Antimicrobial Stewardship in the Emergency Department

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KEYWORDS

• Antibiotics • Antimicrobial stewardship • Emergency department
• Quality improvement • Infectious diseases

KEY POINTS

- The emergency department is a critical setting for antimicrobial stewardship efforts given the frequency of infectious disease encounters and its major role in hospital admissions and acute care outpatient encounters.
- Institutional support, especially for a physician champion, is critical for the success of any emergency department–based antimicrobial stewardship intervention.
- The biomarker procalcitonin and influenza assays are effective means to differentiate viral from bacteria causes of respiratory tract infections and thereby safely reduce unnecessary antibiotic prescribing.
- Emergency department stewardship efforts for urinary tract infections should focus on avoiding routine screening urinalyses for patients without urinary complaints and reducing treatment of asymptomatic bacteriuria.
- Clinical cure rates for uncomplicated abscesses are marginally improved with antibiotics following incision and drainage. The decision to prescribe antibiotics should involve shared decision making, which includes discussion of the risk/benefit ratio.

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INTRODUCTION

Antimicrobials are unique among all classes of therapeutics in that they decrease in effectiveness over time and in direct relation to the frequency of use.[1] Pathogen resistance develops in response to selective pressure associated with all antibiotic prescribing but is accelerated by inappropriate use. Antimicrobials are critically important medications that affect not only the patient receiving them but also the surrounding community. A substantial increase in global rates of infections related to resistant pathogens, in combination with limited new antimicrobial agents in development, has raised concerns of an impending "postantibiotic era" with potential catastrophic consequences for human health.[2]

To address this public health crisis, tremendous efforts have begun to curb the widespread inappropriate use of antimicrobials in human health and agriculture.[3–5] Antimicrobial stewardship refers to efforts aimed at optimizing the use of anti-infective medications. There is a substantial body of literature supporting the ability of hospital antimicrobial stewardship programs to reduce costs while also exerting a positive impact on clinical outcomes.[6] The emergency department (ED) has traditionally been underrepresented as a focus for antimicrobial stewardship efforts. However, policy changes, such as the Joint Commission's antibiotic stewardship accreditation standard (enacted January 1, 2017) and inclusion of stewardship quality metrics in the Centers for Medicare & Medicaid Services Physician Quality Reporting System,[7,8] will increasingly require ED providers to engage in these efforts.[9] This review serves as a primer on antimicrobial stewardship tailored for emergency care providers. To achieve this, we present antimicrobial stewardship from a public health and individual patient safety perspective, review the key domains of stewardship, identify the ED as a critical setting for stewardship efforts, summarize commonly implemented stewardship interventions, and provide stewardship strategies for the most common bacterial infections encountered in the ED.

Public Health Impact of Antimicrobial Misuse

Antimicrobial resistance is a phenomenon in which antimicrobials apply selective pressure on pathogens that, in turn, develop defense mechanisms against that antimicrobial agent's mode of action.[10] Antimicrobial resistance has been occurring since the advent of the first antimicrobial agents; however, the speed and severity of this naturally occurring phenomenon is accelerated by the misuse of antimicrobials.[11] One recent example of this was the increase in macrolide prescribing throughout the 1990s (+388% in ambulatory care).[12,13] *Streptococcus pneumoniae* isolates resistance to macrolides rose dramatically during and after this time period, going from 10% in 1994 to 35% in 1995 and to 50% in 2009.[14]

From 2000 to 2010, antimicrobial use increased by 36% globally and the trend shows no signs of slowing.[15] Moreover, the United States uses a disproportionate amount of antimicrobials per capita, ranking third in the world for total antimicrobial consumption.[15] Antimicrobial resistance is widely regarded as a global epidemic and the conservative estimate for worldwide deaths directly attributable to antimicrobial resistance is 700,000 per year. That figure, however, is projected to swell to 10 million by the year 2050 if current trends continue.[11] Unchecked, the cumulative loss of economic output from antimicrobial resistance by 2050 would amount to 20 to 35 trillion US dollars or roughly double the current US gross domestic product.[11]

