Antibiotic Stewardship for the Intensivist

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KEYWORDS

• Critical illness • Antibiotic stewardship • De-escalation • Duration of therapy

KEY POINTS

- Antibiotic stewardship programs (ASPs) are now required for hospital accreditation.
- The goal of antibiotic stewardship in intensive care units is to ensure timely empiric antibiotic therapy followed by appropriate de-escalation based on clinical data.
- Several clinical trials provide data that shorter durations of antibiotic therapy are as effective as longer duration.
- ICUs should work with hospital ASPs to review antibiotic use and determine areas for improvement and intervention.

BACKGROUND AND INTRODUCTION

Antibiotic stewardship refers to systematic programs, interventions, and recommendations that monitor and guide the use of antibiotics within a health care institution. While a long-term goal of antibiotic stewardship is to reduce the emergence of antibiotic resistance across the population, improved antibiotic use directly impacts the safe care of patients by promoting optimal antibiotic selection and minimizing unintended consequences of antibiotics including *Clostridioides difficile* infection, adverse drug toxicities such as acute kidney injury, and negative impacts on the microbiome. In turn, following best practices in antibiotic prescribing also can lead to a reduction of health care costs.[1–3]

Organized approaches to improve antibiotic use in hospitals began in the 1970s and primarily involved restriction of use of certain antibiotics for which use had to be approved by infectious disease physicians.[4,5] Over the ensuing years, implementation of stewardship initiatives varied widely in scope and practice throughout the United States until 2014 when the Centers for Disease Control and Prevention (CDC) published the Core Elements of Hospital Antibiotic Stewardship Programs (ASPs), which

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Abbreviations	
ASP	Antibiotic Stewardship Program
CAP	community-acquired
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
CRP	C-reactive protein
FiO2	fraction of inspired oxygen
HAP	hospital-acquired pneumonia
IAI	Intra-abdominal infection
ICU	intensive care unit
MRSA	methicillin-resistant Staphylococcus aureus
NAAT	nucleic acid amplification test
NHSN	National Healthcare Safety Network
PCT	Procalcitonin
PEEP	positive end-expiratory pressure
UTI	urinary tract infection
VAP	ventilator-associated pneumonia

outlines the structure and actions needed for successful ASPs, summarized in **Table 1**.[6] Formal requirements for US hospitals to have ASPs began in 2017, when The Joint Commission made the presence of an ASP that meets the CDC Core Elements criteria a standard for hospital accreditation. This was followed by the Centers for Medicare and Medicaid Services (CMS) launching hospital ASPs as a Condition of Participation effective in 2020.[7] Further, since 2024, all US hospitals are required to report antibiotic use and resistance data to the CDC's National Healthcare Safety Network (NHSN).[8]

The practice of antibiotic stewardship is particularly important within intensive care units (ICUs) because (1) patients in the ICU are critically ill, including many with severe infections; (2) patients in the ICU have invasive devices and undergo invasive procedures (eg, central lines, urinary catheters, ventilators, continuous renal replacement therapy, and extracorporeal membrane oxygenation) that put them at higher risk for infection, including those caused by antibiotic-resistant organisms; and (3) patients in the ICU receive the highest volume of broad-spectrum antibiotics in the hospital. However, improving antibiotic use in the ICU setting can be challenging due to clinical uncertainty about which patients have infections and which are at risk for infections due to antibiotic resistant organisms. While patients with septic shock must receive early appropriate antibiotic therapy to reduce mortality, unnecessary antibiotic use in patients without infection or excessively broad therapy for infections where narrow-spectrum antibiotics can be used can put patients at risk for antibiotic adverse events and future antibiotic-resistant infections.[9,10] This article will identify approaches for ICUs to partner with hospital ASPs and discuss stewardship strategies that can be incorporated into daily ICU care with the goal of optimizing antibiotic use and patient outcomes.

