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SPECIAL FEATURE

Antimicrobial Stewardship in Critical Care

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Dr. Guttendorf reports no financial relationships relevant to this field of study.

WHAT IS ANTIMICROBIAL STEWARDSHIP?

In 2012, antimicrobial stewardship (AMS) was defined in a policy statement by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS) as "coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration."[1] Dyar et al expanded this definition to focus on the importance of responsible antimicrobial use by all healthcare providers: "A coherent set of actions which promote using antimicrobials responsibly."[2] This better defines the outcome standards and processes of stewardship that hospitals should strive to meet. The concept and subsequent operationalization of AMS has been developing over several decades, but gained particular support over the last several years, in part due to The Joint Commission's new AMS standard instituted in 2017, mandating that all hospitals, acute care access centers, and nursing care centers establish an evidence-based AMS program.[3] The primary objectives of AMS are to improve clinical outcomes related to antimicrobial treatments, minimize toxicities, reduce costs, and, most importantly, reduce antimicrobial resistance.[1] This review will discuss some of the key principles and practices related to successful AMS programs, particularly as they relate to critical care.

IMPACT OF THE PROBLEM

The Centers for Disease Control and Prevention (CDC) reported that in U.S. acute care hospitals, about 30% of prescribed antibiotics are either unnecessary or inappropriate.[4] Additionally, the CDC estimates that more than 2.8 million antibiotic-resistant infections occur in the United States each year, resulting in more than 35,000 deaths.[5] Combating antibiotic resistance is one of the most important objectives of AMS, and global efforts are underway, spearheaded by the

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CDC, the World Health Organization, the European Centre for Disease Prevention and Control (ECDC), and multiple professional organizations to actively address the problem of the growing number of antimicrobial-resistant organisms.[5-7] The issue of multidrug-resistant organisms is particularly germane in critical care, since immunocompromised patients often present with severe illness, sepsis, and multisystem organ dysfunction, requiring prompt recognition and broad empiric therapies that may place them at risk for complications of antimicrobial therapies and limited choices for effective antibiotics.

WHAT ARE THE GUIDELINES?

The CDC has encouraged all U.S. hospitals to adopt AMS and provided guidelines for implementation with the publication of the Core Elements of Hospital Antibiotic Stewardship Programs: 2019 (an update of the original Core Elements published in 2014).[4] The Centers for Medicare and Medicaid Services (CMS) has mandated AMS for hospitals as a condition for receiving national funding.[4]

The CDC Core Elements consist of seven primary components to be included as part of any AMS program. Since 2014, when these were implemented for acute care hospitals, they have been evaluated through the National Healthcare Safety Network's (NHSN) Patient Safety Component Annual Hospital Survey and reported through the CDC. Staff in hospitals complete annual surveys regarding incorporation of each of the core elements. The percentage of acute care hospitals responding to the NHSN annual survey meeting all seven core elements improved from 41% in 2014 to 85% in 2018.[8] (*See Table 1 for the seven Core Elements of Antibiotic Stewardship Programs and the percentage of hospitals incorporating each component in the 2018 NHSN annual survey, http://bit.ly/2FRLHJ8.*)[8]

The joint policy statement (SHEA, IDSA, PIDS) on AMS from 2012 strongly recommends that all hospitals adopt AMS programs and details minimum requirements: 1) multidisciplinary interprofessional teams, including at least a pharmacist, a physician, a clinical microbiologist, and an infection control preventionist; 2) an antimicrobial formulary with recommended drugs to avoid overlaps in coverage; 3) institutional guidelines for management of common infections; 4) additional interventions to improve the appropriate use of antibiotics (tailoring multidrug regimens to avoid redundancy in coverage, treating only positive cultures, instituting appropriately broad empiric coverage, and tailoring as soon as culture results become available); 5) hospital processes to measure and benchmark antimicrobial use; and 6) the creation of regularly updated institution-specific antibiograms.[1]

