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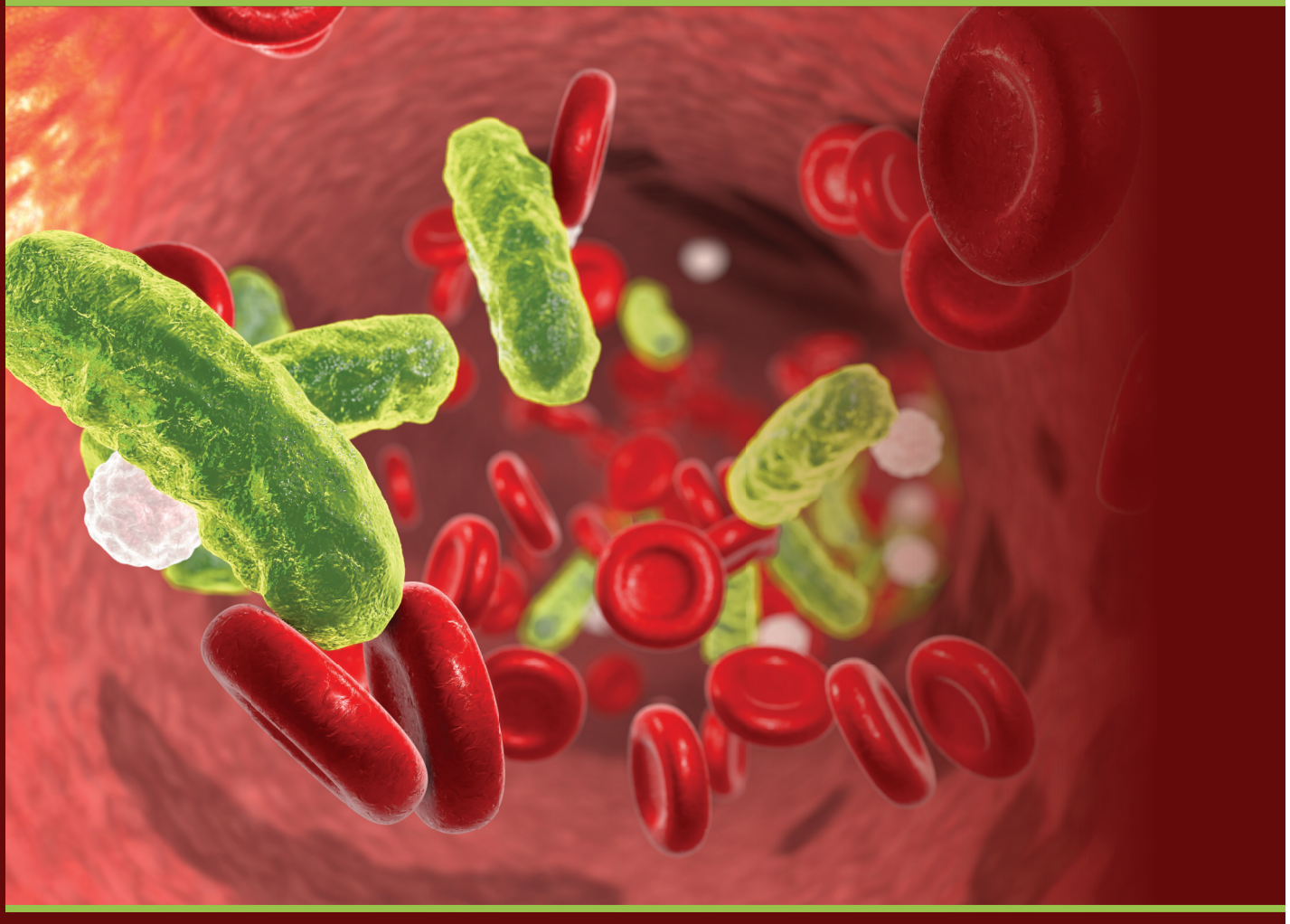
A supplement to *The Nurse Practitioner*

OPTIMIZING PATIENT SURVIVAL FROM DISTRIBUTIVE SHOCK:
A guidelines-based approach



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This is a complimentary continuing nursing education activity supported by an educational grant from La Jolla Pharmaceutical.

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TARGET AUDIENCE

Nurses and nurse practitioners in emergency, acute care, and critical care who may care for patients at risk for distributive shock.

LEARNING OBJECTIVES

After reading the articles in this activity and taking the post-test, participants should be able to:

- Identify diagnostic and assessment criteria for sepsis based on the most recent practice guidelines.
- Select appropriate pharmaceutical treatments for managing patients based on severity and responsiveness to distributive shock resuscitation and vasopressor therapies.
- Identify an evidence-based plan for patient evaluation and monitoring to achieve the best outcomes for patients with distributive shock.

INSTRUCTIONS

- Read all the articles in the supplement and complete the online post-test and evaluation at http://nursing.ceconnection.com/public/modules/9939. Log in with your NursingCenter.com or CEConnection username and password. New users will need to create an account. Registration is free.
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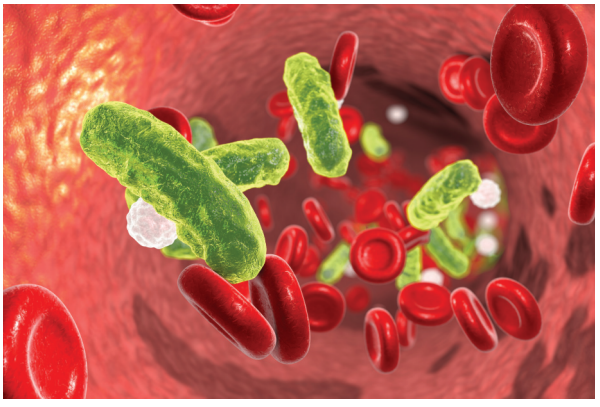
Sepsis-3: The new definitions

Maureen A. Seckel, MSN, APRN, ACNS-BC, CCNS, CCRN, FCCM

ABSTRACT

Sepsis definitions were recently revised by the Third International Sepsis Consensus Definitions for Sepsis and Septic Shock to better align with current understanding of the research, physiology, and management of patients with sepsis. Clinicians must understand these new definitions and their implications for practice. This article reviews the new definitions along with other recent changes in sepsis management.

Keywords: sepsis, Sepsis-3, sepsis bundles, sepsis definitions, septic shock



Patients with sepsis continue to experience significant morbidity and mortality despite coordinated efforts, including the first international sepsis definition conference in 1991. Sepsis is the sixth most common reason for hospital admission in the United States, and patients with sepsis are more likely to have longer hospital stays with higher costs—along with higher rates of discharge to long-term care—than any other discharge diagnosis.[1-3] The Third International Sepsis Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) were published in 2016.[4] This article highlights the significance of these changes and potential practice changes for healthcare providers.

REDEFINING SEPSIS

Sepsis is now defined as "life-threatening organ dysfunction caused by a dysregulated host response to infection" (**Table 1**).[4] Sepsis is the result of an infection and encompasses the patient's response to that infection and resulting organ dysfunction. Because the new definition of sepsis now includes patients with organ dysfunction and increased mortality risk, the term *severe sepsis* has been removed from Sepsis-3.[4]

Systemic inflammatory response syndrome (SIRS) criteria also were removed from the sepsis definition in recognition of their lack of specificity.[4] Although some patients with infections may fit the SIRS criteria, SIRS also may occur in patients with noninfectious conditions such as trauma, burns, surgery, or pancreatitis.[5,6] In addition, the new sepsis definition incorporates the current understanding of sepsis physiology; it includes the host's activation of both proinflammatory and anti-inflammatory responses to infection, which can then lead to organ dysfunction. Patients who have organ dysfunction in response to an infection have a mortality greater than 10%.[4] One of the goals of the new definition was to bring increased awareness and encourage additional assessment of patients with a known sepsis risk.

SEPTIC SHOCK

Septic shock is newly defined as a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality.[4] The new definition includes criteria that help differentiate shock caused by sepsis versus cardiovascular collapse.

The new definition is based on systematic reviews; a meta-analysis; a Delphi study among the consensus group; and large, retrospective cohort studies. Septic shock criteria also have been updated and call for administering vasopressors to maintain a mean arterial pressure (MAP) of 65 mm Hg or greater and maintaining a lactate level greater than 2 mmol/L after adequate volume resuscitation.[4]

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SCREENING FOR SEPSIS

Unlike other medical conditions, such as stroke or acute myocardial infarction, no single clinical test is specifically and directly diagnostic of sepsis. Screening tools can help to identify patients who may require closer assessment for earlier intervention. The sepsis syndrome triad consists of infection, the patient's response to that infection, and the resulting organ dysfunction.

