

The Role of Antimicrobial Stewardship in the Clinical Microbiology Laboratory: Stepping Up to the Plate

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We report the development of a collaborative relationship between antimicrobial stewardship and clinical microbiology that incorporates stewardship practices into daily laboratory rounds. Antimicrobial stewardship involvement on rounds was a welcomed and effective initiative with substantial rates of intervention. New opportunities to positively impact use of antimicrobials and laboratory resources were realized.

Keywords. antibiotic stewardship; collaboration; microbiology.

Inappropriate use of antimicrobials is directly linked to the emergence of multidrug-resistant (MDR) pathogens, adverse effects, and superinfections such as *Clostridium difficile*-associated diarrhea [1]. A concerted effort to promote appropriate selection and use of antibiotics, which in turn should reduce adverse effects and may improve patient outcomes, is the goal of antimicrobial stewardship programs (ASPs) [2].

Antimicrobial stewardship program activities have traditionally been carried out almost exclusively by a pharmacist with oversight from an infectious diseases physician. However, the last decade has seen a dramatic increase in rapid diagnostic microbiology technologies, offering opportunities for ASP interaction with the clinical microbiology laboratory (CML) [3]. There is good evidence that the greatest impact of rapid diagnostic tests occur when implemented in combination with ASP intervention to facilitate timely action and response to the test results [3, 4].

At many academic medical centers (AMCs), microbiology “plate” rounds are an environment for teaching and clinical correlation, providing an opportunity to understand CML

procedures and view culture and organism morphology [5]. Interdisciplinary discussion is encouraged to share information about current cases and acknowledge the expertise and perspective of the attendees, thus improving patient care. Attendees of plate rounds may include clinical microbiologists and trainees of various disciplines (medicine, pharmacy, pathology) and training levels (student, resident, fellow). Historically, ASP members have not been participants, and stewardship activities have not been a major objective of these microbiology plate rounds. In this study, we describe our experience with the addition of an ASP pharmacist to microbiology plate rounds at an AMC, and we describe the stewardship activities occurring during a typical month.

METHODS

At the Medical University of South Carolina, a 725-bed AMC in the Southeastern United States, an ASP was established in 2009. The early focus of the program was on reducing antibiotic use and expenditures through targeted interventions based on auditing of high-cost, broad-spectrum antimicrobials. As the program matured, efforts shifted towards culture- and syndromic-based activities such as patients with positive blood cultures and those infected with MDR organisms. To translate these activities into clinical impact, the ASP pharmacist began attending daily microbiology plate rounds in 2012 to conduct prospective monitoring of critical cultures and to gain a better understanding of the CML workflow and data management. The rationale for the addition of an ASP pharmacist to plate rounds was to provide additional opportunities to promote rational antimicrobial use by optimizing treatment of infected patients while simultaneously reducing unnecessary microbiology workup of poor quality or inappropriately collected specimens, which may in turn enhance patient safety and reduce laboratory and pharmacy expenses.

The stewardship pharmacist attended daily (Monday–Friday) plate rounds, which typically lasted from 30 to 60 minutes. Plate rounds were tailored to the active patient cases and emphasized the CML’s role in diagnosis. During plate rounds, the team reviewed relevant cultures at each workbench, which were organized according to specimen type (eg, blood, urine, respiratory, exudate). Cultures to be reviewed and discussed on plate rounds could be selected from any member on the team. The rounds are a multidiscipline collaborative approach where the input of all parties is valued; however, it was ultimately up to the discretion of the CML director or her designee what workup should be done in each case, after discussion and review with the team members on plate rounds. The actual number of cases

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reviewed during plate rounds was not recorded. However, approximately 10–20 cultures are reviewed during a typical plate rounds session, depending on the requests of the team members and the complexity of cultures being worked up that day.

Stewardship interventions performed by the pharmacist during plate rounds were tracked throughout November 2015. For the purpose of this study, interventions were defined as any action performed by the pharmacist during plate rounds that aided in the workup and/or reporting of cultures. An intervention was considered to be accepted if (1) the request by the pharmacist resulted in a change to the workup and/or reporting of the culture, or (2) the pharmacist provided useful information that resulted in a change to the workup and/or reporting of the culture, or (3) information learned by the pharmacist resulted in a change in patient management. Interventions were considered not accepted if the information or request from the pharmacist did not result in any of these 3 changes.

