A Hospital Pharmacist's Guide to Antimicrobial Stewardship Programs

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Executive Summary

The development of new antibiotics led to marked improvements in the health of Americans beginning in the mid 20th century. However, in recent years antimicrobial resistance has become a major public health problem in the United States. Antimicrobial resistance often is attributed to inappropriate antibiotic use, which is common in U.S. hospitals. Hospital-acquired infections (HAI), increased morbidity and mortality, prolonged hospital lengths of stay, and increased health care costs are among the potential consequences of inappropriate antimicrobial use and antimicrobial resistance. Pathogens that are resistant to all currently available antibiotics have emerged. To make matters worse, the research and development pipeline for antimicrobial agents is essentially empty, lending urgency to the need to use currently available effective agents wisely.

Antimicrobial stewardship—the appropriate selection, dosing, route of administration, and duration of antimicrobial therapy—in conjunction with infection prevention and control measures prevents or slows the emergence of antimicrobial resistance and transmission of antimicrobial-resistant pathogens. Various strategies are used in antimicrobial stewardship programs (ASPs) to improve the quality of antimicrobial therapy, minimize antimicrobial resistance, and optimize clinical outcomes. Reducing health care costs without adversely affecting the quality of care is a secondary goal of ASPs. Pharmacists should assume a prominent role in antimicrobial stewardship because of their knowledge of and influence over antimicrobial use and membership on multidisciplinary committees in hospitals.

Developing and implementing an ASP in the hospital setting can present a challenge, with pitfalls to avoid and barriers to overcome. The process involves developing a proposal to obtain institutional support for the ASP, assembling and leading the ASP core team, analyzing current institutional practices, developing processes to meet ASP goals, analyzing and reporting data demonstrating the impact of ASP processes, and developing and implementing outreach plans directed to key hospital staff. A multidisciplinary effort with the support of hospital administration is essential to success in the process.

PURPOSE

This document is intended as an information resource on implementing antimicrobial stewardship programs for health system pharmacists and other professionals. This document is not intended to provide a comprehensive review of the appropriate use of antimicrobial agents or of the implementation of antimicrobial stewardship programs. Rather, it has been developed to generate ideas that health practitioners can use in their institutions.

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Introduction

The use of antimicrobial agents has increased in hospitalized Americans over the past several decades.[1] By some estimates, half of patients hospitalized in the United States receive antibiotics, and up to half of antimicrobial use may be inappropriate.[1,2] Problems with the excessive and inappropriate use of antimicrobial agents in the United States have been widely recognized for a long time.[3]

The potential consequences of inappropriate antimicrobial use include toxicity, the emergence of antimicrobial resistance, *Clostridium difficile (C. difficile)* and other hospital-acquired infections (HAI), increased morbidity and mortality, prolonged hospital lengths of stay, and increased health care costs.[4–7] In 2002, approximately 1.7 million HAI occurred in U.S. hospitals, resulting in nearly 99,000 deaths.[8] Estimates of the overall annual direct medical costs of HAI in U.S. hospitals ranges from $28 billion to $45 billion in 2007 dollars.[9] Hospital-acquired infections caused by gram-negative bacteria are particularly problematic.[10]

There is a causal relationship between inappropriate antimicrobial use and resistance; changes in antimicrobial use lead to parallel changes in the prevalence of resistance.[11] Antimicrobial resistance is a serious public health concern because of the emergence of multidrug-resistant and extremely drug-resistant microbial species for which there is no effective antimicrobial agent and the paucity of new antimicrobial agents in the research and development pipeline.[3,12,13]

The ESKAPE pathogens—*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae (K. pneumoniae)*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species—are the most troublesome bacterial pathogens in hospitals because they often are resistant to (i.e., escape the effects of) currently available antimicrobial agents and cause HAI.[5] Surgical site infections are a common post-operative complication and account for 14% to 16% of HAI.[14] Resistance rates are high among ESKAPE pathogens associated with surgical site infections.[5]

Antimicrobial resistance is the result of a variety of mechanisms (e.g., producing enzymes that inactivate or destroy the antibiotic, altering the antibiotic target site to prevent the drug from binding, changing the permeability of the cell wall to preventing antibiotic access to the

FIGURE 1

Centers for Disease Control and Prevention Campaign to Prevent Antimicrobial Resistance in Healthcare Settings

TABLE 1

Infection Prevention and Control Methods for Controlling Antimicrobial Resistance in Hospitals[21]

- Hand hygiene
- Contact (i.e., barrier) precautions
- Active surveillance for and decolonization (i.e., eradication) of multidrug-resistant organisms
- Perioperative antimicrobial prophylaxis
- Implementation of best practices for invasive procedures and devices (e.g., removal of unnecessary central catheters, oral disinfection with chlorhexidine for patients on ventilators)
- Disinfection and sterilization of medical devices
- Environmental cleaning

target site, actively pumping the antibiotic from the cell).[3,10,15] The antimicrobial agents to which ESKAPE pathogens are resistant have changed over the years as a result of selective pressure and various mechanisms for resistance (e.g., production of extended-spectrum β-lactamases [ESBLs] by *Klebsiella pneumoniae* [*K. pneumoniae*], *Escherichia coli* [*E. coli*], and other gram-negative pathogens to circumvent effective killing by cephalosporins, monobactams, and penicillins).[15] The mechanisms for resistance of ESKAPE pathogens often confer resistance to more than one agent (i.e., multidrug resistance).[5] A change in the ESKAPE acronym to ESCAPE, with C for *C. difficile* instead of K for *K. pneumoniae* and E for Enterobacteriaceae (which includes *Enterobacter* species, *K. pneumoniae*, *Klebsiella oxytoca*, *E. coli*, and *Proteus mirabilis*) instead of *Enterobacter* species, recently was suggested because of increases in antimicrobial resistance among and the impact of HAI caused by these organisms.[16] The emergence of *K. pneumoniae* carbapenemase (KPC)-producing strains of *K. pneumoniae* and other Enterobacteriaceae currently is a major public health concern.[17] Plasmid-mediated transfer of genes that encode KPCs and other ESBLs severely limits the available options for treating serious infections in critically-ill patients.[10]

To address the lack of antimicrobial agents in the research and development pipeline, the Infectious Diseases Society of America (IDSA) and several other organizations recently launched the "10 x '20 initiative," a call to action to develop 10 new antimicrobial drugs by the year 2020.[18] Federal legislation—the Strategies to Address Antimicrobial Resistance Act (H.R. 2400 known as STAAR)—was introduced in May 2009 to encourage the development of new antimicrobial agents as well as strengthen federal antimicrobial resistance surveillance, prevention and control, and research efforts.[19]

Preventing antimicrobial resistance requires weighing the needs of the individual patient and those of the larger society. Inadequate empiric antibiotic therapy in critically ill patients is associated with increased morbidity and mortality, but indiscriminate use of antibiotics promotes resistance that can affect the entire patient population.[6] Antimicrobial stewardship is a means for achieving balance between providing appropriate care for the individual and protecting public health.