The Healthcare Infection Control Practices Advisory Committee (HICPAC), a federal advisory group that provides guidance to the CDC and the Department of Health and Human Services (HHS), has published similar guidelines for antibiotic stewardship based on the CDC Core Elements.[9] HICPAC also recommends principles of diagnostic testing (rapid diagnostic tests, biomarkers, and molecular testing when appropriate) and principles of treatment, including early source control for infection, empiric broad-spectrum antibiotics appropriate for the severity of infection, optimal dosing based on pharmacokinetics/pharmacodynamics, the shortest effective duration of therapy, and early de-escalation of therapy based on available cultures.[9]

The IDSA and SHEA published a guideline (2016) for implementing an antibiotic stewardship program, based on the best available evidence.[10] The guideline recommends that an infectious disease physician with additional training in stewardship lead the AMS program. The guideline recommends particular interventions for success in antimicrobial stewardship. Two of the common interventions are preauthorization of antibiotics at the time of order entry (requiring providers to get approval before ordering), and prospective audit and feedback (PAF), which allows the provider to order the antibiotic, but AMS team engagement may follow at a later date. Pros and cons of each intervention are delineated, and have been studied. Preauthorization has the advantages of limiting exposure to unnecessary antibiotics and optimizing empiric choices with a review of prior cultures and antibiotic use, but it may result in a delay in initiating therapy and is labor-

intensive for the AMS team. Prospective audit allows the provider more freedom in ordering and can be less labor-intensive for the AMS team. It allows for AMS involvement in review and de-escalation of antibiotics and teaching opportunities for clinicians. Disadvantages of PAF include providers' reluctance to make changes to antibiotics if the patient is noted to be improving, and delays in achieving desired outcomes of reducing overall antimicrobial use. The mechanism of providing feedback to clinicians also is important. The guidelines strongly recommend preauthorization and/or PAF as important strategies over no intervention. Hospitals should decide the most effective and feasible strategy based on available resources.[10]

Implementing facility-specific clinical practice guidelines for specific infections is a weak recommendation. There is a strong recommendation to implement interventions to reduce exposure to antibiotics associated with a high risk of developing *Clostridioides difficile* infection (formerly known as *Clostridium difficile*).[10] Current common practices, such as antibiotic time-outs to review cultures and appropriate tailoring/de-escalation of antibiotics and applying stop orders, are listed as weak recommendations with low-quality evidence.[10] The guidelines recommend against antibiotic cycling as a stewardship strategy.[10] Overall, a number of important strategies and interventions remain understudied.

ANTIMICROBIAL STEWARDSHIP: WHAT WORKS?

Since the IDSA/SHEA guideline for implementation of Antibiotic Stewardship Programs published in 2016,[10] two systematic reviews have been published evaluating AMS programs and other specific interventions.[11,12] Shutz et al reviewed 145 studies, evaluating 14 AMS objectives for four specific outcomes in adult inpatients: clinical outcomes, adverse events, costs, and bacterial resistance.[11] Overall data were available for only nine of the 14 objectives, six of which had significant outcomes. Prescribing empiric therapy via guidelines was associated with a 35% relative risk reduction in mortality (relative risk [RR], 0.65; 95% confidence interval [CI], 0.54-0.80, $P < 0.0001$), and de-escalation in therapy was associated with a 56% relative risk reduction in mortality (RR, 0.44; 95% CI, 0.30-0.66, $P < 0.0001$). Additional improvements in outcome were noted with switching from intravenous (IV) to oral treatment, therapeutic drug monitoring (reduction in nephrotoxicity RR, 0.50; 95% CI, 0.29-0.88, $P = 0.02$), use of a restricted formulary of antibiotics, and bedside consultation, particularly for *Staphylococcus aureus* bacteremia (reduction in mortality RR, 0.34; 95% CI, 0.15-0.75, $P = 0.008$).[11] Davey et al reported a Cochrane Review of 221 studies of antibiotic prescribing practices for hospital inpatients, bundling interventions into restriction and enablement.[12] The duration of antibiotic treatment decreased significantly by 1.95 days (95% CI, 2.22 -1.67). The risk of death was the same in both the intervention and control groups (11%). With AMS interventions, the length of stay was reduced by 1.12 days (95% CI, 0.7 -1.54 days). Both enablement and restriction were independently associated with increased antibiotic policy compliance.[12]