Patient Safety Aspects of Antimicrobial Prescribing

Inappropriate and excessive use of antimicrobials remains a major public health threat; however, messaging to health care professionals and the public has frequently

overlooked individual patient safety concerns. Recent literature suggests that clinicians who demonstrated increased awareness of potential harm from antibiotics during the clinical decision-making process prescribed fewer antibiotics.[16] The risk of antibiotic-associated adverse events varies by class and the overall incidence may be 20%.[17,18] These adverse events can range from minor side effects (eg, diarrhea) to life threatening (eg, anaphylaxis). Antibiotics are the second most common cause of ED visits for adverse drug events with approximately 1 in 1000 prescriptions resulting in an ED visit.[18,19] Although penicillins and cephalosporins account for the highest volume of adverse drug events encountered in the ED, sulfonamides and clindamycin have the highest rates of adverse events per prescription.[18] Of increasing concern is the rising rate of *Clostridium difficile* infection (CDI) and resistant bacteria causing health care–associated infections. Antibiotics are the primary risk factor for development of CDI, estimated at nearly half a million cases and 15,000 attributable deaths each year.[20] Furthermore, an estimated 2 million illnesses and 23,000 deaths annually occur from resistant bacteria in the United States alone.[21]

The Five Ds of Antimicrobial Stewardship

The application of antimicrobial stewardship to human health care has focused on curbing inappropriate use. There are four "Ds" required for optimal antimicrobial prescribing: drug, dose, duration, de-escalation.[22] Ideally, the prescriber selects the right drug (eg, most narrow spectrum), at the right dose (eg, adjusted for patient renal function), for the right duration (eg, shortest to successfully treat infection), and considers de-escalation whenever possible (eg, narrow spectrum based on culture results). A fifth "D" of stewardship, which is perhaps most critical in the context of emergency care, is diagnosis. Prescribing of antibiotics for inappropriate diagnoses (ie, nonresponsive conditions) is prevalent in the ED for all common infection types. This includes upper respiratory tract infections (eg, bronchitis, sinusitis), urinary tract infections (UTI; eg, asymptomatic bacteriuria [ASB]), and skin and soft tissue infections (eg, pseudocellulitis).[23–28]

The Emergency Department: A Critical Setting for Antimicrobial Stewardship

The ED is increasingly the central hub of the US health care system. Annual ED visits continue to climb each year and according to National Hospital Ambulatory Medical Care Survey data annual US ED visits totaled 136.9 million or 43 per 100 persons in 2015.[29] The ED straddles the inpatient and outpatient environment, serving as the primary gateway of entry into the hospital (>80% of all of admissions) and a primary location for acute care encounters (>25%).[30,31] In fact, a recently published analysis of the US health care system concluded that roughly 50% of all medical care occurs in the ED.[32]

Infection is one of the most common reasons that patients seek acute, unscheduled care. The Centers for Disease Control and Prevention (CDC) estimate that 11% (16 million) of annual US ED diagnoses were related to infection.[33] Worsening infection also accounts for 11% of short-term readmissions following ED discharge among Medicare recipients.[34]

Reflecting the infection-related visit rates, antimicrobials are one of the most commonly prescribed drug classes in the ED. The CDC estimates that in 2015 US EDs generated more than 28 million antibiotic prescriptions.[29] Although national data specific to overall ED antibiotic prescribing appropriateness are lacking, a recent single center study in a Veterans Affairs hospital ED identified that 39% of all antimicrobial use was inappropriate.[35] This result is consistent with estimated inappropriate antibiotic use in the inpatient and outpatient clinic settings.[26,36,37]

Cost Impact of Stewardship Interventions

Although not specifically established for the ED setting, inpatient antimicrobial stewardship programs have had substantial cost savings for health systems. A 2016 meta-analysis identified that most stewardship intervention studies demonstrate significant cost savings, through reduced length of stay and drug costs, when included as an outcome.[38] Additionally, a 2017 meta-analysis reported significant reductions in colonization and infection with multidrug-resistance organisms (37%–51%) and CDI (32%).[39] These benefits are enhanced when paired with infection-control programs and CDI rates may be most directly affected by those stewardship programs that restrict use of certain antibiotics.[39,40] Reductions in difficult-to-treat health care–associated infections caused by resistant bacteria and CDIs would yield substantial cost savings for US hospitals given the associated increased lengths of stay and substantial penalties applied by Centers for Medicare & Medicaid Services related to these conditions.[41–43]