ESTABLISHING AND PRACTICING ANTIBIOTIC STEWARDSHIP IN THE INTENSIVE CARE UNIT

Practicing antibiotic stewardship in the ICU is facilitated by its existing collaborative team structure that includes physicians, advanced practitioners, pharmacists, nurses, and respiratory therapists who can all work with the hospital ASP to identify areas and execute approaches for improvements in antibiotic prescribing. It is useful to identify unit-based champions to spearhead stewardship activities because clinicians are

Table 1
Centers for Disease Control and Prevention core elements of hospital antibiotic stewardship programs (2019 update)

Element	Comments
Leadership commitment as demonstrated by funding and resources for program leadership and IT	To function robustly, hospital ASPs must be funded to ensure that AS leads have the time to develop guidelines and perform interventions. Further, IT resources are necessary to ensure access to antibiotic use and resistance data.
Leadership by a physician and pharmacist	Having physician leadership, ideally with IDs training, is essential because ASPs are directing recommendations to physicians and advanced practitioners who must operationalize them. Having pharmacist leadership, ideally with ID or stewardship training, is essential because the pharmacy controls antibiotic dispensing and has pharmacotherapy expertise.
Implementation of core stewardship interventions (preauthorization and prospective audit and feedback) and other interventions to improve antibiotic use	The 2 core AS interventions that ASPs should perform routinely are preauthorization, where the prescriber must obtain approval in real time to use a drug prior to prescribing it (via a text message, phone call, ID consult, use of an order set, etc.) and prospective audit and feedback, where members of the ASP identify and evaluate patients on antibiotics and provide recommendation to stopping or modifying them, usually 48–72 h after they are started. Individual programs will determine which of these 2 interventions to use for each antibiotic and patient care location. ASPs also should perform targeted interventions based on assessments of particular areas where improvement in prescribing is needed.
Monitoring of antibiotic use and other important outcomes	Monitoring antibiotic use and other relevant outcomes (eg, *C. difficile* infections, antibiotic adverse events, emergence of resistant organisms, opportunities to reduce hospital stay) is necessary to target areas for intervention and improvement.
Reporting data to providers and hospital leadership	ASPs should provide feedback to prescribers and leadership regarding overall antibiotic use, appropriate antibiotic use, antibiotic resistance, and outcomes associated with antibiotic use to facilitate education and change.
Education of providers about antibiotic use and resistance	ASPs should develop guidelines, order sets, and other tools to optimize antibiotic prescribing and should lead efforts to educate health care workers regarding their roles in optimizing antibiotic prescribing.

Abbreviations: IDs, infectious diseases; IT, information technology.

more likely to engage if their peers are involved in the process. One champion should be a physician who is respected by other prescribers, such as the medical director of the unit. Depending on the staffing structure of the unit, identification of a physician and advanced practitioner pair may also be an effective approach. In addition, a clinical pharmacist should be included as a champion; many ICUs already have clinical pharmacists embedded in the rounding team, but if this is not the case, then the pharmacy department should be asked to assign a pharmacist to assist with stewardship activities. Consideration can be given to recruiting a nurse champion. Although nurses

are not involved in prescription of antibiotics, they administer them and are at the bedside of patients more often than other health care workers, where they can observe patients for adverse events and problems with antibiotic administration. Furthermore, they can work with rounding pharmacists to prompt daily review of the need for antibiotics by prescribers.

Collectively, these individuals are responsible for engaging with the ICU staff to encourage them to be individual stewards of antibiotic use and with the hospital ASP to review current antibiotic prescribing practices, determine what additional prescribing guidance is needed, and champion and execute interventions to improve antibiotic use. The hospital ASP should provide antibiotic use rates for the ICU, stratified by antibiotic class and benchmarked based on national data reported to the CDC NHSN or relative to other similar units in the hospital. The hospital ASP may have existing data on the appropriateness of antibiotic use in the ICU based on existing interventions or assessments of compliance with local prescribing guidelines.

In discussion with the hospital ASP, consider whether joint antibiotic rounds between hospital ASP staff and ICU providers would be useful. In a prospective cluster randomized cross-over study in 5 academic ICUs in the United States, weekly in-person rounds on patients receiving antibiotics was associated with a modest 16% reduction in antibiotic use (although the reduction varied based on the type of ICU).[11] The most common infectious syndrome intervened upon was pneumonia and the most common recommendation was to set an end date for antibiotic therapy. Such rounds can be time-consuming but may have the benefit of increasing unit engagement and active discussion about stewardship opportunities.

