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COMMENTARY

Preventing the Post-Antibiotic Era by Training Future Pharmacists as Antimicrobial Stewards

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Antimicrobials enable modern medicine, but their efficacy is a limited resource. In the past 20 years, antimicrobial development has slowed dramatically while antimicrobial resistance continues to rise. In response to this, there has been an increased focus on strategically managing antimicrobial use with an approach called "antimicrobial stewardship." Antimicrobial stewardship programs have been endorsed by health systems, professional societies, regulators, and government. These programs have been shown to reduce antimicrobial use, slow the growth of antimicrobial resistance, and improve patient outcomes. This commentary will discuss recent mandates for antimicrobial stewardship, compare current approaches to teaching infectious diseases pharmacotherapy with the skills and knowledge required for antimicrobial stewardship, and provide recommendations for and examples of best practices in training student pharmacists to become antimicrobial stewards.

Keywords: antimicrobial stewardship, antimicrobial resistance, pharmacy curricula, interprofessional education

Antimicrobial Stewardship: What, Why, by Whom, and Says Who?

Antimicrobial resistance is one of the most serious health threats of the 21st century. Resistance is present globally, compromising the ability of clinicians to treat infectious diseases, undermining many advances in health care, and opening the possibility of a future without effective antimicrobial therapy.¹ There is a direct correlation between antimicrobial consumption and development of resistance.^{2,3} For most of the 20th century, the introduction of new antimicrobials outpaced the development of resistance; however, the number of new systemic antimicrobials approved by the Food and Drug Administration has been declining.⁴ The term "antimicrobial stewardship" (AS) was developed to describe the concept of appropriately using and managing antimicrobial agents. It is an approach to patient care that aims to balance effective prevention and treatment of infection with the patient- and population-level adverse consequences of antimicrobial use, particularly antimicrobial resistance. Antimicrobial stewardship programs (ASPs) are multidisciplinary teams of clinicians who systematically review and recommend modifications in antimicrobial use. These programs have become mandated by governmental or regulatory entities across multiple health care settings. Most ASPs have pharmacists both in leadership positions and managing much of the logistics and patient care responsibilities of AS. Studies of ASPs have shown that the presence of interdisciplinary teams who monitor antimicrobial use and provide feedback to prescribers when indicated have decreased antimicrobial use and reversed or slowed the increase in rates of antimicrobial resistance.⁵

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Multiple professional organizations have issued recommendations for the widespread adoption of ASPs with pharmacists as essential members of an interprofessional team, including the Infectious Diseases Society of America, the Society for Healthcare Epidemiology of America, the Society of Infectious Diseases Pharmacists, and the American Society of Health-systems Pharmacists.⁶⁻⁸ In addition, the Centers for Disease Control and Prevention (CDC) included the need for drug expertise provided by a pharmacy leader as one of the core elements in their *Core Elements of Hospital Antimicrobial Stewardship Programs* guidance.⁹

In March 2015, in response to an Executive Order from former President Obama, an interagency Task Force on Combating Antibiotic-Resistant Bacteria released the National Action Plan for Combating Antimicrobial Resistance which provided a roadmap outlining five critical initiatives for combating resistance.^{10,11} Antimicrobial stewardship was named as mission critical for slowing the development and spread of antimicrobial resistance throughout health care. Importantly, the document recommends the Centers for Medicare & Medicaid Services (CMS) consider adopting a policy of requiring ASPs as a Condition of Participation for acute care hospitals and long-term care facilities. CMS has established a targeted implementation window for this policy of 2017-2018.¹² In January 2017, the Joint Commission began monitoring all accredited acute care and long-term care facilities for compliance with their standards calling for establishment of an institutional ASP.¹³

Given the growing national imperative to address antimicrobial resistance, it is incumbent on pharmacy educators to provide future pharmacists with the knowledge and skills necessary to be effective stewards of antimicrobials. Implementation of AS is no longer a niche clinical service or cost-saving initiative; it is a vital and increasingly mandated component of pharmacy practice. While most pharmacists will not be directing ASPs, all pharmacists should incorporate the principles of AS into their clinical practice. Therefore, integrating stewardship principles into pharmacy education will be essential to filling the need established by professional standards and regulatory requirements.

