The Role of the Microbiology Laboratory in Antimicrobial Stewardship Programs

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KEYWORDS

• Antimicrobial stewardship • Microbiology laboratory • Rapid diagnostics
• Antibiogram • Procalcitonin

KEY POINTS

- Rapid diagnostic technologies can decrease the time to identification of microrganisms and resistance genes, potentially leading to reduced time to optimal therapy and improved clinical outcomes. The benefits of rapid diagnostic techniques are enhanced when coupled with antimicrobial stewardship interventions.
- Procalcitonin-guided therapy can reduce antimicrobial consumption by decreasing the initiation of antimicrobial therapy and decreasing the duration of therapy.
- Clinical microbiology laboratories should work closely with antimicrobial stewardship programs to compile institution-specific antibiograms. Antibiograms are frequently used by stewardship programs to make formulary decisions, develop guidelines for empiric therapy, and monitor local resistance rates over time.

INTRODUCTION

The major goals of antimicrobial stewardship programs (ASPs) are to optimize antimicrobial dosing, duration, and route of administration for each patient while minimizing adverse drug events and the emergence of antimicrobial resistance.[1,2] The clinical microbiology laboratory plays an essential role in these stewardship activities. Microbiology laboratories perform timely identification of microbial pathogens and antimicrobial susceptibility testing, and ensure proper attention to the preanalytical components of testing, which are often unrecognized tasks that can impact quality results. For example, most laboratories provide guidelines for appropriate specimen

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collection, enforce rejection criteria for specimens inappropriately submitted, and have established procedures for limiting the work-up of contaminants (eg, blood cultures), all of which could impact antimicrobial use.[3] The preanalytical component of testing is not discussed in detail in this article and additional information can be found in the comprehensive document published by Baron and colleagues.[3]

The last decade has seen an unprecedented plethora of rapid, broad-based, and sensitive diagnostic tests that provide simultaneous organism identification and resistance marker detection. Optimal use of such assays provides tools that increase the effectiveness of antimicrobial stewardship (AS) activities and promote program growth.[4,5] Simultaneously laboratorians and ASP have pursued incorporating biomarkers, such as procalcitonin (PTC), into algorithms to differentiate infectious causes of fever or sepsis from noninfectious inflammatory conditions. Finally, clinical microbiology laboratories are essential for the surveillance of antimicrobial-resistant organisms and for organizing and communicating resistance trends in written form, such as antibiograms.

This article focuses primarily on the rapid tests that have been shown to optimize stewardship activities and reviews the evidence for using PTC. In addition, the value and limitations of antibiograms are also discussed in some detail.

RAPID DIAGNOSTIC TESTS FOR ORGANISM IDENTIFICATION

The past two decades have seen an explosion in the development of rapid diagnostic methods including nonamplified probe technologies, proteomics, and nucleic acid amplification methods combined with microarray technologies. A brief overview of several assays can be found in **Table 1**. These tests can significantly reduce time to organism identification compared with standard methods and lead to faster susceptibility results by detecting resistance markers. Moreover, when incorporated with AS interventions they can reduce the time to effective antimicrobial therapy, overall antimicrobial use, lengths of hospital stay, and hospital costs.[5–17] Summary of the studies evaluating rapid diagnostics can be found in **Table 2**.

Peptide Nucleic Acid–Fluorescence In Situ Hybridization

Peptide nucleic acid–fluorescence in situ hybridization (PNA-FISH) technology (AdvanDx, Inc, Woburn, MA) uses fluorescein-labeled probes that target pathogen-specific 16SrRNA of bacteria or 26SrRNA of yeast. After a blood culture bottle signals growth and a Gram stain is performed, the appropriate PNA-FISH probe can rapidly (20 minutes–1.5 hours) identify several important pathogens.[5] PNA-FISH probes have been cleared by the US Food and Drug Administration (FDA) for the following pathogens: *Staphylococcus aureus* and Coagulase-negative staphylococci; *Enterococcus faecalis* and other *Enterococcus* spp; *Escherichia coli*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa*; *Candida albicans*, *C parapsilosis*, *C tropicalis*, *C glabrata*, and *C krusei*. At this time, PNA-FISH tests do not detect resistance markers. However, a probe that detects the *mecA* gene has been evaluated in a recent clinical trial for FDA approval and will likely be available sometime in 2014 (Karen Carroll, personal communication, 2013).

Forrest and colleagues[6] conducted one of the first studies to evaluate the impact of a PNA FISH assay on patient outcomes. The investigators used an *S aureus* single-probe on positive blood cultures from non–intensive care unit (ICU) patients in conjunction with AS interventions. PNA-FISH results were reported in real time to an ASP that then assessed the need for vancomycin therapy and restricted its release. Investigators reported a significant decrease in median length of hospital stay from