ICUs should strive to perform daily interventions to improve antibiotic prescribing, rather than rely solely on the hospital ASP to prompt changes in antibiotic use. Consideration should be given to integrating into daily rounds the Four Moments of Antibiotic Decision Making, a framework designed to ensure optimal antibiotic prescribing using a structured approach at critical time periods of antibiotic decision making (**Table 2**) that has been associated with decreased antibiotic use and hospital onset *C difficile* infections in the United States; application of the Four Moments to specific ICU situations is discussed further in this article.[12,13] A daily discussion regarding antibiotic therapy for each patient during rounds, known as an antibiotic time-out, has been associated with reduced antibiotic use and mortality in a medical/surgical ICU in Japan and more appropriate antibiotic use in medical/surgical floor units.[14,15]

Reasons for selection of specific antibiotics, plans for de-escalation, and planned duration of therapy should be documented in progress notes to ensure that clinical reasoning about antibiotic therapy is available to all caregivers. Particular attention to antibiotic decision making and documentation should occur at the time of transition of patients out of the ICU setting; if antibiotics can be stopped or narrowed, doing this before transfer will minimize patient exposure to unnecessary antibiotics. ICU ownership of antibiotic decisions creates a culture of self-stewardship among all members of the team and is useful especially in hospitals with fewer stewardship resources.[11]

TARGETS FOR ANTIBIOTIC STEWARDSHIP IN THE INTENSIVE CARE UNIT

General Considerations for Antibiotic Stewardship in the Intensive Care Unit

Decisions regarding empiric therapy

A detailed discussion of approaches to select and administer empiric antibiotic therapy can be found in this edition. The time that empiric antibiotics are being considered provides an opportunity to step back and consider whether they are needed. Much

Table 2
The 4 moments of antibiotic decision-making[65]

Moment Questions	Timing of Question	Comment
Moment 1: Does my patient have an infection that requires antibiotic?	When initiation of antibiotics is being considered	Some patients may have a very low risk of having an infectious cause of their symptoms and others may not need antibiotics immediately.
Moment 2: Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should I initiate?	When the decision has been made to start antibiotics	Relevant cultures should be obtained prior to antibiotics whenever possible; avoid *panculturing* and base the decision regarding what culture to send on the likely infectious source. Empiric therapy should be based on what organisms are likely to cause the suspected infectious process, the severity of illness, and characteristics of the host. Ideally, guidelines for empiric therapy for common infectious processes already exist in the institution; they should be developed collaboratively between the hospital ASP and ICU providers and be based on the hospital formulary and antibiogram data.
Moment 3: Can I stop antibiotics? Can I narrow therapy or change from IV to oral therapy?	On every subsequent day of antibiotic therapy	This moment has been referred to as a daily time out. It should occur every day a patient is on antibiotics and ideally should be integrated into rounds.
Moment 4: What duration of antibiotic therapy is needed for my patient's diagnosis	When it is clear what infectious process is being treated and the patient has response to therapy	In general, most infectious processes can now be treated with courses lasting 7 days or fewer based on studies including randomized trials.

attention has been paid to rapid antibiotic administration in patients with suspected sepsis, in part related to implementation of the CMS SEP-1 bundle, leading to increased broad-spectrum antibiotic use across the United States over the past 10 years.[16] While receipt of antibiotics within 1 hour is critical and lifesaving in patients with septic shock, patients who do not meet such criteria, such as those with fever, may not benefit from immediate antibiotic therapy.[17] In a quasi-experimental study evaluating patients suspected of having an infection (based on clinical assessment of the patient including presence of fever or elevated white blood cell count) in a SICU, conservative management, consisting of collecting appropriate cultures and waiting to start antibiotics until microbiology data suggested evidence of infection, was associated with lower all-cause mortality (13% vs 27%) and more initially appropriate therapy (74% vs 62%) compared to aggressive management with immediate initiation of antibiotics.[18] While these results may not be applicable to all ICU patient populations, they suggest that consideration of obtaining additional evaluation before starting antibiotics in patients who are not demonstrating evidence of septic shock should be considered.

Further, studies have demonstrated that 10% to 25% of patients presenting to the ICU with sepsis have noninfectious causes of their symptoms, usually either cardiovascular or noninfectious respiratory syndromes.[19] Multiple conditions can mimic sepsis (**Table 3**) and patients initiating antibiotics and continuing on antibiotics for sepsis should be evaluated for these if a source of infection is not clear or if they are not responding to antibiotic therapy.[19]

To ensure that prescribers know what agents are recommended for empiric therapy and that they can be ordered in a timely fashion, guidelines and ordersets specific to the ICU setting should be available at the point of care. Organizing guidelines and ordersets according to suspected source of infection (eg, septic shock with unknown etiology; community, hospital, and ventilator associated pneumonia; urinary tract infection; intraabdominal infection) nudges prescribers to consider what additional management and testing is needed based on the likely infection and allows for tailored antibiotic selections based on the organisms associated with each syndrome.

