DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK (DASON)

Antimicrobial Stewardship News

Volume 4, Number 5, May 2016

Spotlight on stewardship: The new IDSA/SHEA Antibiotic Stewardship Guidelines

The Centers for Disease Control (CDC) and the Society for Healthcare Epidemiology of America (SHEA) jointly released new antibiotic stewardship guidelines in April[1]. These guidelines focus on specific evidence-based strategies to help assure that Antibiotic Stewardship Programs (ASP) will be effective, successful, and sustainable. This newsletter reviews and prioritizes key strategies highlighted in these guidelines and discusses how DASON can help local hospitals implement these recommendations.

Priority 1: Preauthorization and Prospective Audit with Feedback:

IDSA/SHEA guidelines recommend that all hospitals implement programs for mandating preauthorization of certain classes of antibiotics and/or develop a mechanism for prospective audits of antibiotic use that are coupled with feedback of recommendations to clinicians. Such programs are considered to be pillars for all ASPs. Preauthorization models require approval of restricted antibiotics prior to administration. Prospective audit and feedback (PAF) models attempt to alter prescriber decision making after administration of an antibiotic(s). Both preauthorization and PAF models, when done correctly, improve the appropriateness of antibiotic use and save money. Preauthorization models have been shown to be associated with reductions in total antibiotic use, reductions in antibiotic resistance and fewer *C. difficile* infections (CDI); without causing adverse impacts on patient outcomes[2-4]. However, preauthorization models are labor intensive and require enough trained staff to provide 24-hour coverage for drug approvals.

PAF models similarly reduce antibiotic use, reduce antibiotic resistance, and reduce rates of CDI. However, unlike preauthorization models, PAF models use persuasive methods to effect change.

A Cochrane review comparing the impact of preauthorization to persuasive measures (including PAF), showed that preauthorization led to measurable effects on antimicrobial prescribing at one month, and less colonization and infection with resistant organisms and *C. difficile* at 6 months. However, preauthorization and persuasive measures equally modified prescribing behavior and colonization/infection rates at 12 and 24 months. [5]. The relative pros and cons of each model is summarized in Table 1.

DASON Response: Both or either preauthorization or PAF should indeed be part of most ASPs. Thus programmatic and personal resources should be committed to creating and implementing one or both models. We are available and willing to work with your institution to help you decide which model is best for your ASP or if both models should be implemented. In addition, we can help you assess (measure) the impact of such programs and sustain either or both models.

Table 1. Comparison of Preauthorization and Prospective Audit and Feedback Strategies for Antibiotic Stewardship

Preauthorization	Prospective Audit and Feedback
Advantages	
• Reduces initiation of unnecessary/ inappropriate antibiotics	• Can increase visibility of antimicrobial stewardship program and build collegial relationships
• Optimizes empiric choices and influences downstream use	• More clinical data available for recommendations, enhancing uptake by prescribers
• Prompts review of clinical data/ prior cultures at the time of initiation of therapy	• Greater flexibility in timing of recommendations
• Decreases antibiotic costs, including those due to high-cost agents	• Can be done on less than daily basis if resources are limited
• Provides mechanism for rapid response to antibiotic shortages	• Provides educational benefit to clinicians
• Direct control over antibiotic use	• Prescriber autonomy maintained
	• Can address de-escalation of antibiotics and duration of therapy
Disadvantages	
• Impacts use of restricted agents only	• Compliance voluntary
• Addresses empiric use to a much greater degree than downstream use	• Typically labor-intensive
• Loss of prescriber autonomy	• Success depends on delivery method of feedback to prescribers
• May delay therapy	• Prescribers may be reluctant to change therapy if patient is doing well
• Effectiveness depends on skill of approver	• Identification of interventions may require information technology support and/or purchase of computerized surveillance systems
• Real-time resource intensive	• May take longer to achieve reductions in targeted antibiotic use
• Potential for manipulation of system (eg, presenting request in a biased manner to gain approval)	
• May simply shift to other antibiotic agents and select for different antibiotic-resistance patterns	

Priority 2: Designing an intervention to reduce use of antimicrobial agents strongly associated with an increased risk of CDI:

ASP interventions that reduce the use of clindamycin, cephalosporins, and/or fluoroquinolones have been consistently associated with reductions in rates of hospital acquired CDI.

DASON Response: We believe that reducing the use of the preceding classes of antimicrobial should be a local priority, because these drugs are closely linked with an increased risk of developing CDI. Our team has developed practical experience and they can provide practical advice on methods and strategies to reduce the overall use of these drugs without adversely affecting patient outcomes. For example, programs that assess and monitor prescribing habits for the above agents are particularly important during outbreaks of influenza and influenza-like illnesses. Our pharmacists will continue to work with each member hospital to develop local strategies to improve prescribing habits and practices related to these agents.