Antimicrobial Stewardship

Antimicrobial stewardship involves the appropriate selection, dosing, route of administration, and duration of antimicrobial therapy (i.e., the prudent use of antibiotics).[11] The wise use of antimicrobial agents is a key strategy in the Centers for Disease Control and Prevention Campaign to Prevent Antimicrobial Resistance in Healthcare Settings (Figure 1).[20] Use of antimicrobial stewardship in combination with infection prevention and control efforts limits the emergence and transmission of antimicrobial-resistant pathogens.[3,4,11] Table 1 lists infection control methods for preventing the emergence and spread of antimicrobial resistance in hospitals.[21] Compliance with hand hygiene and other infection prevention and control measures in hospitals typically is poor.[21]

The primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing the unintended consequences of antimicrobial use (e.g., toxicity, selection of pathogenic organisms, emergence of resistance).[11] Reducing health care costs without adversely affecting the quality of care is a secondary goal of antimicrobial stewardship. [11]

In 2007, IDSA and the Society for Healthcare Epidemiology of America (SHEA) released guidelines for developing an institutional program to enhance antimicrobial stewardship.[11] The American Society of Health-System Pharmacists (ASHP) provided input into the development of and endorsed the guidelines. According to IDSA and SHEA, effective antimicrobial stewardship programs (ASPs) are evidence-based and can improve patient care and be financially self-supporting.[11]

Core Strategies

Two proactive core strategies form the foundation of an ASP, with various supplemental elements depending on local practice patterns and resource availability, according to IDSA/SHEA guidelines. The potential advantages and disadvantages of these core strategies and supplemental elements are listed in Table 2.

Prospective audit with direct intervention and feedback to the prescriber involves evaluating the appropriateness of orders for antimicrobial agents, contacting the prescriber if the order is inappropriate, and recommending alternative therapy.[11,22] Feedback to prescribers may be oral or written. Failure to follow written recommendations may raise legal concerns; providing oral feedback without permanent documentation in the patient medical record may avoid these concerns.[23] Prospective audit with intervention and feedback may be adapted to the practice setting, with a limited scope and frequency of interventions (e.g., Monday through Friday instead of 7 days/week) at institutions with limited resources.[26]

Formulary restriction and preauthorization requirements involves limiting the use of certain antimicrobial agents to specific indications, durations of therapy, physician services, prescribers, or patient populations.[22,24] The nature of the restriction often depends on institutional antimicrobial resistance patterns and patient safety issues related to antimicrobial agents. Formulary restriction and preauthorization can serve an educational purpose.[22] In some institutions, preauthorization requirements are used primarily for educational purposes, and the requirements are not strictly enforced.[24] In these institutions,

TABLE 2

Potential Advantages and Disadvantages of IDSA/SHEA Core Strategies and Supplemental Elements of Antimicrobial Stewardship Programs[11,22-25]

Core Strategies	Advantages	Disadvantages
Prospective audit with direct intervention and feedback	■ May reduce inappropriate antimicrobial use ■ May serve an educational purpose to modify future prescribing ■ Allows prescribers to maintain autonomy	■ Difficulty identifying patients with inappropriate therapy and communicating with prescribers
Formulary restriction and preauthorization requirements	■ May result in immediate and substantial reductions in antimicrobial use and costs	■ May increase staffing requirements ■ May delay order implementation while approval is obtained from an authorized prescriber, with the potential for adverse patient outcomes ■ May increase use of and resistance to alternative antimicrobial agents ■ Perceived loss of prescriber autonomy

(Continued next page)

TABLE 2 *(Continued)*

Supplemental Elements	Advantages	Disadvantages
Education	■ May influence prescribing behavior and promote acceptance of ASP strategies	■ Only marginally effective in modifying prescribing behavior when used without active intervention
Evidence-based guidelines and clinical pathways	■ May improve antimicrobial use and eliminate practice variations	■ Adherence may be poor
Antimicrobial cycling[a]	■ May minimize resistance by providing diversity in antimicrobial use	■ Insufficient data available demonstrating long-term effectiveness in reducing antimicrobial resistance ■ Many patients excluded because of drug allergies, toxicity, or other concerns ■ Potential for nonadherence due to prescriber lack of awareness of currently scheduled agent ■ May increase antibiotic costs
Antimicrobial order forms	■ May reduce inappropriate antimicrobial use ■ May facilitate implementation of guidelines and clinical pathways	■ Potential for inappropriate interruption in therapy due to automatic stop orders
Combination therapy[a]	■ May improve clinical outcomes and prevent resistance in certain types of patients and situations	■ Often redundant and unnecessary ■ Insufficient data available demonstrating improved clinical outcomes and prevention of resistance
Streamlining or de-escalation of therapy	■ Reduces antimicrobial exposure, selection of resistant pathogens, and health care costs	■ Prescriber reluctance to de-escalate therapy when cultures are negative and clinical improvement has been observed
Dose optimization	■ Tailors therapy to patient characteristics, causative organism, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the antimicrobial agent	■ Nursing staff concerns about incompatibilities when prolonged infusions are used based on pharmacokinetic considerations
Parenteral-to-oral conversion	■ May decrease length of hospital stay and health care costs ■ May reduce the risk of complications from intravenous access	■ Difficulty identifying patients in whom conversion is appropriate

ASP = antimicrobial stewardship program; IDSA = Infectious Diseases Society of America; SHEA = Society for Healthcare Epidemiology of America

[a] Not routinely recommended in IDSA/SHEA guidelines

requests for restricted agents trigger an infectious diseases consultation, which serves as an opportunity to provide education, improves antimicrobial use, and reduces resistance and health care costs. Formulary restriction and preauthorization and prospective audit with intervention and feedback are not mutually exclusive.

