

## REVIEWS

# Infections, Bacterial Resistance, and Antimicrobial Stewardship: The Emerging Role of Hospitalists

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The care of patients with serious infections both within and outside healthcare settings is increasingly complicated by the high prevalence of resistant or multidrug-resistant (MDR) pathogens. Moreover, infections caused by MDR versus susceptible bacteria or other pathogens are associated with significantly higher mortality, length of hospital stay, and healthcare costs. Antimicrobial misuse or overuse is the primary driver for development of antimicrobial resistance, suggesting that better use of antimicrobials will translate into improved patient outcomes, more efficient use of hospital resources, and lowered healthcare costs. Antimicrobial stewardship refers to the various practices and procedures utilized to optimize antimicrobial use. The primary goal of antimicrobial stewardship is to improve patient outcomes

and lower antimicrobial resistance and other unintended consequences of antimicrobial therapy. Secondary goals are to reduce length of hospital stays and healthcare-related costs. Hospitalists are increasingly involved in the care of hospitalized patients throughout the United States. Expertise in managing conditions requiring hospitalization, and experience in quality improvement across a wide range of clinical conditions, make hospitalists well positioned to participate in the development and implementation of hospital-based antimicrobial stewardship programs designed to improve patient outcomes, reduce antimicrobial resistance, and provide more efficient and lower-cost hospital care. *Journal of Hospital Medicine* 2012;7:S34–S43. © 2012 Society of Hospital Medicine.

Healthcare-associated infections (HAIs) are important causes of morbidity and mortality in the United States and other countries.<sup>1–3</sup> Moreover, treatment of HAIs is frequently complicated by involvement of bacterial pathogens resistant to 1 or more antibiotics or antibiotic classes,<sup>4</sup> and sometimes bacteria resistant to all or nearly all currently available agents.<sup>5–7</sup> The rapid emergence of resistant bacteria both in and out of the hospital setting can affect empiric antimicrobial choices across all patients. The effort to avoid undertreating or not covering resistant bacteria can lead to overuse of wide-spectrum antimicrobials. Antimicrobial use—and especially antimicrobial overuse or misuse—has been linked with increased antimicrobial resistance,<sup>8–17</sup> leading to worsened clinical outcomes with increased length of hospital stay and healthcare costs. Table 1 defines the various lines of evidence supporting a causal relationship between antibiotic use and emergence of antimicrobial resistance.<sup>18,19</sup>

Optimal management of patients with bacterial infections, both HAIs and those that originate in the community, involves a focus on treatment that maximizes clinical outcomes for the individual patient,

while also inhibiting or slowing the development of antimicrobial resistance and its spread to other patients. Antimicrobial stewardship is a term describing the various clinical strategies that have been devised to maximize the benefits and minimize the costs of antimicrobial therapy through judicious use of these agents.<sup>18,20,21</sup> This article examines the developing patterns of resistance among key bacterial pathogens in the hospital and associated healthcare settings, the costs associated with HAIs (specifically, those caused by resistant pathogens), and the various strategies or programs that have been developed by governmental agencies, individual healthcare institutions, and other organizations to optimize the use of antibiotics to improve patient outcomes and minimize healthcare costs. The value that the hospitalist can bring to the development and/or implementation of institutional antimicrobial stewardship programs is explored.

## ANTIMICROBIAL RESISTANCE AND HAI TRENDS FOR KEY BACTERIAL PATHOGENS

Bacterial pathogens including Enterobacteriaceae (*Klebsiella pneumoniae*, *Enterobacter* spp, *Escherichia coli*, and *Proteus* spp, among others), *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Enterococcus faecium*<sup>22,23</sup> are increasingly prevalent in healthcare settings, and particularly troublesome to manage due to increasing resistance. Data from the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN) have shown that, in intensive care units (ICUs), 16% of HAIs are due to multidrug-resistant (MDR) pathogens.<sup>4</sup> These 16% have the highest mortality and

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Additional Supporting Information may be found in the online version of this article.

**Received:** May 19, 2011; **Revised:** August 9, 2011; **Accepted:** August 28, 2011

2012 Society of Hospital Medicine DOI 10.1002/jhm.978

Published online in Wiley Online Library (Wileyonlinelibrary.com).

length of hospital stay, and are associated with the highest healthcare costs.<sup>24,25</sup> Infections caused by MDR pathogens are more important than their actual numbers, because treatment decisions are driven by the intent to cover these MDR pathogens, even if that means providing excessively broad coverage for most patients. Moreover, the 16% mentioned above are only the tip of the iceberg, as many more HAIs will occur outside of the ICU, particularly catheter-associated urinary tract infections (CAUTI) and surgical site infections, as these patients are often not sick enough to require ICU care. There is little information on the prevalence of HAIs outside of the ICU setting, the role of MDR bacteria in these infections, and the associated costs, mortality, and effects on length of stay.