Campion and Scully specifically reviewed the literature evaluating optimization and de-escalation of antibiotics in the intensive care unit (ICU).[13] Beneficial strategies identified for the ICU include employing empiric guidelines for antibiotic use, collecting appropriate specimens and using molecular diagnostics, optimizing antibiotic dosing, and reducing the total therapy duration. Empiric antibiotic therapy in sepsis should be directed at the suspected location of infection and known risk factors, such as immunosuppression and prior antibiotic exposure, not solely on providing gram-positive, gram-negative, *Pseudomonas*, and methicillin-resistant *Staphylococcus aureus* (MRSA) coverage. Prior IV antibiotic use, poor functional status, and comorbid conditions may increase the risks of multidrug-resistant organisms. Dual gram-negative coverage (the use of two agents with different mechanisms of action) for empiric coverage of infection, particularly in patients at risk for resistant organisms or reduced susceptibility, may be a useful strategy in critically ill patients, particularly when the susceptibility pattern for antipseudomonal beta-lactam antibiotics is < 90%. A beta-lactam plus aminoglycoside may provide better empiric coverage over beta-lactam alone or beta-lactam plus fluoroquinolone.[13]

Biomarkers, molecular diagnostics, and procalcitonin are tools to help clinicians in antibiotic prescribing and de-escalation. Molecular diagnostics analyze the nucleic acids of organisms for identification and for common mechanisms of resistance, providing results much more rapidly than conventional testing.[13-15] Earlier identification of a specific organism limits the time on empiric therapy and facilitates earlier tailoring of antibiotics to the specific organism. Identification of resistance patterns can facilitate earlier escalation of therapy to more appropriate antibiotics. Molecular tests can be applied to many types of culture samples (blood, urine, sputum, stool), but are more costly than traditional culture. The use of procalcitonin levels, which rise in the setting of bacterial infection, can facilitate the tapering of antibiotics, but is not recommended to be used as a marker to initiate antibiotic therapy.[16] Other optimization strategies include the use of pharmacokinetics and pharmacodynamics to adjust drug dosing in critically ill patients who may have increased volume of distribution and in those with rapidly changing renal function, and the use of extended duration of infusion for beta-lactam antibiotics to improve efficacy.[13]

AMS in the ICU requires a multi-professional approach, aggressive management of critically ill patients, appropriate empiric therapy, and willingness to de-escalate therapy when appropriate culture data support it. New diagnostic tools using molecular diagnostics to identify causative organisms and resistance mechanisms can facilitate earlier and more appropriate tailoring to specific therapy. A comprehensive AMS approach can help improve antimicrobial utilization, reduce broad-spectrum antimicrobial use, reduce colonization with multidrug-resistant organisms, and reduce costs.[16] AMS is the responsibility of everyone involved in the care of critically ill and hospitalized patients. Education of prescribers is important, particularly regarding the benefits of AMS; early and specific culturing of sites; appropriate empiric therapy; early tailoring of antibiotics to specific culture data; the conduction of an "antibiotic time-out" at 48 to 72 hours after antibiotic initiation to actively review culture results and patient progress and determine de-escalation; intravenous to oral route adjustment; and discussion of definitive duration of therapy. Preauthorization and PAF are effective tools, particularly when coupled with face-to-face feedback to the prescribing clinician. Additional research is required to specifically address the most effective tools for successful AMS. ■

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ABSTRACT & COMMENTARY

Longer Antibiotic Courses for Pneumonia Do Not Improve Outcomes, But Cause More Adverse Effects

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Dr. Hammond reports no financial relationships relevant to this field of study.

SYNOPSIS: Two-thirds of general medicine patients with pneumonia received excess antibiotic therapy, with 93.2% of the unnecessary duration occurring after hospital discharge. Excess antibiotic therapy did not improve mortality or morbidity outcomes, although each additional antibiotic day was associated with 3% increased odds of antibiotic-associated adverse drug events.