ANTIMICROBIAL STEWARDSHIP INTERVENTIONS FOR THE EMERGENCY DEPARTMENT

Antimicrobial stewardship interventions can generally be characterized into two broad categories: system-level and provider-level. An alternative method of categorizing stewardship interventions uses the classification of "horizontal" to indicate broad, system-level interventions aimed at reducing inappropriate antibiotic prescribing overall (eg, formulary restrictions), whereas "vertical" refers to interventions targeting specific antibiotics or infection types.[44] Naturally, there is some overlap between these classifications because antimicrobial stewardship interventions often involve multiple components and system-level care change processes often simultaneously influence behavior at the provider level. In 2016, a joint guideline on implementing antimicrobial stewardship programs was published by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America.[45] This document includes evidence-based recommendations for the most commonly used stewardship interventions and is an excellent resource for those looking to initiate ED stewardship programs.[46]

OVERVIEW OF SYSTEMS-LEVEL INTERVENTIONS

Physician and pharmacist leadership is an essential first step when operationalizing an ED antimicrobial stewardship program. Antimicrobial stewardship efforts should be multidisciplinary, collaborative, patient-centered, and fully supported by hospital administrators. An ED physician champion can serve as liaison between the stewardship program leadership and front-line clinicians to facilitate intervention implementation and provision of bidirectional feedback. Successful antimicrobial stewardship in the ED is multifaceted; however, system-level interventions fit broadly into four categories: (1) culture follow-up programs, (2) formulary restrictions, (3) pharmacist initiatives, and (4) antibiograms.

Emergency Department Culture Follow-up Programs

In the ED setting, all patients diagnosed with an acute infection are discharged home without available culture and susceptibility results. As such, structured culture follow-up programs are one of the first process improvements that should be considered to improve antimicrobial stewardship in the ED. The basic concept of a structured culture follow-up program is that all clinical cultures are to be reviewed by ED staff with

attention to any discrepancies between the empirically prescribed antimicrobial therapy and the reported culture and sensitivity. If a patient is receiving inappropriate or suboptimal antimicrobial therapy, the ED staff (typically a nurse or pharmacist) consults with the emergency physician and adjusts the regimen. If appropriate, a new prescription is called to the patient's outpatient pharmacy and the patient is contacted and counseled about the culture results and new antimicrobial prescription. Direct contact with the patient is key to effective stewardship, because staff may need to counsel patients about regimen compliance and answer any patient questions. As dedicated ED pharmacists become more commonplace, research suggests that the pharmacist-physician dyad outperforms the nurse-physician in this role.[47] One study found that having ED pharmacists take over the culture follow-up program saved 50 hours of cumulative emergency physician clinician time per month and decreased infection-related readmissions by 12% with no change in reported adverse drug events.[48]

Emergency Department Formulary Restrictions

Because the initial encounter for many episodes of care occurs in the ED, antimicrobial decisions made by emergency care providers often impact subsequent inpatient and outpatient therapy choices. As such, limiting the ED use of certain broad-spectrum antibiotics is one strategy to ensure that the efficacy of these agents is preserved over time.[49] A common method for implementing formulary restrictions is to establish a defined ED formulary that excludes specific antibiotics.[50] Another formulary restriction method is to establish ED criteria for use of certain antimicrobials. In this case, the ED prescriber must give their rationale for the selection of a particular antimicrobial. Typically, this is accomplished via computer-physician order entry, where the prescriber must select the criteria for use from a prepopulated menu.[51] The decision to restrict an antimicrobial or antimicrobial class is typically based on local resistance patterns and cost considerations when there is a less expensive but equally effective alternative antibiotic. Unintended consequences, such as delays in administration of broad-spectrum therapy in sepsis, should be considered in any formulary restriction policy.

Emergency Department Pharmacist

The presence of a dedicated ED pharmacist is often considered a key component of a collaborative, multidisciplinary ED practice, rather than a stand-alone, measurable intervention.[52] Nevertheless, multiple studies have demonstrated that ED pharmacists can exert a specific positive impact on antimicrobial stewardship through various roles, including: assisting in the appropriate selection and dosing of empiric antibiotics, enforcing formulary restrictions, adjusting regimens based on organ function/illness severity, structured follow-up on positive cultures, providing education on antimicrobial stewardship, and performing quality improvement projects related to antimicrobial stewardship.[47,48,53–62]

Emergency Department Antibiograms

An ED antibiogram is "a periodic summary of antimicrobial susceptibilities of local bacterial isolates [from the ED], submitted to the hospital's clinical microbiology laboratory."[63] It is typically updated annually and used by clinicians and pharmacists to assess ED susceptibility rates, as an aid in selecting empiric antimicrobial therapy, and in monitoring ED resistance trends over time. In practice, many low-volume facilities do not have an ED-specific antibiogram because the minimal number of isolates required to report resistance for a particular organism are not available. Solutions to this problem include constructing a biannual antibiogram or pooling data with other

local EDs to construct a regional ED antibiogram. Common challenges that occur when first reporting a dedicated ED antibiogram include difficulty separating ED data from hospital-wide data, difficulty separating screening data from diagnostic data, and difficulty ensuring that the data from admitted patients are not counted twice.