State of Antimicrobial Stewardship Education in Pharmacy Curricula

In 2014, more than 500 graduating pharmacy students from 12 pharmacy schools in the United States participated in a survey about their knowledge and attitudes of appropriate antimicrobial use.¹⁴ These future pharmacists planned on practicing in varied patient care settings, with 53% of respondents planning on entering practice immediately after graduation. Among respondents, the vast majority (94%) believed strong knowledge of antimicrobials was important for their pharmacy careers and more than 80% desired more education on antimicrobial resistance and appropriate use of antimicrobials. However, most felt unprepared to advance stewardship goals with only 54% agreeing that their education was "good or very good" in preparing them to streamline or de-escalate antimicrobial therapy, a core stewardship function of pharmacists. This is in contrast to the more traditional infectious diseases topics taught in the pharmacy curriculum, where a majority (73%) felt their education had been good or very good in preparing them to monitor for efficacy and safety of the chosen antimicrobial therapy.

In 2016, the American College of Clinical Pharmacy (ACCP) published a revised pharmacotherapy didactic curriculum toolkit to serve as a guide for curricular development at pharmacy colleges.¹⁵ The toolkit identified 37 topics under infectious diseases, grouped into tiers based on the priority for students to provide competent pharmacist care in that topic by the time they graduate. AS is listed as a Tier 2 competency, alongside 24 other topics, primarily infectious diseases and syndromes (eg, prostatitis). Although the inclusion of AS in a list of essential topics is encouraging, the prioritization of the topic and the lack of specific tools for incorporating stewardship education into curricula weaken the impact of the recommendation.

In contrast to a specific set of facts about infectious disease or therapy, AS is a process of optimizing outcomes associated with antimicrobial use for individual patients and, ultimately, society. The disease-state-based approach teaches students as if they are managing the patient from diagnosis to discharge, with responsibility for most aspects of patient care. While this does occur, it is more common for pharmacists to become involved in the care of the infected patient after an initial diagnosis and choice of empiric therapy have been made. Correspondingly, the model many ASPs use is one of prospective audit and feedback, reacting to initial prescribing decisions to optimize care instead of providing initial treatment recommendations. Teaching students to apply the principles of AS in the manner in which pharmacists typically perform it is essential and may require a rebalancing within pharmacy curricula from a focus on teaching pharmacotherapy based on guideline-recommended empiric therapies to one that also emphasizes pharmacotherapy optimization. It is this latter role to which pharmacists can frequently contribute, regardless of specialization or degree of training.



Figure 1. Antimicrobial Stewardship Knowledge Pyramid.

Recommendations for Integrating Antimicrobial Stewardship into Pharmacy School Curricula

Recognizing traditional approaches to teaching infectious disease (ID) pharmacotherapy does not emphasize the AS role of pharmacists. We recommend that faculty incorporate AS concepts into curricula throughout didactic and experiential training. Knowledge and skills related to AS are acquired over the entire arc of a pharmacist's career, progressing based on the training and specialization a pharmacist pursues. The Antimicrobial Stewardship Knowledge Pyramid describes a hierarchy of knowledge and skills for pharmacists at three levels of training/practice: the foundational learner – pharmacy student; the everyday steward – general practitioners or pharmacy specialists outside of infectious diseases (critical care, transplant, etc.) and PGY-1 everyday-stewards-in-training; and the stewardship leader specialist stewardship pharmacy practitioner and stewardship-leaders-in-training (PGY-2-IDs, fellows, or practitioners completing stewardship certificate programs) (Figure 1). Pharmacy schools should integrate the objectives for foundational learners into their curricula (Table 1). The majority of these objectives could be incorporated into one to two contact hours of pharmacotherapy or incorporated into sections of multiple ID pharmacotherapy lectures and reinforced across advanced pharmacy practice experiences (APPEs) to buttress the concept that all pharmacists are stewards of antimicrobial use. As noted above, having a strong ID pharmacotherapy curriculum and associated outcomes does not ensure students gain proficiency in the principles and process of AS. To help reconcile this potential gap, below we propose several practical suggestions for threading AS training into the curriculum.