SOURCE: Vaughn VM, Flanders SA, Snyder A, et al. Excess antibiotic treatment duration and adverse events in patients hospitalized with pneumonia: A multihospital cohort study. *Ann Intern Med* 2019;171:153-163.

In acutely ill patients with a community-acquired pneumonia (CAP), multiple randomized, controlled trials have demonstrated similar or improved patient outcomes with three- to five-day antibiotic courses compared to seven- to 14-day courses.[1] Although data are less prevalent for the duration of treatment for healthcare-associated pneumonia (HCAP), the last guidelines published in 2004 suggested a shorter duration of antibiotic therapy (seven to eight days).[2] However, a lack of explicit recommendations for using the shortest course of antibiotics possible for CAP and HCAP may affect antibiotic prescribing practices in the general medicine population. This multicenter cohort study was performed to examine predictors of and outcomes associated with excess duration of antibiotics in CAP and HCAP across 43 hospitals in Michigan.[3]

Adult patients admitted to a general medicine service in one of 43 participating hospitals in Michigan were included if they were admitted for CAP or HCAP treatment and were discharged from the hospital between January 2017 and April 2018. Those who were admitted to an intensive care unit or were severely immunocompromised were not included. Approximately 60% of patients had severe pneumonia (pneumonia severity index class IV or V), with 55% having uncomplicated CAP, 19% having complicated CAP, and 27% having HCAP. Overall, 67.8% of patients received excess antibiotics based on guideline recommendations. The median durations for both CAP and HCAP were eight days, with median excess durations of two days for CAP and one day for HCAP. In total, this resulted in 2,526 excess antibiotic days per 1,000 patients hospitalized with CAP or HCAP. The vast majority of these excess days (93.2%) occurred after hospital discharge, with an additional five days of treatment after discharge being most common despite patients frequently needing zero or one additional day of therapy based on guideline recommendations. Patients from all hospitals were affected, with a range of patient discharges affected between 38.1% and 95.0% depending on the hospital.

Variables associated with excess antibiotic treatment duration on multivariable regression analysis included positive respiratory culture result (predicted excess days per patient 3.2, adjusted rate ratio (aRR) 1.49; 95% confidence interval [CI], 1.33-1.68), each day of hospital stay (excess days 0.2, aRR 1.02; 95% CI, 1.02-1.02), receipt of high-risk antibiotic in the 90 days prior to admission (excess days 2.9, aRR 1.17; 95% CI, 1.10-1.25), and CAP diagnosis (excess days 3.2, aRR 1.43; 95% CI, 1.32-1.55). Documentation of total antibiotic treatment duration in the hospital discharge summary was protective for excess antibiotic duration (aRR 0.78; 95% CI, 0.70-0.87). Most outcomes were similar at 30 days between the appropriate duration and excess duration groups, including mortality (1.9% vs. 2.0%, adjusted odds ratio per excess day [aOR] 1.01; 95% CI, 0.97-1.05), readmission (14.1% vs. 11.3%, aOR 1.00; 95% CI, 0.98-1.03), and emergency department visit (11.4% vs. 10.9%, aOR 0.98; 95% CI, 0.95-1.01). However, antibiotic-associated adverse drug events (ADEs) occurred more frequently in the excess duration group (3.4% vs. 4.8%, aOR 1.03; 95% CI, 1.00-1.06).

■ COMMENTARY

Two-thirds of general medicine patients with a pneumonia received excess antibiotic therapy, with 93.2% of the unnecessary duration occurring after hospital discharge. Although the reasons for these practices were not recorded, the authors hypothesized that the most likely culprits affecting these durations were implied rather than explicitly stated recommendations for antibiotic durations in pneumonia guidelines, the wait for finalized culture results to be available, and a lack of national policy efforts focused on treatment durations. Since patient outcomes were not improved because of excess antibiotic durations, providers may feel more comfortable aligning their treatment durations with more contemporary data for shorter courses. In fact, it may be possible to use one- to five-day antibiotic courses for CAP in many cases, which may allow for further reductions in antibiotic use.[4]

