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Antimicrobial Stewardship: Importance for Patient and Public Health

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The discovery of potent antimicrobial agents was one of the greatest contributions to medicine in the 20th century. When introduced, they had an immediate and dramatic impact on the outcomes of infectious diseases, making once-lethal infections readily curable. Unfortunately, the emergence of antimicrobial-resistant pathogens now threatens these advances. Resistance is a serious health threat that affects the clinical outcome of patients as well as results in higher rates of adverse events and healthcare costs.

The seriousness of the health impact of antibiotic resistance and the limited pipeline of new antibiotics has combined to make antibiotic resistance a major public health crisis. Unfortunately, there are already patients every day who contract infections that cannot be treated with currently available antibiotics. The crisis of antibiotic resistance has been highlighted by academicians, practicing clinicians, professional societies, and public health agencies [1–9]. What can be done to address this crisis? There is no question that antibiotic use is the most important modifiable factor in tackling the problem of antibiotic resistance. Although principles of appropriate use have been encouraged since the introduction of antimicrobials, abiding by them is now more urgent than ever. The discouraging fact is that for decades now, a huge percentage of antibiotic use in both inpatient and outpatient settings is either totally unnecessary or incorrectly prescribed [5,10]. The good news is that we do have a solution to this problem. Since their inception, antimicrobial stewardship programs have proven highly successful in improving antibiotic use. Published studies demonstrate that these programs can improve patient outcomes, reduce adverse events (including *Clostridium difficile*), reduce readmission rates, and even reduce antibiotic resistance [11–

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16]. The proven benefits of antimicrobial stewardship programs have led to increasing calls for their implementation in all hospitals.

In the past, one of the downsides to efforts to promote antimicrobial stewardship programs has been the emphasis on cost savings as the primary rationale. Although this approach can be effective in making appeals to hospital administrators to garner financial support for stewardship programs, the emphasis on savings has shifted the focus away from the true reasons to implement stewardship programs. As defined in the Infectious Diseases Society of America (IDSA)/Society of Healthcare Epidemiology of America (SHEA) guidelines [5], the primary purpose of stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms (such as *Clostridium difficile*), and the emergence of resistance. It is these benefits of antimicrobial stewardship programs that should be the focus. In fact, they must become the focus if we hope to generate support for stewardship among patients, policy makers, and clinicians. This *Clinical Infectious Diseases* supplement takes an important step in seeking to shift the focus on antimicrobial stewardship away from costs and onto quality improvement.

Resistance: A Need for Action

The impact of antimicrobial resistance is high. The Centers for Disease Control and Prevention (CDC) estimates that each year in the United States, at least 2 million people acquire serious infections with bacteria that are resistant to 1 or more of the antibiotics designed to treat those infections [6]. At least 23 000 people die each year as a direct result of these antibiotic-resistant infections [6]. Many more die from other conditions that were complicated by an antibiotic-resistant infection. Antibiotic-resistant infections add considerable and avoidable costs to the already overburdened healthcare system. In most cases, antibiotic-resistant infections require prolonged and/or costlier treatments, extend hospital stays, necessitate additional healthcare encounters, and result in greater disability and death compared with infections that are easily treatable with antibiotics.

Although the concern of antimicrobial resistance has increased over the past decade with emergence of increasing numbers of multidrug-resistant organisms (eg, carbapenem-resistant Enterobacteriaceae), the emergence of antimicrobial resistance has long been a worry. The phenomenon of bacterial resistance was already expressed by pioneers of antimicrobial discovery. Both Gerhard Domagk, the discoverer of sulfonamide drugs, and Alexander Fleming, the discoverer of the penicillins, articulated this in their respective Nobel Prize acceptance speeches:

“If treated patients are not subjected to a very thorough check-up, penicillin—like the sulphonamides—is being misused, with the inevitable result that resistant strains will survive” (Domagk, 1939) [17].

“It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them ... there is the danger that the ignorant man may easily under dose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant” (Fleming, 1945) [18].

More recently, organizations such as the CDC and the World Health Organization have declared antimicrobial resistance a public health crisis and “a threat to national security” [6, 7].

The development and spread of antibiotic resistance is multifactorial, and no single intervention can solve the problem. However, experience has shown that improving the use of antibiotics in hospitals can play an important role in addressing antibiotic resistance. Evidence supports that antimicrobial stewardship programs dedicated to improving antimicrobial use can both reduce use and reduce resistance [15, 16].