Table 2 provides an example of how the foundational learner objectives can be mapped directly to each of the revised accreditation standards for the entrylevel Doctor of Pharmacy degree set forth by the Accreditation Council for Pharmacy Education (ACPE).¹⁶ The table also includes examples of potential learner activities and assessment tools. Incorporating AS in this manner has the advantage of providing opportunities to assess more difficult portions of the 2016 ACPE Accreditation Standards, specifically interprofessional collaboration (Standard 3.4) and personal and professional development (Standard 4 including selfawareness, leadership, innovation and entrepreneurship, and professionalism).

Table 1. Antimicrobial Stewardship Learning Objectives for Foundational Learners

- A. Integrate antimicrobial knowledge from the foundational sciences, eg, mechanism of action or spectrum of activity, to evaluate their potential value in individuals and populations.
- B. Recognize and efficiently collect relevant patient data, eg, infectious signs & symptoms.
- C. Formulate an appropriate assessment and plan for a specific patient.
- D. Delineate common stewardship strategies, eg, formulary restriction, prospective review and feedback.
- E. Describe the roles and responsibilities of various members of the interprofessional antimicrobial stewardship team.
- F. Communicate AS recommendations to patients and members of the interprofessional team in a variety of settings to promote health and wellness for individuals and communities.
- G. Educate patients and health care professionals on foundational antimicrobial stewardship concepts and empower them to practice as stewards.
- H. Identify opportunities for antimicrobial stewardship throughout the continuum of patient care, including hospital pharmacy, community pharmacy, transitions of care, and long-term care settings.
- I. Provide examples of successful, interprofessional antimicrobial stewardship models in various practice settings.
- J. Describe the importance of antimicrobial stewardship in improving public health.
- K. Identify the role of the pharmacist in empiric and definitive antimicrobial selection.
- L. Demonstrate confidence, flexibility, and self-awareness, particularly when providing antimicrobial stewardship recommendations.

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	Student		
	Learner		
ACPE Standard	Objective(s) ^b	Student Learner Activities	Assessments
Standard 1: Foundational	Knowledge		
I.I Foundational Knowledge	A	Evaluate patient alerts/cases (eg, bug-drug mismatch or multidrug-resistance alerts) and select which therapy(s) to cover the specific pathogen; ^c Bugs & Drugs Tournament, eg, Jeopardy. ^c	Alert review rubric Tournament Examination Preceptor evaluation
Standard 2: Essentials for	Practice and Ca	ire	
2.1 Patient-Centered Care	В, С	Develop a care plan for a specific patient; Review an ASP's daily activities, classifying the	Rubrics (for care plan, root cause analysis, etc.)
2.2 Medication Use Systems Management	D, H	type of initiatives, and providing feedback to improve efficiency and quality; Develop a root cause analysis to prevent	Examination Student reflection Preceptor evaluation
2.3 Health and Wellness 2.4 Population-Based Care	F, I	antimicrobial associated adverse event, eg, development of fatal <i>C. difficile</i> - associated diarrhea;	
	I, J	Counsel patients in a health fair on CDC's Get Smart About Antibiotics Campaign; Provide AS recommendations through various media, eg, in person, via phone, in documented notes;	
		Teach antimicrobial resistance as a public health threat.	
Standard 3: Approach to	Patient Care		
3.1 Problem-Solving	C, F	Simulate patient cases with an IPE team, eg,	Rubrics (for simulated cases,
3.2 Education		medicine, nursing, social work, physical	care plans, communications,
3.3 Patient Advocacy		therapy;	etc.)
3.4 Interprofessional	G	Develop a care plan for a specific patient;	Student reflection
3 5 Cultural Sensitivity	G	Provide AS recommendations through various media eg in person via phone in	Preceptor evaluation
3.6 Communication		documented notes;	
		Incorporate education into AS recommendations;	
	E, F, G, I	Counsel patients with beta-lactam allergies;	
	C, G	Counsel patients in a health fair on CDC's Get Smart About Antibiotics Campaign;	
	F, G, L	Present an in-service to educate other health care professionals on new AS initiatives.	
Standard 4: Personal and	Professional De	velopment	
4.1 Self-Awareness	K, L	Compose reflection regarding role of all	Rubrics (for interview
4.2 Leadership	F, G, H, K	pharmacists as stewards and novel ways to incorporate AS into various practice settings (expanding beyond hospital AS programs);	presentation, care plans, etc.) Student reflection
		Interview and present a local pharmacist's perspective on AS (including non-hospital pharmacists);	