Furthermore, each additional antibiotic day was associated with a 3% increased odds of an antibiotic-associated ADE. The most common ADE was diarrhea; however, the short study duration precluded the authors from evaluating the impact of antibiotic days on resistance development. In a recent study of more than 7,000 critically ill adults, researchers observed that each additional day of broad-spectrum beta-lactam therapy beyond day 3 was associated with a 4% increased risk of new resistance development.[5] Consequently, the long-term implications of excessive antibiotic durations in CAP and HCAP are uncertain and likely are worse than those reported in this study. A particular emphasis may be placed on leveraging the electronic health record to guide providers to an appropriate treatment duration based on days of therapy already received in the hospital and the treatment indication. This may help allay

concerns about treatment duration while streamlining the discharge process. ■

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ABSTRACT & COMMENTARY

Efficacy of Vitamin C Infusion on Outcomes in Sepsis-Induced ARDS

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Dr. Sharma reports no financial relationships relevant to this field of study.

SYNOPSIS: In this randomized, double-blinded, placebo-controlled trial, intravenous vitamin C infusion did not influence a change in the modified Sequential Organ Failure Assessment score from the time of infusion to four days compared to placebo.

SOURCE: Fowler AA 3rd, Truwit JD, Hite RD, et al. Effect of vitamin C infusion on organ failure and biomarkers of inflammation and vascular injury in patients with sepsis and severe acute respiratory failure: The CITRIS-ALI randomized clinical trial. *JAMA* 2019;322:1261-1270.

The CITRIS-ALI trial randomized critically ill patients with sepsis and acute respiratory distress syndrome (ARDS) to a vitamin C infusion delivered every six hours for 96 hours or an identically compounded placebo solution. Patients were included if they had ARDS by the Berlin definition, had suspected or proven infection, and had two of four of the systemic inflammatory response syndrome (SIRS) criteria (i.e., temperature > 38°C or < 36°C, tachycardia > 90 beats/minute, tachypnea > 20 breaths per minute, leukocytosis > 12,000, or leukopenia < 4,000 cells/microliter). All criteria had to be met within a 24-hour period to be included, and patients had to be randomized within 48 hours of meeting ARDS criteria. Patients were excluded if they were not expected to survive, had an allergy to vitamin C, were pregnant, or if they had an interstitial lung disease (ILD), alveolar hemorrhage, diabetic ketoacidosis (DKA), or an active kidney stone. The primary outcome was a change in Sequential Organ Failure Assessment (SOFA) scores at 96 hours after the start of infusion and a change in inflammatory biomarker levels (C-reactive protein [CRP] and thrombomodulin) at 168 hours. There were multiple (46) prespecified secondary outcomes, the most relevant of which were mortality, intensive care unit (ICU)-free days, and ventilator-free days.

The SOFA score was modified ("mSOFA" score) to exclude bilirubin because of multiple missing values. The authors contended that the exclusion of a SOFA component does not affect its predictive validity based on previously published data. Overall, 1,262 patients were screened for eligibility, and 170 patients were randomized to each group. The largest proportion (~50%) were excluded because of inability to consent, being outside of the 48 hours since meeting ARDS criteria, or receiving home oxygen. The two groups were well matched for all demographic characteristics, and baseline mSOFA scores were identical (9.8 vs. 10.3). Baseline demographics and proportion of comorbidities were comparable between groups. Baseline oxygenation (PaO_2/FiO_2 and the oxygenation index) also was comparable. Conservative fluid management was instituted in both groups as described in the FACTT-lite protocol.

The authors concluded that a 96-hour vitamin C infusion did not reduce the severity of illness scores over four days compared with placebo. The authors did find a difference in three of the 46 prespecified secondary outcomes: reduced mortality at 28 days, a decrease in the number of days in the ICU to day 28, and hospital-free days to day 60 favored the vitamin C

infusion group. There were no differences in the other 43 prespecified secondary outcomes. Additionally, inflammatory biomarker levels (CRP, procalcitonin, angiopoietin, receptor for advanced glycation end [RAGE] products, tissue factor pathway inhibitor [TFPI] levels, and thrombomodulin) were not attenuated over the course of the four days of observation.