Whether formulary restriction and preauthorization reduces antimicrobial resistance in the institution is unclear because this strategy may increase the use of and resistance to an alternative antimicrobial agent, a phenomenon known as "squeezing the balloon".[11,24] The effectiveness of preauthorization requirements may depend on the education, training, and skills of the authorized prescribers.[11]

Supplemental Elements

Education is the most commonly used supplemental element.[11] However, active intervention (e.g., prospective audit and intervention) is required with education because passive education alone (e.g., provision of seminars and written guidelines) is only marginally effective in modifying prescribing behavior.[11] Repeated education is needed because of changes over time in antimicrobial resistance patterns and staff turnover.[22]

Evidence-based guidelines and clinical pathways that take into consideration the institutional formulary and local microbiology and antimicrobial resistance patterns may improve antimicrobial use and eliminate practice variations.[11] These guidelines and clinical pathways should be developed with multidisciplinary input. Adherence to national guidelines typically is poor because of their lack of local applicability.[24] Tailoring guidelines and clinical pathways to address local microbiology and resistance patterns improves the likelihood of adherence.[11] Education and feedback should be provided to prescribers on antimicrobial use and patient outcomes to facilitate implementation of guidelines and clinical pathways.[11,27] Guidelines and clinical pathways should be updated periodically.[28]

Antimicrobial cycling is the scheduled substitution of a specific antimicrobial agent or class for another agent or class to prevent or reverse antimicrobial resistance.[11] Cycling provides heterogeneity (i.e., diversity) in antimicrobial use, which may minimize the selection pressure that leads to resistance.[11,29] This selection pressure is low during periods when the use of an agent or class is low.[24] However, there are insufficient data about the long-term effectiveness of antimicrobial cycling for preventing or reversing antimicrobial resistance, so this practice is not routinely recommended in the IDSA/SHEA guidelines.[11] The cost of antimicrobial agents could increase during cycling if use is insufficient to meet minimum quantities needed to obtain favorable contract prices.[23]

Antimicrobial order forms with automatic stop orders and requirements for the prescriber to justify antibiotic use can prevent excessively long and other inappropriate antimicrobial therapy. Paper or electronic forms may be developed. Incorporation of antimicrobial order forms into computerized physician order entry (CPOE) systems minimizes the time required to complete forms.[22] Staff access to paper antimicrobial order forms is a consideration in institutions without CPOE systems. Order renewal requirements should be explained to prescribers to avoid inappropriate interruption in therapy from the use of automatic stop orders.[11]

Combination therapy in theory may improve clinical outcomes and prevent resistance in certain types of patients and situations. For example, critically-ill patients with serious infections suspected to be caused by multidrug-resistant pathogens may respond better to empiric therapy with a broad spectrum of coverage (e.g., a broad-spectrum β-lactam antibiotic, an aminoglycoside or fluoroquinolone, and an agent to which methicillin-resistant *Staphylococcus aureus* is susceptible) than to monotherapy with a more narrow spectrum of activity.[11] However, combination therapy often is redundant and unnecessary, and there are insufficient data supporting its use to improve clinical outcomes or prevent resistance. Therefore, combination therapy is not routinely recommended to prevent the emergence of resistance in the IDSA/SHEA guidelines.[11]

Streamlining or de-escalation of therapy involves the discontinuation of inappropriate or redundant empiric antimicrobial therapy based on culture and antimicrobial susceptibility data usually obtained on the third day of empiric antibiotic therapy (e.g., discontinuing broad-spectrum

therapy and initiating targeted therapy with a more narrow spectrum of activity suited to the isolated pathogen).

Dose optimization is a strategy that takes into consideration patient characteristics (e.g., age, weight, renal function), the causative organism, site of infection (e.g., bone), and pharmacokinetic and pharmacodynamic characteristics of the antimicrobial agent.[11] The pharmacokinetic and pharmacodynamic considerations enter into antimicrobial use guidelines.

Parenteral-to-oral conversion for antimicrobial agents with excellent bioavailability when the patient's condition permits can decrease the length of hospital stay and health care costs.[11] Developing institutional guidelines with clinical criteria for conversion can facilitate use of this strategy.

Various combinations of the core strategies and supplemental elements listed in Table 2 are used in hospitals. De-escalation of therapy on the third day of empiric antibiotic use is widely used with prospective audit with intervention and feedback.

Care Bundles

Care bundles are groups of evidence-based best practices that improve care, with a greater improvement achieved when the practices are used as a group within a specific time frame than when each practice is used alone.[30] Care bundles involve practices (usually three or four) that are necessary and sufficient to improve quality (i.e., lack of any one practice diminishes the likelihood of success in improving quality).[31] Measurement of compliance with the bundle is straightforward and dichotomous (i.e., all or nothing, with yes/no determinations at various checkpoints).[30,31]

Care bundles can provide education and clinical decision support and facilitate documentation of decisions. [30] The use of care bundles ensures a systematic approach so that the delivery of care is consistent for all patients based on established local evidence-based guidelines.[30] Auditing compliance with care bundles serves as a means for performance monitoring of processes of care that can lead to quality improvement.[30] Care bundles have been used successfully to reduce HAI by the Institute for Healthcare Improvement in its 100,000 Lives Campaign, a national initiative with a goal of saving 100,000 lives in hospitalized patients through improvements in the safety and effectiveness of health care.[32]

TABLE 3

Proposed Care Bundles for Antibiotic Prescribing[30]

