore is not recommended in the treatment of septic shock unless norepinephrine is triggering serious arrhythmias, cardiac output is elevated, and blood pressure is persistently low, or inotropes or vasopressors and low-dose vasopressin fail to raise MAP sufficiently.[9] Vasopressin and dopamine are not considered first-line agents, but may be used as salvage therapy.[9] An experimental angiotensin II medication has shown promise in a recent trial after improving blood pressure and reducing doses of concomitant vasopressors within three hours in patients with vasodilatory shock.[33]

Ongoing critical care assessments. *Noninvasive hemodynamic monitoring.* The 2012 SSC guidelines called for invasive hemodynamic monitoring to reassess volume status and tissue perfusion. This recommendation was revised in 2015 to include noninvasive measures, such as a repeated focused examination (after initial fluid resuscitation) incorporating vital sign assessment; cardiopulmonary, capillary refill, pulse, and skin findings; or bedside cardiovascular ultrasound and dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge. These changes were made after three trials did not demonstrate the superiority of a central venous catheter to other noninvasive means.[26, 34-36]

Invasive hemodynamic monitoring. Based on provider discretion, in the presence of persistent hypotension that does not respond to crystalloid IV fluid resuscitation, a central venous catheter may be inserted to monitor both central venous pressure and central venous oxygen saturation. Although invasive hemodynamic monitoring was recommended for patients with a lactate level above 4 mmol/L in earlier SSC

guidelines, the 2016 guidelines suggest using dynamic measures instead, which have demonstrated greater accuracy.[12] These include passive leg raises, stroke volume measurement, and variations in systolic pressure or pulse pressure on ventilators.

Remeasure lactate. To evaluate peripheral tissue perfusion, serum lactate should be remeasured after delivery of the 30 mL/kg bolus of crystalloid IV fluids. A serum lactate level > 2 mmol/L despite adequate volume resuscitation, combined with vasopressor requirements to maintain a MAP of at least 65 mmHg, is associated with a hospital mortality rate above 40% and should prompt further diagnostic evaluation and therapeutic intervention to improve tissue perfusion.[5]

The one-hour bundle was developed to treat sepsis as a medical emergency with the same degree of urgency as trauma and stroke.

GOVERNMENTAL MEASURES TO PREVENT SEPSIS

Health care providers and hospitals are held accountable for patient outcomes. The Centers for Medicare and Medicaid Services (CMS) provide greater reimbursement for better performers, assessing a 1% payment reduction to hospitals ranking in the lowest quartile with respect to preventable hospital-acquired infections, including sepsis.[37] In October 2015, sepsis became a Joint Commission core measure; hospital reimbursement is now tied to adherence to the SSC sepsis bundles.[38] All of the SSC bundle elements must be met to ensure adherence and improve patient outcomes. The Institutes of Medicine (IOM)—now known as the Health and Medicine Division of the National Academies of Sciences, Engineering, and Medicine—Joint Commission, CMS, and Institute for Healthcare Improvement have called for increased transparency regarding practice outcomes.[39] The New York State Department of Health has mandated public reporting of sepsis survival and bundle compliance since 2013, and the subsequent reductions in in-hospital mortality[40] should lead other states to follow suit. By implementing evidence-based practice guidelines and standards to improve patient safety and clinical outcomes, hospitals can provide clinically effective care, thereby minimizing the incidence of sepsis and readmissions, while increasing reimbursement.

LEADING THROUGH EVIDENCE-BASED PRACTICE

The IOM has called for 90% of clinical decisions and interventions to be evidence based by the year 2020.[41] Achieving this goal will require health care providers to identify gaps in translating research to clinical practice and to implement proven decision-making tools, protocols, and policies. Integrating sepsis CDS tools into EHRs promotes prompt recognition and treatment of sepsis.

