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Collaborative Antimicrobial Stewardship

Working with Microbiology



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KEYWORDS

- Antimicrobial stewardship • Role of microbiology laboratory
- Infectious diseases diagnosis • Rapid testing • Molecular panels • Antibiogram
- *Clostridium difficile*

KEY POINTS

- The microbiology laboratory should be integrated into antibiotic stewardship programs.
- Rapid diagnostic technologies have the potential of decreasing time to appropriate therapy and improving patient care, and should be implemented in consultation with clinicians, clinical microbiologists, and the antibiotic stewardship team.
- Antibiotic stewardship teams are helpful to guide clinician use of the microbiology laboratory and interpretation of antimicrobial susceptibility results.

INTRODUCTION

Inappropriate and excessive use of antibiotics contributes to the emergence of antimicrobial resistance and adverse patient outcomes including *Clostridium difficile* infection (CDI), adverse drug reactions, and other antimicrobial-related patient morbidities.^{1,2} The primary goal of an antimicrobial stewardship program (ASP) is to optimize the appropriate use of antimicrobials, improve patient outcomes, reduce adverse sequelae of antimicrobial use, and decrease the emergence and spread of multidrug-resistant infections.^{3,4} The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America published guidelines in 2007 and updated them in 2016 to assist hospitals to develop and implement ASP and activities.^{5,6} Moreover, in 2014 the Centers for Disease Control and Prevention defined seven core elements for successful ASPs,⁷ and in 2016 the Joint Commission issued

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regulatory guidance for these programs.⁸ These guidelines suggest that ASPs actively collaborate with clinical microbiology.

At Wake Forest Baptist Health (WFBH), an 850-bed tertiary care center with a large cancer center and transplant services, our ASP has been active for 20 years. From the earliest days WFBH's clinical microbiology laboratory director has collaborated with the antimicrobial stewardship (AS) team. This strong partnership between the ASP team and laboratory has been extremely fruitful and has resulted in many successful initiatives to improve patient care. In addition, this collaboration has been helpful to address the challenges of assimilating new outpatient and inpatient clinical facilities into our rapidly expanding health care system. These challenges include finding solutions for the integration of diverse existing susceptibility reporting cascades, infectious diseases testing practices, antimicrobial formularies, and ASPs for newly assimilated hospitals and clinics. In this review, we discuss the collaborative efforts undertaken by our AS team with the microbiology laboratory, illustrating our experience, insight, and some successes and challenges we have encountered.

COLLABORATION WITH THE MICROBIOLOGY LABORATORY

The clinical microbiology laboratory is an essential part of the ASP team and plays an important role in the promotion of appropriate antimicrobial use, surveillance for resistant pathogens, and prevention of nosocomial infections. Conversely, the ASP team is an extremely important entity to advise, support, and expand clinician outreach for the microbiology laboratory. The collaborative tasks between our AS team and the microbiology laboratory include selecting antimicrobial susceptibility testing panels and cascade reporting, reviewing the annual antibiogram, evaluating new methodologies for the diagnosis of infectious diseases, standardizing antimicrobial reporting throughout the health system, educating and communicating with providers, and providing interpretation of test results to guide appropriate use of antimicrobials (Table 1). These functions require not only close collaboration of the AS team with the clinical microbiology laboratory, but also the support and expertise of informatics, and hospital leadership, so that providers accept and follow resulting clinical guidance. The acceptance of the recommendations by the clinical providers at large is of the utmost importance for the long-term success of any implemented program or intervention and the AS team can often facilitate such acceptance.