Other Critical Needs for Antimicrobial Stewardship

Although antibiotic resistance is the crisis that is precipitating the current push for antimicrobial stewardship programs, it is important to note that there are a number of other patient safety issues that these programs address.

Clostridium difficile is a major threat to patients in hospitals. The emergence of the BI/NAP1 epidemic strain of *C. difficile* has led to sharp increases in morbidity and mortality. The CDC estimates that there are roughly 250 000 *C. difficile* cases resulting in 14 000 deaths among hospitalized patients each year in the United States [6]. Antimicrobial stewardship has proven to be a highly effective strategy in combating *C. difficile* in hospitals. Several single-center studies in the United States have shown significant reductions in *C. difficile* that follow the implementation of stewardship programs [19, 20]. More impressively, national data from the United Kingdom show even more impressive drops in *C. difficile* associated with reductions in use of key antibiotics [21].

Stewardship programs have also demonstrated effectiveness in improving the use of antibiotics in surgical prophylaxis and in helping clinicians optimize dosing in patients with renal insufficiency [22]. Whereas most of the studies on these improvements have examined process measures, there is little doubt that starting patients on proper surgical prophylaxis both contributes to preventing surgical site infections and reduces potential adverse events.

Finally, there is the most important patient safety issue—the proper treatment of infections. As the hospitalized population becomes sicker and more complicated, and antibiotic resistance continues to grow, the management of infections in hospitals is more challenging than ever. It should come as no surprise, then, that a program focused on improving antibiotic use would improve the treatment of infections, and this has been demonstrated. A study by Fishman et al showed that infections that were managed with the assistance of an antimicrobial stewardship program resulted in a 70% increase in infection cures and an 80% decrease in treatment failures [23].

SHIFTING THE FOCUS OF THE STEWARDSHIP RATIONALE

It has been well documented that antimicrobial stewardship programs are highly cost effective. Published studies, mostly from larger hospitals, have consistently put the annual cost savings of stewardship programs at \$200 000–\$900 000 [5, 24, 25]. One of the most dramatic recent examples came from the University of Maryland, where a stewardship

program was able to help reduce antibiotic expenditures by roughly \$3 million over a 3-year period. Unfortunately, the program was discontinued and there was an immediate increase in antibiotic expenditures of roughly \$2 million over the next 2 years [24]. It is also important to note that most of the cost studies of stewardship programs have only looked at direct pharmacy costs for antibiotics. When other potential savings, such as reduced lengths of stay and reduced readmission rates, are factored in, the savings become even more dramatic.

The cost-benefits of antimicrobial stewardship make it an easy sell for hospitals, especially in an era of increasing cost constraints. And although these cost-benefits have been helpful to promote support for stewardship, they seem to have become the predominant rationale for stewardship programs. As a result, antimicrobial stewardship has not become a core component of the patient safety movement and has not found many advocates among patient groups and non-infectious disease specialists. If we are to truly advance the state of antimicrobial stewardship, we must make it clear that it fits well within the context of patient safety.

HOW WE CAN MAKE PROGRESS ON STEWARDSHIP

Making antimicrobial stewardship a part of the patient safety effort will help bring new support and energy that must be translated into useful actions. Both the CDC and the American Hospital Association have highlighted the urgent need for antimicrobial stewardship programs [10, 25], but hospitals must now do the difficult work of making this a reality. To help with this, the CDC has developed a document called *Core Elements for Antibiotic Stewardship Programs*, which outlines 7 elements that have proven to be essential to successful programs [26]. While outlining these keys to success, this document also underscores the need for flexibility in implementing these elements in the diverse types of hospitals in the United States. Additional action on the regulatory front could also be important in making stewardship a reality in all hospitals. IDSA, SHEA, and the Pediatric Infectious Diseases Society have all called for antimicrobial stewardship programs to be added to the Centers for Medicare and Medicaid Services' hospital Conditions of Participation, which would likely have a huge impact on the wide implementation of these programs [27].

In conclusion, in light of the serious threat of emerging antimicrobial-resistant pathogens and the realization that new drugs to effectively treat these pathogens are several years away, it is crucial that antimicrobial stewardship programs be put into practice now to provide for optimal patient outcomes and preserve antimicrobials for future use. The articles in this supplement focus on various strategies and interventions for implementation of effective stewardship.

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