Bangladesh J Med Microbiol 2019; 13 (2): 25-29
Bangladesh Society of Medical Microbiologists

Review Article

Antimicrobial Stewardship: Laboratory to Clinical Microbiology: A Road Map

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Summary

Antimicrobial stewardship refers to a set of coordinated strategies to improve the use of antimicrobial medications with the goal of enhancing patient health outcomes, reducing resistance to antibiotics and decreasing unnecessary costs.

While clinical microbiologists with clinical pharmacists are considered the main leaders of antimicrobial stewardship programs, clinical microbiologists can play a key role in these programs.

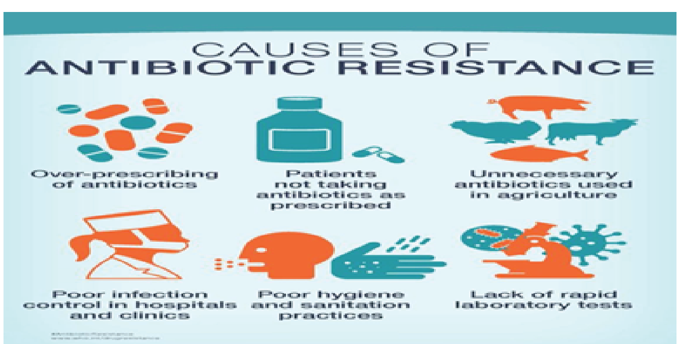
This review is intended to provide a comprehensive discussion of the different components of antimicrobial stewardship in which microbiology laboratories and clinical microbiologists can make significant contributions, including cumulative antimicrobial susceptibility reports, enhanced culture, and guidance in the pre analytic phase, rapid diagnostic test availability, provider education, and alert and surveillance systems.

Key words: antimicrobials, antimicrobial stewardship, clinical microbiologist, optimal use, role, rapid tests.

Introduction

Antimicrobial stewardship is a key instrument to facilitate the appropriate use of antimicrobials and therefore to minimize the emergence of multidrug-resistant (MDR) pathogens, adverse effects and superinfections such as *Clostridium difficile*-associated diarrhea.[1]

The emergence of antimicrobial resistance are due to lack of a microbiologically confirmed diagnosis, laboratory test errors, failure to submit appropriate specimens for culture, misuse of microbiology resources and a general overreliance on empirical antimicrobial therapy with attendant disregard of microbiological results.[2]



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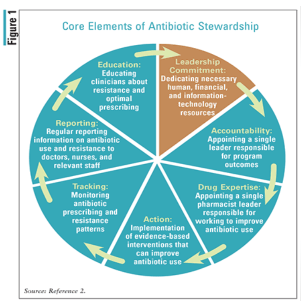
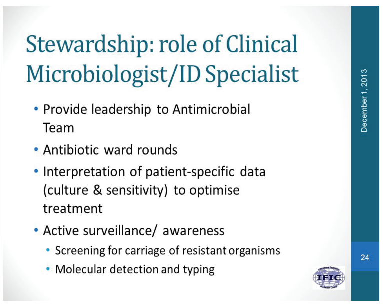
A concerted effort to promote appropriate selection and use of antibiotics, which in turn should reduce adverse effects and may improve patient outcomes, is the goal of antimicrobial stewardship programs (ASPs).[3]

Several organizations, including the Infectious Disease Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), and the American Society of Health System Pharmacists (ASHP), have identified antimicrobial stewardship as having an important role in today's health care environment.[4]

The optimum hospital-based antimicrobial stewardship program consists of an oversight group of three individuals: a clinical pharmacologist with a Pharm.D. degree plus 2 years of fellowship training in infectious diseases, preferably obtained in a training program approved by the American College of Clinical Pharmacy; a board-certified infectious disease physician; and a board-certified doctorate-level director of the clinical microbiology laboratory. Preferably, all of these individuals should be full-time employees of the institution in which the stewardship program resides. It is expected that the infectious disease physician and clinical microbiology laboratory director would devote a portion of their effort to the program.