Decisions regarding reevaluation and de-escalation

Once a patient's primary process has been identified, there is an opportunity to reevaluate the clinical situation and consider de-escalation or cessation of antimicrobials. De-escalation includes changing an antibiotic from a broad-spectrum class to a narrower spectrum class, stopping unnecessary antimicrobials, shortening durations of therapy, defining end dates for antimicrobials, and switching from intravenous to oral therapy. De-escalation has been evaluated in multiple studies, including in a systematic review of 13 studies in ICU patients in whom de-escalation to narrower therapy was associated with a 28% reduced risk of death compared to continued broad-spectrum antibiotic therapy.[20–22] Although studies evaluating outcomes associated with de-escalation can be associated with biases such as confounding by indication in which patients who are improving clinically are more likely to have antibiotics de-escalated and independently more likely to survive, overall the evidence suggests

Table 3
Common sepsis mimics[66]

System	Mimics
Cardiac	Arrhythmia, heart failure, and acute coronary syndrome
Pulmonary	Aspiration, acute respiratory distress syndrome, asthma exacerbation, bronchiectasis exacerbation, and pulmonary embolism
Gastrointestinal	Liver failure, bowel obstruction, bleed, mesenteric ischemia, pancreatitis, and volvulus
Central nervous system	Autonomic dysfunction, seizure, stroke, and intracranial hemorrhage
Endocrine	Adrenal insufficiency, diabetic ketoacidosis, myxedema coma, and thyroid storm
Hematology	Antiphospholipid syndrome, malignancy, hemophagocytic lymphohistiocytosis, and tumor lysis
Rheumatology	Gout, Still's disease, lupus, and vasculitis
Drugs/toxins	Overdose, withdrawal, toxicity, malignant hyperthermia, neuroleptic malignant syndrome, and serotonin syndrome
Other	Anaphylaxis, compartment syndrome, heat stroke, hypovolemia, burns, and tissue ischemia

that de-escalation is not harmful. A recent study evaluating de-escalation among patients with suspected sepsis in 236 US hospitals demonstrated that there is room for improvement with only 29.4% of patients having antibiotics narrowed or stopped despite the finding that it was associated with a lower odds of acute kidney injury and mortality.[23]

De-escalation can be assisted by evaluation of clinical and surveillance cultures. For example, the negative predictive value of nares swabs that do not indicate the presence of methicillin-resistant *Staphylococcus aureus* (MRSA) has been shown to be above 90% in multiple studies evaluating several sites of infection, suggesting that cessation of antibiotic therapy directed at MRSA can be stopped, particularly when the prevalence of MRSA infection is low.[24–26] It is important to note that positive predictive value of MRSA nares swabs is low; thus, positive swabs should not be used as the sole reason to continue anti-MRSA antibiotic therapy. Clinical cultures or rectal swabs that do not show evidence of organisms that require treatment with carbapenems can be used to assist in de-escalation to noncarbapenem antibiotics.[27–31]

Consideration can be given to using inflammatory biomarkers, most commonly procalcitonin (PCT), as an aid to facilitate de-escalation. Clinical trials evaluating procalcitonin algorithms, the majority of which have been open-label and performed outside of the United States, have included different populations and used different algorithms (although most algorithms recommended antibiotic discontinuation if the procalcitonin level drops less than 0.5 mcg/L or by 80% from the peak level).[32,33] Several studies have had poor algorithm compliance, indicating that rules may be difficult to implement at the bedside. Trials involving ICU patients over the past 20 years have been summarized in several meta-analyses that suggest that use of PCT-guided algorithms to inform de-escalation is associated with a reduction in antibiotic duration (1–2 days) and a modest decrease in mortality. The recent ADAPT Sepsis Trial was a multicenter, double-blinded study comparing a PCT-guided protocol and a C-reactive protein (CRP)-guided protocol to standard care in patients admitted to ICUs with sepsis expected to continue antibiotics for at least 72 hours.[34] This rigorous trial demonstrated a 1-day reduction in antibiotic duration (9.8 days vs 10.7 days) and no difference in mortality (20.9% vs 19.4%) in the PCT arm and no change in antibiotic duration in the CRP arm. Overall, use of PCT-based algorithms in the ICU may be useful in achieving modest reductions in antibiotic use, although given the long-courses of antibiotics used in studies of PCT ($\sim$ 9–10 days), regular evaluation of the need for continuing antibiotics daily may allow for the same or greater reductions in use. If PCT is used to inform de-escalation decisions, an algorithm should be developed with input from the hospital ASP and end-users, and periodic evaluation of compliance with the algorithm should be assessed.

