ASHP *Advantage* E-Newsletter **September 2011**

Why Focus on Antimicrobial Stewardship?

Nearly half of antimicrobial use in hospitals is unnecessary or inappropriate.[1] Inappropriate antimicrobial use has been linked with antimicrobial resistance, which is associated with increased mortality, prolonged hospital lengths of stay, and increased health care costs.[2,3] Approximately 99,000 deaths are attributed to hospital-acquired infections at a cost of $28 billion to $33 billion every year in the United States.[4]

The research and development pipeline of antimicrobial agents to fight infections caused by resistant pathogens is essentially empty.[5] The wise use of currently available antimicrobial agents is needed to stem the emergence of resistance to and loss of effectiveness of these agents. Antimicrobial stewardship, an activity that includes the appropriate selection, dosing, route of administration, and duration of antimicrobial therapy, has been shown to improve antimicrobial use and reduce antimicrobial resistance, mortality, hospital length of stay, and health care costs.[6-13] Optimizing clinical outcomes while minimizing unintended consequences of antimicrobial use is the primary goal of antimicrobial stewardship.[14] A reduction in health care costs without adversely affecting the quality of care is a secondary goal.[14]

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Hospital Use of Antimicrobial Stewardship Programs

Use of antimicrobial stewardship programs (ASPs) was among the items recently reported from the 2010 ASHP national survey of pharmacy practice in hospital settings.[15] Roughly two of five (43.5%) of hospitals had an ASP. The percentage of hospitals with an ASP increased with hospital size from 31.6% for small hospitals with fewer than 50 beds to 83.0% for hospitals with 600 or more beds. The pharmacist's primary role was one of leadership and accountability in nearly half (48.5%) of hospitals with ASPs, with pharmacists serving primarily in a clinical support role in another 36.2% of hospitals and data analysis in another 13.1% of hospitals. Few hospitals with ASPs (2.2%) reported a lack of pharmacist involvement.

A variety of strategies were used to improve antimicrobial use in these ASPs, including national or local guidelines (90.1%), daily review of orders for targeted antimicrobial agents with feedback to prescribers (77.3%), formulary or prescribing restrictions for targeted antimicrobial agents (74.0%), education of individual or groups of prescribers (68.7%), and use of clinical decision support technology at the time of order entry (31.1%). Strategies involving education or information technology were more commonly used in large hospitals than in smaller facilities. Antimicrobial cycling (the scheduled substitution of a specific antimicrobial agent or class for another agent or class to prevent or reverse antimicrobial resistance) was not commonly used regardless of hospital size (5.9% overall, with a range from 2.2% to 10.5%). The methods used by hospitals to assess the impact of the ASP included evaluating antibiotic-use patterns (81.6%), bacterial resistance and infection control data (77.5%), expenditures and costs (59.0%), and patient outcomes (49.7%). The methods used varied by hospital size, with expenditures and costs relied on to a smaller extent than other methods at small hospitals compared with larger hospitals.

Institutional Impact Antimicrobial Stewardship Mentored Initiative

ASHP Advantage is conducting a multidisciplinary educational initiative to facilitate improvement in antimicrobial use in health systems through implementation of ASPs. Developed by a multidisciplinary educational steering committee of experts in antimicrobial stewardship and infectious diseases, this initiative comprises innovative educational activities and tools. Featured educational programming includes on-demand home study activities and live interactive webinars. Information about this programming, a discussion guide on implementing ASPs in health systems, and a resource center with links to organizations, guidelines, tools, and readings related to antimicrobial stewardship are available at the initiative Web portal at **http://www.leadstewardship.org**.

Activities include the Institutional Impact Antimicrobial Stewardship Mentored Initiative through which pharmacist ASP experts provide an on-site evaluation of selected ASP practices in health systems. The following participating health systems recently were announced:

Inova Alexandria Hospital
Alexandria, Virginia

Interim LSU Public Hospital
New Orleans, Louisiana

St. Mary's Hospital
Madison, Wisconsin

Texas Health Harris Methodist Hospital Southwest Fort Worth
Fort Worth, Texas

The Christ Hospital
Cincinnati, Ohio

New Policy Paper on Combating Antimicrobial Resistance

Earlier this year the Infectious Diseases Society of America (IDSA) released a policy paper for combating antimicrobial resistance.[16] Specific recommendations for legislative action and funding were made to the U.S. Congress, including establishment and support of ASPs in all health care settings (e.g., hospitals, long-term care facilities, long-term acute care facilities, ambulatory surgical centers, dialysis centers, outpatient clinics, private practices). These ASPs should be required as a condition of participation in the federal Medicare and Medicaid programs or through another regulatory mechanism, according to IDSA. An antibiotic innovation and conservation fee was proposed, with 75% of the revenue used to fund new antibiotic development and 25% used to fund antimicrobial stewardship.