Antibiograms should be used to guide ED-specific recommendations for empiric treatment of all common bacterial infections.

Overview of Behavioral Interventions

The ED has unique challenges to implementing quality improvement interventions because of frequent interruptions, high-volume care, the need for rapid decisions with limited information, variation in staff over different shifts, and concerns related to patient satisfaction.[64–66] Furthermore, even though emergency care providers may appreciate the public health implications of growing antimicrobial resistance, changing practice is difficult for a multitude of reasons. To ensure each patient gets the right antibiotic at the right dose and for the right duration, or avoid an antibiotic when not indicated, effective interventions to change prescribing behavior are critically needed.

Traditional educational approaches are not effective at producing long-lasting changes in clinical practice. Although education-only interventional studies have been published, it is more common to see education included as part of a steward intervention bundle.[67,68] These typically encompass provision of education on best practice guidelines and provision of associated clinical decision support systems. For example, clinical decision support systems have been demonstrated to improve ED antibiotic decision making for community-acquired pneumonia and uncomplicated UTIs.[69–71]

Beyond simple education-based interventions, evidence from behavioral economics and the psychology decision-making literature suggests that audit and feedback, academic detailing (ie, one-on-one education), behavioral nudges, and peer comparisons can improve prescribing outcomes.[72–74] Because emergency care providers often rely on heuristics given constraints of time and limited information, behavioral interventions that take into account workflow and decision-making processes have the potential to significantly impact change by targeting specific barriers and facilitators. For example, multifaceted stewardship interventions have been demonstrated to improve ED antibiotic prescribing for pneumonia,[75–78] UTIs,[79,80] skin and soft tissue infections,[81] and sepsis.[82]

Audit and feedback

Randomized controlled trials (RCT) of audit and feedback conducted in primary care practices demonstrate that feedback can significantly improve appropriate antibiotic prescribing.[72,83] One large RCT conducted in this setting used a peer comparison feedback intervention that took advantage of social motivation and found that being labeled a top performer or not top performer was an effective means to reduce inappropriate antibiotic prescribing for respiratory tract infections.[72] However, several studies have demonstrated a reversal of stewardship gains after discontinuation of audit and feedback, suggesting the need for ongoing efforts to achieve sustainability.[84,85]

Public commitments

Simple interventions that rely on social motivation and accountability to patients and peers, such as posters placed in examination rooms and letters with a commitment to avoid potentially harmful antibiotic use, has resulted in 20% absolute reduction in

prescribing.[73] Given the higher acuity and rapid pace of ED care relative to clinic settings (ie, illness or time restrictions preventing patients from reading posters) and absence of treatment areas associated with individual physicians, the effectiveness of physician pledges in this setting is unknown. Emergency care providers may be more likely to be judicious about antibiotic avoidance when they have committed publicly to avoiding patient harm and related materials can be used for patient education.

OVERVIEW OF DIAGNOSTIC INTERVENTIONS

Diagnostic stewardship interventions are divided into three categories: (1) cultures, (2) organism identification assays, and (3) biomarkers. Although traditional cultures are not available to impact prescribing at the point of care, they are a critical component to enhance the downstream tailoring of antibiotic therapy for post-ED care in the inpatient and outpatient setting. Infection-specific cultures (eg, sputum, urine, wound) may assist in the tailoring or discontinuation of antibiotic therapy but are not routinely advised for uncomplicated UTIs, skin and soft tissue infections, or pneumonia. Additionally, although blood cultures are a core component of sepsis care, routine blood cultures should not be obtained for uncomplicated pneumonias, UTIs (including pyelonephritis), or skin and soft tissue infections because of low clinical utility and the risk of contamination resulting in false positives and unnecessary antibiotic prescribing.[86–89]

With the emergence of molecular assays that can rapidly identify organisms, such as methicillin-resistant *Staphylococcus aureus* (MRSA), there has been increased interest in using these in the ED for stewardship applications. These compliment more traditional organism identification assays, such as group A β-hemolytic *Streptococcus* for pharyngitis and influenza. Finally, procalcitonin (PCT) is a biomarker approved in 2017 by the Food and Drug Administration to assist with antibiotic prescribing decisions for respiratory tract infections.[90] PCT joins C-reactive protein, which is the other biomarker that has been tested as an antibiotic stewardship intervention.[91] Each of these interventions is covered next in more detail in their respective condition specific stewardship section.

