Pharmacy’s Role in Antimicrobial Stewardship
Establishing Guidelines, Fostering Partnerships, and Measuring Long-Term Results

ONE CANNOT UNDERESTIMATE THE IMPORTANCE OF IMPLEMENTING AN effective antimicrobial stewardship program in your organization – nor pharmacy’s involvement in it. The pressing reasons for performing a drug use evaluation (DUE) of antibiotics are the improvement of patient care outcomes and the minimization of costs to your institution. The process involves considering the efficacy and toxicity of drugs in particular patient populations, reviewing related evidence and literature and determining its relevance to your institution, and finally comparing the cost of equally efficacious agents. You will often be able to make decisions that have financial benefits, but – first and foremost – the primary goal of such a program is to identify those agents that are most efficacious in your patient population.

An antimicrobial stewardship group has two core members: an infectious disease specialist from the medical staff and a pharmacist trained in infectious diseases. Clinical microbiology is also an important member of this team. These parties, each equipped with complementary expertise, can outline antimicrobial use guidelines for your physicians based on the analysis of antibiograms and culture and susceptibility data. Agents of equal efficacy can then be compared to identify the most cost-effective therapy for your institution.

Also, keep in mind that the impact on the pharmacy drug budget is not the only dollar figure to consider in developing your antimicrobial stewardship program. For instance, the most appropriate treatment for a fungal blood infection might be more expensive than a less efficacious one, but the patient in question will have a quicker recovery and a shorter hospital stay. These “softer” cost savings should not be ignored when evaluating antibiotic use in your organization and developing prescribing guidelines.

Identifying Targeted Therapies
It is difficult to provide a hard and fast rule for identifying the specific agents you should target as part of your antimicrobial stewardship program, partly due to the variance in effectiveness for any antibiotic over time. However, begin by looking at correlations between problematic microbial resistance patterns and high dispensing volumes, as well as drugs in the same class that have no novel function. Fluoroquinolones and cephalosporins are two such classes that provide the opportunity to minimize formulary therapeutic duplication.

Your patient mix also will invariably affect your needs for antibiotic agents. A rural community hospital and a large teaching facility will likely have significant differences in their formularies, as the latter may see transplant and cancer patients, as well as other patients at high risk for infection. In that vein, small community hospitals, for instance, will likely have little – or perhaps no – need for broad-activity agents like meropenem, imipenem, or ertapenem.

It may also behoove your facility to evaluate the use of antifungal agents, which are beginning to account for a larger portion of facilities’ antimicrobial budgets. Review the types of patients most commonly seen in your hospital and choose an antifungal agent with demonstrated efficacy data. For instance, it can be very costly to have several triazoles or echinocandins on formulary, and by evaluating your patient population, you should be able to dispense just one agent in either of these classes. However, some agents are aggressively marketed to physicians and, as such, it may be difficult to get your medical staff behind one agent. Provide solid evidence for the antifungal agent you select, and explain your decision-making process to physicians. Doing so may make them more willing to accept your decisions.

Fostering a Partnership Between Pharmacy and Physicians
It is vital that you develop criteria for the appropriate use of anti-infectives in conjunction with your medical staff. Once the criteria are established, you must partner with the medical staff to affect change in your institution and to eventually evaluate your program’s success in positively impacting antibiotic use. Working with a physician advocate can help pharmacists influence broad prescribing trends. Identify a physician who is genuinely interested in the program and who shares pharmacy’s goal of creating guidelines that will improve patient care.

As mentioned earlier, while there are financial benefits to antimicrobial stewardship, avoid making it your primary goal, as you could end up polarizing the pharmacy and medical staff. You will likely be able to garner more physician interest if you create a multi-faceted program based on improving patient care – an issue that should strike a chord with your medical staff.

It is also important that you demonstrate to your potential physician partners the value they will derive from the program. Since pharmacists and physicians have aligned goals for improved patient care, physicians are generally very receptive to improved antimicrobial dosing in their patients. This is complemented by a stewardship program’s educational initiatives, which can highlight the importance of prudent antimicrobial use and the role of the infectious diseases expert. Keep in mind that infectious disease physicians depend on consultations for their livelihood, and the idea that an antimicrobial stewardship program will decrease physician consultations can poison the well. So be sure to communicate that the program, if it works properly, will actually increase the number of consultations for infectious disease practitioners. Also, hospitals are often willing to fund the director of the antimicrobial stewardship program at some level, to reimburse the physician for time devoted to the program. It may also be helpful to gather input from other sub-specialties in...
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Periodic Reviews of Antimicrobial Use Guidelines

Generally speaking, review and revise your empiric guidelines for antibiotic use annually, but also make revisions in response to situations as they come up throughout the year. Hospitals are not be able to sustain a high rate of decreased costs for the long term. The target will continually move, and you should not feel defeated if you do not see significant net drug savings year after year. Given annual drug price increases, even if you to keep your anti-infective costs flat from one year to the next, you may have actually cut 10% to 15% of your budget.

A decrease in hospital-associated infections may result from the implementation of an antimicrobial stewardship program. With effective stewardship, over the long-term, you should be able to minimize the number of resistant pathogens in your environment. Infections caused by resistant organisms are more difficult to treat and result in longer lengths of stay. With recent rule changes regarding reimbursement, these hospital-acquired infections can quickly have a significant negative impact on the institution’s bottom line.