The Modified Early Warning Score (MEWS) was developed in 2001 to identify hospitalized patients at risk for clinical deterioration. The MEWS takes into account all components of the qSOFA (systolic blood pressure, respiratory rate, and mental status), as well as heart rate and temperature.[42] Points are assigned based on values for each physiologic parameter. Scores of 5 or higher are associated with an increased

Nursing Assessment for Sepsis

Complete a comprehensive history and physical examination, considering the following:

- medical history, including such chronic diseases as diabetes, pulmonary or renal disease, malignancy, or HIV; and organ transplant, splenectomy
- surgical and procedural history
- current use of medications suggestive of immune suppression or acute illness, including antibiotics
- any recent infections
- any potential sources of infection, such as wounds, incisions, or catheter use
- recent hospitalization (within 30 days, for example)
- recent travel
- presence of risk factors, including extremes of age (adults > 65 or children), male sex, severe burn injury, recent trauma, malnutrition, alcohol use or abuse, drug abuse, low socioeconomic status, fragility, debilitation, long-term care facility residence, prolonged ICU stay
- presence of SOFA (for ICU patients) or qSOFA (for non-ICU patients) criteria

Next steps:
If the definition of sepsis is met, begin the one-hour sepsis bundle; if sepsis is not present, continue care and monitor patient for worsening of condition.

Putting It All Together: When Sepsis Is Suspected

Three scenarios illustrate the assessment of patients with suspected sepsis in the ICU, a nursing home, and a clinic.

Nursing Considerations	**Patient 1:** A 62-year-old man admitted to the ICU two days ago for respiratory failure	**Patient 2:** An 80-year-old woman in a nursing home with new-onset altered mental status	**Patient 3:** A 45-year-old man who presented to a clinic with painful urination and flank pain
History and physical exam	T: 100.6°F (38.1°C) HR: 105 beats per minute RR: 24 breaths per minute BP: 94/48 mmHg On ventilator: FiO_2, 60%; PaO_2, 75 mmHg; PaO_2:FiO_2, 125 mmHg WBC: 14 mm^3 UOP: oliguria History: COPD, recent exacerbation Medications: methylprednisolone 50 mg daily × 10 days, albuterol nebulizer every 4 hours Exam: not responsive; cool, clammy skin; rapid thread pulses, 1+; blood glucose, 187 mg/dL	T: 101.2°F (38.4°C) HR: 110 beats per minute RR: 28 breaths per minute BP: 105/50 mmHg History: bedbound, very thin and fragile, with diabetes and rheumatoid arthritis Medications: metformin 1,000 mg daily, adalimumab 80 mg injection Exam: confusion; chills; warm, dry skin; weak pulses, 1–2+; BMI, 21 kg/m^2; stage 2 sacral decubitus ulcer; blood glucose, 175 mg/dL	T: 99.9°F (37.2°C) HR: 85 beats per minute RR: 24 breaths per minute BP: 116/72 mmHg History: otherwise healthy, on metoprolol 50 mg daily for controlled hypertension Exam: alert and oriented; heart sounds, S1S2; warm, dry skin; pulses, 3+
Risk factors present?[a]	Yes • Older adult • Chronic illness with recent exacerbation • Taking immunosuppressive medication • Probable infectious source: pulmonary	Yes • Older adult • Chronic illness • Taking immunosuppressive medication • Possibly malnourished, with low BMI • Wound present	No
SOFA criteria present?	Yes, score of 9 • PaO_2:FiO_2: < 200 mmHg (score: 3) • MAP: < 70 mmHg (score: 1) • GCS: 10-12 (score: 2) • creatinine: 3.5–4.9 mg/dL (score: 3)	Not used in outpatient setting	Not used in outpatient setting
qSOFA criteria present?	SOFA criteria to be used when patient is in the ICU	Yes • RR: ≥ 22 breaths per minute • GCS: < 15	No
Symptoms of hypoperfusion present?[b]	Yes • Altered mental status • Hypotension • Hypoxemia • Oliguria • Hyperglycemia	Yes • Altered mental status • Hyperglycemia	No
Does patient meet diagnosis for sepsis?	Yes	Yes	No
What is the next step?	Begin 1-hour sepsis bundle	• Transfer to hospital • Begin 1-hour sepsis bundle	• Continue care from home • Monitor for worsening of condition

BMI = body mass index; BP = blood pressure; COPD = chronic obstructive pulmonary disease; CRF = chronic renal failure; FiO_2 = fractional inspired oxygen; GCS = Glasgow Coma Scale score; HR = heart rate; MAP = mean arterial pressure; PaO_2 = partial pressure of arterial oxygen; qSOFA = quick Sequential Organ Failure Assessment; RR = respiratory rate; SOFA = Sequential Organ Failure Assessment; T = temperature; UOP = urinary output; WBC = white blood cell count.