Table 2. San	ple Curricula	ar Mapping for	Antimicrobial	Stewardship	Content in	the Pharmacy	^r Curriculum ^a

ACPE Standard	Student Learner Objective(s) ^b	Student Learner Activities	Assessments
4.3 Innovation and Entrepreneurship4.4 Professionalism	F, H, L F, G, K, L	Develop a care plan for a specific patient, focusing on the de-escalation efforts once a physician's plan is already in place (requiring more leadership and innovative communication); Participate in class forum to discuss creative ways to persuade prescribers to accept AS recommendations.	Preceptor evaluation

Table 2. (Continued)

Abbreviations: AS=antimicrobial stewardship; ASP=antimicrobial stewardship program; IPE=interprofessional education ^aMost content will fit into Pharmacotherapy coursework or APPEs; yet certain activities, eg, public health concepts, could be incorporated into other, earlier coursework

^bRefers to the pharmacy student learning objectives listed in the first tier of the Antimicrobial Stewardship Knowledge Pyramid (Figure 1) ^cActivity may overlap with ID Pharmacotherapy content in the existing curriculum

Incorporate stewardship concepts early in the curriculum

Efforts can be made to incorporate AS awareness into early coursework and to teach AS as a public health initiative. Taking this step supports the 2016 ACPE Accreditation Standards specifically related to health and wellness (Standard 2.3) and population-based care (Standard 2.4). Through the use of available public health resources, such as the CDC Get Smart About Antibiotics materials, pharmacy faculty can introduce students to the importance of judicious antimicrobial use even prior to teaching detailed information regarding drug therapy.¹⁷ In schools with foundational curricula, opportunities for integration may be identified in first- and second-year courses related to microbiology, immunology, pathophysiology, pharmacokinetics, patient care laboratories and social and administrative sciences. In schools with integrated block curricula, these discrete courses may not exist, but opportunities for discussing AS concepts within infectious disease-related modules can still be identified. Additional opportunities to discuss AS concepts also exist within coursework regarding health care utilization, pharmacy practice, and other introductory courses.

Teach and assess student knowledge of pertinent AS terminology

We recommend ID pharmacotherapy instructors teach AS terminology in ways similar to those used to teach other introductory ID pharmacotherapy principles such as laboratory tests and spectra of antimicrobial coverage. At a minimum, all students should be able to define the terms antimicrobial stewardship, empiric therapy, de-escalation, and definitive therapy. Threading terminology consistently throughout diseasestate discussions will prepare students for language they should use in practice. Formal assessment of student competency in antimicrobial stewardship terminology is encouraged.

Incorporate "antimicrobial stewardship plan" and "antibiotic time-out" into case-based learning

Case-based learning is a frequently used modality in pharmacotherapy curricula. Infectious diseases cases in pharmacotherapy textbooks and those facilitated in the classroom typically follow a standard medical case format, and instructors expect that the student present a pharmacotherapy plan based upon analysis of the case. Often, this plan includes the selection of the correct empiric antimicrobial, dose, route, and duration of therapy with recommendations for monitoring for safety and efficacy. The plan expectation may not, however, include direct assessment of AS responsibilities of the pharmacist. We propose that revising the case-learning process to include a targeted "Antimicrobial Stewardship Plan" will foster student appreciation of the importance of antimicrobial re-evaluation beyond the initial plan. It is neither practical nor necessary for all ID pharmacotherapy cases to span timeframes of days to weeks to accomplish this. Instructors can encourage students to reflect on an antimicrobial stewardship plan for any case using antimicrobial agents, even if only developing hypothetical or "high-level" recommendations. Reflections can help the student connect with the importance of AS despite a lack of clinical practice experience. A primary goal is for the student to gain confidence in an approach founded on AS principles. A few examples of AS plans and reflection points are shown in Table 3.