Although the SIRS criteria have been removed from the current sepsis definition, they may still remain useful for identifying infection and can be used to

TABLE 1. Sepsis definitions, 1992–2016[4,16,17]

Definitions/criteria	Sepsis-3 (2016)	Sepsis-2 (2001)	Sepsis-1 (1992)
Sepsis	Life-threatening organ dysfunction caused by dysregulated host response to infection	Unchanged	Systemic response to the presence of infection with change to two or more SIRS criteria: • Temperature >100.9° F (38.3° C) or <96.8° F (36° C) • Heart rate >90 • Respiratory rate >20 breaths/min or $Paco_2$ <32 mm Hg • WBC >12,000 cells/mm^3, <4,000 cells/mm^3, or >10% immature bands
Severe sepsis	Deleted	Unchanged	Sepsis with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status.
Septic shock	Sepsis with underlying circulatory and cellular/metabolic abnormalities profound enough to substantially increase mortality	Unchanged	Sepsis with hypotension, despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. Patients who are on inotropic or vasopressor agents may not be hypotensive at the time the perfusion abnormalities are measured.

TABLE 2. Sepsis and septic shock bundles[14,18]

Sepsis Within 3 hours of presentation	• Measure lactate level. • Obtain blood cultures prior to administering antibiotics. • Administer broad-spectrum or other antibiotics. • Administer 30 mL/kg crystalloid for hypotension or lactate ≥4 mmol/L
Sepsis or septic shock Within 6 hours of presentation	Repeat lactate if initial lactate is elevated (>2 mmol/L).
Septic shock Within 6 hours of presentation	• Administer vasopressors to maintain a MAP ≥65 mm Hg. • Reassess volume status and tissue perfusion by either option (licensed independent practitioner): Option 1: Focused exam with all five components; vital signs, cardiopulmonary exam, capillary refill exam, peripheral pulse exam, and skin exam Option 2: Any two of the following: central venous pressure central venous oxygen saturation, bedside cardiovascular ultrasound, passive leg raise or fluid challenge

TABLE 3. SOFA score[11]

Score		0	1	2	3	4
Respiration	Pao_2/Fio_2 (P/F ratio) mm Hg	>400	≤400	≤300	≤200 with respiratory support	≤100 with respiratory support
Coagulation	Platelets $10^3/mm^3$	>50	≤150	≤100	≤50	≤20
Liver	Bilirubin mg/dL	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12
Cardio-vascular		No hypo-tension	MAP <70 mm Hg	Dopamine ≤5 mcg/kg/min or dobutamine (any dose)	Dopamine >5 mcg/kg/min or epinephrine ≤0.1 mcg/kg/min or norepinephrine ≤0.1 mcg/kg/min	Dopamine >15 mcg/kg/min or epinephrine >0.1 mcg/kg/min or norepinephrine >0.1 mcg/kg/min
Central nervous system	GCS score	15	13–14	10–12	6–9	<6
Renal	Creatinine mg/dL	<1.2	1.2–1.9	2.0–3.4	3.5–4.9	>5
	Urine output				<500 mL/24 hours	<200 mL/24 hours

help broadly identify or screen patients who may be at risk for sepsis.[4,7,8] Earlier recognition and assessment of infection and sepsis can lead to earlier implementation of the components of the treatment bundles; this implementation also may lead to better outcomes and decreased patient mortality (**Table 2**).[7] Screen patients for infection upon entry to the healthcare system and routinely after admission, and include assessment for tissue hypoxia and new organ dysfunction.

QUANTIFYING TISSUE HYPOXIA

Lactate levels have been used as a marker of tissue hypoxia due to inadequate oxygen delivery in patients with sepsis.[9] However, lactate levels cannot be used in isolation as a test for sepsis but only as an adjunctive assessment tool. Elevated lactate levels can be attributed to lactic acidosis from tissue hypoxia (type A) or from nontissue hypoxic states (type B) resulting from the use of beta-agonists, diabetic ketoacidosis, liver failure, and other conditions.[10]

QUANTIFYING ORGAN FAILURE

The Sequential Organ Functional Assessment (SOFA) score is used in critical care to describe organ dysfunction or failure and is based on several important concepts (**Table 3**).[11] Organ failure is a continuum, and clinicians need a tool that describes its degrees of severity rather than a simple number or score. Patients with a suspected infection and a SOFA score of 2 or greater have an increased (greater than 10%) risk of mortality.[12] The SOFA score requires laboratory work and assessments that are best performed in an ICU, and it has a better predictive value when used in that setting. For patients with chronic conditions (that is, those with a higher baseline score), a change in SOFA score of 2 or more points also signals higher morbidity risk.

TABLE 4. qSOFA score[4,12]

A positive qSOFA is a score of 2 or greater based on these clinical criteria:	
GCS	≤13 or altered mental status
Systolic BP	≤100 mm Hg
Respiratory rate	≥22 breaths/minute

QUICK SOFA (QSOFA) SCORE

As part of Sepsis-3, a new scoring system was developed that could be easily and quickly implemented in most clinical settings outside the ICU without technology or laboratory tests (**Table 4**). The qSOFA score consists of three clinical components: the patients' Glasgow Coma Scale (GCS) score, systolic BP, and respiratory rate.[12] Altered mental status may be used as a surrogate for GCS score and describes a lower GCS score. Patients who have a suspected infection and qSOFA score of 2 or greater have a greater risk for morbidity due to sepsis.

This new measure was retrospectively tested in several large patient databases.[12] Patients with infection and a positive qSOFA score had higher mortality and longer ICU stays than patients who did not, and the gSOFA score was predictive in patients who were not in the ICU.

ADDITIONAL CHANGES

Since October 2015, the Centers for Medicare and Medicaid Services (CMS) has used and will continue to use the 2003 definitions of sepsis, severe sepsis, and septic shock to capture mandated reported data based on discharge diagnosis. There are no plans to revise the sepsis CMS core measure, or SEP-1, to implement public reporting or payment penalties through fiscal year 2017.[13]

These forthcoming guidelines also may influence changes to the sepsis treatment bundles. However, the Surviving Sepsis Campaign bundles already have incorporated the new Sepsis-3 definitions into their recommendations for sepsis screening and management.[14] Recommendations include initial screening for suspected or confirmed infection, screening for organ dysfunction and management of sepsis, and identifying and managing initial hypotension. The qSOFA may be an additional tool to help identify patients who are at increased risk.

The CDC also has recently implemented a comprehensive sepsis campaign to improve patient safety by increasing clinician and patient awareness of the condition that incorporates the new definitions. The campaign focuses not only on early recognition and treatment but also on preventing sepsis, and provides education for clinicians, patients, and their families.[15]

IMPLICATIONS FOR PRACTICE

Although the new definitions will be progressively incorporated into clinical use, clinicians should expect a period of discordance as the sepsis literature and research catches up with the 2016 definitions for sepsis and septic shock. Using the new definitions will help clinicians and researchers understand which interventions improve outcomes and which resources are needed. Sepsis teams should work to incorporate the new definitions into their sepsis protocols and coding. Clinicians should not only be aware of the new definitions but also their facility's policies and protocols for screening and managing patients with sepsis. **JAAPA**

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Understanding sepsis and septic shock

Paul Szczybor, PA-C, DFAAPA

ABSTRACT

Although sepsis outcomes have improved in recent years, overall morbidity and mortality remain high. Sepsis is common but frequently unrecognized by clinicians at initial patient presentation. This leads to treatment delays and poor outcomes. This article reviews the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) and discusses current management for sepsis.