[a] Risk factors include young or old age, immunosuppression (such as post–organ transplant, splenectomy, HIV, chemotherapy), wounds, addictive habits, invasive catheter or IV lines, chronic illnesses (such as diabetes, COPD, CRF, malignancies, or malnutrition), debilitation, major surgery or trauma, extensive burns, and anemia.

[b] Symptoms of hypoperfusion are altered mental status, hypotension, hypoxemia (PaO_2:FiO_2 < 300 mmHg), oliguria, and hyperglycemia.

risk of death and ICU admission.[42] The MEWS has been adapted at many facilities to help nurses evaluate subtle signs of deterioration, increase use of rapid response teams, and increase nurses' confidence in their patient assessments.[43] The score can be calculated by the EHR system or manually on every shift by nursing staff. A rising MEWS should prompt nurses to consider possible sources of infection. When used appropriately in the hospital setting, the MEWS has been shown to reduce the number of code blues by as much as 50%.[43]

When used appropriately in the hospital setting, the MEWS has been shown to reduce the number of code blues by as much as 50%.

Customized sepsis screening tools can be incorporated into EHRs, using best practice advisories or components of the SOFA, qSOFA, and SIRS criteria, based on facility preferences. As nurses are at the forefront of patient care, it is important to couple such screening tools with nurse-initiated provider notification (see *Putting It All Together: When Sepsis Is Suspected*). The Society for Healthcare Epidemiology of America, in association with the IDSA, American Hospital Association, and Joint Commission, has compiled a *Compendium of Strategies to Prevent Healthcare-Associated Infections in Acute Care Hospitals*. All sections are available for download at www.shea-online.org/index.php/practice-resources/priority-topics/compendium-of-strategies-to-prevent-hais.

RESEARCH OPPORTUNITIES

The quest to determine best practices in the areas of fluid resuscitation, screening tools, and early goal-directed therapy continues to provide numerous research opportunities in the areas of fluid resuscitation, screening tool validation, and efficacy of early goal-directed therapy on mortality and adverse events.

Although more conservative fluid resuscitation than that recommended by the SSC has been shown to increase the number of ventilator-free days and to decrease ICU days, there have been no significant findings regarding reduced mortality rates.[44] Large randomized trials are needed to determine the fluid resuscitation measures that optimally affect mortality rates.

The validation of the screening tools used to identify sepsis provides another opportunity for future research. When Churpek and colleagues compared the qSOFA, SIRS criteria, MEWS, and National Early Warning Score (NEWS) in predicting in-hospital mortality and critical care transfer in non-ICU patients, they found that the qSOFA was more accurate than the SIRS criteria but less accurate than the MEWS or NEWS.[45] As this study was performed in only one academic institution, further investigation and validation is needed to increase the external validity of these screening tools.

Finally, what is the effect of early goal-directed therapy on mortality and adverse events? The Australasian Resuscitation in Sepsis Evaluation trial, as well as a meta-analysis by Rusconi and colleagues, found that early goal-directed therapy did not decrease mortality but caused no significant adverse events.[34,46] Additionally, Rusconi and colleagues found no difference in hospital mortality rates, length of required organ support, or length of hospital stay. A limitation of this meta-analysis is that the therapies administered, especially IV fluid volume, varied widely across the studies evaluated, and early antibiotic administration, which is both common practice and part of bundled early goal-directed therapy, was noted in all trials.[46] ▼

For eight additional continuing nursing education activities on the topic of sepsis, go to www.nursingcenter.com/ce.