Interventions were collected into 9 categories (Table 1). Clinical liaison services included providing pertinent clinical information to aid CML staff in appropriate culture workup and/or susceptibility testing. Because CML staff do not have time to investigate every complex and/or polymicrobial culture in the electronic health record, the additional information provided by the pharmacist on the circumstances (anatomical location, clinical relevance, hospital setting [bedside versus operating room]) under which the specimen was collected was invaluable.

Table 1. Intervention Type and Outcome from Interdisciplinary Microbiology Plate Rounds

Intervention Type*	N (%)
Antibiotic allergy	3 (3.5)
Bug-drug mismatch	2 (2.4)
Clarification of specimen ordering/handling	1 (1.2)
Clinical liaison services	36 (42.4)
Infection vs colonization	4 (4.7)
MDR organism	19 (22.3)
Mixed cultures	5 (5.9)
Rapid diagnostics	5 (5.9)
Reporting	15 (17.6)
Intervention Outcome	N (%)
Avoid inappropriate antimicrobial de-escalation	1 (1.2)
Avoid inappropriate antimicrobial escalation	3 (3.5)
Avoid treatment of colonization	1 (1.2)
Avoid unnecessary microbiology workup	12 (14.1)
Clarify culture reporting	15 (17.6)
Clarify microbiology workup	19 (22.4)
De-escalated spectrum of activity	8 (9.4)
Ensure appropriate therapy for MDR organism	6 (7.1)
Initiate therapy	1 (1.2)
No change	7 (8.2)
Optimize therapy	11 (12.9)
Reduced duration of therapy	1 (1.2)

Abbreviations: MDR, multidrug resistant.

*Individual interventions could qualify for multiple types of intervention.

Management of MDR organisms involved the review and optimization of antibiotic selection, culture reporting, and need for additional testing of salvage antimicrobials (eg, ceftaroline, fosfomycin, polymyxins, tigecycline). Clarification of reporting included releasing of hidden/restricted antimicrobials (eg, daptomycin, ertapenem).

RESULTS

A total of 85 interventions were made by the ASP pharmacist over the course of 19 plate rounds (mean 4.5 interventions/day). The majority of interventions were on blood (29%), urine (29%), and exudate cultures (27%). The most common intervention (Table 1) was liaison services between the CML staff and clinicians (42%). Management of MDR organisms (22%) and clarification of culture and antimicrobial susceptibility result reporting (18%) were also common. Interventions were accepted in 81 (95%) of 85 cases. There were 4 cases of MDR urinary tract infections in which the intervention made by the pharmacist did not result in any modification to the culture or management of the patient. A change of antimicrobial therapy was made in 33% of patients (19% de-escalation and 14% escalation of antimicrobial therapy). The most frequent outcomes of these interventions (Table 1) were broadly classified as follows: clarification of culture workup/reporting (40%) to reduce time to clinically actionable results, optimization of antimicrobial therapy (31%), and avoidance of unnecessary culture workup (14%). Table 2 shows examples of common stewardship interventions during these interdisciplinary plate rounds that have positively affected patient care and led to decreased costs for both microbiology and the pharmacy.

DISCUSSION

Confronting the growing antibiotic resistance crisis will require a determined multidisciplinary effort across the entire health-care spectrum [6]. We found the addition of an ASP pharmacist on microbiology plate rounds to be a valuable tactic. Working closely with the CML, the stewardship pharmacist was able to enhance patient care by recommending optimal selection of antimicrobial therapy to providers based on patient-centric culture results. Although it is likely that in many cases the managing healthcare team would have eventually consulted with the CML director for additional information (eg, alternative testing for antibiotic allergy or reporting antimicrobial susceptibility data for hidden/restricted agents), the presence of a pharmacist on plate rounds allowed for a real-time discussion and ensured interventions were made in a timely manner as soon as the information was available to avoid delays in selecting the most appropriate therapy. In fact, there is strong evidence that merely reporting a microbiology test result infrequently leads to actionable events without an active messenger [3]. In addition, the presence of a stewardship pharmacist on microbiology plate rounds helped to facilitate engagement in antimicrobial

Table 2. Examples of Common ASP Interventions Resulting From Interdisciplinary Microbiology Plate Rounds and Their Potential Clinical Impact