### *K pneumoniae* Carbapenemases and Community-Acquired Methicillin-Resistant *Staphylococcus aureus*

*K pneumoniae* carbapenemase (KPC) is a prime example of the emergence and rapid spread of a new resistance pattern that affects prescribing patterns. Emergence of KPC as the primary source of carbapenem resistance in Enterobacteriaceae<sup>26</sup> is critically significant, as carbapenems are recommended first-line therapy for serious infections caused by extended-

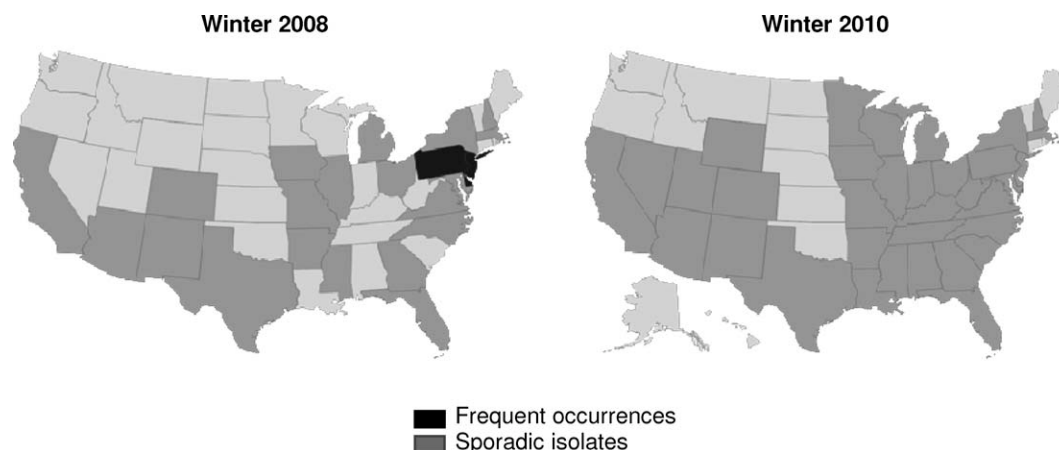
spectrum  $\beta$ -lactamase (ESBL)-producing *K pneumoniae* or other Enterobacteriaceae. One particularly remarkable fact about KPC-producing bacteria is the speed at which they have spread since first emerging. Figure 1 from the CDC illustrates the rapid spread of KPC-producing bacteria within the United States, from winter 2008 to May 2010. International spread has also been rapid and extensive. The first case of a KPC-producing bacteria outside the United States was reported in France in February 2005, in an 80-year-old man who was admitted to a Parisian hospital 2 to 3 months after having a medical procedure performed in a New York City hospital, suggesting intercontinental transfer from the United States.<sup>27</sup> Since then, KPC-producing pathogenic bacteria have been identified in the Caribbean, South America, Europe, Israel, and China.<sup>28–30</sup> It is clear that once resistant bacteria emerge, they have the potential to spread very rapidly within and between countries, challenging currently available antimicrobial agents and complicating the treatment of serious infections.

Consideration of *S aureus* skin and skin-structure infections highlights the fact that the barrier between hospital and community is now beginning to be crossed, further complicating prescribing decisions. The classic risk factors for resistance may no longer be reliable in determining best empiric treatment. In a landmark study, Moran et al. demonstrated the large percentages of outpatients in the United States with skin or soft-tissue infections (SSTIs) involving community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA).<sup>31</sup> *S aureus* was isolated from 76% (320/422) of adults presenting to 11 university-affiliated emergency departments with acute, purulent SSTIs in August 2004, 59% of whom were infected with MRSA. More than half the patients in the study (57%) were initially treated with antibiotics to which MRSA isolates were not susceptible.<sup>31</sup> In the hospital, it has been shown that most invasive MRSA infections now actually have their onset outside of the healthcare setting,<sup>32</sup> and that increasing numbers of hospitalized