Priority 3: Certain IV agents should have pharmacy-driven pharmacokinetic (PK) monitoring:

Hospitals should develop programs to adjust dosing of aminoglycosides to improve their efficacy and reduce their risk of producing side effects in patients. Aminoglycoside PK monitoring programs are designed to increase the frequency of measuring drug level to assure that serum drug concentrations remain within the therapeutic range. Despite the cost of implementing such programs and measuring drug levels, these programs result in lower overall costs, mainly because of reduced nephrotoxicity. Other studies have also shown that aminoglycoside PK monitoring is associated with reduced risks of nephrotoxicity, shorter hospital stays, and lower mortality[6, 7].

The impact of vancomycin PK monitoring programs has not been as extensively evaluated as programs that provide aminoglycoside PK monitoring. However, the authors of one randomized controlled study reported that pharmacy-initiated PK monitoring resulted in lower risks of nephrotoxicity and lower costs even though overall patient outcomes remained the same. [8].

DASON Response: Our pharmacists have considerable experience on how to implement PK monitoring programs. We also can help local hospitals assess their existing PK monitoring programs and improve them in some cases.

Priority 4: ASP should implement interventions to improve the timing and frequency of oral antimicrobial use

ASP interventions that increase oral antibiotic use reduce cost and hospital stay. These interventions target either initial oral drug administration or timely switch from IV to equivalent oral agent (IV to PO switch). Early oral antibiotic administration strategies should be incorporated into routine pharmacy activities.

DASON Response: DASON strongly supports early conversion of parenteral to oral (PO) antibiotic administration in appropriate settings and patient groups. Such policies need to be carefully constructed and implemented so that clinicians have guidance when such conversions are appropriate, what groups of patients are suitable for early conversion, and how to dose oral agents in these patients. If you are interested in either beginning such a program, or modifying/improving your existing parenteral-to-oral switch program, please contact your pharmacy liaison.

Priority 5: ASP implemented syndromic guidelines and interventions to reduce antimicrobial duration:

Antimicrobial Stewardship Programs should develop facility-specific guidelines for selected common and important infectious syndromes such as pneumonia. These guidelines should be provided to local clinicians along with practical and clear educational materials about how to implement these recommendations. Hospitals that have created such facility specific guidelines, particularly for conditions such as pneumonia, have been able to document 1) a higher frequency of appropriate initial therapy, 2) more frequent use of appropriate narrower-spectrum antibiotic regimens, 3) earlier appropriate switches from IV to oral therapy, and 4) overall shorter durations of therapy.[9, 10]

Syndrome guidelines should include a recommended duration of therapy for each specific infectious syndrome. Recently published randomized controlled trials have shown that a shorter duration of antimicrobial therapy may be appropriate for several common infectious syndromes such as SSTI, pneumonia, and UTIs. Table 2, taken from the guidelines, lists the randomized trial evaluating duration of therapies for specific clinical syndromes.

DASON response: The IDSA/SHEA guidelines highlight the importance of creating and implementing facility specific syndromic guidelines. Such guidelines at a minimum should include recommendations to specify (and in most cases reduce) the total duration of antibiotic therapy. We encourage all of our member hospitals to develop syndrome specific guidelines for community acquired pneumonia and include specific recommendations for the recommended total duration of therapy as there are good data to support such recommendations and because shorter courses of therapy are proven to be safe and effective. Our pharmacist-liaisons will gladly assist you in creating and implementing such guidelines.

Table 2. Meta-analyses and Examples of Randomized Clinical Studies Comparing Shorter Versus Longer Duration of Antibiotics

Reference	Clinical Condition/Population	Treatment Duration, d	Clinical Outcome[a]
Meta-analyses			
Dimopoulos et al, 2008 [123]	Adults and children with CAP	3–7 vs 5–10	Clinical success, relapse, mortality, adverse events
Pugh et al, 2011 [124]	Adults with VAP	7–8 vs 10–15	Antibiotic-free days[b], recurrence[b]
Dimopoulos et al, 2013 [125]	Adults with VAP	7–8 vs 10–15	Relapse, mortality, antibiotic-free days[c]
Randomized clinical trials			
Chastre et al, 2003 [127]	Adults with VAP	8 vs 15	Mortality, recurrent infections[d]
El Moussaoui et al, 2006 [128]	Adults with CAP	3 vs 5	Clinical and radiological success
Greenberg et al, 2014 [129]	Children with CAP	5 vs 10	Treatment failure[e]
Hepburn et al, 2004 [130]	Adults with cellulitis	5 vs 10	Clinical success
Sandberg et al, 2012 [131]	Adult females with acute pyelonephritis	7 vs 14	Clinical efficacy, adverse events
Talan et al, 2000 [132]	Women with acute uncomplicated pyelonephritis	7 vs 14	Bacteriologic and clinical cure[f]
Runyon et al, 1991 [133]	Adults with spontaneous bacterial peritonitis	5 vs 10	Mortality, bacteriologic cure, recurrence
Saini et al, 2011 [134]	Neonatal septicemia	2–4 vs 7 (with sterile culture)	Treatment failure
Sawyer et al, 2015 [135]	Adults with intra-abdominal infection	4 vs ≤10	Composite of surgical site infection, recurrent intra-abdominal infection, or death
Bernard et al, 2015 [136]	Adults with vertebral osteomyelitis	42 vs 84	Cure at 1 y by independent committee and secondary outcomes

Abbreviations: CAP, community-acquired pneumonia; VAP, ventilator-associated pneumonia.