Keywords: sepsis, septic shock, organ dysfunction, sequential organ failure assessment, lactate, procalcitonin

Since the turn of the 20th century, the medical community has recognized that sepsis is a life-threatening condition associated with high morbidity and mortality. Research on the topic, however, was hampered by the lack of a standard definition or nomenclature. In 1992, the American College of Chest Physicians (ACCP)/Society of Critical Care Medicine (SCCM) consensus paper, published in *Chest*, recommended standardized terminology that would bring consistency in clinical trials:

- *Sepsis* was defined as the presence of the systemic inflammatory response syndrome (SIRS) in a patient with a known or suspected source of infection. SIRS was defined as the presence of two or more of the following parameters: heart rate greater than 90 beats/minute; respirations greater than 22 or $PaCO_2$ less than 32 mm Hg; white blood cell count greater than 12,000 cells/mm^3, less than 4,000 cells/mm^3, or with greater than 10% bands; and a temperature greater than 38° C (100.4° F) or less than 36° C (96.8° F).
- *Severe sepsis* indicated sepsis with organ dysfunction, hypoperfusion, or hypotension.
- *Septic shock* was defined as persistent hypotension despite adequate fluid resuscitation.[1]

In 2001, the International Sepsis Definitions Conference reassessed these definitions, and although a few changes were made to expand the signs and symptoms of sepsis, the basic definitions were left intact.[2] Twenty-five years after the first consensus, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) made a significant shift in how sepsis was defined. The Sepsis-3 task force of 19 international experts was originally convened by the SCCM and the European Society of Intensive Care Medicine in 2014. By the time their report was published in *JAMA* in 2016, it had been endorsed by 31 medical societies worldwide.[3]

SEVERE SEPSIS IS NOW SEPSIS

The Sepsis-3 definitions have moved away from describing the inflammatory response to focus on the resulting organ dysfunction. Definitions were simplified to include only *sepsis* and *septic shock* (the term *severe sepsis* was eliminated). Sepsis now is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.[3] Essentially, the body's response to the infection is injuring its own tissues and organs.[3]

Sepsis pathobiology is complex and modulated by biochemical, genetic, and endogenous factors. The body's normal response when host immune cells

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recognize a pathogen is a highly regulated release of proinflammatory and anti-inflammatory mediators. The end result is typically homeostasis between infection control and tissue repair. The immune system's response to infection begins at a local level and may result in local organ dysfunction as well as variable systemic physiologic responses (such as fever, tachycardia, tachypnea, and leukocytosis) depending on the location and severity of infection. The dysregulated response that is the core feature of sepsis occurs when the proinflammatory cascade predominates beyond the local level and causes a generalized, systemic response resulting in an unbalanced net inflammatory state.

The release of proinflammatory factors through protein signaling pathways largely is responsible for organ dysfunction in patients with sepsis. For example, both tumor necrosis factor (TNF)-alfa and interleukin (IL)-1 are released with the initial infectious insult, triggered by neutrophils and macrophages. TNF-alfa and IL-1, in turn, are involved in secondary mediator release of prostaglandins and nitric oxide, both powerful vasodilators responsible for some of the early hemodynamic changes in sepsis. These cytokines also activate abnormalities in the coagulation cascade that can lead to adverse microvascular changes at the organ level. These are just a few of the better-understood immune-mediated pathways of organ dysfunction; many other pathways outside the immune system are thought to also play a role in sepsis-related organ dysfunction.

Septic shock, considered a subset of sepsis, is defined by Sepsis-3 as sepsis in which underlying circulatory and metabolic abnormalities are profound enough to substantially increase mortality.[3] Clinically, this translates to a patient who:

- meets sepsis criteria
- requires vasopressors to maintain a mean arterial pressure of 65 mm Hg or greater, despite adequate fluid resuscitation
- has a serum lactate level greater than 2 mmol/L.[3]

These patients frequently develop multiorgan failure and in-hospital mortality can exceed 40%.[3] Central venous access is required in these critically ill patients and norepinephrine is recommended as the first-line vasopressor.

SIRS criteria are no longer used to diagnose or define sepsis as they were found to be too sensitive, nonspecific, and did not necessarily indicate a life-threatening response. SIRS may simply reflect an appropriate host response.[3] SIRS is a measure of inflammation, not organ dysfunction, and occurs in many hospitalized patients with infection, including those who never develop organ dysfunction. Patients with significant morbidity and mortality risk may lack SIRS criteria. In a research setting, patients with SIRS criteria who do not develop sepsis or organ dysfunction demonstrated poor discriminant validity and those with sepsis but no SIRS criteria demonstrated poor concurrent validity. Based on these findings, SIRS criteria were considered a poor tool for predicting the development of sepsis and provide little information on organ dysfunction. Early diagnosis of sepsis and organ dysfunction are key to reducing morbidity and mortality in patients with sepsis.

The new definitions are meant to simplify terminology when discussing sepsis and improve consistency in sepsis research. Before Sepsis-3, the nomenclature suggested that sepsis was a syndrome that followed a spectrum or specific course from SIRS to sepsis to severe sepsis to septic shock. This is not always the case. Although the components of SIRS are clinically important and remain important in monitoring and screening patients for infection or physiologic stress, they are not considered a good marker for sepsis (that is, the dysregulated response to infection or organ failure) and are not valid predictors of patient morbidity and mortality.

For practicing clinicians, the new terminology may improve communication among peers, support staff, and family—a patient either has sepsis and responds to fluid resuscitation with adequate hemodynamic stability, or has septic shock and requires vasoactive medication for hemodynamic support.

The *International Classification of Diseases, Ninth Revision* (ICD-9), and ICD-10 codes have compounded the problem of varied terminology for sepsis.[3] Many ICD terms such as *sepsis syndrome* and *septicemia* are not consistent with consensus nomenclature, creating disparity between accepted medical practice, documentation, and billing and coding.[3] The Sepsis-3 guidelines recommend specific ICD-10 codes based on the new terminology: R65.20 for sepsis and R65.21 for septic shock.

EARLY DETECTION USING SOFA CRITERIA

Because sepsis is characterized by life-threatening organ dysfunction, the focus needs to be on a rapid determination of organ function in patients with infection, so immediate resuscitation and antibiotics can be started.

In an article published in conjunction with Sepsis-3, Seymour and colleagues showed that the sequential organ failure assessment (SOFA) score is an effective tool to predict sepsis-related organ dysfunction and subsequent mortality.[4]

Six organ systems are scored based on the degree of dysfunction.

- Respiratory system—vascular hyperpermeability, neutrophil-related cascade responsible for further tissue injury
- Coagulation—activation of intravascular coagulation by inflammatory cytokines, disruption in fibrinolysis, increased consumption and decreased production of natural anticoagulants, systemic thrombin generation. Dysfunction in coagulation affects most organs and causes endothelial injury.
- Hepatic system—hypoperfusion, disruption of intracellular and extracellular bile salt transport (caused by hypoxia, hypoperfusion, and inflammatory cytokines)
- Cardiovascular—hypoperfusion, myocardial depression, disruption of electrolyte homeostasis (calcium, phosphate)
- Central nervous system—hypoperfusion, cellular damage, mitochondrial and endothelial dysfunction, disruption of electrolyte homeostasis, disturbances to neurotransmitters
- Renal system—hypoperfusion, damage or dysfunction of tubular epithelial cells.

A SOFA score of 2 or greater over baseline correlates to an overall mortality risk of 10% in a general hospital population with presumed infection. This is greater than the overall mortality of 8.1% for ST-segment elevation myocardial infarction, a life-threatening condition.[3] Depending on a patient's baseline level of risk, a SOFA score of 2 or greater identified a 2- to 25-fold increased risk of dying compared with patients with SOFA scores less than 2.[3]

Using a scoring tool involving six organ systems is laborious and waiting for laboratory results can be impractical when early recognition and rapid resuscitation are keys to improving outcomes. Retrospective statistical analysis suggests that three criteria in patients with infection indicate increased mortality due to organ dysfunction:

- alteration in mental status
- systolic BP of 100 mm Hg or less
- respirations of 22 or more.[3,4]

Clinicians can use this new measure, termed qSOFA (for quick SOFA), without waiting for laboratory values in patients with a known or suspected infection. The task force suggested that qSOFA criteria be used to prompt clinicians to further investigate for organ dysfunction, to initiate or escalate therapy as appropriate, and to consider referral to critical care.[3] Positive qSOFA criteria also should prompt consideration of possible infection in patients not previously recognized as infected.[3]

Seymour and colleagues analyzed several large hospital databases to explore construct validity and criterion validity of several models assessing clinical criteria for sepsis.[4] SIRS, SOFA, and qSOFA were among the models evaluated in this study. They found that in the ICU setting, the predictive validity for hospital mortality using SOFA was statistically greater than both SIRS and qSOFA, and qSOFA was significantly greater than SIRS.[4] Outside the ICU, the predictive validity of qSOFA was statistically greater than both SOFA and SIRS.[4] The study supports qSOFA as a quick tool for clinicians to detect a clinically significant change and sepsis risk in the hospital units where patients are outside the close surveillance of the ICU.