CONDITION-SPECIFIC STEWARDSHIP APPROACHES

Respiratory Tract Infections

Antibiotic prescriptions for nonbacterial respiratory tract infections (eg, bronchitis, sinusitis, otitis media, nonspecific URI) represent the most frequent source of unnecessary antibiotic prescribing in ambulatory care settings.[26] Although simply avoiding antibiotic prescribing for nonindicated conditions would make a significant impact on stewardship, there are clinical scenarios that involve diagnostic uncertainty, which can also drive overuse. For example, patients with viral respiratory infections (eg, influenza) may have radiographic infiltrates on chest radiograph, which traditionally would prompt a diagnosis of pneumonia and prescription of antibiotics. One potential solution to this dilemma are influenza assays, which have been demonstrated in a series of studies to reduce the number of patients presenting to the ED with respiratory tract infection symptoms who receive antibiotic therapy.[92–95] More broadly, recently commercialized multiplex rapid viral panels have been proposed as a potential solution to improve antibiotic prescribing for respiratory conditions.[45,96,97] However, several clinical studies, one of which included discharged ED patients, suggest that the broader viral panel results did not significantly change antibiotic prescribing outside of those involving a positive influenza result.[98,99] It remains to be seen whether incorporating rapid multiplex viral panel results as part of an ED antimicrobial stewardship program could improve their impact.[45]

PCT is a biomarker upregulated by the presence of bacterial infection and attenuated by viral infections.[100] A 2017 Cochrane review that included data from 32 RCTs concluded that PCT-guided antibiotic therapy in the acute care setting is effective in reducing antibiotic prescribing without any adverse effect on patient safety or outcomes.[101] Based on the available data, PCT was approved by the Food and Drug Administration in 2017 to assist with antibiotic decision making in patients with lower respiratory tract infections (eg, pneumonia).[90] The impact of PCT on US ED antibiotic prescribing is unknown because it has not been widely adopted. Epidemiologic data indicate that a bacterial pathogen was identified in less than 15% of patients admitted with pneumonia as diagnosed by the presence of an infiltrate on chest radiograph.[102] This fact suggests a large potential role for PCT in helping to identify pneumonias that are not bacterial in origin.

In cases where the provider has decided to treat suspected pneumonia with antibiotics, stewardship should focus on the selection of optimal empiric therapy. Although recommended for community-acquired pneumonia in the 2007 guideline, increasing national rates of macrolide resistance among *S pneumonia* isolates means there is a diminishing role for macrolide monotherapy in the treatment of community-acquired pneumonia.[103,104] Selection of β-lactam plus doxycycline or azithromycin versus a respiratory fluoroquinolone should be based on patient factors (eg, comorbidities, potential for medication interactions) and local resistance patterns. Another important area for improved stewardship is to eliminate the use of reflex broad-spectrum antibiotic prescribing for patients meeting the traditional definition of health care–associated pneumonia (HCAP): recent admission, residing in a long-term care settings, chemotherapy, or hemodialysis.[105] Because of its poor discriminatory ability for patients at risk for pneumonia caused by resistant organisms referred to as PES (*Pseudomonas aeruginosa*, *Enterobacteriaceae* extended-spectrum β-lactamase-positive, and MRSA),[106] HCAP is no longer considered an appropriate basis for initiation of broad-spectrum antibiotics in ED patients being admitted with pneumonia.[107,108] A recently published prediction score, drug resistance in pneumonia, demonstrated improved diagnostic performance characteristics as compared with HCAP but has not yet been widely validated.[109] Initial studies suggest drug resistance in pneumonia (DRIP) can reduce broad-spectrum antibiotic prescribing without adverse clinical outcomes but further research is needed before widespread implementation.[110–114]

Urinary Tract Infections and Asymptomatic Bacteriuria

UTIs are one of the most common discharge diagnoses made in the ED and the CDC reports that treatment of UTIs in US hospitals could be improved in nearly 40% of cases.[36] To optimize ED stewardship for UTIs efforts should focus on improved diagnostic processes (eg, when to order a urinalysis [UA] and how to correctly interpret it), reduced overtreatment of ASB, and selection of appropriate empiric antibiotics.