SELECTION OF ANTIMICROBIAL SUSCEPTIBILITY PANELS AND CASCADE REPORTING

Once a year, the ASP staff and the director of the microbiology laboratory review the current antimicrobial susceptibility panels and the corresponding set of tested antimicrobials. Updated panel contents are reviewed focusing on the addition of new agents or the modified antimicrobial concentrations that are tested that may be relevant to our specific treatment guidelines. To ensure that the laboratory is providing the most clinically relevant antimicrobial susceptibility results, our program routinely validates and implements new breakpoint recommendations from the Clinical and Laboratory Standards Institute (CLSI).⁹

In addition to the standard rules for cascade reporting recommended by CLSI,⁹ our program developed additional rules for antimicrobial susceptibility reporting so that results for some agents are "hidden." Hidden susceptibilities are often agents that would be problematic for treating selected infections (such as fluoroquinolones for invasive *Staphylococcus aureus*). This facilitates a final goal of promoting the use of the right agent for the right patient. A "hidden" susceptibility result must be approved

Efforts/Tasks	Comments
Selecting antimicrobial susceptibility testing panel for routine testing	At least once a year the current panels are reviewed to assess where changes are needed
Review of the reporting cascade	To ensure that the agents reported are included in our formulary and are the preferred agents for treatment
Preparation of cumulative susceptibility reports (antibiogram)	Annual reports are prepared for the different services within the main hospital and for the hospitals in our health care system
Standardization of agents in formulary and reporting of antibiotics throughout the health care system	Because the results are entered in the same electronic system, it is important to have the same rules and recommendations for reporting
Assessment of rapid diagnosis tests	Selection of tests is done to maximize clinical usefulness
Deciding what new agents can be available to testing and when to use them	Provide recommendations for testing of newer agents not included in panels, but that can be tested by other methods
Providing interpretation of microbiology tests and cultures	Adding comments to reports to facilitate interpretation
Diagnostic stewardship	Identify areas that need clarification for ordering, collection, or change in methodology to avoid misuse of antibiotics
Education to providers	Multiple options for education including laboratory rounds

by the ASP member on call (or a consulting infectious diseases provider) before the microbiology laboratory can report the results for that agent in the electronic medical record. This reporting algorithm has guided providers to select an agent from among those reported, which are usually of narrow spectrum or enhanced efficacy, or are considered first-line therapy for the organism isolated. Some of our reporting rules for antimicrobial susceptibility results are described in [Table 2](#).

PREPARATION OF ANTIBIOGRAMS

An antibiogram or cumulative susceptibility report is the summary of the local rate of antimicrobial susceptibility for the organisms most frequently isolated from clinical specimens. The antibiogram serves as a resource for clinicians choosing empiric antibiotic therapy. By tracking changes in the antibiogram year after year, the antibiogram helps stewardship programs to identify emerging resistance or to document improvements in susceptibility rates after targeted interventions. The microbiology director has traditionally been responsible for preparing and validating the data for the annual antibiogram according to the rules described in the CLSI M-39 document.¹⁰

Stewardship personnel, including pharmacists, have a vested interest in the antibiogram because of its potential impact on antibiotic prescribing. For this reason, stewardship pharmacists often work with the microbiology laboratory to populate

Rule	Rationale
Daptomycin tested but not reported for staphylococci and enterococci	Promote antibiotic stewardship
Linezolid reported for respiratory cultures of <i>Staphylococcus aureus</i> but not blood cultures	
Ceftaroline tested but not reported	
Cascaded reporting of linezolid for enterococci (only reported if vancomycin resistant)	
Cascaded reporting of cefepime and ceftazidime for Enterobacteriaceae (only reported if ceftriaxone resistant)	
Cascaded reporting of aminoglycosides for gram-negative rods	
Trimethoprim/sulfamethoxazole reported for wound cultures of <i>S aureus</i> but not blood cultures	
Fluoroquinolones and rifampin tested but not reported for staphylococci	
Tetracycline reported for wound and urine cultures but not blood cultures	
Perform D-test for staphylococci and streptococci that are erythromycin resistant and clindamycin susceptible	
β -Lactams not reported for oxacillin-resistant staphylococci	

susceptibilities, validate the data, and format the antibiogram so it is user (clinician) friendly. Color coding can help designate certain antibiotics as preferred based on enhanced susceptibility. Some institutions also add relative antibiotic cost information to the antibiogram to further assist clinicians at the point of antibiotic prescribing.