Acute care: initiation of therapy
■ Document clinical rationale for antibiotic initiation
■ Collect and send appropriate specimens to microbiology laboratory
■ Select antibiotic therapy according to local policies (i.e., local antimicrobial susceptibilities) and risk group (exclude drug allergy)
■ Consider removal of foreign body/drainage of pus/surgical intervention
Acute care: continuation of therapy
■ On a daily basis, consider de-escalation, parenteral-to-oral conversion, or discontinuation of antibiotic therapy based on clinical signs and symptoms and laboratory test results
■ Monitor serum antibiotic concentrations in accordance with local policies
Surgical prophylaxis
■ Select antibiotic therapy based on local guidelines (i.e., local antimicrobial susceptibilities) and type of surgery (exclude drug allergy)
■ Give first dose within guideline-defined time before incision
■ Discontinue antibiotic therapy within guideline-defined time after first preoperative dose or surgical end time

The use of care bundles has been suggested for antimicrobial stewardship in the acute care and surgical settings (Table 3), with input from local microbiologists and pharmacists and adaptation of the care bundle to meet institutional needs.[30] The primary goals of an acute care antibiotic bundle are to select the antibiotic most likely to cure the patient while simultaneously minimizing the risk of side effects, resistance to the antibiotic, and *C. difficile* infection (CDI).[30] The primary goals of a surgical antibiotic prophylaxis bundle are to

decrease the incidence of surgical site infections, while simultaneously reducing the risk of side effects and resistance to the antibiotic.[30]

At a tertiary care center, improved compliance with quality indicators was associated with implementation of an antibiotic care bundle for internal medicine and surgery patients receiving an antipseudomonal β-lactam antibiotic, vancomycin, fluoroquinolone, linezolid, or aminoglycoside.[33] The quality indicators included documentation of treatment rationale, collection of appropriate culture specimens, appropriate empiric antibiotic selection, and de-escalation of antibiotic therapy. Clinical outcomes were not assessed.

Pulcini and colleagues identified four key process measures for the reassessment of inpatient empiric antibiotic use after approximately 3 days of treatment based on published literature.[34] These measures include presence of an antibiotic plan (drug, dose, route of administration, dosing interval, and planned duration), a review of the diagnosis, adjustment of the antibiotic therapy (e.g., streamlining, discontinuation) based on positive microbiological results if available, and documented consideration of parenteral-to-oral conversion if therapy was initiated using the intravenous (i.v.) route. These four measures were grouped to form a care bundle as a fifth measure. Compliance with this day 3 bundle required completion of all four process measures. The feasibility of using the five measures of care was evaluated over a 15-week period. The investigators judged the measures suitable for reassessing empiric antibiotic use after 3 days, with data collection that was sustainable over the 15-week period. Full (100%) compliance with the care bundle was achieved after 15 weeks. Clinical outcomes were not assessed.

Additional experience with antibiotic care bundles is needed. Methodologic flaws limit the validity of published reports of studies evaluating the impact of interventions to improve hospital antibiotic use.[35,36]

Information Technology

The information technology infrastructure at a hospital often dictates which of the core strategies and supplemental elements in Table 2 can be used. This infrastructure may comprise a CPOE system and electronic clinical decision support system, with electronic alerts (e.g., warnings about the need to reassess empiric antibiotic therapy after 3 days). Systems with the capability for obtaining comprehensive data on a real-time basis are valuable for conducting ASP activities. Many of the core strategies and supplemental elements listed in Table 2 (e.g., automatic stops as part of standardized antimicrobial orders) may be incorporated into CPOE systems. In the future, interfaces between the clinical laboratory and the CPOE system will facilitate the use of evidence-based guidelines and clinical pathways based on culture and antimicrobial susceptibility data and renal and hepatic function test results by providing guidance in antibiotic selection and dosing.

Information technology may be used to gather, sort, and analyze antimicrobial drug use data to create databases and identify, prioritize, and target problems with prescribing that involve specific physician services, types of patients, hospital units, or antimicrobial agents.[11] Information technology also can streamline the analysis of data pertaining to antimicrobial resistance to yield meaningful information about the impact of ASP activities. A lack of information technology often is the biggest barrier to implementing an ASP, although an extensive database and sophisticated information system are not necessarily required for a successful ASP.

Role of the Pharmacist in Antimicrobial Stewardship

A statement about the pharmacist's role in antimicrobial stewardship and infection prevention and control recently was released by ASHP.[37] Promoting optimal use of antimicrobial agents (Table 4), reducing the transmission of infections, and educating health professionals, patients, and the public about antimicrobial stewardship and infection prevention and control are key pharmacist responsibilities. Pharmacist efforts to promote optimal use of antimicrobial agents and contributions to the success of ASPs are well documented.[2,38–40] According to ASHP, pharmacists should assume a prominent role in antimicrobial stewardship because of their knowledge of and influence over antimicrobial use and membership on multidisciplinary committees in the institution.[37]

TABLE 4

Pharmacist Functions that Promote Optimal Use of Antimicrobial Agents[37]

- Promoting multidisciplinary collaboration in the institution to ensure optimal patient outcomes from prophylactic, empiric, and therapeutic uses of antimicrobial agents
- Making recommendations for appropriate antimicrobial agent selection, dose optimization, timely initiation of therapy, therapeutic monitoring, and de-escalation of therapy
- Working with the pharmacy and therapeutics committee or its equivalent to develop policies and procedures for restricted antimicrobial use and therapeutic interchange, treatment guidelines, and clinical care plans
- Generating and analyzing quantitative data on antimicrobial drug use for use in performing analyses of clinical and economic outcomes
- Collaborating with microbiology laboratory and infectious diseases personnel to ensure the timely reporting of microbial susceptibility test results for individuals and hospital-wide and unit-specific microbial susceptibility data to prescribers
- Using information technology for surveillance of antimicrobial resistance, preparation of reports on antimicrobial use and outcomes, and developing clinical decision support tools
- Encouraging safe medication management practices for antimicrobial agents using efficient and effective systems to reduce the risk for errors and adverse effects

Pharmacist involvement in the pharmacy and therapeutics (P & T) committee is instrumental in providing antimicrobial stewardship because this committee has the authority to manage antibiotic use in the institution. Pharmacists also should participate in the infection prevention and control committee; this involvement is critical to the success of antimicrobial stewardship efforts.[37] Antimicrobial stewardship efforts are unlikely to succeed without effective infection prevention and control measures.