AN UNRECOGNIZED KILLER

Too often, providers diagnose an infection but fail to recognize sepsis, putting patients at risk for higher morbidity and mortality. Former CDC Director Tom Frieden, MD, MPH, described sepsis as "an unrecognized killer (and) a medical emergency."[5] Clinicians should apply the qSOFA scoring to patients suspected of an acute infection, prompting them to recognize sepsis sooner and begin immediate IV fluid resuscitation and aggressive antibiotic therapy. At the recommendation of the Surviving Sepsis Campaign, many institutions developed sepsis screening and performance improvement programs aimed at early recognition of sepsis. Because the lack of recognition prevents timely therapy, sepsis screening is associated with earlier treatment and decreased mortality.[6-9]

The Surviving Sepsis Campaign supports the Sepsis-3 definitions and offers clarification. In response to the Sepsis-3 document, they recommend that the continued appropriate first step in screening patients for sepsis should be to identify infection by assessing patients for signs and symptoms of infection. If clinical judgment suggests potential infection, the clinician should follow the institution's sepsis pathway, which typically includes obtaining lactate levels, blood or other cultures as appropriate, starting empiric antibiotics, and obtaining laboratory studies to evaluate for organ dysfunction.

The Centers for Medicare and Medicaid Services also is implementing mandated, quality-of-care core measures for sepsis, similar to those for acute myocardial infarction and pneumonia.

MANAGEMENT

Administer fluid resuscitation After a clinician recognizes sepsis in a patient, the Surviving Sepsis Campaign recommends an initial IV fluid bolus of 30 mL/kg within the first 3 hours.[6] Administering 0.9% sodium chloride solution or balanced crystalloids such as lactated Ringer solution for the initial bolus is appropriate because these fluids expand intravascular volume. The idea of a 2- to 3-L IV crystalloid bolus seems excessive and risky to many clinicians but improving perfusion is the goal. Keep in mind that patients with sepsis tend to be markedly vasodilated and have increased microvascular permeability. The release of proinflammatory mediators leading to endothelial cell dysfunction also affects perfusion.[10] A patient history of heart failure or chronic kidney disease (CKD) should not dissuade clinicians from giving an appropriate (30 mL/kg) fluid bolus. Retrospective studies show worse outcomes in patients with heart failure or CKD who received less-aggressive initial fluid boluses.[11,12]

After the initial 30 mL/kg bolus, additional IV fluid administration should be guided by frequent reassessment of the patient's hemodynamic status. Perform a thorough clinical examination and evaluate available physiologic variables, including heart rate, BP, SaO_2, respiratory rate, temperature, and urine output, as well as other noninvasive or invasive monitoring when available.[6] A previous resuscitation strategy known as early goal-directed therapy had been recommended, but this protocol has been challenged following its failure to show a mortality reduction in three subsequent large multicenter randomized controlled trials.[6,13] Routine use of colloids, such as albumin, as a resuscitative fluid is not recommended as colloids provide no mortality benefit.[14] Also, hydroxyethyl starch should never be used in patients with sepsis or in any critically ill patient due to an increased risk of mortality and acute kidney injury.[15]

Monitor lactate levels Although elevated lactate levels alone do not indicate sepsis or septic shock, serial measurements of serum lactate can be a guide to resuscitation in patients presenting with elevated lactate levels thought to be due to tissue hypoperfusion.[6,16] Studies have shown a 22% relative risk reduction in mortality when lactate levels decreased by more than 20% in the first 8 hours of resuscitation.[17,18] Many protocols recommend checking the patient's serum lactate levels every 4 to 6 hours until they normalize. Using the reduction of lactate levels as one of many endpoints in resuscitation can aid clinical decisions as well as be a predictor of mortality.

Start empiric antibiotics ASAP Although establishing vascular access and initiating aggressive fluid resuscitation are very important when managing patients with sepsis and septic shock, prompt IV infusion of antimicrobials also is a priority.[6] Rapid administration of appropriate antibiotics is essential to improve outcomes. In patients with sepsis or septic shock, each hour delay is associated with an increase in mortality.[6,19] Delays also make acute kidney injury, acute lung injury, and other organ dysfunction more likely and increase length of stay.[6,20-23] Administering antibiotics within 1 hour is recommended as a reasonable minimum target once sepsis is recognized.[6] Whenever possible, obtain blood cultures and other appropriate, site-specific cultures before starting antibiotics. However, if cultures cannot be obtained promptly, do not delay antibiotic administration.

Choose the right antibiotic Failure to choose the right antibiotic is associated with a substantial increase in morbidity and mortality. Empiric regimens should err on the side of overinclusiveness.[6]

Antibiotic choices should focus on the source of infection, the host, and the likely pathogen.

- *Source:* Consider the source or site of infection with respect to likely pathogens and drug penetration to that site.
- *Host:* Consider the patient's age and comorbidities, recent antibiotic use, as well as possible immunosuppression (for example, splenectomy, HIV, neutropenia), invasive devices (such as central venous access devices and indwelling urinary catheters), and the environment in which the patient developed the infection (for example, the community, long-term care facility, or acute care hospital).
- *Pathogen:* Assess risk factors for infection with multidrug-resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus*, *Pseudomonas,* and *Acinetobacter* when treating nosocomial infections or patients from a long-term care facility, acute care hospital, or those recently treated with antibiotics or known to be colonized with a multidrug-resistant organism.[6]

For example, if a patient with no significant comorbidities comes from home with pneumonia and

has a qSOFA score of 2 or greater, the diagnosis is sepsis due to community-acquired pneumonia (CAP). After initiating a 30 mL/kg IV crystalloid bolus, appropriate antibiotics would be ceftriaxone and azithromycin or levofloxacin. These antibiotics cover the most common community-acquired bacteria, including atypical organisms, and have excellent lung penetration.

On the other hand, if the patient presents from a long-term care facility or was recently hospitalized, the provider may need to be concerned about Gram-negative organisms, particularly *Pseudomonas*, as well as MRSA. Appropriate antibiotics would include an antipseudomonal cephalosporin such as cefepime or an antipseudomonal penicillin such as piperacillin/tazobactam plus vancomycin to cover MRSA.

Start broadly and narrow quickly The Surviving Sepsis Campaign recommends empiric, broad-spectrum therapy with one or more antibiotics for patients presenting with sepsis or septic shock to cover all likely pathogens. They also stress that empiric therapy be narrowed once the pathogen is identified and its sensitivities established and/or adequate clinical improvement is noted. De-escalate to the narrowest effective agent when a pathogen is identified. When a pathogen is not identified, de-escalate based on the patient's clinical improvement and consider other biomarkers such as procalcitonin.

Monitor procalcitonin During the past decade, the role of biomarkers in the diagnosis and management of infections has been extensively explored.[6] Procalcitonin measurements, in particular, are early and extremely specific to bacterial infections as well as predictive for severity. Procalcitonin is helpful in differentiating bacterial and nonbacterial infections in patients.[24] Procalcitonin levels less than 0.1 ng/mL indicate an extremely low likelihood of bacterial infection; levels greater than 2 ng/mL are strongly suggestive of sepsis.[25] Procalcitonin also can help clinicians shorten the course of antibiotics. A value of less than 0.5 ng/mL in a patient with SIRS, without clear evidence of infection, and with negative cultures can be used to support the clinician's decision to discontinue antibiotics.[25]

Control the source of infection In addition to early recognition, aggressive resuscitation, and early appropriate antibiotic therapy, clinicians also need to be mindful of the anatomic source of the infection. Procedures such as draining an abscess or empyema, inserting a percutaneous nephrostomy tube, removing an infected hemodialysis catheter, or performing an exploratory laparotomy must be done as soon as medically and logistically practical after the diagnosis is made. Interventions within 6 to 12 hours after diagnosis are usually sufficient to improve survival in most patients.[6]

CONCLUSION

Despite recent improvements, sepsis and septic shock prevalence is increasing and mortality remains high. Early recognition; aggressive IV fluid resuscitation; timely, appropriate, empiric antibiotics; and source control are key to improving morbidity and mortality. Using the new Sepsis-3 definitions, in particular applying qSOFA criteria, can help clinicians make the diagnosis faster and start treatment sooner, resulting in better patient outcomes. **JAAPA**

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Pharmacologic management of distributive shock using vasoactive agents

Luana Atherly, PhD

Alpha and beta refer to the agonist activity at the adrenergic receptor sites.