Modern health care systems are often challenged with standardizing antibiograms to serve many stakeholders within the system. The system's stakeholders include staff working in different settings, such as clinics, nursing homes, long-term care facilities, community hospitals, and tertiary care medical centers. Developing antibiograms that serve each of these settings is difficult. It is important to identify stewardship staff or liaisons at each location who can provide the local perspective about the patient populations served, the antibiotic formulary, the most common infections encountered, and any resistance concerns.

Depending on the structure of the health system, it may be advantageous to consolidate antibiogram data for multiple system locations, especially if the locations have common characteristics (eg, community hospitals or clinics in the same geographic area). Consolidating antibiogram data can also improve the sample size for organisms that are infrequently cultured. However, there are barriers in developing antibiograms to serve multiple locations in a health system. It is possible that different locations use different assays for susceptibility testing or that the antibiotics tested are different because of inconsistent formularies. By working with microbiology, a system stewardship program can help standardize and align these processes, making consolidated antibiograms feasible and improving consistency in the use of antibiotics throughout the system.

Antibiograms are limited in that they provide single antibiotic-pathogen pair susceptibility rates. The adequacy of any single agent prescribed as empiric therapy may not

be acceptable in clinical practice, particularly for life-threatening infections among patients with risk factors for antibiotic-resistant bacteria. The addition of a second antibiotic can improve adequacy of empiric therapy, and the optimal combination of antibiotics should be directed by local microbiology data. Specifically, microbiology and stewardship personnel should work together to construct combination antibiograms that represent institution-specific bacterial pathogens for a particular disease and ultimately to determine recommendations in local empiric treatment guidelines, as our team has successfully done.¹¹

IMPLEMENTATION OF RAPID TECHNOLOGIES FOR THE DIAGNOSIS OF INFECTIOUS DISEASES

New diagnostic techniques, a rapid turnaround time for pathogen identification, and accurate interpretation of susceptibility results are important tools for a patient-centered selection of appropriate therapy. Throughout the years, our AS team has reviewed many new laboratory techniques and methodologies that allow rapid identification of organisms and their mechanisms of resistance. The local assessment of clinical usefulness of these tests for our patient population has been an important factor for hospital administration in their decision to acquire a new piece of equipment testing methodology. Some of the most relevant technologies for rapid testing in the microbiology laboratory that have been evaluated and implemented by our AS team are described next.

Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Technology for Identification of Organisms

There is no doubt that matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) has revolutionized the way that laboratories identify microorganisms. This technique identifies an unknown organism by analyzing the proteins present, separating them according to mass, charge, and the time it takes for each of the proteins to travel from the inoculation site to the detector end of the instrument. Based on these parameters, the instrument generates a protein spectrum that is then compared with the spectrums included in the database of the instrument.^{12,13} The main advantages of MALDI-TOF are the speed and accuracy for identifying microorganisms. The instruments have high performance characteristics and robust databases to identify the most common organisms isolated from clinical specimens.¹⁴ Overall, identification is achieved 2 to 24 hours earlier for gram positives, and 24 to 72 hours earlier for gram-negative rods and yeasts compared with traditional systems of identification.^{13,15} Furthermore, MALDI-TOF is able to accurately identify fastidious or difficult to identify organisms that laboratories were previously unable to identify with conventional identification methodologies. The reporting of unusual organisms that are occasionally identified by MALDI-TOF can have unintended consequences because clinicians may be unfamiliar with the organism reported or with their potential pathogenicity and this can potentially lead to unnecessary antimicrobial treatment. Consultation with our ASP team is recommended for assessment of reporting language in the medical record and how clinicians might respond to a *Staphylococcus epidermidis* result as compared with a “coagulase-negative staphylococcus” report. Studies have shown that rapid identification of an organism by MALDI-TOF can improve time to appropriate antibiotic treatment, but only when associated with ASP collaboration.^{16–19}

The laboratory at WFBH implemented MALDI-TOF technology in 2014 and our AS team has been fundamental in educating providers on how to use the early

identification result to implement empiric therapy by providing reliable local antibiogram reports. Overall at our institution, the implementation of MALDI-TOF has clearly improved turnaround time for identification of organisms. Although MALDI-TOF does not provide susceptibility testing, many organisms have predictable susceptibility, and in these cases, rapid identification results in appropriate patient management.