Once it is determined there is no infection or low suspicion for infection, ICU teams should not feel compelled to complete a course of therapy; stopping antibiotics while the patient remains hospitalized facilitates on-going monitoring to ensure that they remain stable off therapy. Decisions around stopping and narrowing therapy can be challenging; some examples of how to approach different clinical scenarios in the ICU are described in **Table 4**.

Syndrome-Specific Considerations for Stewardship in the Intensive Care Unit

Bloodstream infections

Several antibiotic stewardship opportunities are available for patients with bacteremia. Early diagnosis of the causative organism as well as the presence of common resistance genes can be achieved via multiplex nucleic acid amplification tests (NAATs) performed on organisms growing in blood cultures. This information, often available

Table 4
Framework for decision-making around antibiotic de-escalation and cessation

Scenario	Action
An alternative nonbacterial etiology is identified (eg, pulmonary embolism, aspiration)	Stop antibiotics
A bacterial infection is identified and clinical culture data are available	Narrow or broaden therapy as appropriate
A bacterial infection is identified but clinical culture data are not available (eg, HAP and nonpurulent cellulitis)	Antibiotic regimen based on likely pathogens informed by local susceptibility data and surveillance culture data if available
Neither a bacterial or a nonbacterial etiology is identified and the patient is better	Stop antibiotics and monitor (avoid predetermined courses of antibiotics)
Neither a bacterial or a nonbacterial etiology is identified and the patient is not better	Additional workup for infectious and noninfectious processes. Limit antibiotic course to 7 days for most patients.

within hours, allows clinicians to escalate or deescalate antibiotic therapy before final culture data has been obtained.[35,36] Use of rapid diagnostic tests for bloodstream infections is associated with decreased mortality, length of hospitalization and time to appropriate therapy, but only when combined with involvement of ASPs. Thus, it is important that ICUs work with the hospital ASP to develop specific guidance around what antibiotic therapy is indicated for certain organisms and resistance markers. De-escalation based on blood culture susceptibility results should be performed for all patients. In a recent, pragmatic, randomized trial of patients with Enterobacterales bacteremia in 21 Spanish hospitals, de-escalation from antipseudomonal beta-lactams to narrow spectrum antibiotics, including oral therapy (specifically ampicillin, trimethoprim-sulfamethoxazole, cefuroxime, ceftriaxone, amoxicillin-clavulanic acid, ciprofloxacin, or ertapenem) compared to continued antipseudomonal beta-lactam treatment was associated with similar cure rates (90% vs 89%) and fewer severe adverse events (24% vs 32%).[37] Several observational studies have found no difference in outcomes between oral and intravenous therapy for Gram negative bacteremia, and there is a clinical trial underway to further investigate this question.[38,39]

Short courses of antibiotic therapy are appropriate for most cases of uncomplicated bacteremia.[40,41] The BALANCE trial evaluated all types of bacteremia, excluding *Streptococcus aureus* and *S lugdunensis,* infections that require prolonged courses of antibiotic therapy (such as endocarditis), and immunocompromised patients (neutropenia, solid organ transplant, hematopoietic stem cell transplant), and found that 7 days of therapy was noninferior to 14 days of therapy (90 day mortality 14.5% vs 16.1%).[42] The most common sources of infection were urinary (42.7%), intra-abdominal (19.1%), and pulmonary (13.4%); the most common organisms were *Escherichia coli* (43.3%) and Klebsiella species (15.6%); and 55% of patients were in the ICU at the time of enrollment.[42] The majority of bacteremia episodes in the BALANCE trial were caused by Gram negative organisms (>70%); thus the finding that 7 days of therapy is adequate is most robust for these infections. However, the study suggests that uncomplicated bacteremias caused by *Enterococcus* species (7.3%), *S pneumoniae* (4.3%), and beta-hemolytic streptococci (4%) also can be treated with shorter course therapy in most cases.