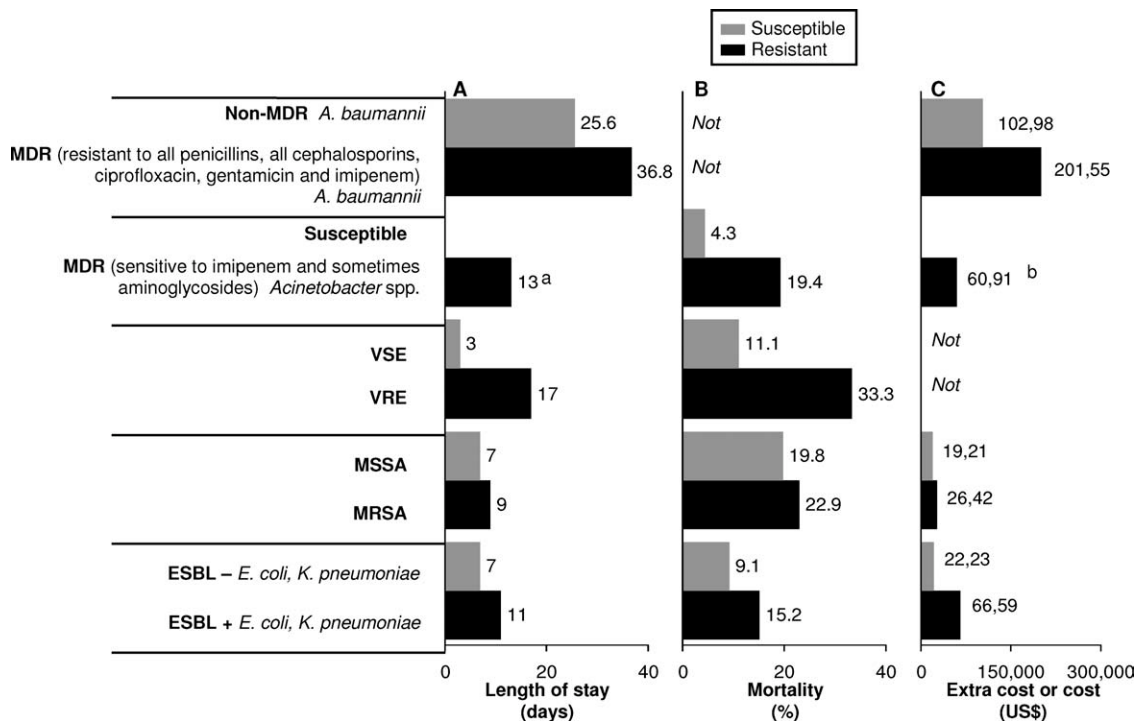
**TABLE 1.** Observations That Support Causal Associations Between Antimicrobial Use and Emergence of Antimicrobial Resistance

|  |
|--|
| Changes in antimicrobial use are paralleled by changes in the prevalence of resistance   |
| Antimicrobial resistance is more prevalent in healthcare-associated bacterial infections vs community-acquired infections                              |
| Patients with healthcare-associated infections caused by resistant strains are more likely than control patients to have received prior antimicrobials |
| Areas within hospitals that have the highest rates of antimicrobial resistance also have the highest rates of antimicrobial use                        |
| Increasing duration of patient exposure to antimicrobials increases the likelihood of colonization with resistant organisms                            |

NOTE: Adapted from Dellit et al.<sup>18</sup>



**FIG. 1.** Rapid spread of *Klebsiella pneumoniae* carbapenemase-producing bacteria within the United States, from winter 2008 to May 2010. (CDC unpublished data).



**FIG. 2.** Association of multidrug resistance of several MDR bacteria with (A) length of stay, (B) mortality, and (C) cost of hospitalization. (Data from Sipahi, 2008) (ESBL, extended-spectrum  $\beta$ -lactamase; MDR, multidrug resistant; MRSA, methicillin-resistant *S aureus*; MSSA, methicillin-susceptible *S aureus*; VRE, vancomycin-resistant *Enterococcus*; VSE, vancomycin-susceptible *Enterococcus*.) <sup>a</sup>Represents additional hospital days attributable to infection with MDR *A baumannii*, as determined in a multivariate model including all variables predictive of duration of hospitalization. <sup>b</sup>Represents additional mean increase in hospitalization cost attributable to infections with a MDR-resistant versus susceptible bacteria.

patients are now developing infections associated with CA-MRSA strains >72 hours after admission.<sup>33–38</sup> Thus, it is becoming increasingly difficult to determine whether an invasive *S aureus* infection encountered in either a healthcare facility or community setting involves a sensitive organism, healthcare-associated MRSA, or a CA-MRSA pathogen, directly impacting treatment choices across all patients we care for with skin and skin-structure infections.