Name	Recommendation	Indications	Mechanism of action	Usual dose range	Monitoring	Adverse events
Norepinephrine[1]	Strong recommendation to use as first-choice vasopressor in septic shock[1]	Restoring and maintaining BP[2]	Alpha, $beta_1$, $beta_2$[3]	0.02-0.25 mcg/kg/min[3]	BP, infusion rate, MAP[2]	Bradycardia, dysrhythmias[2]
Vasopressin[1]	Weak[1]	Increasing BP in adults with vasodilatory shock who remain hypotensive despite fluids[4]	V1 receptor[3]	0.01-0.07 U/min[3,4] (add up to 0.03 U/min to norepinephrine in managing septic shock)	MAP	Bradycardia, tachydysrhythmias, hyponatremia, myocardial ischemia[4]
Dopamine	Weak[1] (should be avoided in most cases as it increases risk of dysrhythmias and death)	Correcting hemodynamic imbalances present in shock due to myocardial infarction (MI), trauma, endotoxic septicemia, open-heart surgery, renal failure, and cardiac decompensation[5]	Alpha, $beta_1$, dopamine[3]	2-20 mcg/kg/min up to 50 mcg/kg/min[5]	Urine output, blood volume, cardiac output, BP, distribution of peripheral perfusion, cardiac contractility, infusion rate[5]	Dysrhythmias, tachycardia, bradycardia, atrial fibrillation (AF)[5]
Epinephrine[1]	Weak[1]	Emergency treatment of allergic reactions including anaphylaxis[6]	Alpha, $beta_1$, $beta_2$[3]	0.05-2 mcg/kg/min[3]	Urine output, blood volume, cardiac output, BP, distribution of peripheral perfusion, cardiac contractility, rate of infusion[6]	Ventricular dysrhythmias, hypertension, angina, cerebral hemorrhage, tachycardia, palpitations, tachydysrhythmias, vasoconstriction, stress cardiomyopathy[6]
Dobutamine[1]	Weak[1]	Short-term treatment of adults with cardiac decompensation and persisting hypoperfusion despite fluid resuscitation and alternate vasoactive medications	$Beta_1$	2-20 mcg/kg/min[3]	Heart rate, BP, hypersensitivity[7]	Increased heart rate, increased BP, hypotension, ventricular ectopic activity, infusion site reactions[7]

(*CONTINUED*)

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Name	Recommendation	Indications	Mechanism of action	Usual dose range	Monitoring	Adverse events
Milrinone[1]	Weak[1]	Short-term IV treatment of acute decompensated heart failure[8]	Phosphodiesterase inhibition[3,8]	0.4-0.6 mcg/kg/min after loading dose[3]	ECG, BP, heart rate, infusion rate[8]	Supraventricular and ventricular dysrhythmias, hypotension, angina, torsades de pointes, headache, bronchospasm, infusion site reactions, anaphylactic shock[8]
Levosimendan[1]	Weak[1]	Short-term treatment of acutely decompensated chronic heart failure where conventional therapy is insufficient[9]	Calcium sensitizer, potassium channel opener[9]	0.1 mcg/kg/min after loading dose of 6-12 mcg/kg over 10 minutes[9]	ECG, BP, heart rate, urine output[9]	Supraventricular tachycardia, AF, hypotension, ventricular extrasystoles, tachycardia, headache[9]
Phenylephrine[1]	Use in patients with septic shock should be limited until more research on clinical outcomes is available.[1]	Increasing BP in adults with clinically significant hypotension from vasodilation in setting of septic shock or anesthesia[10]	Alpha[3]	0.2-2.5 mcg/kg/min[3]	BP, heart rate[10]	Decreased cardiac output, and decreased renal and splanchnic blood flow, bradycardia[3,10]

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Managing the hospitalized adult with pneumonia

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ABSTRACT

Pneumonia is a commonly encountered diagnosis in the inpatient and outpatient settings. Timely diagnosis and management is crucial in any healthcare setting but especially in hospitalized patients. This article reviews the classifications, diagnosis, and treatment of pneumonia according to the most recent guidelines.

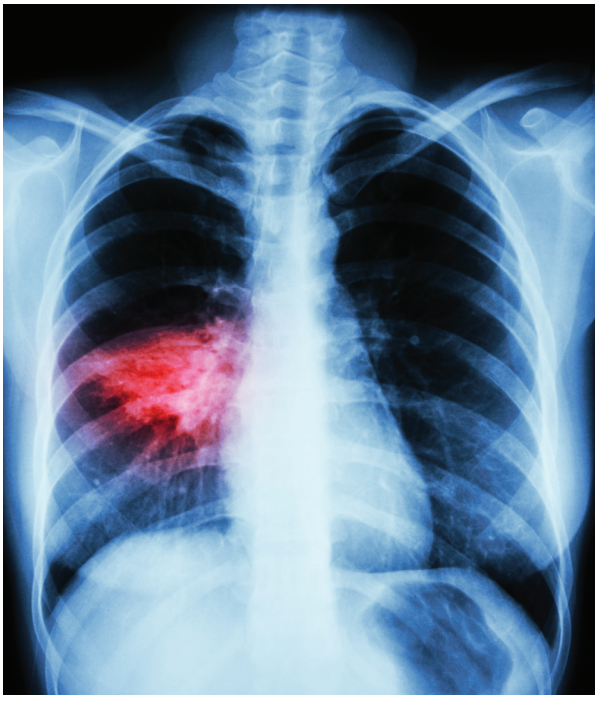
Keywords: pneumonia, guidelines, hospitalized adults, diagnosis, management, antibiotics

Pneumonia is a common diagnosis across all healthcare settings and accounts for about 1 million hospital admissions per year.[1] Diagnosing and treating pneumonia appropriately and promptly can reduce patient morbidity and mortality.[1,2] This article focuses on managing pneumonia in hospitalized adults.

Correctly classifying a patient's type of pneumonia is important because different pathogens require different treatments. The three main classifications of pneumonia are community-acquired (CAP), hospital-acquired (HAP), and ventilator-associated (VAP).[3,4] The most recent CAP guidelines from the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) were published in 2007; an update is expected this year.[3,4] The IDSA/ATS guidelines for HAP and VAP were updated in 2016.[4]

CLASSIFICATIONS

CAP is the most common type of pneumonia.[3] The most common causes in outpatients are *Streptococcus pneumoniae* (20% to 60%), *Haemophilus influenza* (3% to 10%), viruses (2% to 15%), and atypical organisms, including *Mycoplasma pneumoniae* (6%),



Chlamydophila pneumoniae (2% to 5%), and *Legionella* species (2%).[5,6] Atypical organisms are not detectable on Gram stain and cannot be cultivated on standard bacteriologic media.[3] The common organisms seen in the outpatient setting also apply to patients with CAP who are being treated in the hospital; however, the rates of occurrence vary slightly.[3,7] *Staphylococcus aureus* and organisms associated with aspiration also should be considered in hospitalized or at-risk patients.[3] Although estimated prevalences exist for each pathogen, isolating a specific bacterial organism is not always possible, so treatment often is empiric and based on probable organisms.

HAP develops at least 48 hours after a patient is admitted to the hospital, and is not present on admission.[4] Unlike VAP, HAP is not associated with mechanical ventilation. By definition, VAP develops at least 48 hours after intubation and mechanical ventilation.[4] The organisms responsible for HAP and

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VAP differ from CAP; HAP and VAP present with higher rates of Gram-negative organisms, such as *Escherichia coli, Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*.[4] Associated Gram-positive organisms include methicillin-sensitive *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA). HAP and VAP also carry higher rates of anaerobic and polymicrobial infections compared with CAP.[4]

HAP and VAP are associated with significant increases in patient morbidity and mortality and resource use.[3,4] VAP can prolong mechanical ventilation by 7 to 11 days and can increase the length of hospitalization by almost 2 weeks. This can translate to a cost increase of more than $40,000 per patient per hospital stay.[3] Because of these factors, clinicians must focus on the prevention, prompt diagnosis, and treatment of HAP and VAP.

The 2005 IDSA/ATS guidelines identified a fourth classification, healthcare-associated pneumonia (HCAP), which was eliminated in the 2016 guidelines.[4] HCAP encompassed a patient population at high risk for difficult-to-treat organisms: recently hospitalized patients, those living in long-term care facilities, and those in frequent contact with the medical community. However, increasing evidence has shown that many patients previously meeting criteria for HCAP are not truly high-risk for multidrug-resistant pathogens, as was previously believed. These patients received broad-spectrum antibiotics, which increased the rate of treatment-related complications.[4] The IDSA/ATS guidelines for CAP, to be published this summer, will address this high-risk patient population.