Strengthening and rapid enactment of the Generating Antibiotic Incentives Now (GAIN) Act (H.R. 6331 in the 111th Congress, and H.R. 2182 in the 112th Congress) were called for by IDSA to provide incentives to stimulate antibiotic research and development and safeguards to ensure that approved antibiotics are used appropriately.[17] The GAIN Act was introduced by Representative John "Phil" Gingrey, M.D. (R-Georgia) and contains provisions for extending the data exclusivity period for new antibiotics used for treating or preventing infection with certain resistant pathogens; priority or fast track review by the Food and Drug Administration (FDA) of antibiotics; study of the need for incentives to encourage the research, development, and marketing of new antibiotics; and review and revision of FDA guidelines for clinical trials of antibiotics.

Other IDSA legislative recommendations included strengthening and rapid enactment of the Strategies to Address Antimicrobial Resistance Act (known as STAAR and H.R. 2400 in the 111th Congress) to improve antibiotic surveillance, data collection, research, and prevention and control efforts.[18] The STAAR Act was introduced in 2009 to encourage the development of new antimicrobial agents as well as strengthen federal antimicrobial resistance surveillance, prevention and control, and research efforts.[18] Representative Jim Matheson (D-Utah) plans to reintroduce the legislation in the near future.[19]

Answers to Frequently Asked Questions

Several live interactive webinars on ASPs were conducted by ASHP Advantage this summer. The webinars have been archived and are available on demand at the initiative Web portal (**www.LeadStewardship.org**). Participants submitted questions for the faculty to address.

Q: What practical advice do you have for improving the time to first dose of antimicrobial therapy without eliminating preauthorization requirements designed to prevent inappropriate antimicrobial use?

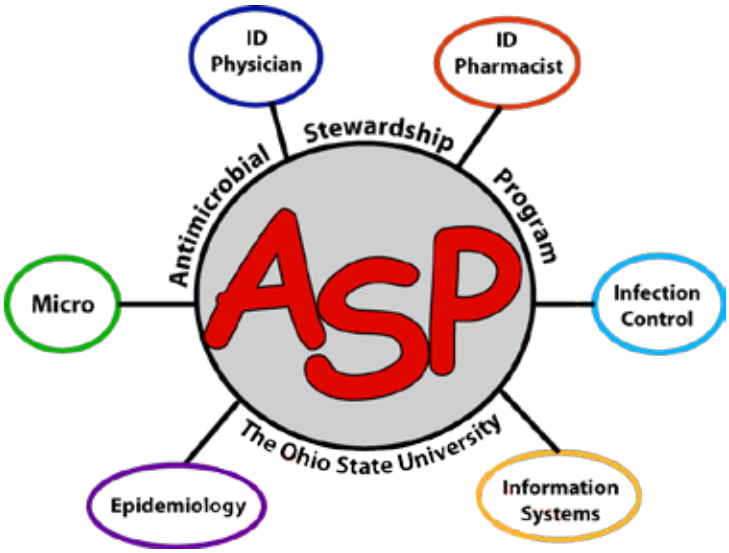
A: The use of preauthorization requirements is a common strategy for preventing inappropriate antimicrobial use and antimicrobial resistance, but delays in initiating antimicrobial therapy can result. The prompt initiation of antimicrobial therapy can be critical to ensure optimal patient outcomes. At University of Kentucky HealthCare, we immediately dispense the first dose, with formulary restrictions and preauthorization requirements enforced only for subsequent doses.[20] This approach strikes a balance between preventing the excessive antimicrobial use that promotes resistance and incurring the delays in therapy that adversely affect clinical outcomes.

—Craig Martin, Pharm.D., BCPS

Q: What is the structure of your antimicrobial stewardship team?