Multiplex Molecular Assays

For many years, molecular detection of a single organism, such as methicillin-resistant *S aureus*, has shown its clinical usefulness for a single-drug-resistant organism.^{20,21} In the last decade, however, there has been a dramatic increase in the development of multiplex molecular assays designed to detect multiple pathogens associated with an infectious syndrome rather than one specific organism. These multiplex polymerase chain reaction (PCR) assays are usually offered as a “panel,” which can simultaneously detect, in a single specimen, the pathogens most commonly associated with an infectious syndrome, such as bloodstream, meningitis/encephalitis, respiratory, or gastrointestinal infections.²²

The implementation of rapid methods must be critically evaluated considering test volume, patient population, and availability of laboratory personnel and clinical support to ensure that the diagnostic technology selected is appropriate for the clinical service at a particular institution. Overuse or inappropriate use of these rapid tests may increase costs without providing the expected improvements in diagnosis and patient care.²³ In addition, many multiplex tests are not reimbursed by third-party payers in the outpatient setting, which can lead to serious economic consequences for the health care system and patient. ASPs affiliated with the clinical laboratory are of value to determine whether test parameters, such as sensitivity, specificity, and positive and negative predictabilities, are useful for implementation. In addition they can help develop protocols that identify appropriate patients for testing and subsequent test interpretation.

(Table 3) describes selected molecular panels that we have implemented and our experience with their use. This table also shows a description of the requirements for ordering these molecular panels.

Blood culture identification panels

One of the most important factors influencing treatment outcomes of patients with bloodstream infections is appropriateness of early antimicrobial therapy.^{24,25} In addition to the prompt initiation of effective therapy, avoidance of unnecessary exposure to broad-spectrum antibiotics is important to limit adverse events and prevent the emergence of antibiotic resistance. The main advantage of rapid blood culture identification panels is that they identify the organism 1 to 3 hours after the blood culture has signaled positive compared with 24 to 48 hours using traditional methodologies. Furthermore, these panels can also identify genetic elements of resistance mechanisms, making them useful for selecting antibiotic therapy for multidrug-resistant organisms.^{22,26}

At WFBH, we implemented the Biofire FilmArray Blood Culture Identification Panel (BioMerieux, Durham, NC), but because of current resource allocation do not use this panel for all blood cultures. To optimize cost-effectiveness and target patients at greatest risk, we elected to use this test routinely only for blood cultures from patients located in an intensive care or oncology units. We studied the impact of panel implementation for patients with noncontaminant gram-positive bacteremia and found improvements in AS metrics as shown in Fig. 1. These improvements were attributed to

Panel	Requirement/Recommendations for Ordering	Comments
RVP	Recommended in immunosuppressed patients with high risk for respiratory complications, and patients with severe respiratory infections that need to be admitted	No test of cure, no repeats of negatives unless new symptoms Encourage no testing or use the rapid flu test if influenza is suspected
GIP	Community-acquired diarrhea of ≥ 7 d duration, travel-related diarrhea, severe presentation (bloody diarrhea, dehydration), immunocompromised status, or norovirus suspected	No test of cure, no repeats of negatives The following comment is included in each report: "No antimicrobial therapy is recommended for mild illness with symptoms < 7 d"
MEP	High suspicion of infectious meningitis/encephalitis CSF with signs compatible with infectious process and at least 50 WBCs	If suspecting HSV, order the stand-alone HSV, which has higher sensitivity Culture must be ordered at the same time Likelihood of false positive, correlate with other tests and clinical presentation

Abbreviations: CSF, cerebrospinal fluid; GIP, gastrointestinal panel; HSV, herpes simplex virus; MEP, meningitis/encephalitis panel; RVP, respiratory viral panel; WBC, white blood cells.

the shortened time to organism identification and the ability to detect resistance. Median time to identification improved by 29 hours. Implementation of the panel also improved stewardship metrics for patients with blood cultures positive with a likely contaminant. For patients with blood culture contaminants, our study demonstrated a reduction in days of antibiotic therapy, shorter length of hospital stay, and fewer tests for vancomycin levels.