### ***Clostridium difficile*-Associated Disease**

Indiscriminate and unnecessary use of antibiotics offer our patients no benefit, while exposing them to adverse effects of antibiotics, including allergies, rashes, and diarrhea among many potential other unintended consequences. *C difficile*-associated disease is an increasingly problematic pathogen in the hospital setting that has been linked to unintended antibiotic effects.<sup>22,39,40</sup> *C difficile* infection is not only costly in dollars, it is also a potentially fatal condition and has been linked to prolonged hospital stays and increased healthcare costs.<sup>41–44</sup> Improved infection control measures<sup>45–49</sup> and better use of antibiotics through antibiotic stewardship programs<sup>50–55</sup> have been shown to reduce the incidence of *C difficile* infection.

### **COSTS OF HAIs AND ANTIMICROBIAL RESISTANCE**

HAIs are an important and growing problem in the United States.<sup>56</sup> Klevens et al. estimated that approxi-

mately 1.7 million individuals hospitalized in the United States in 2002 had HAI, leading to 98,987 deaths.<sup>1</sup> Estimates of annual hospital costs in the United States related to HAIs range from \$28 to \$48 billion.<sup>57</sup> Antimicrobial resistance is a major driver of mortality, increased length of hospital stay, and hospital costs associated with HAIs.<sup>24,25</sup> A recent review by Sipahi<sup>25</sup> summarizes recent studies examining the impact of resistant and MDR bacterial infections (Figure 2).<sup>58–66</sup> It is dramatically clear that infections due to resistant and MDR bacteria more often result in death, are associated with longer hospital stays, and are considerably more expensive to treat.

A number of factors can lead to the increased hospital costs associated with infection with a resistant or MDR bacteria. These include the need to use more expensive antibiotics, increased length of hospital stay, delayed appropriate antibiotic therapy, increased treatment toxicity (and costs associated with managing these toxicities), and increased frequency of surgical interventions required to control infection.<sup>25,67</sup>

The savings that could be realized through reduction in antimicrobial resistance was evaluated recently by Roberts et al.<sup>68</sup> Using a sensitivity analysis for a sample of high-risk adult patients hospitalized in an urban public teaching hospital in 2000, the authors determined that reducing the antimicrobial-resistant infection rate by 3.5% (from 13.5% to 10.0%) would have saved the study hospital \$910,812 (in 2008 US\$), when using lowest cost and length of stay

figures. The calculated societal savings, for reduced mortality and lost productivity associated with the reduced antimicrobial-resistant rate, was \$1.8 million. Hence, the analysis showed a minimum overall medical (hospital) and societal savings of \$2.7 million for this single hospital with a cohort of 1391 patients. The projected savings would be dramatically higher if the reduced antimicrobial-resistant rate was generalized to all hospitals throughout the United States.

## ORGANIZATIONAL AND GOVERNMENTAL EFFORTS ADDRESSING ANTIMICROBIAL RESISTANCE AND HAIs

Given the relationships between antimicrobial use and resistance, and between antimicrobial resistance and morbidity, mortality, length of hospital stay, and healthcare costs, it is not surprising that we have seen a variety of programs and initiatives begun by either government agencies or healthcare organizations aimed at reducing antimicrobial resistance and HAIs.

### The Joint Commission

The Joint Commission is an independent, not-for-profit organization that accredits and certifies >18,000 healthcare organizations/programs in the United States.<sup>69</sup> The Joint Commission issues annual National Patient Safety Goals (NPSG). Hospital compliance with these goals is a critical component of the accreditation process.<sup>70</sup>

The seventh goal of The Joint Commission's NPSG is to reduce the risk of HAIs,<sup>70</sup> the key features of which are listed in Table 2. The methodology recommended to achieve compliance includes infection control programs and implementation of evidence-based practices to prevent HAIs due to MDR microorganisms in acute-care hospitals. This presumably could include development and implementation of an institutional antimicrobial stewardship, or components of a program, to reduce antimicrobial resistance within the hospital.

### Centers for Medicare and Medicaid Services

The Deficit Reduction Act of 2005, Section 5001(c), requires the Secretary of Health and Human Services to identify conditions that are: (1) high cost or high volume, or both; (2) result in assignment of a case to a diagnosis-related group that has higher payment when the code is present as a secondary diagnosis; and (3) could reasonably have been prevented through application of evidence-based guidelines.<sup>71</sup> The Centers for Medicare and Medicaid Services (CMS), which develops and administers Medicare and Medicaid payment and coverage policies, "encourages" hospitals to reduce the occurrence of these preventable problems through reduced payments when these events occur. Among the Hospital Acquired Conditions (HAC) that CMS considers reasonably preventable are a number of HAIs, particularly