In addition to CAP, HAP, and VAP, consider other causes of pneumonia, including aspiration, viral, and fungal.

DIAGNOSTIC TESTING

Although a patient's clinical presentation and microbiologic test results may support the diagnosis of pneumonia, a chest radiograph is the gold standard test, with the presence of an infiltrate being diagnostic.[3] However, clinical suspicion of pneumonia is still crucial because a radiograph may miss an early infiltrate. Repeat radiographic testing may be indicated in 1 to 2 days if clinical suspicion is high and the patient has failed to improve clinically.[8] Do not withhold empiric antibiotic treatment in this scenario.

A chest CT usually is not required to diagnose pneumonia but can be a useful adjunct in certain scenarios (for example, to evaluate for differential diagnoses such as a pulmonary embolus or malignancy, or for further anatomic characterization when the clinical picture remains unclear). CTs have a 20% higher sensitivity, but the six-fold increase in cost and significantly higher radiation exposure must be considered.[9]

The reported sensitivity of blood cultures in pneumonia is only 0.5% to 14%, and low rates of secondary bacteremia from CAP have led researchers to examine the clinical value and cost-effectiveness of routine blood cultures.[10] Pretreatment blood cultures are recommended if the patient meets criteria for severe CAP (**Table 1**): admitted to the ICU, immunocompromised, asplenic, actively abuses alcohol, underlying liver disease, or presence of cavitary infiltrates on imaging.[3] Obtain blood cultures in patients who are not responding to therapy or exhibit evidence of clinical deterioration, and in all patients with HAP or VAP.[4] Obtaining cultures after antibiotics are administered decreases the yield of culture results by at least 50%.[11] In patients with multiple risk factors for bacteremia, blood cultures obtained after antibiotic administration may still be positive in up to 15% of patients, and therefore are still warranted.[3]

Sputum cultures are associated with low sensitivity and high rates of false-positive results. Many bacterial species identified on sputum cultures are normal oral or nasopharyngeal flora or colonizers of the respiratory tract; although these organisms are present in respiratory secretions, they may not be responsible for the patient's pneumonia.[3] Any positive sputum culture should be interpreted within the context of the clinical setting, as it is important to rule out normal flora or colonization. Bronchoalveolar lavage via bronchoscopy typically yields better results than sputum cultures but bronchoscopy only is required for a select population of patients with pneumonia. Bronchoscopy can be useful if a patient is failing to improve and the causative organism remains unknown. Diagnostic indications for bronchoscopy include evaluation of lung masses or nodules, mediastinal lymphadenopathy or masses, hemoptysis, or suspected airway obstruction. Therapeutic indications include treatment of mucus impaction, control of hemoptysis, and endotracheal tube placement.[12,13]

Respiratory pathogen panels can identify organisms by polymerase chain reaction (PCR) testing to aid in the diagnosis of pneumonia. These panels can be especially useful in the winter. Different types and

brands of panels test for different pathogens. Most viral pathogen panels test for influenza A and B, parainfluenza, respiratory syncytial virus (RSV), human rhinovirus/enterovirus, human metapneumovirus, adenovirus, and coronavirus. The bacterial respiratory pathogen panel can test for organisms such as *Streptococcus pneumoniae*, *C. pneumoniae*, *M. pneumoniae*, *Staphylococcus aureus*, *L. pneumophila*, and *Bordetella pertussis*. These tests are obtained via nasopharyngeal swab and have as high as 90% sensitivity and 80% specificity.[14] However, these tests often lack standardization and depend on proper collection technique to yield the most accurate results. Timing of results of PCR testing can vary based on setting and location. Although some panels may be available as a rapid test, confirmatory tests may take more time in hospitals that send the tests out to a third-party facility for processing. In periods of peak influenza activity, do not withhold treatment while awaiting results if clinical suspicion for influenza pneumonia is high.

Urine antigen tests are available to detect *Streptococcus pneumoniae* and *Legionella* spp. These tests can yield quick results and have higher sensitivity and specificity than sputum and blood cultures but their availability may be limited. The yield of these tests is not affected by the antibiotic administration before obtaining the sample. However, no antibiotic sensitivity is available with the results.[3] Serologic testing can be used to identify certain atypical organisms, including *M. pneumoniae, L. pneumophila*, and *C. pneumoniae*.[3]

Biologic markers sometimes can be used to support a bacterial cause of pneumonia, and procalcitonin is one marker that has been studied for this use. Procalcitonin is secreted by parenchymal cells in response to bacterial toxins and should be elevated in patients with bacterial infections. Theoretically, procalcitonin levels should be normal or low in patients without a bacterial infection (that is, those with a viral pneumonia).[15] However, several studies have shown no effect on mortality with the use of procalcitonin.[16,17] The 2016 IDSA/ATS HAP/VAP guidelines recommend that clinicians use clinical criteria alone (without procalcitonin) to determine whether to initiate antibiotics for patients with pneumonia.[4] Procalcitonin originally was recommended only for de-escalation of antibiotics—if the patient's procalcitonin levels begin to trend down, consider de-escalating the antibiotic regimen. Conversely, a recent meta-analysis demonstrated that use of procalcitonin to guide antibiotic treatment in patients with acute respiratory infections reduced antibiotic exposure and adverse reactions and improved survival.[18] This was the first meta-analysis to demonstrate that procalcitonin-guided antibiotic treatment yielded statistically significant results. However, these findings did not translate to the primary care setting, and data were poor for VAP. Other biomarkers, such as C-reactive protein and soluble triggering receptor expressed on myeloid cells 1 (sTREM-1), were not found to be helpful in the decision to initiate antibiotics in patients with pneumonia.[4]

Arterial blood gas (ABG) analysis is essential in patients with signs of respiratory distress on physical examination. Patients who are significantly tachypneic could benefit from an ABG analysis to determine potential underlying acid-base disturbances and to help formulate an appropriate treatment plan.[19] ABG analysis findings can determine appropriate noninvasive ventilation strategies, such as the use of bilevel positive airway pressure or a high-flow nasal cannula. Invasive mechanical ventilation is indicated if the patient fails noninvasive ventilation strategies

TABLE 1. Criteria for severe CAP[3]

One major criterion or three minor criteria qualify for severe CAP.

Major criteria
- Invasive mechanical ventilation
- Septic shock with the need for vasopressors

Minor criteria
- Respiratory rate of 30 or greater (or need for noninvasive ventilation)
- PaO_2/FiO_2 ratio of 250 or less (or need for noninvasive ventilation)
- Multilobar infiltrates
- Confusion or disorientation
- Uremia (blood urea nitrogen level of 20 mg/dL or greater)
- Leukopenia (white blood cell count of less than 4,000 cells/mm^3) as a result of infection alone
- Thrombocytopenia (platelet count of less than 100,000 cells/mm^3)
- Hypothermia (core temperature less than 36° C [96.8° F])
- Hypotension requiring aggressive fluid resuscitation
- Also consider hypoglycemia (in patients without diabetes), acute alcohol abuse or withdrawal, hyponatremia, unexplained metabolic acidosis or elevated lactate level, cirrhosis, and asplenia

for hypoxemic, hypercapnic, or mixed respiratory failure, as well as for airway protection, if the patient must be sedated for procedures, or for patients with airway obstruction.[4]

THE IMPORTANCE OF APPROPRIATE TRIAGE

One of the most important decisions a clinician can make for a patient with pneumonia is whether the patient is best managed as an outpatient or requires admission to a medical or surgical unit or the ICU.[3,20] A delay in escalating to the proper level of care has been shown to significantly increase 30-day mortality. Furthermore, a delay of more than 6 hours in transferring a patient to the ICU has resulted in increased hospital length of stay and higher in-hospital mortality.[20] Clinicians can use clinical predictor tools to determine the appropriate level of care for patients with pneumonia and to estimate associated mortality risk. Two common clinical predictor tools are the British Thoracic Society criteria, also known as the CURB-65 score, and the Pneumonia Severity Index (PSI). The CURB-65 score considers five risk factors—**C**onfusion, **U**remia, **R**espiratory rate, low **B**P, and age **65** years or older—estimates the patient's 30-day mortality, and suggests the appropriate level of care (for example, outpatient management versus inpatient management versus ICU admission). The PSI considers 20 different risk factors, including patient demographics, coexisting illnesses, physical examination findings, and laboratory and radiographic findings, in estimating mortality. Unlike the CURB-65, the PSI does not suggest the appropriate level of care for patients. The clinical predictor tools do not consider certain factors, such as whether a patient can take oral medications or the availability of outpatient support resources; therefore, clinical predictor tools should never replace clinical judgment.[3]