Optimal use of rapid diagnostic tests, including multiplex molecular blood culture panels, is best done in conjunction with dedicated stewardship personnel who provide

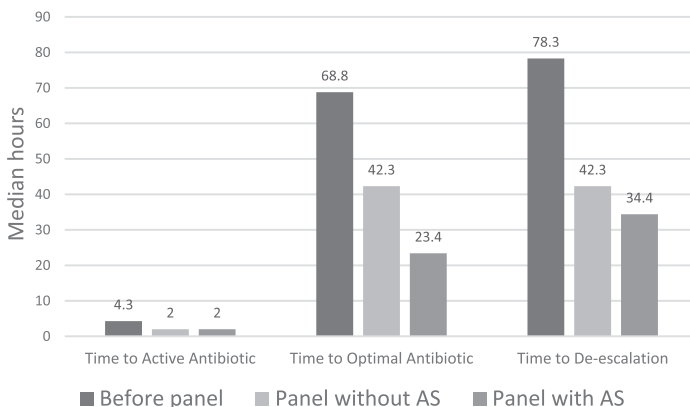


Fig. 1. Impact of a rapid blood culture panel with or without antibiotic guidance on stewardship metrics for noncontaminant gram-positive bacteremia.

antibiotic guidance at the time results are available.^{27–31} At WFBH, the AS team and microbiology staff collaborated to evaluate an approach for communicating positive blood culture panel results. Instead of reporting positive cultures to the nurse, results were reported directly to a stewardship pharmacist who relayed the result to the responsible provider along with antibiotic guidance. This method of communicating positive cultures improved stewardship metrics beyond what the rapid panel could achieve alone (see [Fig. 1](#)).

Some hospitals, however, may struggle to maintain this model of reporting 24 hours a day, 7 days a week. After initial implementation of molecular blood culture testing with AS team reporting, we later elected to report results using in-basket functionality within the electronic medical record in conjunction with traditional reporting to nurses. Inpatient acute care pharmacists received the in-basket results instead of a dedicated stewardship pharmacist. Such passive reporting of panel results did not achieve the same improved stewardship metrics. Time to optimal therapy and time to de-escalation regressed back to levels close to the traditional method of only reporting to nurses (data not shown). Our experience highlights the need for dedicated stewardship personnel along with rapid diagnostics to achieve the best outcomes.

Respiratory viral panels

Respiratory tract infections are one of the most common causes of morbidity and mortality in all age groups, and the clinical presentation of different organisms are often similar. Furthermore, a large portion of lower respiratory tract infections is caused by viruses, mycoplasma, and chlamydia. A multiplex PCR for respiratory viruses and difficult-to-culture bacteria, including pertussis, is now a frequently used panel test for respiratory infections. Testing for respiratory viruses other than influenza is controversial because many argue that detecting viruses for which there is no treatment may not be clinically important. Others state that identifying noninfluenza respiratory viruses is beneficial because it decreases additional testing, provides valuable information for epidemiologic and infection prevention purposes, and limits the use of antibiotics.³²

At WFBH, the first respiratory viral panel (RVP), a multiplex PCR for respiratory viruses, was implemented in 2009 around the time of the 2009 H1N1 influenza A pandemic. Initially it was mostly used for the diagnosis of influenza, but it quickly became a useful tool for assessing patients with other respiratory infections. Currently, the laboratory uses a multiplex PCR assay that includes 15 respiratory viruses and four bacterial pathogens. To begin with, microbiology and stewardship staff positioned the RVP for use in immunocompromised patients or those with moderate to severe respiratory infections needing hospitalization. Tests could be ordered without preauthorization or other restriction. Over time, the volume of ordered RVPs has substantially increased, with the maximum volume observed during the months of influenza activity. The high cost of the test and escalating RVP volume underscores the importance of diagnostic stewardship and prudent use of this test. In addition, test performance depends on collecting proper nasopharyngeal swabs and physicians and nurses should be trained on the procedure.