**TABLE 2. National Patient Safety Goals (NPSG)**

Goal 7: Reduce the Risk of Healthcare-Associated Infections

NPSG.07.03.01

- Implement evidence-based practices to prevent healthcare-associated infections due to multidrug-resistant organisms in acute-care hospitals
- Note: This requirement applies to, but is not limited to, epidemiologically important organisms such as methicillin-resistant *Staphylococcus aureus*, *Clostridium difficile*, vancomycin-resistant enterococci (VRE), and multidrug-resistant Gram-negative bacteria

NPSG.07.04.01

- Implement evidence-based practices to prevent central line-associated bloodstream infection
- Note: This requirement covers short- and long-term central venous catheters and peripherally inserted central catheter (PICC) lines

NOTE: Available at: [http://www.jointcommission.org/npsg\\_7\\_healthcare-associated\\_infections\\_webinar/](http://www.jointcommission.org/npsg_7_healthcare-associated_infections_webinar/)

CAUTI, vascular catheter-associated infections, and various surgery-related SSTIs. Importantly, the CMS policy is still in effect as of April 2011, and there are no signs of its being repealed or modified in the foreseeable future.

### The CDC Get Smart and Get Smart for Healthcare Programs

The Get Smart campaign, initiated by the CDC in 1995, focused on providing information to parents about the appropriate and inappropriate use of antibiotics to treat common childhood infections, as well as about the dangers of antibiotic resistance.<sup>72</sup> The goal of Get Smart is to reduce unnecessary antibiotic use and the spread of antibiotic resistance in the community by reducing the pressure exerted by parents on physicians to overuse or misuse antibiotics. Hence, the primary focus in this setting is on patient/parent education. The Get Smart campaign has been highly successful, with a significant reduction in antibiotic prescriptions after initiation of the campaign, across a range of infections for which antibiotics are generally or often not warranted.<sup>73</sup> The success of Get Smart is also largely responsible for the improvement in antibiotic prescribing for childhood middle ear infections observed in the CDC *Healthy People 2010* program.<sup>74</sup> The actual performance achieved in 2007 (the latest year reported) exceeded the *Healthy People 2010* target.<sup>75</sup>

Building on the success of Get Smart for community-acquired infections, a similar CDC campaign (Get Smart for Healthcare) has been undertaken to improve antibiotic usage and reduce antibiotic resistance in inpatient healthcare facilities.<sup>76</sup> The specific goals of Get Smart for Healthcare are to improve patient safety through better treatment of infections, reduce emergence of antimicrobial-resistant pathogens and *C difficile*, and heighten awareness of the challenges posed by antimicrobial resistance in healthcare settings. To help accomplish these ends, the CDC has partnered with the Institute for Healthcare Improvement (IHI), an independent, not-for-profit organization dedicated to closing the gap between the



**TABLE 3.** Summary of Antimicrobial Stewardship Strategies

| Strategy              | Procedure   | Personnel  | Advantages  | Disadvantages  |
|-----------------------|---|--|---|--|
| Education/ guidelines | Creation of guidelines for antimicrobial use<br>Group or individual education of clinicians by educators  | Antimicrobial committee to create guidelines<br>Educators (physicians, pharmacists)  | May alter behavior patterns<br>Avoids loss of prescriber autonomy   | Passive education likely ineffective   |
| Formulary restriction | Restrict dispensing of targeted antimicrobials to approved indications  | Antimicrobial committee to create guidelines<br>Approval personnel (physician, infectious diseases fellow, clinical pharmacist)                    | Most direct control over antimicrobial use<br>Individual educational opportunities                              | Perceived loss of autonomy for prescribers<br>Need for all-hours consultant availability |
| Review and feedback   | Daily review of targeted antimicrobials for appropriateness<br>Contact prescribers with recommendations for alternative therapy                           | Antimicrobial committee to create guidelines<br>Review personnel (usually clinical pharmacist)   | Avoids loss of autonomy for prescribers<br>Individual educational opportunities                                 | Compliance with recommendations  |
| Computer assistance   | Use of information technology to implement previous strategies<br>Expert systems provide patient-specific recommendations at point of entry (order entry) | Antimicrobial committee to create rules for computer systems<br>Personnel for approval or review (physicians, pharmacists)<br>Computer programmers | Provides patient-specific data where most likely to impact care (point of care)<br>Facilitates other strategies | Significant time and resource investment to implement sophisticated systems              |

NOTE: Adapted from MacDougall and Polk.<sup>82</sup>

healthcare that currently exists and the healthcare that should exist.<sup>77</sup> Together, they have identified a number of primary drivers to improve antibiotic use: timely and appropriate initiation of antibiotics; appropriate administration and de-escalation; data monitoring and transparency; and improving knowledge of, and engagement in, antimicrobial stewardship efforts, which are the focus of the next section. With respect to data monitoring, many in the healthcare community hope that, through the Get Smart program, we will soon have better sources of data, not just for the ICU, but across the entire hospital setting. This would help providers get a better sense of where resistance is located, thereby enabling better development of action plans to deal with the problem.