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Example of Student's Antimicrobial Stewardship Plan/Reflection

Case study presents a patient with recurrent UTI (h/o ESBL+ E.coli UTI 3 months ago); student

and De-escalation plan	appropriately recommends empiric therapy with meropenem.
	Student's Antimicrobial Stewardship Plan: Look for urine culture & susceptibility results in 24-48 hours. If no evidence of ESBL producer, contact prescriber to switch to alternate targeted therapy. Oral agent if possible to facilitate discharge, with total of 10 days of therapy (pending organism).
	Student Reflection: It is important to consider past clinical history and patient risk factors when selecting empiric treatment. In order to use antimicrobials according to the principles of antimicrobial stewardship, it is important to follow the patient's test results to change from empiric to targeted therapy. I can advocate for this patient by contacting the prescriber in a timely fashion based on test results, and communicating my recommendations for therapy change.
Antibiotic Time Out at 48 hours (Inpatients)	 Antibiotic Time Out Review: Day 2 of ceftriaxone/azithromycin for r/o pneumonia. Procalcitonin normal, BNP elevated but trending downward. WBC normal, patient improved with diuretics. Student's Antimicrobial Stewardship Plan: Contact MD to suggest DC antimicrobials.
	 Antibiotic Time Out Review: Day 2 of piperacillin/tazobactam, ciprofloxacin, vancomycin for HCAP. Sputum culture results = <i>S.pneumoniae</i>, susceptible to ceftriaxone. Pt afebrile, WBC trending downward, O₂ requirements decreasing. Student's Antimicrobial Stewardship Plan: Contact MD to change to ceftriaxone monotherapy.
	Student Reflection: The first case reminds me that antibiotics are not benign medications, and I should evaluate whether a patient's symptoms could be due to a non-infectious cause (like heart failure) when doing the antibiotic time out. It is my job to discuss any concerns I have with a patient's antibiotic therapy with the prescriber. Discontinuing antibiotics when they are not needed saves the patient from unnecessary costs, and potentially from a superinfection like <i>C. difficile.</i> The second case reinforces my commitment to contact prescribers when I identify an opportunity to change from empiric to targeted therapy. Allowing unnecessary antibiotics to be given even a day longer might place my patient at increased risk for related toxicities.
Outpatient Pharmacy	Young, otherwise healthy female patient presents to community pharmacy with prescription from urgent care for azithromycin for "bronchitis" she has had for 2 days.
	Antimicrobial Stewardship Plan: Ask if a CXR was performed at urgent care. If CXR clear or not assessed, call urgent care MD to discuss likely viral etiology and encourage delaying antimicrobial therapy. MD discussion may include discussion of risks of azithromycin toxicity, <i>C. difficile</i> superinfection, and drug-drug interactions. Teach patient about importance of using antibiotics only when needed for bacterial infections. Recommend appropriate symptomatic over-the-counter therapies. Screen for/recommend/administer influenza and pneumococcal vaccines as appropriate.
	Student Reflection: Outpatient pharmacies are often very busy, and patients are in a hurry to get their medication. Asking a few simple questions can take less than a minute, and the pharmacist might be able to assess that an antibiotic isn't needed. We need to be committed to educating patients and providers when we see antibiotic prescriptions that may not be needed. When I am a pharmacist working in the retail setting, I want to use CDC Get Smart handouts to educate my patients that taking an antibiotic doesn't help if the infection is due to a virus.