[a] There were no statistically significant between-group differences in outcomes unless otherwise noted.

[b] Shorter course was associated with more antibiotic-free days (mean difference, 4.02; 95% confidence interval [CI], 2.26–5.78) and fewer VAP recurrences due to multidrug-resistant organisms (odds ratio [OR], 0.44; 95% CI, .21–.95), without adverse effects on other outcomes. For VAP due to nonfermenting gram-negative bacilli, however, shorter course was associated with more recurrences (OR, 2.18; 95% CI, 1.14–4.16).

[c] Shorter course was associated with more antibiotic-free days (mean difference, 3.40 days; 95% CI, 1.43–5.37).

[d] Shorter course was associated with more antibiotic-free days (13.1 v 8.7 days; $P < .001$) and no increase in recurrent infection except in the subset with nonfermenting gram-negative bacilli.

[e] The 5-day, but not the 3-day, course was not inferior to the 10-day course.

[f] Shorter course was associated with higher bacteriologic (99% vs 89%; 95% CI, .04–.16; $P = .004$) and clinical cure rates (96% vs 83%; 95% CI, .06–.22; $P = .002$).

Priority 6: Avoiding pitfalls: Don't rely only on didactic material for stewardship

Educational materials should augment but not supplant active stewardship. IDSA/SHEA guidelines recommend that leaders of antibiotic stewardship activity be infectious disease physicians and pharmacists with **additional training in stewardship.**

DASON response: Active stewardship leads to improved patient outcomes and reduces the emergence of resistant bacteria. Our team of infectious diseases physicians and liaison pharmacists who all have additional training and practical experience in antibiotic stewardship principles and practice will continue to help your hospital develop cutting edge stewardship and create and disseminate educational material designed to augment and enhance your active stewardship program.

Take Home Points:

1. Effective antimicrobial stewardship improves patient outcomes and saves money.
2. As a DASON member, you have access to ID physicians and pharmacists trained in antimicrobial stewardship to help you create, implement, and measure the success of your ASP.
3. Local ASPs should focus on 1) preauthorization programs and/or direct feedback to prescribers, 2) attempt to monitor and reduce the use of specific selected classes of antibiotics that are proven to increase the risk of CDI, 3) implement pharmacy-driven PK monitoring programs, 4) develop and implement programs and protocols that promote the early appropriate conversion of parenteral to oral antibiotic administration in appropriate groups of patients, 5) develop and implement local facility-specific protocols for selected common infectious syndromes such as community-acquired pneumonia.
4. Educational materials are important; however, they are not sufficient. Local antibiotic stewardship programs active interventions designed to improve prescribing practices and patient outcomes.

References:

1. Barlam, T.e.a., *Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Disease Society of America and the Society for Healthcare Epidemiology of America.* Clinical Infectious Disease, 2016.
2. Metjian, T.A., et al., *Evaluation of an antimicrobial stewardship program at a pediatric teaching hospital.* Pediatr Infect Dis J, 2008. **27**(2): p. 106-11.
3. White, A.C., Jr., et al., *Effects of requiring prior authorization for selected antimicrobials: expenditures, susceptibilities, and clinical outcomes.* Clin Infect Dis, 1997. **25**(2): p. 230-9.
4. Buising, K.L., 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**(3): p. 608-16.
5. Davey, P., et al., *Interventions to improve antibiotic prescribing practices for hospital inpatients.* Cochrane Database Syst Rev, 2013. **4**: p. CD003543.
6. Streetman, D.S., et al., *Individualized pharmacokinetic monitoring results in less aminoglycoside-associated nephrotoxicity and fewer associated costs.* Pharmacotherapy, 2001. **21**(4): p. 443-51.
7. Kemme, D.J. and C.I. Daniel, *Aminoglycoside dosing: a randomized prospective study.* South Med J, 1993. **86**(1): p. 46-51.
8. Fernandez de Gatta, M.D., et al., *Cost-effectiveness analysis of serum vancomycin concentration monitoring in patients with hematologic malignancies.* Clin Pharmacol Ther, 1996. **60**(3): p. 332-40.
9. Ostrowsky, B., et al., *Antimicrobial stewardship and automated pharmacy technology improve antibiotic appropriateness for community-acquired pneumonia.* Infect Control Hosp Epidemiol, 2013. **34**(6): p. 566-72.
10. Capelastegui, A., et al., *Improvement of process-of-care and outcomes after implementing a guideline for the management of community-acquired pneumonia: a controlled before-and-after design study.* Clin Infect Dis, 2004. **39**(7): p. 955-63.