Because of the persistence of myths around the diagnosis of UTI, optimizing the ordering of UAs and urine cultures can have a profound impact on antibiotic prescribing.[115] In ideal circumstances, the UA should only be used as a diagnostic test for UTI in the setting of clinical symptoms and suspicion for infection. Because it can identify the presence of bacteria in asymptomatic patients, a UA should not be routinely sent as a screening test for UTI.[116] Provider-level examples of inappropriate UA ordering include confirming a verbal nursing order for a UA on a patient with no urinary symptoms because the patient is confused, because the sample "looks dirty," or simply because "the patient had to pee, so I collected a sample doc…should I send it?"[117] Perhaps even more commonplace are the system-level examples of inappropriate

UA ordering. One common example is UAs sent on asymptomatic patients because the order is included on a default order set (eg, abdominal pain, psychiatric clearance, trauma). In either scenario, ordering a UA for a patient with a low pretest probability for UTI puts the ED clinician in a position where the positive predictive value of the UA is greatly diminished and the likelihood of the patient receiving unnecessary antibiotics is greatly increased.

The potential for misdiagnosis and overtreatment is compounded when urine cultures are ordered inappropriately, because the urine culture results are typically reviewed days later, often by a staff member who is not personally familiar with the patient's signs and symptoms. The two most basic stewardship interventions to reduce ordering of inappropriate urine cultures are to avoid the use of reflex urine cultures and to remove urine cultures from most order sets. Emergency care providers can also combat the ordering of inappropriate urine cultures by implementing two key practice changes. First, they can recognize patient populations that are high-risk for ASB (indwelling Foley catheter, long-term care) and avoid sending a UA or urine culture if the patient is not having symptoms. Second, they can add clarity to the situation and improve downstream care by documenting a diagnosis of "asymptomatic bacteriuria" if a UA (whether ordered intentionally or unintentionally) shows bacteria for an asymptomatic patient.

The key to understanding why a significant portion of antimicrobials given for UTI are unnecessary hinges on one's appreciation of what ASB is and what patient populations are at-risk for having ASB. ASB is defined as "isolation of bacteria in an appropriately collected urine sample from an individual without signs or symptoms referable to a urinary infection."[118] Transient ASB is common in healthy reproductive-age women (2%–5% prevalence) and even more common during pregnancy (2%–11% prevalence).[119] These patients may test "positive" 1 day and then have an unremarkable UA the next day after voiding. If the patient is tested during a period of transient ASB, they are at risk for being prescribed unnecessary antimicrobials.

In certain specialty populations, patients' bladders are colonized with nonpathogenic bacteria, meaning that they test "positive" at any time. In the long-term care population, the prevalence of ASB varies widely (5%–50%) because the presence of ASB typically corresponds to the patient's level of functional impairment. For example, up to 50% of patients with spinal cord injury or paralysis exhibit ASB. Most notably, the prevalence of ASB in patients with indwelling catheters is nearly 100%, meaning that *any* UA sent in this patient population looks "positive" if the ED clinician does not have a high index of suspicion for ASB.[118]

Emergency care providers commonly treat ASB, because this practice was standard of care for decades. The logical fallacy is that ASB progresses to pyelonephritis. This pathophysiology was observed in pregnant patients when the urine culture was first developed and the assumption was that the same was true for all patients. This false assumption led to the general treatment of ASB in all patient populations. In fact, according to national infectious disease guidelines, treating ASB is only acceptable in three niche clinical scenarios: (1) preurologic procedure, (2) immediately postrenal transplant, and (3) *once* in early pregnancy (only if present on two separate urine cultures).[116]

Another common but controversial example of treating ASB that merits its own discussion is whether or not to order a UA on older adults presenting with altered mental status or functional decline with no urinary symptoms, fever, or clinical instability. The current literature suggests that UTI is not a common cause of altered mental status in the elderly and that the premature incorrect diagnosis of UTI can lead to anchoring bias and prevent the clinician from uncovering the true (often multifactorial) cause of

the altered mental status (eg, dehydration, hypoxia, polypharmacy, sundowning, sensory impairment).[120,121] Schulz and colleagues[115] summarize a reasonable approach to this challenging patient population, asserting that older adults "with acute mental status changes accompanied by bacteriuria and pyuria, without clinical instability or other signs or symptoms of UTI, can reasonably be observed for resolution of confusion for 24 to 48 hours without antibiotics, while searching for other causes of confusion."