Current IDSA/SHEA guidelines call for a clinical pharmacist with infectious diseases training and an infectious diseases physician to serve as core members of a multidisciplinary antimicrobial stewardship team.[11] The team often is directed by these two core members. The current IDSA/SHEA guidelines reflect a change from previous guidelines in which pharmacists played a smaller role and were expected to defer requests for therapeutic information and recommendations to physicians.[41] The prominent role for pharmacists in antimicrobial stewardship called for in current IDSA/SHEA guidelines represents an opportunity for pharmacists to assume an expanded role in and responsibility for collaborative drug therapy management based on their knowledge of pharmacokinetics and pharmacodynamics. The director of pharmacy should make a commitment to antimicrobial stewardship and assume a leadership role in promoting the role of pharmacists as antibiotic use experts in the institution when interacting with other department heads and hospital administration. The director of pharmacy in collaboration with an infectious diseases leader or other medical staff champion also should lead the effort to formally introduce antimicrobial stewardship to the organization.

According to IDSA/SHEA guidelines, the pharmacist who serves as a core member of the antimicrobial stewardship team should be knowledgeable about the appropriate use of antimicrobial agents and receive appropriate training to achieve and maintain this expertise.[11] In a joint opinion published in 2009, the Society of Infectious Diseases Pharmacists (SIDP) and the Infectious Diseases Practice and Research Network (ID PRN) of the American College of Clinical Pharmacy (ACCP) recommended completion of a postgraduate year (PGY) 1 residency and a PGY2 residency in infectious diseases, board certification as a pharmacotherapy specialist, and assembly of a portfolio of educational experiences to maintain qualifications for pharmacists who wish to practice in infectious diseases.[42] These two organizations encourage infectious diseases training programs to seek accreditation and advocate the development of a certification examination in infectious diseases.[42] Until a certification examination in infectious diseases becomes available, SIDP and the ACCP ID PRN suggest that

board-certified pharmacotherapy specialists seek added qualifications in infectious diseases from the Board of Pharmaceutical Specialties. Some PGY2 residency training programs in infectious diseases are accredited by ASHP. The SIDP maintains online listings of infectious diseases fellowships, residency training programs, continuing education programs, and other educational resources (www.sidp.org). Many fellowships in infectious diseases have a strong research focus, with less emphasis on clinical training in a patient care setting.[42]

The limited availability of and substantial time investment required to complete infectious diseases fellowships and residency training programs have limited the number of pharmacists with these credentials. Recruiting pharmacists with infectious diseases training can be difficult for institutions with budgetary constraints because of competition for qualified candidates from the private sector with greater financial resources.

The burden for providing antimicrobial stewardship falls on pharmacists without infectious diseases training in many institutions, and a lack of specialized training should not be viewed as an insurmountable barrier to implementation of an ASP.[36] A need for pharmacists without infectious diseases training to assume responsibility for antimicrobial stewardship because of a lack of sufficient numbers of pharmacists with such training in the United States is acknowledged by ASHP in its statement on the pharmacist's role in antimicrobial stewardship and infection prevention and control.[37] Pharmacists without specialized training in infectious diseases often can contribute to antimicrobial stewardship through medication order review and detection of orders for restricted antimicrobial agents, without proper authorization, or inconsistent with clinical pathways or protocols. However, time constraints and discomfort due to a lack of training may limit the contribution of these individuals.[24] In many hospitals without infectious diseases pharmacists, routine pharmacy services take priority over antimicrobial stewardship activities, compromising the success of antimicrobial stewardship efforts. Consistent antimicrobial stewardship efforts by pharmacists whose time and responsibilities are devoted to these efforts are needed for program success. The success of antimicrobial stewardship efforts relies heavily on the cooperation of pharmacists without infectious diseases training, even in hospitals with pharmacists who have such training.

TABLE 5

Informal ID Educational Opportunities for Hospital Pharmacists

■ Identify a mentor with ID expertise for case discussions
■ Attend rounds with an ID physician
■ "Shadow" a clinical microbiologist
■ Join ID professional organizations
■ Attend ID professional meetings
■ Participate in ID-related continuing education programs
■ Subscribe to ID list-servs
■ Sign up for electronic alerts with tables of contents for ID-related periodicals
■ Read basic primers, review articles, and practice guidelines on ID topics
■ Conduct or participate in an ID journal club
■ Attend ID-related morbidity and mortality case reviews

ID = infectious diseases

Pharmacists may use a variety of methods to improve their knowledge of microbiology and infectious diseases pharmacotherapy without making the large time investment associated with infectious diseases fellowships and residencies. A certificate program in antimicrobial stewardship, with Web-based, live, and practical workplace components, is available from MAD-ID Making a Difference in Infectious Diseases Pharmacotherapy (www.mad-id.org/), a not-for-profit foundation for continuing education in infectious diseases pharmacotherapy.

The SIDP currently is developing a certificate program for pharmacists that will be available online and for which continuing education credit will be available. The certificate program is intended to supplement not supplant infectious

diseases fellowships and residency training programs.

Pharmacists might augment their infectious diseases knowledge by identifying a pharmacist or physician mentor with infectious diseases expertise, attending rounds with infectious diseases physicians, and arranging to work alongside a clinical microbiologist on a short-term basis in their workplace (Table 5). Discussing patient cases with a mentor can be a good learning experience for the pharmacist. Attending infectious diseases-related professional meetings and participating in infectious diseases-related continuing education programs also can be helpful. Obtaining basic references (e.g., the Clinical and Laboratory Standards Institute *Performance Standards for Antimicrobial Disk Susceptibility Tests*) and readings in the published literature (e.g., basic primers, review articles, practice guidelines from authoritative sources) are other cost-effective ways of preparing pharmacists to participate in antimicrobial stewardship.[43] The resource center at ASHP's Antimicrobial Practice Improvement Program in Hospitals Web site (www.ashpadvantage.com/stewardship/) provides links to useful Web-based resources.

Developing and Implementing an ASP

The development and implementation of an ASP in the hospital setting is a potentially daunting task, with many potential pitfalls to avoid and barriers to overcome. Developing a proposal to obtain institutional support for the ASP, assembling and leading the ASP core team, analyzing current institutional practices, and developing processes to meet ASP goals are key steps in the implementation process. Other steps include analyzing and reporting data demonstrating the impact of ASP processes, and developing and implementing outreach plans directed to key hospital staff. Because pharmacists serve as core members of antimicrobial stewardship teams and other multidisciplinary committees and have considerable knowledge of antimicrobial use in the institution, they might spearhead the development and implementation of an ASP.