To evaluate whether RVP testing improved stewardship metrics at WFBH, microbiology and stewardship staff collaborated to determine the impact of RVP testing on the use of antibiotics for respiratory infections. We conducted a prospective study of nonimmunocompromised inpatients tested with the RVP and measured antibiotic use associated with respiratory infection. Results of the study showed that providers were more likely to discontinue or de-escalate antibiotics if the RVP is positive

(Table 4). Hospital length of stay and attributable mortality was not changed. Microbiology and stewardship teams need to balance improved stewardship metrics associated with the test with its cost and high volume burden to the laboratory. Thus, although the escalating cost of RVP testing is concerning, it may be offset by reduced antibiotic expense and improved use. At WFBH the stewardship team is currently implementing diagnostic stewardship for the RVP to decrease the volume and improve the selection of patients for testing.

Gastrointestinal panels

Infectious diarrhea is caused by bacterial, viral, and parasitic pathogens and remains a significant health care burden worldwide.³³ Although gastrointestinal infections are severe in immunosuppressed, pediatric, and elderly patients, most of these infections are self-limiting and do not need antimicrobial treatment.³⁴ Conventional testing for gastrointestinal pathogens lacks sensitivity and takes 3 to 5 days for the results to become available. With the gastrointestinal panels, results are available in 2 to 3 hours and it can detect the most important bacterial, parasitic, and viral pathogens causing diarrhea in the United States. Because the results are available the same day that the sample is submitted, the patient is still symptomatic and this may lead to antibiotic treatment. For that reason, at WFBH, a comment is included with each gastrointestinal panel result with recommendations to prevent misuse of antibiotics. Questions on whether treatment is necessary, such as for positive tests for enteropathogenic *Escherichia coli*, are referred to the stewardship pager.

In addition to improving diagnostic accuracy, this assay has helped us to quickly detect and control norovirus outbreaks as well as a *Salmonella* spp outbreak involving multiple counties in our region.

Meningitis/encephalitis panel

This panel from BioFire can rapidly detect the pathogens most commonly associated with this syndromic infection. However, the published evaluation of the performance of this panel showed false positives particularly for *Streptococcus pneumoniae*.³⁵ A false-positive result may not only lead to unnecessary therapy, but more importantly, false-positive results may delay or halt the pursuit of the true diagnosis.³⁶ In addition, providers should be aware that the sensitivity for detection of the different pathogens included in the panel varies considerably. For this reason, at WFBH when suspecting herpes simplex virus (HSV) infection,

Table 4
Impact of RVP testing on antibiotic use at WFBH

Outcome	Negative RVP (n = 100)	Positive RVP ^a (n = 50)	P Value
Antibiotic discontinued by 24 h, n (%)	2 (2)	5 (10)	.04
Antibiotic de-escalated by 24 h, n (%)	8 (8)	13 (26)	<.01
Antibiotic DOT, median (range), d	9 (1–35)	6 (1–53)	.03
Antibiotic duration, median (range), d	4.1 (0.5–14.9)	3.5 (0.2–24)	.09
Length of hospitalization, median (range), d	4.3 (0.4–39.9)	3.6 (0.9–26.0)	.25
In-hospital mortality, n (%)	3 (3)	2 (4)	.75

Abbreviation: DOT, days of antibiotic therapy.