The 2007 IDSA/ATS guidelines established criteria for severe CAP in order to identify high-risk patients with CAP. Consider ICU admission for patients with one major criterion or three minor criteria (**Table 1**).[3]

For patients with sepsis and suspected pneumonia, use the sequential organ failure assessment (SOFA) score from the 2016 Sepsis-3 guidelines to estimate mortality and identify patients who should be transferred to a higher level of care.[21]

TREATMENT

CAP Administer antibiotics as soon as possible in patients with a suspected or confirmed diagnosis of CAP caused by bacteria. Treatment delays can lead to morbidity and mortality. **Table 2** summarizes current empiric antibiotic treatment recommendations for CAP.[3]

When treating a patient with any type of pneumonia, consider whether the patient has risk factors for pseudomonal or MRSA infections. Risk factors for pseudomonal infections include use of antibiotics in the past 90 days, history of a pseudomonal infection within the last year, prolonged hospital stay (5 or more days), time spent in the ICU during hospital stay, mechanical ventilation, malignancy, immunosuppression, cystic fibrosis, HIV/AIDS, alcohol abuse, and chronic obstructive pulmonary disorder. Risk factors for MRSA include end-stage renal disease, IV drug abuse, and antibiotic use within the past 90 days.[3] Recognizing these risk factors early is important, as this will affect antibiotic selection.

HAP and VAP The 2016 IDSA/ATS guidelines emphasize basing empiric antibiotic therapy on local antibiograms. Each clinical institution should have an up-to-date antibiogram to guide patient-specific treatment plans. The first-line treatment regimens for HAP and VAP are to use a single drug—either piperacillin-tazobactam, cefepime, levofloxacin, imipenem, or meropenem—to empirically cover for *Staphylococcus aureus* in patients with HAP and *Staphylococcus aureus, P. aeruginosa,* and other Gram-negative bacteria in patients with VAP.[4] In patients with either HAP or VAP, if methicillin-sensitive *Staphylococcus aureus* is isolated, the preferred treatments are oxacillin, nafcillin, or cefazolin.[4]

Certain patients with HAP or VAP should be covered for MRSA with vancomycin or linezolid (**Table 3**).[4] All of the pharmacologic agents recommended for first-line therapy of HAP and VAP provide some antipseudomonal coverage; however, certain high-risk patients should be double covered with two antipseudomonal agents (**Table 4**).

Transition hospitalized patients to oral antibiotics when they show signs of clinical improvement, are hemodynamically stable, and can tolerate oral medications. Patients do not have to be observed in the hospital while transitioning from parenteral to oral therapy.[3,4]

TREATMENT DURATION

The IDSA/ATS CAP guidelines recommend treatment for 5 to 7 days.[3] A longer treatment duration is warranted in certain patients, such as those with necrotiz-

ing pneumonia, lung abscesses, or empyemas. HAP and VAP have previously been treated for up to 21 days but the guidelines recommend a 7-day course as long as the patient is showing signs of clinical improvement.[4] This is based on meta-analyses that found no difference in terms of mortality, clinical cure, or recurrent pneumonia with a short course of treatment.[4] Shorter duration of antibiotic therapy leads to improved rates of antibiotic resistance, fewer complications such as *Clostridium difficile* colitis, and lower overall cost. Shorter durations also are associated with increased patient adherence to treatment.

OTHER CONSIDERATIONS

Aspiration pneumonia Risk factors for aspiration include any condition associated with reduced or altered consciousness, loss of ability to maintain an airway, and reduction in gag reflex.[22] Existing dysphagia, older age, postoperative state, neurologic disorders, anatomic defects, poor oral hygiene, and gastroesophageal reflux disease also increase a patient's risk for aspiration.[22]

A patient with aspiration pneumonia typically has a right lower lobe infiltrate on imaging.[22] Appropriate antibiotics for treatment of aspiration pneumonia include piperacillin-tazobactam, ampicillin-sulbactam, clindamycin, and amoxicillin-clavulanate to cover anaerobic pathogens.[4,23] Follow proper aspiration precautions and have patients undergo a swallow evaluation by a speech therapist who can outline proper diet or liquid alterations to minimize the risk of recurrence.

Be sure to differentiate an acute aspiration event from aspiration pneumonia. No clinical benefits have been associated with using prophylactic antimicrobial therapy for patients with an acute aspiration pneumonitis.[24] Clinical suspicion for pneumonia should be present before initiating antimicrobial therapy.[24]

Viral pneumonia Viruses are a common cause of CAP.[25] Rates of viral pneumonia are higher in the outpatient setting but patients with viral pneumonia also are commonly hospitalized, especially during the winter months.[7] The most common viruses are influenza A and B, RSV, parainfluenza, coronavirus, and human metapneumovirus.[25] Less common viral pathogens include herpes simplex virus, varicella zoster, and cytomegalovirus (CMV). These less common pathogens typically occur only in immunocompromised patients.[26] The diagnosis can be clinical but respiratory pathogen panels or sputum cultures can aid in determining the specific viral cause.

TABLE 2. Recommended empiric antibiotics for CAP[3]

Outpatient treatment
- Previously healthy patient with no use of antibiotics in the past 90 days: macrolide or doxycycline
- Patient with comorbidities such as chronic heart, lung, liver, or renal disease; diabetes; alcohol abuse; malignancy; asplenia; immunosuppression; or use of antibiotics in the past 90 days: respiratory fluoroquinolone (moxifloxacin or levofloxacin) or beta-lactam plus macrolide

Inpatient non-ICU treatment
- Respiratory fluoroquinolone (moxifloxacin or levofloxacin) or beta-lactam and macrolide

Inpatient ICU treatment (choose one)
- Beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) and azithromycin
- Respiratory fluoroquinolone

Special considerations
- In patients with suspected pseudomonas, administer an antipneumococcal, antipseudomonal beta-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) and one of the following: a respiratory fluoroquinolone, an aminoglycoside and azithromycin, or an aminoglycoside and an antipneumococcal fluoroquinolone. For patients allergic to penicillin, substitute aztreonam for the beta-lactam.
- If MRSA is suspected, add vancomycin or linezolid.

TABLE 3. Empiric MRSA coverage for patients with HAP or VAP[3]

Cover patients with HAP if
- they have used antibiotics in the past 90 days
- they are in a unit in which more than 10% to 20% of *Staphylococcus aureus* isolates are MRSA
- the prevalence of MRSA is not known
- they are at high risk of death because of the need for mechanical ventilation or had septic shock at the time HAP was diagnosed

Cover patients with VAP if
- they have a risk factor for antibiotic resistance, such as antibiotic use in the past 90 days, septic shock at the time of VAP, acute respiratory distress syndrome preceding VAP, 5 or more days of hospitalization before VAP, or acute renal replacement therapy before onset of VAP
- they are in a unit in which more than 10% to 20% of *Staphylococcus aureus* isolates are MRSA
- the prevalence of MRSA is not known

Few recommendations are available for the treatment of viral pneumonias. Consider early treatment (within 48 hours of symptom onset) with oseltamivir, zanamivir, or rimantadine in patients with influenza, depending on the strain.[27] Secondary bacterial pneumonias can develop, and antibiotic coverage may be appropriate even if a virus has been isolated.[28] Encourage patients to get an influenza vaccination before the onset of influenza activity in the community, optimally before the end of October.[27]

Fungal pneumonia Consider fungal pneumonia depending on the patient's clinical presentation and characteristic radiologic findings such as pulmonary nodules or cavitary lesions. Obtain a thorough history of the patient's state of residence and/or recent travel to areas with endemic fungal infections, such as California's San Joaquin Valley and states in the Midwest.