Donna Lester is an adjunct clinical assistant professor, Tonja Hartjes is a clinical associate professor, and Amanda Bennett is an adult gerontology acute care NP, all in the Adult-Gerontology Acute Care Nurse Practitioner Program at the University of Florida College of Nursing, Gainesville. Contact author: Donna Lester, dhlester@verizon.net. *The authors and planners have disclosed no potential conflicts of interest, financial or otherwise.*

REFERENCES

1. Centers for Disease Control and Prevention. *Sepsis: basic information* 2018. https://www.cdc.gov/sepsis/basic/index.html.
2. Fleischmann C, 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):259-72.
3. Centers for Disease Control and Prevention. *Sepsis: data and reports*. 2017. https://www.cdc.gov/sepsis/datareports/index.html.
4. Torio CM, Moore BJ. *National inpatient hospital costs: the most expensive condition by payer, 2013*. Rockville, MD: Agency for Healthcare Research and Quality; 2016 May. Healthcare cost and utilization project (HCUP) statistical brief #204; https://www.hcup-us.ahrq.gov/reports/statbriefs/sb204-Most-Expensive-Hospital-Conditions.jsp.
5. Singer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315(8):801-10.
6. Gaieski DF, et al. Benchmarking the incidence and mortality of severe sepsis in the United States. *Crit Care Med* 2013;41(5):1167-74.
7. National Institute of General Medical Sciences. *Sepsis*. Bethesda, MD: National Institutes of Health; 2018 Jan. Fact sheets; https://www.nigms.nih.gov/education/pages/factsheet_sepsis.aspx.