Developing a Proposal to Obtain Institutional Support for an ASP

Obtaining approval from administration for an ASP is difficult in most hospitals because of competition for limited resources, so a strong business case and strategic plan for the ASP are vital to gaining support. Proposals must be compelling and based on sound arguments and solid data.

The proposal should provide justification for the program based on the institutional costs and consequences of inappropriate antimicrobial use (i.e., adverse effects, resistance, morbidity, mortality, and HAI). An evidence-based toolkit for estimating the cost of HAI and antimicrobial resistance, *What Every Health Care Executive Should Know: The Cost of Antibiotic Resistance*, is available from the Joint Commission at no charge to health care organizations, executives, and clinicians. Published estimates of the costs of HAI also are available.[44]

Although an ASP may reduce the hospital length of stay, it is best not to use the savings associated with reductions in length of stay as part of the cost justification for an ASP because multiple factors affect length of stay.[45] The relationship between antibiotic use and length of stay is complex, and it often is difficult to demonstrate a direct cause-and-effect relationship between antimicrobial stewardship and length of stay.

The proposal should demonstrate the need for the ASP by providing examples from the published literature and selected institutional data on the prevalence of HAI caused by resistant organisms, bacterial susceptibilities to antimicrobial agents from antibiograms, and antimicrobial use patterns and costs that illustrate problems. Antibiograms are reports compiled by the clinical microbiology department that indicate the susceptibility of various pathogens to different antibiotics, and these reports may be obtained for specific hospital locations where unique resistance patterns often develop (e.g., surgical and medical intensive care units) as well as the overall institution. Problems with HAI caused by resistant organisms (e.g., methicillin-resistant *Staphylococcus aureus*) and antimicrobial use that can lead to resistance or increase costs (e.g., an excessive duration of use, especially involving the unnecessary use of the parenteral route once the oral route becomes

an alternative) and the implications of failure to address the problems should be described in the proposal.

Guidelines and recommendations for establishing an ASP from authoritative groups, especially IDSA and SHEA, should be outlined in the proposal. The SHEA recently called for efforts to achieve a goal of zero HAI, and this goal could provide impetus for the implementation of an ASP.[46]

The financial implications for the hospital of Centers for Medicare & Medicaid Services (CMS) reimbursement policies for infection-related "never events" also should be addressed in the proposal because they provide justification for ASP implementation. In an effort to improve the quality of care in hospitals, CMS discontinued payment for never events—preventable medical errors that result in serious consequences for the patient—beginning in October 2008.[47] The agency considers certain HAI avoidable never events.[48]

The impact on institutional image of publicly-reported infection-related national quality indicators should be mentioned in the proposal to strengthen the argument for ASP implementation. The Joint Commission and National Quality Forum require reporting by hospitals of various core performance measures (e.g., appropriate antibiotic section and timely administration for pneumonia) to facilitate quality comparisons among hospitals.[49] The Joint Commission's National Patient Safety Goal 7 to reduce the risk of HAI provides added impetus for ASP implementation because it requires the implementation of evidence-based practices to prevent HAI due to multidrug-resistant organisms (NPSG.07.03.01) and surgical site infections (NPSG.07.05.01), with elements of performance that address prophylactic antimicrobial use in surgical patients.[50] Failure to meet NPSGs could affect Joint Commission accreditation decisions.

The Surgical Care Improvement Project (SCIP) is a national initiative developed by CMS, the Centers for Disease Control and Prevention, and various organizations to improve the safety of surgical care by reducing postoperative complications by 25% before 2010.[51] Because surgical site infections are a common complication and account for 14% to 16% of HAI, several SCIP performance measures address the appropriate selection, time of initiation, and time of discontinuation of prophylactic antibiotic therapy in surgical patients.[14] The need for these SCIP performance measures to provide a favorable impression of the institution lend support to proposals for ASP implementation.

The proposal should outline the goals of the ASP based on the scope of the problems identified and available resources. The ASP should be tailored to meet institutional needs, but the goals should be realistic. Short- and long-term goals should be identified through a formal strategic planning process. The "low-hanging fruit" might be targeted initially to maximize results from limited resources. This approach involves focusing first on activities that are easy or inexpensive to implement or associated with proven benefits and goals that are readily achieved. Initial efforts might focus on only one or a few antibiotics or types of infections. Pharmacists at many small institutions perform effective antimicrobial stewardship activities despite the lack of a formal, well-funded program.

In preparing the proposal, an attempt should be made to quantify the resource requirements and associated costs for the ASP. These costs can be substantial, especially for personnel (e.g., physician compensation) and information technology. As with other requests for funding, it may be wise to request a larger amount than the minimum required to implement and conduct the ASP, with the expectation that a smaller amount of funding will be provided.

The costs of the ASP should be presented in the context of the potential for improved patient safety and clinical outcomes from the investment. The potential net cost savings or costs avoided (e.g., avoiding continuation of a recent trend of increasing costs) from an ASP also should be quantified, if possible.[23] The hospital finance department can be helpful in providing cost figures for the proposal.

The proposal for an ASP might call for pilot testing activities on a limited basis, with plans for hospital-wide expansion at a later date if success is demonstrated with pilot testing. The proposal might specify a target cost savings from the pilot program and stipulate that savings realized at the end of the pilot program will be used to fund

salaries for new staff dedicated to the ASP. Future growth and needs (e.g., personnel, equipment) of the ASP should be anticipated.

The director of pharmacy and an infectious diseases physician should play instrumental roles in developing the proposal and negotiating with hospital administration for the ASP. The proposal should seek adequate authority as well as financial support from administration for the ASP. A commitment from hospital administration for the ASP is critical to the success of the program; financial support alone does not suffice.[24] A survey of infectious diseases pharmacists at North American hospitals with an ASP revealed uncertainty about program effectiveness in improving patient outcomes, controlling antimicrobial resistance, and decreasing medication costs, and these perceptions were attributed to a lack of institutional support for the ASP.[52]

Assembling and Leading the ASP Core Team

A clinical pharmacist with infectious diseases training, infectious diseases physician, and ideally a clinical microbiologist, infection control professional, information system specialist, and hospital epidemiologist should be designated for the ASP core team, according to IDSA/SHEA guidelines.[11] The infectious diseases physician member of the core team plays a vital role in lending legitimacy to the ASP.[24] Other influential "key opinion leaders" (i.e., champions) among the medical staff should be identified, and their early buy-in and support for the ASP should be sought.