Antimicrobial Stewardship Program Structure





Antimicrobial stewardship programs have been shown to be beneficial in numerous health care settings, from small community health care centers to nursing homes and academic urban hospitals.[5]

Infectious disease diagnostic testing needs to fulfill a variety of different roles in clinical practice and research. including:

- ***Identifying pathogens*** to guide selection of antimicrobial agents, de-escalation from broad spectrum to narrow-spectrum agents, and/or discontinuation of antimicrobial treatment
- ***Identifying resistance genes or markers*** that may predict antibiotic treatment failure
- ***Determining virulence factors*** that modify the expression of resistance to antimicrobial agents in vivo
- ***Identifying antimicrobial susceptibility*** to available antibiotic agents (inhibition of in vitro pathogen growth) to help predict which antimicrobial agents are likely to effectively treat the infection
- ***Measuring biomarkers*** as indicators of host response to infection or high-risk conditions.
- ***Distinguishing viral from bacterial causes of infection*** to avoid or discontinue antibiotics for nonbacterial (viral, fungal, or parasitic) infections
- ***Providing point-of-care testing***, eg, at the patient's bedside or in outpatient clinics, in addition to traditional skilled laboratory-based services
- ***Supporting clinical trials*** to improve the efficiency of studies evaluating new antibiotics.[6]

Being able to make the right diagnosis is usually a prerequisite to providing effective therapy. Recommendations for drug choice, dosing, or duration may be useless if the diagnosis is wrong. Filice et al. assessed the accuracy of diagnosis and appropriateness of therapy from the medical records of 500 randomly selected hospitalized patients who received antimicrobials. While prescribed antimicrobials were appropriate in the majority (62%) of the cases when the diagnosis was considered accurate on the basis of clinical, radiologic, and laboratory findings, anti-infective appropriateness was abysmal (5%) when the diagnosis was incorrect.[7]

The timely availability of accurate and clinically significant microbiology results is critical for optimal antibiotic use and related clinical outcomes.[8] For example, a positive blood culture Gram stain read as Gram-negative bacilli but later identified as Listeria monocytogenes could significantly delay the provision of effective therapy, leading to an adverse outcome, even death.[9] While microbiology laboratories can provide selective reporting and interpretation of results to promote the judicious use of antimicrobials.

The delayed results of traditional bacterial cultures and antimicrobial susceptibility testing, which may take up to several days to obtain, remain one of the major barriers to providing optimal therapy.[10] This is especially important for severe infections such as sepsis and septic shock, for which a delay in initiating effective therapy is a strong predictor of death.[11] Emerging of Rapid Diagnostic Testing (RDT) methods include a large variety of technologies and vary greatly in terms of complexity, price, speed, and the ability to identify single or multiple pathogens.

The key to successful RDT is the twinning of these technologies to an antimicrobial stewardship team that can notify clinicians about test results and guide their use in initiating or modifying antimicrobial therapy, for without this link between clinical microbiologists and antimicrobial stewardship, the rapid results run the risk of floating adrift at sea.[12]

The CLSI first published guidelines for the analysis and presentation of cumulative susceptibility test data in 2002 and updated them most recently in 2018. They included 10 recommendations. The clinical microbiologist is in an excellent position to understand how these recommendations influence the utility of the reports and to contribute to antimicrobial stewardship programs on the basis of this expert knowledge.

One way microbiology laboratories can significantly impact diagnostic accuracy and the quality of antimicrobial prescribing is by providing guidance in the preanalytic phase, i.e., guidance for selecting the appropriate test or culture according to the patient's syndrome, obtaining optimal collection of clinical specimens, and interpreting microbiology test results. Because poorly collected specimens may result in the recovery of commensal or colonizing organisms and are often rejected[13], clinicians need instruction in the appropriate timing and technique of specimen collection.

While new antibiotics should be used with care and only when indicated, some clinicians might find their use urgent, especially when the new agents fill a void in the therapeutic arsenal. Microbiology laboratories stay abreast of new drug development and assess the laboratory's capacity to test the activity of new agents against appropriate pathogens. Information on clinical breakpoints, quality control, and other drug particularities may be limited when new drugs first come to market or when older drugs, e.g., polymyxins, reemerge as therapies of necessity. Thus, a laboratory that previously evaluated, experimented, or validated testing for a specific new drug may play a critical role in the process of approval by a pharmacy and therapeutics committee.