The CDC has recently expanded its Web site on antimicrobial stewardship, now providing extensive support and resources for program development and implementation at: <http://www.cdc.gov/getsmart/healthcare/>. In addition to urging the development of stewardship programs at all healthcare facilities, they propose 2 novel tools for use with every hospitalized patient who is prescribed antibiotics. According to the CDC<sup>78</sup>:

All Clinicians Should:

#### Dose, Duration, Indication

Too often antibiotics in hospitals are continued unnecessarily simply because clinicians caring for the patient do not have information indicating why the antibiotics were started initially or for how long they were to be continued. This challenge is compounded in today's healthcare system where primary responsibility for patient care is frequently transitioned from one clinician to another. Ensuring that all antibiotic orders are always accompanied by a dose, duration, and indication will help clinicians change or stop therapy when appropriate.

#### Get Cultures

Antibiotic therapy can be best optimized when it can be tailored to specific culture results. Knowing the susceptibility of the infect-

ing organisms can lead to narrowing of broad-spectrum therapy, changing therapy to better treat resistant pathogens and to stopping antibiotics when cultures suggest an infection is unlikely. . . .

A number of other government initiatives have been developed to address the issues of HAIs, antimicrobial resistance, and improved antimicrobial stewardship. These are beyond the scope of the present article, but include the United States Department of Health and Human Services (HHS) action plan to prevent HAIs,<sup>79</sup> and the CDC campaign and action plan to prevent and combat antimicrobial resistance,<sup>80,81</sup> among others.

## ANTIMICROBIAL STEWARDSHIP IN HOSPITALS AND THE HOSPITALIST'S ROLE

As recently defined, antimicrobial stewardship is "a system of personnel, informatics, data collection, and policy/procedures that promote the optimal selection, dosing, and duration of therapy for antimicrobial agents throughout the course of their use."<sup>20</sup> In simple words, the right antibiotic, at the right dose, at the right time, and for the right duration. The primary goals of antimicrobial stewardship are to reduce patient morbidity and mortality, prevent or slow the emergence of antimicrobial resistance, and reduce adverse drug effects, including secondary infections, such as *C difficile*-associated diarrhea.<sup>18,20</sup> Secondary goals include a reduction in hospital length of stay and healthcare expenditures, without adversely impacting quality of care. These goals are entirely in line with those of the hospitalist, who can play a critical role in the prevention and successful management of these infections. Optimal effects are expected when antimicrobial stewardship is combined with implementation of effective infection control measures within the hospital setting.

### Antimicrobial Stewardship Strategies

Table 3 provides an overview of various general strategies/procedures employed as components of antimicrobial stewardship programs.<sup>82</sup> The 2 most common are: (1) formulary restriction and preauthorization for specific agents; and (2) prospective audit with intervention and feedback.<sup>18,20</sup> Both approaches can and have been used to improve antimicrobial stewardship and to achieve at least some of its goals, and each is associated with advantages and disadvantages, as outlined in Table 3 and reviewed elsewhere.<sup>18,20,21,83</sup> Other strategies, such as education and use of guidelines and clinical pathways, tend to be used to supplement or complement either a general formulary restriction/preauthorization, or prospective audit/review and feedback approach to antimicrobial stewardship. It is important to note that, as in other areas such as venous thromboembolism prophylaxis, education alone is insufficient to drive changes in prescribing patterns and thereby reduce resistance. Healthcare informatics are increasingly being utilized to improve the management of infectious diseases. These can be simple programs that better assemble information about hospital-pathogen epidemiology. They can also be sophisticated systems, designed to standardize the antimicrobial order sets and medical logic modules, that guide treatment options by connecting patient-specific information with guideline recommendations and local resistance patterns.<sup>18,20,84,85</sup>

Two early, randomized, prospective studies illustrate the potential benefits and general receptiveness of clinicians to use of an audit/review and feedback approach to institutional antimicrobial stewardship. The first study randomized adult inpatients receiving  $\geq 1$  parenteral antibiotic for  $\geq 3$  days to an intervention ( $n = 141$ ) or control group ( $n = 111$ ).<sup>86</sup> In the intervention group, a clinical pharmacist and infectious diseases fellow reviewed the initial therapy prescribed by the primary care physician and the patient's progress 3 days after therapy initiation, and at that point offered suggestions for subsequent antibiotic therapy. The feedback or suggestions were communicated via nonpermanent chart note. In total, 85% of the physicians implemented the suggestions, and there were no significant differences between the intervention and control group for clinical or microbiologic endpoints. However, per-patient antibiotic charges were significantly lower in the intervention versus control group (\$1287.17 vs \$1673.97;  $P = 0.05$ ), which yields an estimated \$390,000 in annualized savings for the 600-bed tertiary-care hospital.