^a Viruses detected by RVP include influenza (38%), respiratory syncytial virus (20%), metapneumovirus (20%), rhino/enterovirus (18%), and coronavirus (4%).

particularly in neonates, we recommend ordering the stand-alone HSV PCR test in cerebrospinal fluid, which has higher sensitivity than the HSV target included in the meningitis/encephalitis panel (MEP). The main benefit of the MEP is the rapid result, which could help to select appropriate therapy and prioritize resource use. In addition, it has been useful for the determination of whether droplet isolation or secondary chemoprophylaxis is required for *Neisseria meningitidis*. Because of the potential for false-positive results and the possibility for the detection of latent or reactivated viruses, results from MEP must be carefully assessed. At WFBH, MEP orders are not routinely processed on specimens with less than 50 WBC/dL unless approved by a consulting infectious disease or AS team member. All positive results for bacterial pathogens are correlated with culture to confirm the diagnosis.

DIAGNOSTIC STEWARDSHIP

Diagnostic stewardship refers to the appropriate use of laboratory testing to guide patient management and treatment in real time, with the goal of enhancing clinical outcomes and limiting the spread of antimicrobial resistance.³⁷ The goals of the ASP and the microbiology laboratory are intertwined, inasmuch as laboratory results direct antibiotic decision making. All phases of the diagnostic effort, the preanalytical phase, the analytical phase, and postanalytical phase, are critical elements of the testing process because they significantly impact diagnostic accuracy and the antimicrobials prescribed in response to test results.³⁸ Overuse of unnecessary testing increases the likelihood of false-positive test results that may lead to erroneous diagnoses and inappropriate antibiotic usage. Therefore, the ASP and microbiology laboratory must collaborate to design diagnostic stewardship processes aimed at achieving collective goals. At WFBH, the ASP and microbiology laboratory identified areas that could benefit from diagnostic stewardship. One of our most successful initiatives involves testing for CDI.

Testing for Clostridium difficile Infection

The enzyme immunoassays (EIA) to detect the presence of toxins were initially the most commonly used tests for the diagnosis of CDI, but their low sensitivity resulted in false-negative results. In 2009, WFBH converted to nucleic acid amplification test (PCR) for the diagnosis of CDI and observed a two-fold increase in the number of diagnoses. Growing concerns regarding overdiagnosis of CDI led us to evaluate CDI diagnoses at WFBH in 2015. Clinical specimens submitted for PCR testing were tested concurrently with an EIA that simultaneously tests for *C difficile* antigen and toxin. Members of the ASP performed chart review for each patient and made assessments of the likelihood of CDI while blinded to the EIA results. The analysis showed that the EIA was a better predictor of CDI and confirmed our suspicion of overdiagnosis by using PCR alone. The evaluation also identified common reasons for diarrhea that led to unnecessary CDI testing, many of which were iatrogenic. Several initiatives to improve patient selection for testing and the pretest likelihood for CDI were not successful. These included electronic medical record best practice advisories or algorithms, and nurse and provider education.

Supported by the data in our assessment, we converted to EIA testing in April 2016, ahead of guidelines by European and American societies that recommend a high-sensitivity EIA assay as a first step followed by a high-specificity toxin test.^{39,40} Included in the report for each EIA result, we added an explanatory comment (Table 5) for clinical decision support. PCR testing is still available at WFBH, but

Table 5 Clinical decision support for interpretation of <i>Clostridium difficile</i> EIA results	
Result Combination	Interpretation and Comment
Antigen positive, toxin positive	Interpretation: Positive for toxigenic <i>C difficile</i> . Comment: These results are consistent with <i>C difficile</i> infection. Detection of both antigen and toxin are expected when <i>C difficile</i> infection is present.
Antigen positive, toxin negative	Interpretation: <i>C difficile</i> present but toxin not detected. Comment: This pattern is most consistent with <i>C difficile</i> colonization (occurs in 20% of hospitalized patients). There is no indication to treat <i>C difficile</i> colonization and anti- <i>C difficile</i> antibiotics do not prevent subsequent infection. Antimicrobial therapy and proton pump inhibitors should be avoided. Consideration should be given to medication causes of diarrhea, such as laxatives, stool softeners, colchicine, metformin, HIV protease inhibitors, antibiotics, or certain chemotherapy agents, among others. Enteral feeds are also a common cause of diarrhea. If symptoms and signs are consistent with colitis and risk factors are present for <i>C difficile</i> (eg, recent antibiotic exposure), additional testing using <i>C difficile</i> PCR may be performed, but testing requires prior authorization by the AS team.
Antigen negative, toxin positive	Interpretation: Undetermined. Comment: Toxin positivity should not occur without antigen positivity. Consider repeat testing if clinically indicated.
Antigen negative, toxin negative	Interpretation: Negative for toxigenic <i>C difficile</i> . Comment: There is no evidence of <i>C difficile</i> infection. Consider other causes of diarrhea. Consideration should be given to medication causes of diarrhea, such as laxatives, stool softeners, colchicine, metformin, HIV protease inhibitors, antibiotics, or certain chemotherapy agents, among others. Enteral feeds are also a common cause of diarrhea.