Category	Intervention or Examples	Potential Clinical Impact
Antibiotic allergy	<ul style="list-style-type: none"> • Identification of penicillin allergic patients prompts earlier <i>in vitro</i> susceptibility testing of alternative agents 	<ul style="list-style-type: none"> • Faster <i>in vitro</i> susceptibility data • Avoid delay in time to appropriate therapy
Antimicrobial resistance markers	<ul style="list-style-type: none"> • Methicillin-resistant vs methicillin sensitive <i>Staphylococcus aureus</i> (PCR, PBP_{2a} chromogenic agar) • Vancomycin-resistance in <i>Enterococcus</i> spp (PCR) • KPC-producing organisms (in facilities where these are uncommon) 	<ul style="list-style-type: none"> • Shorter time to effective and/or optimal therapy • Cost savings (supplement to anti-MRSA pneumonia therapy duration of treatment limits)
Bug-drug mismatch from emergency department or outpatient clinics	<ul style="list-style-type: none"> • Alert provider to untreated pathogens (yeast, <i>S aureus</i>, GNR) from critical sterile sites (blood, CSF, etc) • Alert provider to discordant result • Suggest alternative agents 	<ul style="list-style-type: none"> • Decrease time to appropriate therapy • Prevent unnecessary hospitalization • Avoid IV/IM administration or PICC insertion (eg, fosfomycin for MDR cystitis)
Clarification of improper specimen/culture ordering	<ul style="list-style-type: none"> • Endotracheal specimen ordered as a BAL or vice versa • Abdominal abscess ordered as abdominal fluid • CF culture in non-CF patient 	<ul style="list-style-type: none"> • Decrease unnecessary/excessive microbiology workup
Clinical liaison services	<ul style="list-style-type: none"> • Reporting organism in mixed urine culture of patients with bacteremic urosepsis • Review prior patient history, cultures from OSH 	<ul style="list-style-type: none"> • Established source of bacteremia allows for conversion to oral therapy in some situations • Modification of therapy and/or microbiologic workup based on previous culture and susceptibility results
Infection vs colonization	<ul style="list-style-type: none"> • Assist with assessment of clinical presentation and clinical correlation for lower respiratory cultures and urine cultures, etc 	<ul style="list-style-type: none"> • Avoid unnecessary antimicrobial utilization • Decrease unnecessary/excessive microbiology workup
MDR organisms	<ul style="list-style-type: none"> • Earlier <i>in vitro</i> susceptibility testing of alternative/salvage antimicrobials (tigecycline, polymyxins) • Earlier involvement of infectious diseases consultant 	<ul style="list-style-type: none"> • Decrease delay in time to appropriate therapy • Improve patient outcomes
Mixed cultures	<ul style="list-style-type: none"> • Predominance vs polymicrobial • Liaison service between provider and microbiologists to determine extent of work up of mixed cultures in a more timely fashion • Requirements for <i>in vitro</i> susceptibility testing for all isolates vs selective isolates 	<ul style="list-style-type: none"> • May prevent unnecessary escalation of antibiotic treatment and may decrease time to appropriate therapy • Avoid unnecessary/excessive microbiology workup • Streamlining of antimicrobial regimen for polymicrobial infection
Optimal dose selection	<ul style="list-style-type: none"> • Actual MIC for a given antimicrobial agent 	<ul style="list-style-type: none"> • Optimize the therapeutic regimen based on pharmacokinetic and pharmacodynamic principles
Rapid diagnostics (PCR, MALDI-TOF)*	<ul style="list-style-type: none"> • Create clinical pathways to increase utilization of results 	<ul style="list-style-type: none"> • Shorter time to effective and/or optimal therapy • Decrease broad-spectrum antimicrobial utilization
Reporting*	<ul style="list-style-type: none"> • Avoid inappropriate/suboptimal <i>in vitro</i> susceptibility results for site specific cultures (early-generation cephalosporins for inducible AmpC beta-lactamase-producing Gram-negative bacilli in blood cultures) 	<ul style="list-style-type: none"> • Decrease inappropriate prescribing, therapeutic failures, and metastatic infections • Increase appropriate antimicrobial selection

Abbreviations: ASP, antimicrobial stewardship program; BAL, bronchoalveolar lavage; CF, cystic fibrosis; CSF, cerebrospinal fluid; GNR, Gram-negative rod; IDSA, Infectious Diseases Society of America; IM, intramuscular; IV, intravenous; KPC, *Klebsiella pneumoniae* carbapenemases; MALDI-TOF, matrix-assisted laser desorption ionization time-of-flight; MDR, multidrug resistant; MIC, minimum inhibitory concentration; MRSA, methicillin-resistant *Staphylococcus aureus*; OSH, outside hospital; PBP_{2a}, penicillin binding protein 2A; PCR, polymerase chain reaction; PICC, peripherally inserted central venous catheter.