Another opportunity for stewardship in UTI care involves the selection of appropriate empiric therapy. Ciprofloxacin, once the mainstay of outpatient UTI and pyelonephritis treatment, is rapidly losing its efficacy against *Escherichia coli* with resistance rates averaging 35% in the United Sates.[122] Therefore it should no longer be considered a universal first-line agent for UTI and empiric therapy should be based on local resistance patterns (ie, ED antibiogram). For most patients with an uncomplicated UTI and normal renal function, we recommend nitrofurantoin or trimethoprim and sulfamethoxazole (TMP-SMX) if local *E coli* resistance rates are less than 20%.

Catheter-Associated Urinary Tract Infections

Catheter-associated UTIs are a significant source of hospital-acquired infection and thus represent a core component of ED infection prevention and antimicrobial stewardship. One national study estimated that 65% of urinary catheters placed in the ED potentially could have been avoided.[123] At the provider-level, clinicians should be aware that urinary catheters should not be placed for incontinence, ease of nursing care, or urine output measuring.[124] All catheters placed in the ED should have a plan for removal in place at the time of initial placement, so that clinical inertia does not result in a catheter being in place longer than is medically necessary. If an ED has a nurse-initiated protocol for catheter placement, the HOUDINI acronym outlines appropriate reasons for placement of a urinary catheter: *H*ematuria, gross; *O*bstruction, urinary; *U*rologic surgery; *D*ecubitus ulcer—open sacral or perineal wound in incontinent patient; *I*nput and output critical for patient management or hemodynamic instability; *N*o code/comfort care/hospice care; *I*mmobility caused by physical constraints.[125]

Skin and Soft Tissue Infections

Antimicrobial stewardship considerations in the management of skin and soft tissue infections vary depending on the type of infection. The avoidance of antibiotics following incision and drainage (I&D) of uncomplicated abscesses has been a mainstay of ED antimicrobial stewardship since it was included as part of the American College of Emergency Physician's initial Choosing Wisely recommendations in 2013.[126] This guidance was based on a series of RCTs that failed to demonstrate clinical benefit for systemic antibiotics following I&D.[127]

However, two recently published large RCTs did demonstrate a statistically significant reduction in treatment failure and development of recurrent abscesses with TMP-SMX and clindamycin following I&D.[128,129] These results have prompted some to conclude that antibiotics should become standard of care following I&D of uncomplicated abscesses.[130] Given the societal ramifications of potential increased bacterial resistance related to routine antibiotic prescribing for the hundreds of thousands of patients with uncomplicated abscesses treated in the United States alone each year, a critical analysis of these trial results is necessary.

First, it is important to recognize that the narrow margin of benefit observed for antibiotics in these trials is associated with high numbers needed to treat ranging from 7 to 14.[128,129] Even if applying the results from Daum and colleagues,[129] highest demonstrated margin of benefit observed using a composite definition of treatment failure,

which included development of future abscesses, approximately 70% of patients do not require antibiotics to successfully resolve their abscess. Additionally, there were no cases of sepsis or infection-related mortality observed among the more than 2000 trial participants, suggesting that withholding antibiotics for uncomplicated abscesses would not compromise patient safety.[128,129]

Moving forward, emergency care providers should attempt to balance the marginal treatment benefit from post-I&D antibiotics with patient safety and public health considerations. One potential solution is to engage in shared decision making, which includes discussions about the numbers needed to treat for this condition and safety risks related to antibiotics. To assist with risk stratification, results from a subgroup analysis of the Talan and colleagues[131] RCT suggest that patients with a history of MRSA or fever are more likely to benefit from antibiotic therapy. Delayed antibiotic prescribing, which substantially reduces the number of antibiotic prescriptions filled without increasing complication rates in patients with suspected respiratory tract infections, is another potential strategy.[132] When providers make a decision to prescribe, the common practice of double coverage for group A ß-hemolytic streptococcus and MRSA (eg, cephalexin plus TMP-SMX) should be avoided given clinical cure rates more than 80% are achieved with TMP-SMX alone.[27,133,134] In terms of dosing, clinical cure rates were similar with lower doses of TMP-SMX (160/800 mg twice daily) as compared with double doses (320/1600 mg twice daily).[128,129] Given increased resistance of *S aureus* isolates to clindamycin in the United States, use of this antibiotic in the treatment of abscesses should be guided by local antibiograms.[135]