Abbreviation: HIV, human immunodeficiency virus.

requires authorization by a member of the ASP. After changing the assay, PCR testing frequency declined by 98%, the rate of International Classification of Diseases-9/10 codes for CDI declined by 65%, the rate of NHSN *C difficile* LabID event rates/10,000 patient days declined by 75%, and the number of patients treated with oral vancomycin declined by 58%. Postimplantation audits showed no increase in CDI morbidity or mortality, or missed cases of inpatient CDI.

Interpretation of Antimicrobial Susceptibility Results

Through the years, we have identified certain antimicrobial susceptibility results that are misinterpreted by clinicians. Such misinterpretation leads to additional but unnecessary testing (eg, “special MIC”) or use of alternative antibiotics. The AS team and microbiology laboratory have developed supporting guidance incorporated within test results to overcome these issues. Examples of comments included in test results

Table 6	
Examples of comments included in the antimicrobial susceptibility testing report	
Organism/Specimen	Comment
<i>Haemophilus influenzae</i> isolated from sterile sites	<i>H influenzae</i> is considered susceptible to ceftriaxone and meropenem even if β -lactamase positive.
<i>H influenza</i> and <i>Haemophilus parainfluenza</i> from respiratory specimens	<i>H influenzae</i> may produce β -lactamase, which causes resistance to penicillin, ampicillin, and amoxicillin. However, <i>H influenzae</i> is generally susceptible to amoxicillin-clavulanate, cefuroxime, cefpodoxime, cefdinir, ceftriaxone, and azithromycin even if β -lactamase positive.
Group B streptococcus from vaginal/rectal swab for screening pregnant women	Group B streptococci are universally susceptible to ampicillin, penicillin, and cefazolin and testing is not necessary. If the clindamycin is reported as susceptible, the result has been confirmed by D test, and the organisms should be considered susceptible to clindamycin.
<i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , and <i>Proteus mirabilis</i> from clean-catch urine Cefazolin breakpoints for urine are applied	In the treatment of uncomplicated urinary tract infections, cefazolin susceptibility predicts susceptibility to the oral cephalosporins cephalexin, cefuroxime, cefpodoxime, and cefdinir. Cephalexin is cost-effective, but QID dosing (normal renal function) is less convenient than the other oral cephalosporins, which are dosed BID. Isolates resistant to cefazolin but susceptible to ceftriaxone may be susceptible to cefpodoxime.
Carbapenem-resistant enterobacteriaceae	Based on additional testing the following comment is added: carbapenamase-producing organism. Consult AS team for treatment recommendations.

are listed in [Table 6](#). Furthermore, special or extrasusceptibility testing must be approved by a member of the AS team.

SUMMARY

Rapid methodologies, particularly multiplex molecular panels, represent a paradigm shift in the diagnosis of clinical infectious diseases. The main benefit of rapid assays is the potential for improving patient care, particularly when associated with AS support. Local implementation of rapid methods, preparation of antibiograms, and interpretation of antimicrobial susceptibility tests should be done in partnership with pharmacy and clinicians versed in AS. This will ensure appropriate test use, a clear understanding of test characteristics and result interpretation, and opportunities for expert opinion to influence antimicrobial treatment.

DISCLOSURE

The authors have nothing to disclose.

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