A: The ASP at the Ohio State University Medical Center (OSUMC) uses a team approach to improving patient care (Figure). Infectious disease pharmacists, infectious disease physicians, clinical microbiologists, infection control personnel, epidemiologists, information system specialists, and others collaborate to manage antimicrobial use in the institution. Each member of the multidisciplinary team at OSUMC has a unique education and makes a valuable contribution to optimizing antimicrobial use and minimizing antimicrobial resistance. These health care professionals can accomplish much more by working as a team than alone.

Figure.
Team Approach to Improving Patient Care Through Antimicrobial Stewardship at OSUMC



—Debra A. Goff, Pharm.D., FCCP

Q: How do you handle clinician hesitation to de-escalate antimicrobial therapy in a patient with negative cultures?

A: Clinicians often are reluctant to de-escalate therapy when cultures are negative and clinical improvement has been observed.[21] Ideally, guidelines for de-escalating antimicrobial therapy should be followed in such situations, but published guidelines are not available. Nevertheless, the clinical principles described in the published literature might be used to devise strategies for antimicrobial de-escalation. For example, de-escalation of antimicrobial therapy in surgical intensive care unit (ICU) patients with fever and pulmonary infiltrates was achieved at one medical center by using a clinical pulmonary infection score (CPIS)—a diagnostic algorithm based on readily available clinical, radiographic, and microbiological criteria—to identify patients with ventilator-associated pneumonia (VAP) and differentiate them from patients with a clinical pneumonia syndrome with a non-infectious etiology. Use of the CPIS made feasible the discontinuation of empiric antimicrobial therapy after 3 days in patients with a low CPIS and negative pulmonary cultures without increasing mortality or ICU length of stay.[22] It also reduced antimicrobial costs and resistance.

In an attempt to minimize mortality, patients with hospital-acquired pneumonia, including VAP, typically receive as empiric therapy a three-drug regimen that provides coverage against methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa (P. aeruginosa)*. Guidelines of the American Thoracic Society and Infectious Diseases Society of America for managing hospital-acquired, ventilator-associated, and healthcare-associated pneumonia suggest that antimicrobial therapy may be de-escalated by discontinuing coverage for MRSA and *P. aeruginosa* in patients with clinical improvement who were not receiving antibiotics when cultures were obtained if sputum cultures are negative for these pathogens.[23]

—George H. Karam, M.D.

Practice Changes

Participants in the live interactive webinars on ASPs conducted by ASHP Advantage this summer were asked what practice changes they might implement based on the knowledge acquired by participating in the educational activity. The following are examples of practice changes identified by participants:

- Present a business case to hospital administration and obtain support for establishing an ASP.
- Identify champions among the medical staff, especially infectious disease physicians, to promote antimicrobial stewardship in the institution.
- Make an effort to further develop the relationship between the pharmacy and microbiology departments, and investigate the use of new diagnostic tests to differentiate between antimicrobial-resistant and sensitive pathogens, improve antimicrobial clinical decision making, and patient outcomes.
- Increase collaboration with prescribers of antimicrobial therapy.
- Incorporate ASP elements into the computerized physician order entry system as a means for educating prescribers about appropriate antibiotic choices.
- Reassess the timing of initial antibiotic doses and develop strategies to improve timeliness and patient outcomes.
- Implement new policies and procedures to avoid an inappropriate duration of antimicrobial therapy.
- Encourage de-escalation of antimicrobial therapy when appropriate.
- Track clinical data and use a variety of metrics (e.g., days of therapy, not just antibiotic purchases) to evaluate antimicrobial use and illustrate the impact of the ASP.

References

1. Centers for Disease Control and Prevention. Get smart for healthcare. http://www.cdc.gov/getsmart/healthcare/ (accessed 2011 Aug 22).

2. Costelloe C, Metcalfe C, Lovering A et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ*. 2010; 340:c2096. Available at http://www.bmj.com/cgi/pmidlookup?view=long&pmid=20483949.

3. Goff DA. Antimicrobial stewardship: bridging the gap between quality care and cost. *Curr Opin Infect Dis*. 2011; 24(suppl 1):S11-20.

4. U.S. Department of Health and Human Services. Healthcare associated infections. http://www.hhs.gov/ash/initiatives/hai/index.html (accessed 2011 Aug 22).