Pneumonia

Pneumonia is both a common admission diagnosis in the ICU and a common complication in the ICU. Antibiotic stewardship for pneumonia in the ICU is impacted by the dual challenge of ascertaining if the patient has an infection and the causative organism if infection is present. Without both respiratory symptoms and infiltrates on imaging, the diagnosis of pneumonia should be questioned, and the differential should include noninfectious etiologies including pulmonary edema, acute respiratory distress syndrome, and aspiration pneumonitis without pneumonia; antibiotics are not helpful in the treatment of these conditions.[43] In the decompensating patient with pulmonary infiltrates and respiratory distress of uncertain etiology, it is reasonable to initiate treatment of pneumonia, using predetermined guidelines and ordersets for choice of antibiotic; however, the need for continued antibiotics should be evaluated.

A specific microbiologic diagnosis for pneumonia can be facilitated by blood and respiratory cultures, urinary antigens for *S pneumoniae* and *Legionella*, and respiratory virus testing. It is important to recognize that bacterial respiratory cultures can indicate colonization rather than infection and should not be the sole factor in determining if a patient has pneumonia that requires antibiotic therapy. Some institutions have adopted multiplex NAAT respiratory panels that assess for viral and bacterial pathogens and common resistance genes.[44–46] While use of these panels may be associated with modest increases in the time to appropriate antibiotic therapy, they have not been shown to impact patient outcomes, including clinical cure and mortality. This may in part be related to the same uncertainty as to whether detected organisms are causing infection that occurs with traditional respiratory cultures. If a true diagnosis of pneumonia is made, cultures (including negative surveillance cultures) and other data should be used to narrow antibiotic therapy; empiric antibiotics started to cover pseudomonas or MRSA should not be continued if these organisms are not recovered because they grow without difficult in routine bacterial cultures.

Several studies support short durations of therapy for all types of pneumonia seen in the ICU. In a retrospective, propensity-matched cohort study comparing patients with a diagnosis of community-acquired or hospital-acquired pneumonia (CAP or HAP) and median oxygen saturations $\geq$95% without supplemental oxygen, patients treated for 1 to 2 days and those treated for 5 to 8 days had similar hospital mortality (2.1% vs 2.8%) and no differences in 30-day readmissions (16.0% vs 15.8%).[47] A similar study has been conducted among patients suspected of having ventilator-associated pneumonia (VAP) with daily minimum positive end-expiratory pressure (PEEP) of $\leq$ 5 cm H_2O and fraction of inspired oxygen (FiO_2) $\leq$ 40% for at least 3 days.[48] Of the 1290 patients, 259 received 1 to 3 days of antibiotics and 1031 were treated for greater than 3 days, and no differences in time to extubation (9 days in both groups), or hospital mortality (28.4% vs 30.4%) were noted. The patients in these studies may have had nonbacterial or noninfectious syndromes rather than true pneumonia, but both studies suggest that for patients with CAP or HAP who have rapid clinical response and no longer require supplemental oxygen, or patients with VAP who have minimal stable ventilator settings, consideration can be given to very short courses of therapy.

If criteria from the aforementioned studies are not met, guidelines generally recommend 5 days of therapy for CAP and 7 days of therapy for HAP and VAP, based on clinical trials that have demonstrated no difference in mortality or recurrent infections with shorter courses and decreased rates of multidrug resistant pathogens.[49–52] Patients with respiratory viruses who are started on antibiotic therapy due to concern for bacterial superinfection should have these stopped if there is no evidence of such infection. Finally, consideration should be given to early transition to oral therapy

if the patient can tolerate it and has oral therapy options because it is associated with fewer hospital days, shorter duration of antibiotic therapy, and no difference in mortality compared to later transition.[53]