Another potential solution to enhance antimicrobial stewardship in the management of uncomplicated abscesses is the use of rapid molecular MRSA assays.[136] One RCT demonstrated that these assays effectively assist emergency care providers in tailoring antibiotic therapy toward the causative bacteria in abscesses, whereas a retrospective study did not show significant improvements because of low uptake of the results by clinicians.[137,138] The tailoring of therapy is important because antibiotics commonly used to cover MRSA (TMP-SMX and clindamycin) are associated with more than twice the risk of adverse reaction compared with antibiotics with activity against methicillin-sensitive *S aureus* (eg, cephalexin).[18] The rapid detection of MRSA could also be helpful in risk stratification because patients with MRSA-related abscesses were also more likely to benefit from antibiotics in the Talan et al. RCT subgroup analysis.[131]

In the case of cellulitis, the primary areas of focus for stewardship should be improving diagnostic accuracy and appropriate antibiotic selection. A recent study published in the dermatology literature concluded that a significant portion (~30%) of ED cellulitis admissions may actually represent noninfectious dermatologic conditions termed pseudocellulitis.[23] Although this was a retrospective single-center study, the author correctly suggest emergency care providers should be vigilant for cellulitis mimics, such as "venous stasis dermatitis, lymphedema, deep venous thrombosis, gout, and contact dermatitis."[23] Diagnostic accuracy in the ED is improved through simple strategies, such as passive leg raise to observe abatement of erythema as a sign of nonbacterial cause and first considering alternative edema-causing conditions before making the unlikely diagnosis of bilateral lower extremity cellulitis.[139] The double coverage approach for uncomplicated cellulitis has been evaluated in two RCTs, neither of which observed a reduction in treatment failure with the addition of TMP-SMX to a ß-hemolytic streptococcus-active antibiotic (eg, cephalexin).[140,141] Uncomplicated, nonpurulent cellulitis should therefore only be treated after careful consideration of potential mimics and be managed with a single antibiotic active against group A ß-hemolytic *Streptococcus*.

Sexually Transmitted Infections

Sexually transmitted infections (STI) are the most common notifiable diseases seen in ED settings. There was a nearly 40% increase in the number of STI visits to EDs for the time period 2011 to 2013 compared with 2008 to 2010, versus a 2% increase for all diagnoses.[142] A total of 17% of all STI patients are seen in hospital based EDs, with patients presenting to EDs being more likely to be younger, nonwhite, and to have public insurance.[143]

Clinical judgment is often inadequate for diagnosis of STIs, leading to standard practice that involves use of empiric therapy to prevent public health transmission. Given growing evidence of resistant gonorrhea,[144] overuse of antibiotics to treat STDs is an imperative topic to address. A RCT of rapid STI testing with real-time result reporting during the ED visit coupled with specimen self-collection found only 12.9% of patients with symptoms consistent with STI tested positive for chlamydia or gonorrhea. Compared with control subjects (batched nucleic acid amplification testing), patients in the rapid molecular diagnostic group were significantly less likely to receive unnecessary empiric antibiotic treatment, less likely to report missed antibiotic doses, and more likely to be notified of their results. There were no significant differences in charges or health care use measures.[145] These results were mirrored in a recently published quasi-experimental study that also demonstrated the feasibility of rapid STI testing in the ED and observed an associated increase in appropriate antibiotic use.[146]

SUMMARY

Given the increasing role of the ED in the US health care system and magnitude of antibiotic use that occurs in this setting, antimicrobial stewardship programs are an important area of focus to improve clinical outcomes, optimize patient safety, and protect antibiotics as a critical public health resource. Opportunities to enhance antimicrobial stewardship are abundant in the ED. Each of the most common infection types (respiratory tract, urinary tract, skin and soft tissue) have aspects of antibiotic prescribing that could be significantly enhanced and we suggest these are starting points for those looking to initiate ED-based stewardship quality improvement interventions. The most effective stewardship interventions involve a bundle approach, building on the strengths of multiple systems and provider-level approaches to achieve sustainable improvements in appropriate antibiotic prescribing.

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