Table 3. Antimicrobial Stewardship Plan/Reflection Examples

Empiric Therapy Selection

Abbreviations: UTI=urinary tract infection, ESBL=extended-spectrum beta-lactamase, WBC=white blood cell count, DC=discontinue, HCAP=health care-associated pneumonia, CXR=chest X-ray, CDC=Centers for Disease Control and Prevention

vaccination status.

There is a lot I can do for my patients even when they don't receive antibiotics, including educating them on their condition, recommending symptomatic treatments, and assessing

CMS has recently included antimicrobial review at 48 hours for all patients on antimicrobials ("Antibiotic Time-Out") as an element (1.C.12) of its survey of hospital infection control.¹⁸ Many hospital pharmacists play a role in this required review. This review may become even more important to the outpatient pharmacist as it becomes increasingly recognized that prolonged durations of antibiotic courses beyond symptom resolution may be unnecessary.¹⁹ Therefore, it would be helpful to train pharmacy students to evaluate a patient at hour 48 of inpatient antimicrobial therapy or some similar time point. During this "time-out," clinicians evaluate the need for antimicrobials, the choice of agents, their planned duration, and possible scenarios for transitions of care. This would prepare students for APPEs and ultimately practice. Within the pharmacotherapy classroom setting, instructors can modify inpatient-based cases to include longitudinal scenarios, eg, recommendations for 48-hour antimicrobial time-outs or 72-hour culture follow-ups.

Provide learning experiences to understand AS from a broad systems perspective

Education in AS should stress that AS should be performed in all care settings and by all pharmacists who care for patients with infections. Learning experiences within ID pharmacotherapy should offer the student the opportunity to practice application of stewardship principles in various types of pharmacy settings. Although most experience with AS is from the inpatient setting, stewardship programs are being developed across ambulatory, long-term care, and many other care settings, with guidance from new CDC Core Elements for stewardship in outpatient and nursing home settings.^{20,21} Pharmacists in community and ambulatory care settings can evaluate the efficacy and safety of antimicrobials through patient interviews even when access to objective data is suboptimal and contact prescribers in the same manner as they do for other patient safety issues. Pharmacists in long-term care settings can advocate to escalate care when poor response is noted, intervene to modify suboptimal treatment choices, and monitor patients for response, including ordering labs if appropriate. By comparing and contrasting the feasibility and effectiveness of different stewardship strategies in various settings, learners can gain a better understanding of the importance of tailoring stewardship strategies appropriate to the system of interest.

Promote interprofessional AS education

Given the team approach that guidelines for ASPs recommend,^{6,7,9} antimicrobial stewardship is an ideal area for interprofessional education (IPE). Practitioners from multiple professions converge in the care of these

patients and contribute unique points of view. As an example case, a physician chooses an initial empiric choice of intravenous therapy after draining a severe skin infection; a nurse assesses the patient for signs of improvement; a laboratory technician interprets the results of a Gram stain of the drainage; a pharmacist changes therapy based upon the Gram stain, culture results, or laboratory values; and the physician and pharmacist converge to decide on a course of definitive therapy as the patient prepares to transition to an outpatient care environment. Modeling this case in a didactic curriculum gives students of these disciplines the chance to interact in a clinical setting that mimics a professional environment without any roles that are contrived for the sake of creating an IPE experience. Studies have shown such experiences can improve student attitudes toward IP collaboration and self-efficacy in promoting appropriate antimicrobial use.²²

CONCLUSION

The rise of antimicrobial resistance has the potential to reverse many gains achieved by modern medicine in the last century. Pharmacists specialized in infectious diseases have been at the forefront of efforts to provide effective stewardship of antimicrobials. Based on the scale of the problem and the broad mandates for stewardship being implemented, every pharmacist in the next generation will need to demonstrate some ability to serve as an antimicrobial steward. We believe this is well within the scope and capacity of pharmacy school education. What is required is a modest shift of focus in the content already being taught as well as incorporation of stewardship concepts into initiatives already being prioritized for pharmacy schools, such as early experiential learning and IPE.

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