*IDSA/SHEA Stewardship Guideline recommended.

stewardship initiatives and enabled CML staff and trainees of pathology, pharmacy, and medicine to appreciate the importance of rational antibiotic use as healthcare professionals, discouraging the workup of poor quality or inappropriately collected specimens, while also modeling interprofessional teamwork. This is important because education regarding antimicrobial stewardship receives minimal attention in the didactic curriculum of most pathology, pharmacy, and medicine programs.

The CML already plays an essential role in enhancing many ASP activities by ensuring timely and accurate identification of microbial pathogens and antimicrobial susceptibility testing as well as the development of antibiograms. In addition, most laboratories provide guidelines for appropriate specimen collection, impose strict rejection criteria for inappropriately submitted specimens, and have procedures for limiting the workup

of contaminants and cultures with mixed flora, all of which may contribute to ASP goals of limiting inappropriate antimicrobial use [7]. As technological innovations continue to emerge, new rapid diagnostic methods will only increase the need for stewardship tactics to ensure maximal benefits are achieved, as well as to keep healthcare costs under control by helping to minimize unnecessary testing. Evidence of ASP involvement in the CML outside of rapid diagnostic tests is sparse, and it represents an unrecognized and underused environment for development of stewardship initiatives and collaboration. Much like organisms evolve, it is imperative that ASP search for new and meaningful approaches to improve antibiotic use.

Not unlike antimicrobial use, unnecessary and clinical questionable laboratory testing contributes to the rapid growth of healthcare costs and may harm patients by exposing them to avoidable medical interventions, such as antibiotics [8]. Medical

tests have been overused for many years, leading to the launch of the Choosing Wisely campaign by the American Board of Internal Medicine foundation in 2012, which is focused on the avoidance of wasteful or unnecessary medical tests, treatments, and procedures [9, 10]. The American Society for Clinical Pathology participates in the campaign with “right test, right patient, right time, at the right cost.” The Infectious Diseases Society of America participates in the campaign, encouraging clinicians to avoid prescribing antibiotics for conditions that do not warrant treatment (asymptomatic bacteriuria, upper respiratory tract infections, and stasis dermatitis of the lower extremities) as well as avoiding testing for conditions without symptoms, such as presence of *C difficile* in the absence of diarrhea [11]. The presence of an ASP team member on microbiology plate rounds offers an additional means of supporting the goals of Choosing Wisely. In our institution, for example, we were able to improve the communication between the laboratory and clinicians, particularly as it relates to a value versus cost discussion (eg, Does the additional cost of the microbiology laboratory to workup all organisms in a polymicrobial culture provide additional value to the clinician?), avoiding the need for additional organism identification and testing in some instances (Table 1).

This study is not without limitations. Due to the technological advancement (eg, matrix-assisted laser desorption ionization time-of-flight and multiplex polymerase chain reaction blood culture identification platforms) and changes in our microbiology department since 2012 (the last time a pharmacist did not attend plate rounds), a preintervention period for comparison was not used. There would have been inherent imbalances between groups due to the different type of cultures and interventions reviewed and made at plate rounds during each time period. The lack of a comparison group is a limitation that prevents us from making definitive claims on the effectiveness of the pharmacist intervention. However, we believe the descriptive nature of this study still provides preliminary evidence on the usefulness of having an ASP member attend microbiology plate rounds. It is also worth mentioning that this study describes microbiology plate rounds during 1 month (November 2015) and may not have captured any changes/trends in the numbers/types of interventions and outcomes over time since 2012. However, although the number of trainees on plate rounds does vary from month to month, the composition and attendance of core active members (a clinical

microbiologist, laboratory technical staff, and an ASP pharmacist) of microbiology plate rounds remained the same throughout this time period.

CONCLUSIONS

In conclusion, antimicrobial stewardship involvement on microbiology plate rounds was a welcomed initiative with a high rate of accepted recommendations both by laboratorians and by clinicians. Stewardship interventions were diverse and offered new opportunities that positively impacted utilization of antimicrobials and laboratory resources. In addition, antimicrobial stewardship members became familiar with microbiology procedures and practices. Although the concept of microbiology plate rounds is not revolutionary, there is a dearth of literature describing the value of ASP involvement, a potentially absent component of many ASPs. We encourage others to consider ASP activities in the CML, through microbiology plate rounds or other avenues.

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