This issue has been cast in an even brighter light with the recent incidences of MRSA infections. Since the advent of the antibiotic era, most of these therapies have been thought of as relatively non-toxic. We were rarely concerned with administering too much of an antibiotic, and were instead concerned with not giving enough. While you would not expect a physician to put patients on multiple chemotherapy agents simultaneously without a second thought, we frequently do so with antibiotics. Effective stewardship can combat this problem by educating physicians and giving them the tools and evidence they need to prescribe antibiotics appropriately and to address difficult cases. The message is: Use these beneficial drugs wisely, when it is appropriate.
Northwestern Memorial Hospital’s Restricted Antimicrobial Criteria

Amphotericin B: Conventional amphotericin B is not to be used for systemic treatment; it is only available for irrigation or special intravascular uses. For systemic treatment with an amphotericin B product, liposomal amphotericin B (Ambisome) should be used.

Aztreonam: Restricted to use in penicillin-allergic patients (documented history of type I allergy) who require the gram-negative coverage of a beta-lactam type antimicrobial.

Caspofungin: Restricted to use in patients with documented aspergillosis, who are refractory or intolerant to amphotericin-products and voriconazole; empiric antifungal therapy, when necessary in neutropenic patients who remain febrile despite broad spectrum antibiotic therapy; empiric use in patients with yeast bloodstream infections; and with Candida isolates who have documented clinical or microbiologic resistance to fluconazole.

Cefepime: Cefepime is restricted to the treatment of febrile neutropenic patients, empirically as a single agent for broad spectrum gram-positive and gram-negative activity, and in patients with documented gram-negative infections that are resistant to other expanded-spectrum cephalosporins. When cefepime is used for an indication other than a documented gram-negative infection that is resistant to other expanded-spectrum cephalosporins, if an antimicrobial with gram-positive activity (such as vancomycin or clindamycin) is added to the patient’s regimen, cefepime will be automatically discontinued and cefazidime at an equivalent dose will be substituted.

The AUT pharmacist will be responsible for the auto-substitution of cefazidime for cefepime in patients receiving vancomycin. The RPH modification function in Powerchart will be utilized for this effort, in areas where CPOE is active.

Cefoxitin: Restricted to patients with documented rapidly growing mycobacteria (Mycobacterium fortuitum, M. chelonae and M. abscessus) or ID consult

For other indications, use cefazolin 1 g + metronidazole 500 mg.

Cefazolin may be administered by IV push and metronidazole should be infused over 30 minutes. Cefazolin and metronidazole are compatible and may be administered together.

Ceftriaxone: NOW ON FORMULARY—NO AUTO RESTRICTION

Dalfopristin/Quinupristin: Its use should be restricted to patients with vancomycin-resistant Enterococcus faecium infections that are resistant to linezolid or in patients with vancomycin-resistant Enterococcus faecium or MRSA infections, who are unable to receive linezolid.

Daptomycin: Restricted to use by Infectious Diseases Consultation Service only

Dual Antifungal Therapy: Restricted to use by Infectious Diseases Consultation Service only

Imipenem: Restricted to patients with necrotizing pancreatitis and with documented or strongly suspected infections resistant to other antimicrobial agents

Linezolid: Use should be restricted to patients with with documented or strongly suspected VRE infections that are also ampicillin-resistant, or VRE infections that are ampicillin-susceptible in patients with penicillin allergy.

Cefepime is restricted to patients with documented infections resistant to other antimicrobial agents.

MRSA from culture is required for linezolid continuation.

• Culture-documented methicillin-resistant staphylococcal pneumonia who fail to respond to vancomycin

• MRSA infections in patients who exhibit a true allergic reaction to vancomycin

Meropenem: Restricted to cystic fibrosis patients, or patients with a documented Pseudomonas aeruginosa infection resistant to imipenem but susceptible to meropenem

Oxacillin: Restricted to use for prophylaxis in neurosurgery patients with indwelling devices and infectious Diseases Consultation Service only

Tigecycline: Restricted to use by Infectious Diseases Consultation Service only

Vancomycin Oral: Restricted to patients who have failed a minimum of five days of metronidazole or are intolerant to metronidazole

Voriconazole: Restricted to use in patients with strongly suspected or documented aspergillosis or for fungol prophylaxis in high risk bone marrow transplant patients

The following are criteria that help identify patients as being strongly suspected of having aspergillosis:

- Biopsy specimen consistent with aspergillosis

- Halo or air-crescent sign on lung CT

- Radiologic evidence of new pulmonary lesions not attributable to other factors with hyphae consistent with aspergillosis or aspergillus in the sputum

- CT evidence of sinusitis along with BMT, transplantation, or other immunocompromised condition

- Pulmonary symptoms suspicious of aspergillosis in a hematology or BMT patient

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Microbiology Data

Microbiology data is essential to maintaining your empiric antibiotic recommendations and ensuring they are well suited to your institution. Work with your microbi-
ology lab to ensure that data is available on a regular basis, in order to make rational decisions regarding commonly used antibi-
otics and avoid defaulting to antibiotics that no longer show activity in your institution. The microbiology lab should, at a mini-
mum, prepare an annual summary of organ-
ism susceptibility to allow you to make appropriate choices regarding available antibiotics and options included in your antimicrobial use guidelines.

Other Tools
Software platforms for clinical decision sup-
port are available to pharmacists seeking to improve the use of antimicrobials in their facilities. These tools can aid your clinicians in identifying opportunities for dosage adjustments and IV to PO therapeutic sub-
stitutions and in monitoring resistance pat-
ters with up-to-date antibiograms. Clinical intervention and patient monitoring data can be captured in real time and can allow your pharmacists to write rules that are clin-
ically applicable to your institution.

Conclusion
There is much value to be derived from an effective antimicrobial stewardship pro-
gram. When pharmacy and physicians establish a true partnership with common goals, your institution certainly stands to reduce costs, but, most importantly, will be making great strides towards improving patient care and therapeutic outcomes.

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Additional Resources: Infectious Diseases Society of America, Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship: www.idsociety.org

The authors wish to acknowledge Ericka Wilhelms for her contributions to the article.

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