Similarly, a randomized, prospective study by Gums et al. showed that therapeutic intervention by a multidisciplinary antimicrobial team for inpatients receiving suboptimal intravenous antibiotic therapy was associated with a median hospital cost savings of \$2642 per intervention, compared with costs for similar inpatients who did not receive such intervention.<sup>87</sup>

The multidisciplinary team in the study consisted of pharmacists, a clinical microbiologist, and an infectious diseases specialist, who provided the treating physician with recommendations of possible optimal antibiotics, dosages, and rationales based on timely, detailed reviews of relevant microbiologic and clinical data. In total, 89% of physicians in the study implemented the suggestions from the multidisciplinary antimicrobial team. In addition to reduced costs, the intervention versus control group was also associated with significant reductions in the overall length of stay (10.1 vs 14.5 days;  $P = 0.0001$ ), and total non-ICU length of stay (5.7 vs 9.0;  $P = 0.0001$ ). There was no significant difference between the 2 groups for mortality rate.

The results from these studies<sup>86,87</sup> demonstrate how a prospective audit/review and feedback approach to antimicrobial stewardship can be associated with high physician participation and significant cost reductions for participating hospitals,<sup>88</sup> and potentially improve patient outcomes. Antimicrobial stewardship programs overall have a long track record in improving patient outcomes and reducing antimicrobial resistance at the patient level.<sup>89-91</sup>

### The Hospitalist's Role in Antimicrobial Stewardship

Hospitalists can participate in antimicrobial stewardship at a number of levels. On the direct patient care level, they can consistently apply the principles of appropriate empiric therapy, de-escalation, and duration of therapy as presented by Drs Snyderman, Kaye, and File in this supplement. As hospitalists assume a continually increasing role in the care of hospitalized patients throughout the United States,<sup>92</sup> they can directly influence the way medicine is practiced on a daily basis, patient by patient. A 2007 survey conducted by the American Hospital Association (AHA) showed that 58% of the 4897 community hospitals surveyed had hospital medicine programs, and that 83% of hospitals with 200 or more beds had such a program.<sup>93,94</sup> Estimates from the Society of Hospital Medicine (SHM) in July 2010 indicated that currently there were more than 30,000 hospitalists, practicing in 3300 large hospitals.<sup>95</sup> This affords hospitalists the opportunity to improve care across a huge segment of hospitalized patients.

On a departmental or institutional level, hospitalists appear to be especially well positioned to contribute to, and in some cases direct, a hospital's antimicrobial stewardship program. Unique to hospital medicine, and incorporated into the definition of the profession, is the commitment to quality and process improvement, efficient use of hospital and healthcare resources, and an interdisciplinary approach to care.<sup>96</sup> In line with this, hospitalists frequently serve on hospital committees and task forces, are experienced in developing and implementing clinical guidelines, and lead multidisciplinary teams to optimize patient care. For

example, as reported in a recent review, a 2007 Pediatric Research in the Inpatient Setting survey of 208 pediatric hospitalists in the United States and Canada indicated that 92% spend at least some time in administration, 85% serve on hospital committees, and 61% and 52% lead initiatives in practice guidelines and quality improvement, respectively.<sup>97</sup> Hospitalists are therefore especially well positioned to participate, and provide leadership, in hospital antimicrobial stewardship programs.

In 2007, the Infectious Diseases Society of America (IDSA)/Society for Healthcare Epidemiology of America (SHEA) released guidelines for developing institutional programs to enhance antimicrobial stewardship.<sup>18</sup> According to these guidelines, the ideal institutional antimicrobial stewardship program contains an infectious diseases physician and clinical pharmacist with infectious diseases training as core members, along with a clinical microbiologist, an information system specialist, infection control professional, and a hospital epidemiologist. The infectious diseases physician and clinical pharmacist with infectious diseases training are expected to serve as leaders of the team and should be appropriately compensated for time dedicated to the program. Clearly, this is an extensive team requiring a lot of staff. Although optimal, many institutions do not have an infectious diseases physician on staff or an attending who is interested and willing to participate. For many institutions, an even bigger issue is identifying an infectious diseases pharmacist with sufficient skill to manage an antimicrobial stewardship program. As a consequence, many institutions wanting to develop an antimicrobial stewardship program to improve clinical outcomes, reduce antimicrobial resistance, and lower costs will need to “think outside the box” and look for nontraditional leaders to champion and lead their programs. Potential nontraditional leaders include general clinical pharmacists, intensivists, and hospitalists.<sup>98</sup>