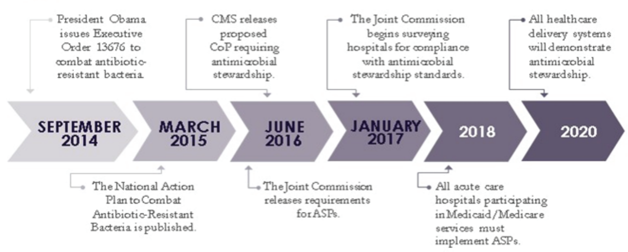
Table I: Objectives and characteristics of assignments and laboratory techniques performed by microbiology laboratories in Antimicrobial Stewardship program.[14]

Objectives and techniques performed by microbiology laboratories	Goals and specificities
Realization of classical microbiological and biochemical tests	Perform microbial identification tests and antimicrobial susceptibility testing by disk diffusion and classical biochemical tests.
Determination of serum procalcitonin	Stratify the risk for generalized infections and guiding systems for administration of antimicrobial agents in cases of sepsis
Methods of implementation for rapid diagnosis	Deploy Reaction Polymerase Chain tests (PCR) and Fluorescence In Situ Hybridization with Nucleic Acid (PNA-FISH) platforms for rapid microbial identification and accurate.
Determination of genotype group and phylogenetic analysis	Implement microbiological enrichment methods and genetic and chromosomal extraction for elucidation of microorganisms and antimicrobial resistance mechanisms.
Identification by Mass Spectrometry Ionisation with assisted laser desorption matrix and by time-of-flight (MALDI-TOF MS).	To implement this new technique which has high sensitivity for microbial identification.
Participation in the clinical guides and protocols and pharmacotherapeutic	Participate in the development and implementation of guidelines and clinical protocols for safe and rational use of antimicrobials

In many countries of the Commonwealth of Nations, clinical microbiologists assume many clinical functions outside the laboratory because many are also trained in ID. For example, clinical microbiologists were present in more than 90% of acute trust antimicrobial stewardship committees in England and Ireland, making microbiology the most represented specialty in recent surveys.[15]

In 2011, the Australian Commission on Safety and Quality in Healthcare promulgated multiple recommendations for antimicrobial stewardship programs, including some pertaining to the role of microbiology services.[16] The commission recommended that clinical microbiologists provide best practices for the rapid diagnosis of common infections.

Figure. National Timeline for Implementing Antimicrobial Stewardship Programs



ASPs, antimicrobial stewardship programs; CMS, Centers for Medicare & Medicaid Services; CoP, Conditions of participation

Another survey in Queensland found that clinical microbiologists were responsible for providing therapy advice and antimicrobial approval in nearly 40% of the institutions surveyed, though half of the facilities did not have access to in-house clinical microbiologists or ID specialists.[17]

In the province of Quebec (Canada), a survey of 68 hospitals in 2008 found that clinical microbiologists participated in 89% of antimicrobial stewardship surveillance programs.[18] In this province, as in some other countries, most microbiologists are also trained and certified as ID specialists.

In the United States, clinical microbiologists' training backgrounds can vary between academic (Ph.D.) and medical (M.D.) training. In the latter, most will follow a pathology track while some, more rarely, will additionally be trained in internal medicine and ID. However, many microbiology laboratories focus on processing specimens and providing quality results without engaging in antimicrobial stewardship programs, which are usually led by ID physicians and pharmacists.[19] Studies performed in California and Florida showed that microbiologists participated in antimicrobial stewardship activities in 26% and 42% of the hospitals surveyed, respectively.[20]

Conclusion

Clinical microbiologists' collaboration with antimicrobial stewardship teams and other clinicians can lead to benefits that are multidirectional. Clinical microbiologists are experts on a multitude of subjects related to antimicrobial stewardship, such as resistance mechanisms, pathogen interaction with the environment, diagnostic testing, and interpretation of susceptibility reports.[21] Their daily decisions as experts in laboratory diagnostics impact clinicians' interpretation of tests and influence patient care. However, the tasks and purposes of clinical microbiologists may not always be fully understood by clinicians.[22] Thus, we strongly encourage the participation of clinical microbiologists in designing and delivering antimicrobial stewardship-related teaching, which is ideally multimodal, including rounds and conferences but also staff bulletins and management guidelines.[23] To be maximally effective, the clinical microbiologist should visit the ward at least occasionally, in addition to providing educational sessions at physician and staff conferences.