8. Hotchkiss RS, et al. Immunosuppression in sepsis: a novel understanding of the disorder and a new therapeutic approach. *Lancet Infect Dis* 2013;13(3):260-8.
9. Dellinger RP, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 2013;41(2):580-637.
10. Rivers E, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001;345(19): 1368-77.
11. Gu WJ, et al. The effect of goal-directed therapy on mortality in patients with sepsis—earlier is better: a meta-analysis of randomized controlled trials. *Crit Care* 2014;18(5):570.
12. Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock: 2016. *Crit Care Med* 2017;45(3):486-552.
13. Bone RC, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 1992;101(6):1644-55.
14. Sprung CL, et al. An evaluation of systemic inflammatory response syndrome signs in the Sepsis Occurrence in Acutely Ill Patients (SOAP) study. *Intensive Care Med* 2006;32(3):421-7.
15. Churpek MM, et al. Incidence and prognostic value of the systemic inflammatory response syndrome and organ dysfunctions in ward patients. *Am J Respir Crit Care Med* 2015; 192(8):958-64.
16. Vincent JL, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure: on behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 1996;22(7):707-10.
17. Makic MBF, Bridges E. Managing sepsis and septic shock: current guidelines and definitions. *Am J Nurs* 2018;118(2): 34-9.
18. Seymour CW, 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):762-74.
19. Freund Y, et al. Prognostic accuracy of Sepsis-3 criteria for in-hospital mortality among patients with suspected infection presenting to the emergency department. *JAMA* 2017; 317(3):301-8.
20. Hayden GE, et al. Triage sepsis alert and sepsis protocol lower times to fluids and antibiotics in the ED. *Am J Emerg Med* 2016;34(1):1-9.
21. Alsolamy S, et al. Diagnostic accuracy of a screening electronic alert tool for severe sepsis and septic shock in the emergency department. *BMC Med Inform Decis Mak* 2014; 14:105.
22. Nguyen SQ, et al. Automated electronic medical record sepsis detection in the emergency department. *PeerJ* 2014;2:e343.
23. Institute for Healthcare Improvement. *Evidence-based care bundles*. Cambridge, MA; 2016. http://www.ihi.org/Topics/Bundles/Pages/default.aspx.
24. Jozwiak M, et al. Implementing sepsis bundles. *Ann Transl Med* 2016;4(17):332.
25. Levy MM, et al. Surviving Sepsis Campaign: association between performance metrics and outcomes in a 7.5-year study. *Intensive Care Med* 2014;40(11):1623-33.
26. Surviving Sepsis Campaign. *Updated bundles in response to new evidence*. Chicago: Society of Critical Care Medicine; 2015. http://survivingsepsis.org/SiteCollectionDocuments/SSC_Bundle.pdf.
27. Levy MM, et al. The Surviving Sepsis Campaign bundle: 2018 update. *Crit Care Med* 2018;46(6):997-1000.
28. Barlam TF, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016;62(10):e51-e77.
29. Thayer S. A procalcitonin-guided algorithm to reduce antibiotic duration. *Nursing2016 Critical Care*;11(6):31-7.
30. Kelm DJ, et al. Fluid overload in patients with severe sepsis and septic shock treated with early goal-directed therapy is associated with increased acute need for fluid-related medical interventions and hospital death. *Shock* 2015;43(1):68-73.
31. Levy MM, et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. *Intensive Care Med* 2010; 36(2):222-31.
32. Reinelt H, et al. Impact of exogenous beta-adrenergic receptor stimulation on hepatosplanchnic oxygen kinetics and metabolic activity in septic shock. *Crit Care Med* 1999;27(2):325-31.
33. Khanna A, et al. Angiotensin II for the treatment of vasodilatory shock. *N Engl J Med* 2017;377(5):419-430.
34. ARISE investigators, ANZICS Clinical Trials Group, et al. Goal-directed resuscitation for patients with early septic shock. *N Engl J Med* 2014;371(16):1496-506.
35. Mouncey PR, et al. Trial of early, goal-directed resuscitation for septic shock. *N Engl J Med* 2015;372(14):1301-11.
36. ProCESS Investigators, et al. A randomized trial of protocol-based care for early septic shock. *N Engl J Med* 2014;370(18): 1683-93.
37. Centers for Medicare and Medicaid Services. *Hospital-acquired condition reduction program fiscal year 2018 fact sheet*. Baltimore, MD; 2018. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Downloads/FY2018-HAC-Reduction-Program-Fact-Sheet.pdf.
38. Centers for Medicare and Medicaid Services. *Hospital inpatient prospective payment system and long-term acute care hospital prospective payment system fiscal year 2016 final rule [PowerPoint presentation]*. Baltimore, MD: Centers for Medicare and Medicaid Services, Medicare Learning Network 2015 Sep 18. https://www.cms.gov/Outreach-and-Education/Outreach/NPC/Downloads/2015-09-18-Long-Term-Care-Presentation.PDF.
39. Wurmser T. The financial case for EBP. *Nurs Manage* 2009; 40(2):12-4.
40. Seymour CW, et al. Time to treatment and mortality during mandated emergency care for sepsis. *N Engl J Med* 2017; 376(23):2235-44.
41. Institute of Medicine. *Evidence-based medicine and the changing nature of healthcare: 2007 IOM annual meeting summary*. Washington, DC: National Academies Press; 2008. Learning healthcare system series. https://www.nap.edu/catalog/12041/evidence-based-medicine-and-the-changing-nature-of-healthcare.
42. Subbe CP, et al. Validation of a modified early warning score in medical admissions. *QJM* 2001;94(10):521-6.
43. Maupin JM, et al. Use of the modified early warning score decreases code blue events. *Jt Comm J Qual Patient Saf* 2009; 35(12):598-603.
44. Silversides JA, et al. Conservative fluid management or deresuscitation for patients with sepsis or acute respiratory distress syndrome following the resuscitation phase of critical illness: a systematic review and meta-analysis. *Intensive Care Med* 2017;43(2):155-70.
45. Churpek MM, et al. Quick sepsis-related organ failure assessment, systemic inflammatory response syndrome, and early warning scores for detecting clinical deterioration in infected patients outside the intensive care unit. *Am J Respir Crit Care Med* 2017;195(7):906-11.
46. Rusconi AM, et al. Early goal-directed therapy vs usual care in the treatment of severe sepsis and septic shock: a systematic review and meta-analysis. *Intern Emerg Med* 2015;10(6): 731-43.