Urinary tract infections

Many hospitalized patients, especially those with indwelling urinary catheters, will have bacteriuria without the presence of an infection.[54,55] Additionally, many patients in the ICU are unable to provide a history to understand if symptoms of a urinary tract infections (UTI) are present. Thus, urine culture stewardship is a critical step for antibiotic stewardship around UTIs in the ICU. Sending urine cultures as part of a general fever workup should be avoided, and as much as possible, urine cultures should only be obtained in patients in whom there is a strong suspicion for UTI, such as the presence of urinary tract abnormalities or localizing symptoms. Because indwelling urinary catheters are a risk for UTI, minimizing their use is desirable. If catheter-associated UTI is suspected, the catheter should be removed before urine cultures are sent; if the patient is stable, removal of the catheter alone may be adequate treatment. Aside from cystitis, which in most cases can be treated with 3 to 5 days of oral therapy, most complicated UTIs can be treated with 7 days of therapy with longer courses being reserved for cases in which source control has not been obtained (eg, infected stones and unresolved functional abnormalities of the urinary tract).[56–59]

Intra-abdominal infections

While many types of intra-abdominal infections (IAIs) are seen in the ICU (eg, cholangitis with associated sepsis, postoperative intra-abdominal abscess, and acalculous cholecystitis), the primary stewardship opportunities for IAIs are de-escalation of empiric antibiotics, usually based on culture data, and minimizing duration of therapy based on the presence of source control. Source control is the mechanical process of removing pathogenic organisms, necrotic tissue, inflammatory exudates, and hardware that drive the systemic sepsis response; source control obtained within 6 hours in community-acquired sepsis was associated with reduced risk of mortality in a recent retrospective study.[60,61] Several studies have demonstrated the benefits of shorter courses of antibiotics after source control of IAIs has been achieved.[62,63] The STOP IT Trial found that patients with IAI who had achieved adequate source control via surgery or percutaneous drain had similar rates of recurrence and mortality when treated with 4 days of antibiotics compared to up to 10 days of antibiotics after surgery. These findings were consistent across several subgroups including patients with higher APACHE scores and who achieved source control via percutaneous drain, and short course therapy has become the standard approach including in ICU patients.[64]

SUMMARY

Antibiotic stewardship should be considered a critical element to optimize the care of the ICU patient. ICU patients presenting with septic shock must receive early and appropriate therapy. At the same time, once a patient has stabilized and the diagnosis is better understood, antibiotics should be tailored or stopped if no infection is likely or if an appropriate course of therapy is complete. Multidisciplinary ICU teams should collaborate with hospital ASPs to review data on antibiotic use; identify targets for improved antibiotic use; develop guidelines algorithms, and order sets specific to ICU antibiotic needs; and determine the best approaches for interventions to ensure that all patients receive the most appropriate therapy.

CLINICS CARE POINTS

- Intensive care unit (ICU) teams should partner with hospital Antibiotic Stewardship Programs to (1) develop and enhance guidelines, order sets, and pathways to ensure that critically ill patients receive timely and appropriate empiric antibiotic therapy, (2) implement approaches to review antibiotic selection and need daily for all patients, and (3) identify specific clinical scenarios where prescribing can be improved and develop targeted improvement interventions.
- ICUs should identify physician, advanced practitioner, pharmacist, and nursing champions to lead and promote local antibiotic stewardship efforts.
- Consider conditions that may mimic infection and sepsis both before starting antibiotics and in patients who are not responding to broad-spectrum antibiotic therapy.
- Antibiotics should be deescalated or stopped whenever possible, and especially before a patient is transferred out of an ICU; stopping antibiotics while a patient is still hospitalized allows for ongoing observation for any infection recurrence.
- Use of inflammatory biomarkers (eg, procalcitonin) is associated with modest reductions in already long durations of antibiotics (eg, 10–9 days) in clinical trials; if used, algorithms for appropriate use should be developed and adhered to.
- In addition to standard culture data, multiplex nucleic acid amplification tests on organisms growing in blood and surveillance cultures (eg, methicillin-resistant *Staphylococcus aureus* nares swabs) can be useful to tailor antibiotic therapy.
- Most cases of uncomplicated gram-negative bacteremia and complicated urinary tract infection can be treated with 7 days of antibiotic therapy.
- Most cases of hospital-acquired pneumonia or ventilator-associated pneumonia can be treated for 7 days (shorter courses are also reasonable when the diagnosis is equivocal or the patient has no oxygen requirement or stable, minimal ventilator requirements (eg, daily minimum positive end-expiratory pressure of $\leq$5 cm H_2O and fraction of inspired oxygen $\leq$40% for at least 3 days).
- Intra-abdominal infection can be treated for 4 days following source control obtained either surgically or via percutaneous drain.

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