The need for physician compensation for ASP efforts as incentive for participation on the ASP team may need to be addressed because lack of compensation can be a barrier to participation.[22] In most hospitals, physicians are compensated for services rendered to individual patients through consultation fees in contrast to hospital personnel who receive salaries.[23] The large time commitment required for participation in ASP activities can deter physician involvement.[24] A volunteer (i.e., uncompensated) physician core team member may not be available as consistently as one who is compensated. In institutions without an infectious diseases physician, an enthusiastic physician champion should serve as a core team member.

The clinical microbiologist member of the core team provides expert input about the use of microbiology susceptibility test panels (especially new assays for rapid diagnosis) and options for sorting among susceptibility data to generate meaningful antibiograms (i.e., without distortion from inappropriate data selection methods). These antibiograms may be based on unit-specific or hospital-wide data on appropriate pathogens and antibiotics for an entire year or a shorter period. Providing guidance in interpreting institutional antibiograms taking into consideration the limitations of the reports (e.g., the inability to draw conclusions from or extrapolate data based on small numbers of isolates) is another contribution of the clinical microbiologist. This input is essential for devising guidelines and clinical pathways for antimicrobial use to prevent or treat infections.

Infection control professionals are integral members of the ASP core team because of the close relationship between antimicrobial stewardship and infection prevention and control efforts. For example, infection control professionals monitor HAI rates, including CDI rates, which reflect resistance patterns.[24]

The information system specialist member of the ASP core team can be instrumental in advising the team about optimal uses of available technology. Hospital epidemiologists have expertise in and can advise the ASP core team about infection surveillance and research methods to use in evaluating the impact of ASP activities.[24]

A lack of personnel to serve on an ASP core team is a potential barrier in some facilities, especially small or rural hospitals. Some facilities lack an infectious diseases physician, often because of a lack of compensation. A physician with a strong interest in infectious diseases should be sought for the ASP core team in these facilities. Although pharmacists have led antimicrobial stewardship efforts in some facilities without infectious diseases physicians, ideally antimicrobial stewardship is a coordinated and equal partnership involving pharmacy and medicine. In institutions without a pharmacist with infectious diseases training, a clinical pharmacist with an interest in but no credentials in infectious diseases or the director of pharmacy could serve as a core team member.

Communication channels should be established to facilitate collaboration between members of the ASP core team and members of the infection control, P & T, medical executive, and other multidisciplinary committees. Networking can promote cooperation and may be mutually beneficial. For example, the clinical microbiology department may be able to use ASP data to justify the addition of new staff and equipment.

Establishing an ASP core team does not preclude the involvement of additional staff in planning and implementing ASP activities. For example, members of the pharmacy staff should be involved in the development of guidelines and policies for antibiotic use. Environmental services staff often participate in infection control efforts related to ASP goals. Other stakeholders (e.g., surgeon, pediatrician) should be involved as needed.[23] Input should be obtained from representatives of hospital departments that will be affected by and involved in ASP activities (e.g., emergency department personnel). Early involvement of these staff can forestall resistance to the ASP.[23]

Analyzing Current Institutional Practices

Problems with current institutional practices for the diagnosis and treatment of infections should be identified by compiling and analyzing data on antimicrobial use and costs for common HAI (e.g., ventilator-associated pneumonia, catheter-associated bloodstream infections) and bacterial susceptibilities to antimicrobial agents from unit-specific and hospital-wide antibiograms. Infection-related national quality indicator data also should be evaluated.

Antibiograms from a 5- or 10-year period might be used to identify trends. Antibiograms are helpful for making decisions about empiric antibiotic therapy because they reflect local microbiology and resistance patterns. However, antibiograms should be interpreted with caution and they should not be used alone to make clinical decisions because of their limitations.[53] Antibiograms may provide misleading information if they are based on small numbers of or duplicate isolates, isolates cultured at a hospital outpatient clinic as well as from inpatients, or isolates that reflect resistance patterns that are subject to rapid change.[53] Patient-specific factors, including the type and severity of infection and prior infections and antibiotic use, should be taken into consideration when prescribing antibiotics.[53]

Obtaining antibiograms is difficult at some institutions because of inadequate microbiology laboratory services. Proposals for ASPs should provide funding for these services to optimize the effectiveness of the program. When robust data pertaining to antimicrobial use and susceptibilities are not available, it may be helpful to consult with infectious diseases physicians about their perceptions of problems at the institution.

Goals for the ASP should be refined to address problems with current institutional practices identified through analysis of antibiograms and antimicrobial use and cost data for common HAI. Infection-related national quality indicator data also should be taken into consideration in establishing ASP goals.

Developing Processes to Meet ASP Goals

The antimicrobial stewardship core strategies and supplemental elements in Table 2 can be applied in various steps in the antimicrobial prescribing process. For example, education, guidelines, and clinical pathways may be used at the time of patient evaluation. When antimicrobial agents are selected, formulary restriction, preauthorization requirements, and prospective audit with direct intervention and feedback may be used as well as education, guidelines, and clinical pathways. Prospective audit with direct intervention and feedback also is used in antibiotic dispensing. Computer-assisted strategies (e.g., antimicrobial order forms integrated into CPOE systems) may be used in selecting and ordering antimicrobial agents. A strategic plan should be devised to implement these strategies and elements as part of institutional processes so that ASP goals are met.

Policies and procedures for antimicrobial prescribing should be revised to accommodate ASP goals and activities, with multidisciplinary input from all stakeholders. In small hospitals and other institutions with limited resources, the hours of operation for ASP activities may be limited. Providing these activities after hours may need to be addressed in policies and procedures.