Reference

1. Lepper MH. Microbial resistance to antibiotics. Ann Intern Med1955; 43:299-315.
2. Dellit TH, Owens RC, McGowan JE 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; 44:159-177.
3. Centers for Disease Control and Prevention. 2014. Core elements of hospital antibiotic stewardship programs. Centers for Disease Control and Prevention, Atlanta, GA. http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html.
4. Joint Commission on Hospital Accreditation. Approved: new antimicrobial stewardship standard. Jt Comm Perspect 2016;36: 3-4.
5. Davey P, Brown E, Charani E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev 2013;4: CD003543.
6. Welcome trust. 2016. Four diagnostic strategies for better-targeted antibiotic use. https://wellcome.ac.uk>default>files.
7. Filice GA, Drekonja DM, Thurn JR, et al. Diagnostic errors that lead to inappropriate antimicrobial use. Infect Control Hosp Epidemiol 2015;36: 949-956.
8. Dellit TH, Owens RC, McGowan JE, 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: 159-177.
9. Weinstein MP. Positive blood cultures. Clin Adv Hematol Oncol 2010;8:850-851.
10. Tenover F, Hindler J. Reporting of the results, p 89-99. In Courvalin P, Leclerq R, Rice LB. (ed), Antibiogram. 2010 ASM Press, Washington, DC
11. Kumar A, Roberts D, Wood KE et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med 2006;34: 1589-1596
12. Bauer KA, Perez KK, Forrest GN, et al. Review of rapid diagnostic tests used by antimicrobial stewardship programs. Clin Infect Dis 2014;59 (Suppl 3): S134-S145.
13. Johns Hopkins Medicine. 2015. Johns Hopkins medical microbiology specimen collection guidelines-updated 6/2016. Johns Hopkins Medicine, Baltimore, MD: http://www.hopkinsmedicine.org/microbiology/specimen/Specimen Collection Guidelines 20
14. Silva AL, Almeida DLM, Monteiro EM, et al. Insight on antimicrobial stewardship in the microbiology laboratory: a review. J Microbiol Exp 2019;7(1): 35-39.
15. Ashiru-Oredope D, Sharland M, Charani E, et al. ARHAI Antimicrobial Stewardship Group.Improving the quality of antibiotic prescribing in the NHS by developing a new antimicrobial stewardship programme: start smart-then focus. J Antimicrob Chemother 2012;67 (Suppl 1): i51-i63.
16. Australian Commission on Safety and Quality in Health Care. 2011. Antimicrobial stewardship in Australian hospitals, January 2011 ed. Australian Commission on Safety and Quality in Health Care, Sydney, NSW, Australia: https://www.safetyandquality.gov.au/our-work/healthcare-associated-infection/antimicrobial-stewardship/book
17. Avent ML, Hall L, Davis L, et al. Antimicrobial stewardship activities: a survey of Queensland hospitals. Aust Health Rev 2014;38:557-563.
18. Nault V, Beaudoin M, Thirion D, et al. Antimicrobial stewardship in acute care centres: a survey of 68 hospitals in Quebec. Can J Infect Dis Med Microbiol 2008;19:237-242.

19. Trivedi KK, Dumartin C, Gilchrist M, et al. Identifying best practices across three countries: hospital antimicrobial stewardship in the United Kingdom, France, and the United States. Clin Infect Dis 2014;59 (Suppl 3): S170-S178.

20. Trivedi KK, Rosenberg J. The state of antimicrobial stewardship programs in California. Infect Control Hosp Epidemiol 2013;34:379-384.

21. American College of Microbiology. 2008. Clinical microbiology in the 21st century: keeping the pace. American Society for Microbiology, Washington, DC: http://www.asm.org/ccLibraryFiles/FILENAME/000000004806/Clinical Microbiology in the 21st Century.

22. Ohl CA, Luther VP. Health care provider education as a tool to enhance antibiotic stewardship practices. Infect Dis Clin North Am 2014;28:177-193

23. Mack MR, Rohde JM, Jacobsen D, et al. Engaging hospitalists in antimicrobial stewardship: lessons from a multihospital collaborative. J hospital medicine 2016;11:576-580