■ COMMENTARY

The plausibility of a clinical effect of vitamin C in the setting of shock and ARDS is well founded. Vitamin C is an antioxidant, and low levels have been demonstrated in the setting of sepsis.[1] Vitamin C also increases the synthesis of norepinephrine and vasopressin, having been defined as a cofactor in the synthesis of these molecules.[2] Furthermore, vitamin C has been shown to attenuate increases in cytokine levels that lead to activation and sequestration of neutrophils in the lungs in vitro.[3] Marik et al published a retrospective before-after study[4] assessing the effect of an infusion of hydrocortisone, vitamin C, and thiamine ("HAT" therapy) in the setting of severe sepsis and septic shock. They found an adjusted odds ratio for mortality of 0.13 in favor of HAT therapy. This study has led to a plethora of studies in various phases of completion and has led, arguably, to a premature adoption of the "Marik Protocol" in some institutions.

This study was designed to assess the effect of vitamin C infusion on relevant molecular and clinical outcomes among patients with ARDS in the setting of sepsis in a medical intensive care unit. Patients who developed sepsis resulting from a surgical intervention or who were in a surgical intensive care unit were excluded. While no randomized trials have yet reported results assessing the benefit of vitamin C in sepsis/septic shock, the authors decided to test their hypothesis that given the downstream salutary effects of vitamin C on the coagulation cascade, there would be a benefit in the setting of sepsis-associated ARDS.

There are a few points worthy of attention with respect to the conclusions of the trial. First, while there was a significant difference between the secondary endpoints of importance (mortality, hospital-free days, and ICU-free days), the authors noted that the study was a proof-of-concept trial not designed to assess a mortality difference. These three endpoints were the only significant differences between the groups in a total of 46 secondary endpoints, and they were "based on analyses that did not account for multiple comparisons and therefore must be considered exploratory." Patients were recruited up to 48 hours after meeting ARDS criteria; as a result, some randomized patients were in an advanced state of disease development, preventing a salutary effect of vitamin C (if any) from taking hold. Second, a large proportion of patients were excluded because either they were unable to provide consent or they were outside the window of randomization. This may have introduced an element of systematic error. Third, the majority of patients in both groups (more than 70%) had ARDS due to a primary thoracic etiology (presumably pneumonia) with a slightly higher proportion (82% vs. 70%) randomized to the vitamin C group. While low tidal volume ventilation affects both ARDS due to pneumonia or aspiration and ARDS due to sepsis (i.e., extrathoracic causes) with respect to a mortality benefit, there are substantial differences in mortality between these two groups (i.e., higher mortality in patients with non-thoracic sepsis).[5] Therefore, a larger trial that includes more patients with ARDS due to sepsis of non-thoracic etiology may reach different conclusions with respect to both primary and secondary endpoints. Fourth, the fluid balance was comparable in both groups at day 1; however, at 96 hours (the primary time endpoint of the study), patients receiving placebo had a statistically significantly different net negative fluid balance of approximately 800 mL compared with the vitamin C group. Fluid balance in the placebo group continued to be negative out to day 7 (net negative approximately 500 mL, not statistically significant). This was despite a conservative fluid strategy instituted in both groups. These differences in fluid balance are comparable to those published in the FACTT trial at day 4 and day 7. Fluid balance clearly has been shown to affect both ventilator-free days and ICU-free days, and the differences in fluid balance here make the differences in the secondary endpoints circumspect. The proportion of patients with acute kidney injury (AKI) was equivalent in both groups at enrollment; however, the proportion needing continuous renal replacement therapy (CRRT) over the ensuing week in either group was not reported, and whether more frequent CRRT was the reason for the greater negative fluid balance in the placebo group cannot be deciphered. Finally, more than half of the patients in each group received corticosteroids, but the dose of steroids administered or the duration was not reported. While this remains controversial, both the dose and duration of corticosteroid therapy may influence outcomes in the setting of ARDS[6] and certainly in the setting of severe community-acquired pneumonia,[7] introducing yet another confounding factor into the results of this study.