Analyzing and Reporting Data Demonstrating the Impact of ASP Activities

Documentation and analysis of data are needed to demonstrate a favorable impact of ASP activities on clinical outcomes, antimicrobial resistance, and health care costs. The appropriate types and sufficient amounts of data must be documented and accessible for an analysis to yield meaningful information.[36]

Data on antimicrobial use and costs, bacterial susceptibilities to antimicrobial agents from unit-specific and hospital-wide antibiograms, surgical site infection and other HAI rates, and infection-related quality indicators should be compared before and after ASP implementation and over time to document the impact of ASP activities and identify trends. Institutional data also should be compared with bench mark data from local hospitals and the published literature.

Antibiograms may be useful as an outcome measure of the success of ASP activities.[53] Guidance in preparing antibiograms is available from the Clinical and Laboratory Standards Institute (*Antibiograms: Developing Cumulative Reports for Your Clinicians Quick Guide*, M39-A3 QG, available at www.clsi.org).

Various process measures (Table 6) and adherence to institutional guidelines, care bundles, and policies and procedures also should be used to evaluate the impact of ASP activities. Antimicrobial resistance rates should not be relied on exclusively to judge the success of the ASP because they may also reflect the impact of infection prevention and control measures and the transfer from long-term-care facilities or other hospitals of patients previously infected or colonized with antimicrobial-resistant pathogens.[21,24]

Cost analyses should take into consideration the costs associated with antimicrobial resistance (e.g., the use of isolation to prevent transmission of multidrug-resistant infection among hospitalized patients) and HAI as well as drug acquisition costs. Aggressive empiric use of high-cost antibiotic therapy can decrease the duration of treatment, hospital length of stay, and hospital costs despite an increase in drug acquisition costs.[45]

TABLE 6

Process Measures for Use in Evaluating ASP Impact

- Justification for antibiotic use
  - Empiric
  - Therapeutic
- Appropriateness of antibiotic drug choice/ avoidance of unnecessary combination therapy
  - Based on spectrum of activity and susceptibility of suspected or documented pathogen
  - Based on drug allergies and potential for toxicity
  - Based on cost
- Appropriateness of antibiotic drug regimen (dose, dosing interval, and route of administration) based on pharmacokinetics and pharmacodynamics
- Appropriateness of time of initiation of antibiotic therapy
  - With respect to time of surgery for prophylactic use
  - With respect to time of cultures for therapeutic use
- Appropriateness of duration of antibiotic therapy/ avoidance of unnecessarily prolonged therapy
- Rate of acceptance of ASP recommendations
- Rate of adherence to institutional guidelines, care bundles, and policies and procedures for antibiotic use

ASP = antimicrobial stewardship program

The results of the data analysis should be reported to hospital administration, the P & T and infection control committees, and other stakeholders to obtain support for program continuation or expansion. An annual report describing ASP activities and outcomes might be prepared. The results of the data analysis also should be used to revise ASP strategies as needed to improve efficacy of the ASP and quality of care (i.e. the ASP data analysis should be integrated with institutional continuous quality improvement efforts).[36] Publication of the results of the data analysis should be explored.

Developing and Implementing Outreach Plans Directed to Key Hospital Staff

Misperceptions about a lack of prescriber autonomy are a major potential barrier to ASP implementation. Physicians may view the ASP as a "cookbook approach" to medicine that eliminates clinical judgment and represents a cost-driven bureaucratic effort by hospital administration or the pharmacy department. In some instances, prescribers have been known to find ways to work around ASP requirements (e.g., wait until after hours to order restricted antibiotics in hospitals with limited hours of operation for the ASP).[23]

Outreach plans should be devised to anticipate and avoid or overcome these problems. The plan should market and build buy-in for the ASP before it is launched by providing education about its rationale, goals, and components.[36] The education can take a variety of forms, including grand rounds, morbidity and mortality conferences, newsletter stories, and a concise one-on-one "elevator pitch." An emphasis on patient safety should be used to dispel misperceptions.[11] The use of guidelines and clinical pathways that reflect published literature, institutional microbiology and resistance patterns, and local practitioner input as the basis for the ASP should be explained to defuse concerns about a lack of autonomy.

All staff who are impacted by the ASP program, including supervisors, should be educated about the rationale, goals, and components of the program in a way that is relevant and meaningful to them to promote adherence to ASP requirements. For example, nursing staff need to understand that the ASP is designed to reduce the need for isolation of patients with HAI due to multidrug-resistant pathogens, which is labor-intensive and time-consuming for nurses as well as costly for the institution. Nursing staff also require an understanding of antibiotic pharmacokinetics and pharmacodynamics because of the impact of continuous infusions on the use of i.v. tubing for other purposes. Pharmacists are uniquely qualified to provide this education because of their education. Staff education about ASP goals and requirements should be provided frequently (at least annually for house officers) for all departments to accommodate new staff. When annual antibiograms become available, education should be provided about the implications for affected staff, including physicians, nurses, and hospital administrators.

Creating a "brand" for the ASP with a slogan and logo can unify and build recognition among hospital staff for various components of the ASP. This branding should be applied to all communications (e.g., memoranda, posters, newsletters, electronic mail), order forms, and computer interfaces (e.g., CPOE screens) used for the ASP. A Web site for the ASP might be established to provide a comprehensive, convenient source of program information for hospital staff.

A one-on-one intervention may be needed to address problems with individual prescribers who appear to undermine or sabotage ASP efforts. Political savvy and diplomacy may be needed to cope with recalcitrant persons. The support of hospital administration in enforcing ASP requirements can be helpful. In some cases, inappropriate prescribing practices reflect long-established habits that are difficult to change. Many prescribers fail to appreciate the urgency of the problem with multidrug resistance, potential for collateral damage (i.e., the selection of resistant pathogens arising from the unnecessary use of broad-spectrum antibiotics), need to reserve effective agents for use only when truly needed, and the impact of prescribing for an individual patient on resistance in the local flora.

Conclusion

Inappropriate antimicrobial use and antimicrobial resistance are major problems in U.S. hospitals that can be addressed through ASPs. Pharmacists play a vital role in leading the development and implementation process and ensuring the success of ASPs. The commitment of hospital administration and a multidisciplinary effort are required for successful ASP implementation. An awareness of the potential pitfalls in and barriers to implementation of an ASP can facilitate the process and lead to success.

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