Although hospitalists are not explicitly mentioned in the IDSA/SHEA guidelines, they seem to be implicitly included. The guidelines state that the development, maintenance, and ultimate success of such programs fundamentally depends on the support and collaboration of hospital administration, medical staff leadership, and local providers.<sup>18</sup> Furthermore, they indicate the desirability for antimicrobial stewardship programs to “function under the auspices of quality assurance and patient safety.” As defined above, these are characteristics that are inherent to hospital medicine. Hence, there appears to be a good match between the activities performed by hospitalists and what the 2007 guidelines indicate is important for an effective antimicrobial stewardship program.

Now is the time for individuals to begin thinking about how best to prepare hospitalists for leadership roles in hospital antimicrobial stewardship programs. We need a well-defined process for either training hos-

pitalists for independent establishment of stewardship programs or establishing partnership with infectious disease specialists for the development of these programs. We need high-level training programs in focused areas of infectious diseases that hospitalists encounter frequently (skin and skin-structure infections, pneumonia, catheter-associated infections, among others). Detailed understanding of the pathogens and their optimal treatment could form the core of such training. Additional education in infection control and the antimicrobial stewardship processes would round out the knowledge needed for a hospitalist to best implement and provide leadership for an antimicrobial stewardship program at his/her own institution. These training programs could be developed and delivered locally, or preferably they could be provided at national training sessions developed and supported through SHM, infectious disease societies, or the CDC.

Partnering with infectious diseases specialists is essential for protocol development and clinical support. This could allow the hospitalist to start a stewardship program on a small scale. It begins with identifying a single important problematic infection area, based on available local data (antibiotic usage, resistance levels, length of stay, *C difficile* rates, mortality, etc). The hospitalist would then work with the infectious disease department/staff to establish a protocol focusing on several of the key areas: diagnosis, optimal empiric therapy, de-escalation (based on cultures and clinical response), transitioning intravenous antibiotics to oral, optimal duration of therapy, and transitioning therapy to the posthospital setting. The protocol would establish best treatment practices and the strategies to implement them (education, standardized order sets, computer decision support, monitoring and feedback, etc). The level of complexity and targeted outcomes need to be tailored to the resources available for implementation. Successful implementation and goal achievement in a small area could then be used to justify additional resources to expand the program. If hospitalists can be engaged in antimicrobial stewardship, both through individual patient care as well as program development, the large and growing number of hospitalists throughout the United States should allow for widespread implementation of antimicrobial stewardship programs.

## CONCLUSIONS

Healthcare-associated infections are increasingly a cause of morbidity and mortality in the United States and other countries, and the management of HAIs is increasingly complicated by involvement of MDR pathogens. Antimicrobial-resistant pathogens are also increasingly involved in infections occurring outside the hospital setting. Infections caused by resistant or MDR pathogens are associated with increased



mortality, longer length of hospital stay, and higher healthcare costs. The prevalence of these dangerous bacteria affects antimicrobial choices across a wider range of patients, particularly when choosing empiric therapy. Together with infection control, antimicrobial stewardship is an attractive solution to the challenges posed by antimicrobial resistance. Development and implementation of an effective institutional antimicrobial stewardship program can improve clinical outcome, reduce antimicrobial resistance and other unintended consequences of antimicrobial overuse/misuse, and lower healthcare costs.

At the forefront of inpatient care, hospitalists are positioned as excellent champions of the principles and practices of antimicrobial stewardship. By adhering to the principles of optimal antimicrobial therapy in their clinical practice, hospitalists can improve care and help reduce resistance on a patient-by-patient basis. At the same time, they may achieve other key hospitalist goals by reducing length of stay and decreasing costs and utilization. Moreover, they are well positioned to participate in, and at times lead, hospital-based antimicrobial stewardship programs. As such, hospitalists are expected to play a critical role in helping to solve the problems of antimicrobial resistance and suboptimal inpatient care, as we move further into the 21st century.

Disclosure: Dr Rosenberg received an honorarium for this work, which was jointly sponsored by the American Academy of CME and GLOBEX through an unrestricted educational grant from Merck & Co, Inc.

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