5. Infectious Diseases Society of America. Bad bugs, no drugs: as antibiotic discovery stagnates…a public health crisis brews. July 2004. Available at: http://www.idsociety.org/WorkArea/showcontent.aspx?id=5554 (accessed 2011 Aug 22).

6. Dellit TH, Chan JD, Skerrett SJ et al. Development of a guideline for the management of ventilator-associated pneumonia based on local microbiologic findings and impact of the guideline on antimicrobial use practices. *Infect Control Hosp Epidemiol.* 2008; 29:525-33.

7. Hermsen ED, Smith Shull S, Puumala SE et al. Improvement in prescribing habits and economic outcomes associated with the introduction of a standardized approach for surgical antimicrobial prophylaxis. *Infect Control Hosp Epidemiol.* 2008; 29:457-61.

8. Bantar C, Sartori B, Vesco E et al. A hospitalwide intervention program to optimize the quality of antibiotic use: impact on prescribing practice, antibiotic consumption, cost savings, and bacterial resistance. *Clin Infect Dis.* 2003; 37:180-6.

9. Cook PP, Catrou P, Gooch M et al. Effect of reduction in ciprofloxacin use on prevalence of methicillin-resistant *Staphylococcus aureus* rates within individual units of a tertiary care hospital. *J Hosp Infect.* 2006; 64:348-51.

10. Buising KL, Thursky KA, Robertson MB et al. Electronic antibiotic stewardship—reduced consumption of broad-spectrum antibiotics using a computerized antimicrobial approval system in a hospital setting. *J Antimicrob Chemother.* 2008; 62:608-16.

11. Cosgrove SE. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. *Clin Infect Dis.* 2006; 42(suppl 2):S82-9.

12. Bauer KA, West JE, Balada-Llasat JM et al. An antimicrobial stewardship program's impact with rapid polymerase chain reaction methicillin-resistant *Staphylococcus aureus/S. aureus* blood culture test in patients with *S. aureus* bacteremia. *Clin Infect Dis.* 2010; 51:1074-80.

13. Kaki R, Elligsen M, Walker S et al. Impact of antimicrobial stewardship in critical care: a systematic review. *J Antimicrob Chemother.* 2011; 66:1223-30.

14. Dellit TH, Owens RC, McGowan JE Jr et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007; 44:159-77.

15. Pedersen CA, Schneider PJ, Scheckelhoff DJ. ASHP national survey of pharmacy practice in hospital settings: Prescribing and transcribing—2010. *Am J Health Syst Pharm.* 2011; 68:669-88.

16. Infectious Diseases Society of America. Combating antimicrobial resistance: policy recommendations to save lives. *Clin Infect Dis.* 2011; 52(suppl 5):S397-S428. Available at: http://cid.oxfordjournals.org/content/52/suppl_5/S397.full.pdf.

17. 112th U.S. Congress. Text of H.R. 2182: Generating Antibiotic Incentives Now Act of 2011. http://www.govtrack.us/congress/billtext.xpd?bill=h112-2182 (accessed 2011 Aug 15).

18. Infectious Diseases Society of America. Strategies to Address Antimicrobial Resistance Act. http://www.idsociety.org/staaract.htm (accessed 2011 Aug 15).

19. Tucker C. New measures, legislation aimed at antibiotic resistance: infections cost millions, end lives. *The Nation's Health.* 2011 July; 41(5):1-12. http://thenationshealth.aphapublications.org/content/41/5/1.4.full (accessed 2011 Aug 15).

20. Martin CA, Armitstead JA, Mynatt RP et al. Moving antimicrobial stewardship from restriction to facilitation. *Am J Health Syst Pharm.* 2011; 68:109-10.

21. Drew RH, White R, MacDougall C et al. Insights from the Society of Infectious Diseases Pharmacists on antimicrobial stewardship guidelines from the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Pharmacotherapy*. 2009; 29:593-607.

22. Singh N, Rogers P, Atwood CW et al. Short-course empiric antibiotic therapy for patients with pulmonary infiltrates in the intensive care unit. A proposed solution for indiscriminate antibiotic prescription. *Am J Respir Crit Care Med.* 2000; 162(2 pt 1):505-11.

23. American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med.* 2005; 171:388-416.

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