It also is important to keep in mind the potential adverse effects of a high-dose vitamin C infusion. Descriptions have included an oxalate nephropathy and interference with point-of-care blood glucose measurements, which is why patients with DKA were excluded. Given the exploratory nature of this trial, it seems premature to recommend vitamin C to all patients with sepsis and ARDS. Careful fluid management is an established intervention with respect to outcomes of interest in this trial, and it ought to be the focus of management

rather than who may benefit from vitamin C. Whether "HAT" therapy makes a difference in the setting of sepsis alone is being studied in a randomized, controlled trial. Whether vitamin C works in a larger trial incorporating more patients with ARDS related to sepsis of non-thoracic origin remains to be seen. ■

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CME/CE INSTRUCTIONS

To earn credit for this activity, please follow these instructions:

1. Read and study the activity, using the provided references for further research.

2. Log on to **ReliasMedia.com** and click on My Account. First-time users must register on the site. Tests are taken after each issue.

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CME/CE QUESTIONS

1. Which of the following is a Core Element of Hospital Antibiotic Stewardship Programs as delineated by the Centers for Disease Control and Prevention?
a. Eliminating the use of cultures before initiating antibiotics
b. Deferring initiation of antibiotics until after culture results become available
c. Tracking to monitor antimicrobial prescribing, resistance patterns, and outcomes
d. Reporting of outcomes to the Centers for Medicare and Medicaid Services

2. In the study by Vaughn et al, which outcome occurred more commonly in the group that received an excess duration of antibiotics compared to an appropriate duration?
a. Antibiotic-associated adverse drug event
b. Development of a new resistant pathogen
c. Emergency department visit
d. Hospital readmission

3. Which one of the following was associated with an infusion of vitamin C with respect to outcomes in acute respiratory distress syndrome associated with sepsis?
a. Better mSOFA scores at 96 hours
b. Better mSOFA scores at 48 hours
c. Improvement in C-reactive protein levels during infusion
d. Improvement in mortality at 28 days

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- identify relevant topics in the practice of critical care medicine;
- utilize recommendations from current clinical guidelines; and
- manage common critically ill patient and ICU administration scenarios.

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Table 1: The Seven Core Elements of Hospital Antibiotic Stewardship Programs and U.S. Hospitals Reporting Implementation in 2018

Core Element	Description of Core Element	Hospital Implementation Reported in 2018
1. Leadership	Dedicate necessary human, financial, and information technology resources.	98%
2. Accountability	Appoint a leader or co-leaders, such as a physician and pharmacist, responsible for program management and outcomes.	96%
3. Pharmacy Expertise*	Appoint a pharmacist, ideally, as a co-leader of the stewardship program to help lead implementation efforts to improve antibiotic use.	97%
4. Action	Implement interventions, such as prospective audit and feedback and/or preauthorization, to improve antibiotic use.	99%
5. Tracking	Monitor antibiotic prescribing, impact of interventions, and other important outcomes and resistance patterns.	96%
6. Reporting	Regularly report information on antibiotic use and resistance to prescribers, pharmacists, physicians, nurses, and hospital leadership.	93%
7. Education	Educate prescribers, pharmacists, nurses, and patients about adverse reactions from antibiotics, antibiotic resistance, and optimal prescribing.	91%

* Previously called "Drug Expertise"
Sources: Centers for Disease Control and Prevention. Core elements of hospital antibiotic stewardship programs. US Department of Health and Human Services, CDC; 2019. Available at: https://www.cdc.gov/antibiotic-use/core-elements/hospital.html. Accessed Jan. 8, 2020.
Centers for Disease Control and Prevention. Antibiotic Resistance & Patient Safety Portal – Stewardship. Hospital antibiotic stewardship. Available at: https://arpsp.cdc.gov/profile/stewardship. Accessed Jan. 8, 2020.