This type of pneumonia is uncommon in the general population but is increasing in incidence in immunocompromised patients.[29] *Aspergillus* spp. were found to be the primary cause of fungal pneumonia in a recent review of pulmonary infections in patients with cancer.[30] Other risk factors for aspergillosis are coinfection with or treatment for CMV infection.[29] The diagnosis of invasive aspergillosis is made by respiratory cultures, and despite treatment with potent antifungal agents such as amphotericin B, the prognosis remains grim, with a mortality of up to 66%.[29,31,32]

Coccidioidomycosis, also known as *valley fever*, is endemic to deserts in the Western hemisphere.[33] Patients become infected by inhaling spores of *Coccidioidomycosis immitis* or *Coccidioidomycosis posadasii*. Clinical presentation consists of rather vague symptoms, including a dry cough, shortness of breath, fatigue, weight loss, fever, arthralgias, and rashes. The disease is diagnosed via serologic testing; complement fixation is the best confirmatory test. Patients with uncomplicated pulmonary coccidioidomycosis require close follow-up as they are at risk for disseminated disease but generally do not require pharmacologic treatment.[34] Patients who require pharmacologic treatment include those who are significantly symptomatic, have diffuse pulmonary involvement, or have concurrent comorbidities or advanced age rendering them frail. The preferred treatment is a 3- to 6-month course of fluconazole (or itraconazole as an alternative).[35] Amphotericin B is reserved for only the most complicated of cases and should be prescribed in conjunction with infectious disease specialists.

Histoplasmosis is endemic in Midwestern states and occurs through inhalation of *Histoplasma capsulatum* fungal spores. Clinical presentation is similar to that of coccidioidomycosis, and the most sensitive means to diagnose this disease is via complement fixation. Treatment consists of itraconazole; amphotericin B is used only for patients with complicated or refractory disease.[36]

TABLE 4. *P. aeruginosa* coverage for patients with HAP or VAP[3]

Patients with structural lung disease, such as cystic fibrosis or bronchiectasis are at high risk for Gram-negative infections and should be double covered for *Pseudomonas* spp.

Double cover patients with HAP if

- they have received IV antibiotics in the past 90 days
- they are at high risk of death because of the need for mechanical ventilation or had septic shock at the time HAP was diagnosed

Double cover patients with VAP if

- they have a risk factor for antibiotic resistance, such as IV antibiotic use in the past 90 days, septic shock at the time of VAP, acute respiratory distress syndrome preceding VAP, 5 or more days of hospitalization before VAP, or acute renal replacement therapy before onset of VAP
- they are in a unit where more than 10% of Gram-negative isolates are resistant to the drugs being considered for monotherapy
- they are in an ICU where local antimicrobial susceptibility rates are not available

CONCLUSION

Pneumonia is common in the inpatient setting. The three main classifications of pneumonia are CAP, HAP, and VAP. Consider viruses, fungi, and aspiration as causes as well as bacteria. Correct classification guides treatment choices as pathogens will differ. In addition to proper classification, prompt diagnosis and treatment are important, as patient outcome may be significantly affected. **JAAPA**

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OPTIMIZING PATIENT SURVIVAL FROM DISTRIBUTIVE SHOCK:
A guidelines-based approach

POST-TEST

EXPIRATION DATE: JULY 2019

All post-tests must be completed and submitted online. See instructions on inside front cover.

1. **Which of the following is *not* part of the sepsis syndrome triad?**
   a. A patient's response to infection
   b. Evidence of infection
   c. Evidence of organ dysfunction
   d. SOFA score

2. **Why are the SIRS criteria no longer used in the diagnosis of sepsis?**
   a. The sensitivity for detecting sepsis was too low, resulting in frequent false negatives.
   b. They are nonspecific, which frequently led to overdiagnosis of sepsis.
   c. They don't adequately reflect the body's response to infection.
   d. They were never part of the original sepsis criteria.

3. **Which of the following is not a condition of septic shock?**
   a. Heart rate greater than 90 beats/minute
   b. Meeting the criteria for sepsis
   c. Required use of a vasopressor to maintain a MAP of 65 mm Hg or greater
   d. Serum lactate level greater than 2 mmol/L

4. **What is the respiratory component of the SOFA criteria?**
   a. Pao_2
   b. Pao_2/Fio_2 ratio
   c. respiratory rate
   d. Sao_2

5. **What are the components of the qSOFA?**
   a. Altered mental status, systolic BP of 100 mm Hg or lower, and respirations of 22 or greater
   b. Temperature greater than 99° F (37.2° C), respirations greater than 22, and white blood cell (WBC) count greater than 12,000 cells/mm^3
   c. Systolic BP less than 100 mm Hg, temperature greater than 99° C, and WBC count greater than 12,000 cells/mm^3
   d. Positive blood cultures, altered mental status, and temperature greater than 99° F

6. **In what setting does the qSOFA have better predictive validity than the SOFA?**
   a. ICU
   b. non-ICU settings
   c. The qSOFA is superior in predictive validity in all settings compared with the SOFA
   d. Both SOFA and SIRS have better predictive validity compared with the qSOFA, regardless of setting

7. **Serial measurements of which laboratory value guide resuscitation in patients with sepsis and evidence of hypoperfusion?**
   a. Pao_2
   b. serum albumin
   c. serum lactate
   d. urine osmolality

8. **Which previous category of sepsis is not recognized as part of Sepsis-3?**
   a. chronic sepsis
   b. recurrent sepsis
   c. severe sepsis
   d. septic shock

9. **What is the term for the phenomenon that occurs when the proinflammatory secondary to an infection spreads beyond the local level, causing a generalized systemic response?**
   a. sepsis
   b. SIRS
   c. septic shock
   d. severe sepsis

10. **According to the Surviving Sepsis campaign, what is an appropriate fluid bolus for a patient newly diagnosed with sepsis?**
    a. 5 mL/kg 0.9% sodium chloride solution
    b. 10 mL/kg lactated Ringer solution
    c. 20 mL/kg 0.45% sodium chloride solution
    d. 30 mL/kg 0.9% sodium chloride solution

11. Your patient meets qSOFA criteria for sepsis. For reasons beyond your control, there will be a 20- to 30-minute delay in getting the first blood culture collected and sent for laboratory evaluation. What should you do?

a. Wait to administer IV antibiotics until the first culture has been drawn, even if it takes several hours before the first dose.
b. Administer IV antibiotics immediately; collect a culture specimen as soon as possible.
c. Wait up to 90 minutes after the diagnosis of sepsis has been made to administer IV antibiotics. If cultures have not been drawn by then, give the antibiotics.
d. Cultures do not have to be drawn unless antibiotic therapy fails.

12. Which drug has the strongest recommendation as a first-line agent for distributive shock?

a. dopamine
b. epinephrine
c. norepinephrine
d. vasopressin

13. According the 2016 IDSA/ATS guidelines, which of the following is no longer a classification of pneumonia?

a. community-acquired
b. healthcare-associated
c. hospital-acquired
d. ventilator-associated

14. Why are *L. pneumophila, C. pneumoniae,* and *M. pneumoniae* considered atypical causes of CAP?

a. They are less common than other causes of CAP such as *S. pneumoniae*.
b. They only occur in certain endemic areas.
c. They are not detectable on Gram stain or cultivatable on standard bacteriologic media.
d. They only occur in significantly immunocompromised patients.

15. Which of the following is not considered a minor criterion for severe CAP?

a. hyperthermia (temperature greater than 38° C [100.4° F])
b. respiratory rate of 30 or greater
c. leukopenia (WBC count less than 4,000 cells/mm^3)
d. hypothermia (temperature less than 36° C [96.8° F])

16. Which of the following is *not* a risk factor for MRSA infection?

a. IV antibiotic use within 90 days
b. end-stage renal disease
c. IV drug abuse
d. alcohol abuse

17. Which statement is correct about diagnostic testing in hospitalized patients with suspected pneumonia?

a. Chest CT is always required to make the diagnosis.
b. Blood cultures have a high sensitivity for detecting the pulmonary pathogen.
c. Sputum culture carries a high false-positive rate.
d. Urine antigen testing is highly sensitive for most likely pathogens.

18. What is one advantage of the CURB-65 over the PSI clinical predictor tool?

a. The CURB-65 can suggest an appropriate level of care.
b. The CURB-65 considers the patient's ability to take oral medications.
c. The CURB-65 can predict mortality; the PSI can only predict length of hospital stay.
d. The PSI has fewer questions and is easier to use but the CURB-65 has better predictive reliability.

19. According to the IDSA/ATS guidelines, what is the duration of antibiotic therapy for HAP and VAP?

a. There was no consensus for treatment duration.
b. 7 days, as long as the patient is showing signs of clinical improvement
c. 14 to 21 days
d. 21 days or until the patient has had 3 days of no symptoms, whichever is greater

20. Which statement is correct about viral pneumonias?

a. Laboratory testing for viral causes is unavailable.
b. Secondary bacterial infections can develop and antibiotic coverage may be appropriate.
c. The most common viral cause is CMV.
d. Multiple treatment options are available for most viral causes of pneumonia.

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