MAD-ID Newsletter

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MAD-ID
MAKING A DIFFERENCE IN INFECTIOUS DISEASES®

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In this issue

Happy Holidays from MAD-ID
Things are getting better!

As we approach the holiday season, MAD-ID would like to express our gratitude for our community for the work that you all are doing for patients during the COVID-19 pandemic. We have much to be excited about and thankful for as therapeutics advance and vaccines become available.

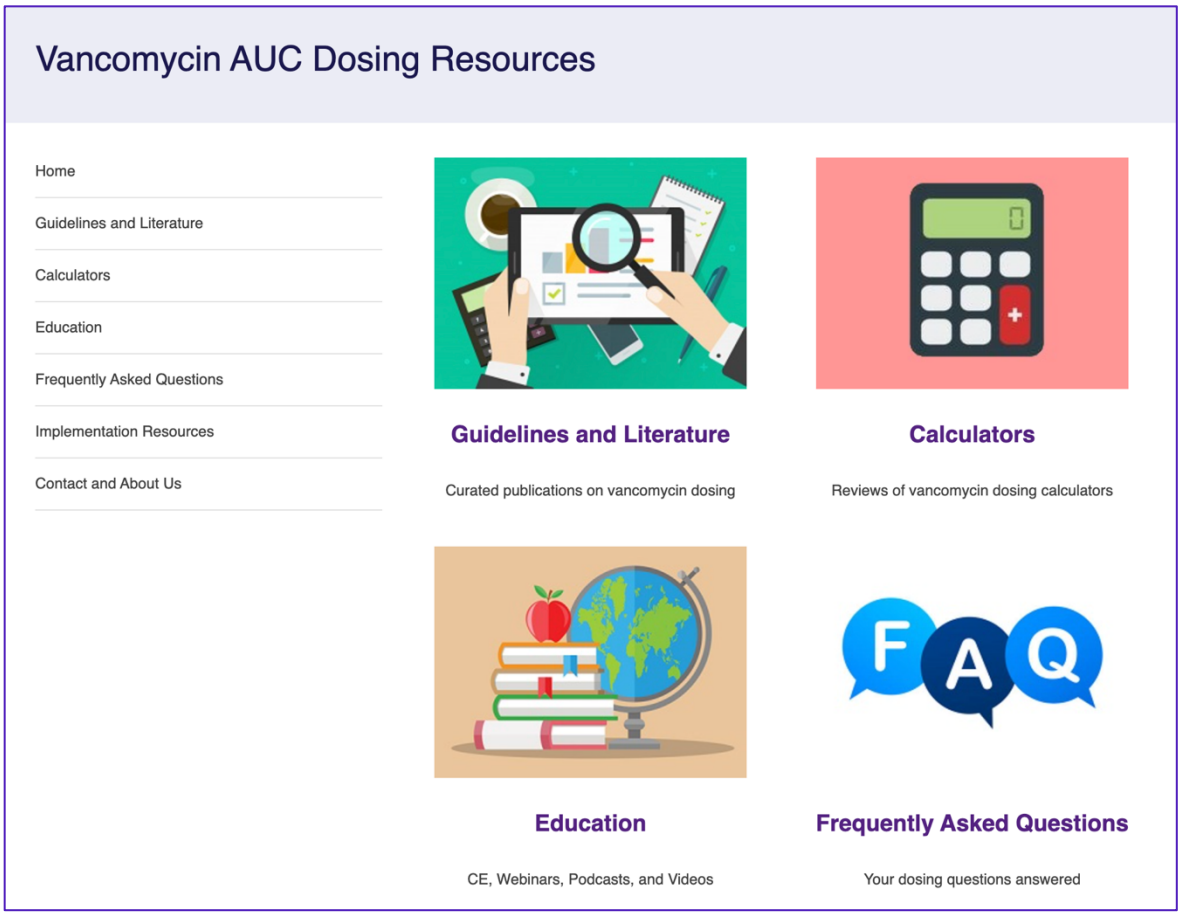
We know that conference education and travel may still be in flux for many of you as we approach the 2021 year and we are committed to telling you as soon as possible how MAD-ID 2021 will be held. But our planning committee members and speakers continue to work on excellent and engaging content for either live or virtual settings. We can't wait to get back together to talk about solutions and support in the challenges we continue to face in antimicrobial resistance.

From everyone at MAD-ID, have a happy and safe holiday. We hope to see you soon!

Announcing the MAD-ID Vancomycin AUC Dosing Resource Page

Find all of the tools you need including guidelines, literature, calculators, implementation resources, and the opportunity to contact an expert, for FREE.

https://mad-id.org/vancomycin/



Ongoing Advocacy for Antimicrobial Stewardship and Resistance

In the last newsletter we updated you on the *Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (*PASTEUR*) Act*, introduced by Sen. Michael Bennet (D-CO) and Sen. Todd Young (R-IN) to support the development of new antibiotics and promote appropriate use of existing ones, helping to limit the increase and spread of resistant infections. Since then, MAD-ID joined other organizational partners through S-FAR in a letter of support for the PASTEUR Act. In addition, MAD-ID supported an S-FAR letter to the Biden-Harris Transition Team to highlight the problem of antimicrobial resistance and to request that the incoming administration prioritize the federal response and reinvigorate efforts to sustain antibiotic development.

Looking Forward to MAD-ID 2021

Whether live or virtual, MAD-ID 2021 will have some outstanding sessions. This year we are planning these fantastic topics in classroom workshops and didactic sessions:

- Effective Use of EMR Programming to Implement Antibiotic Guidelines/Pathways
- Dose Optimization of Beta-Lactams
- Supporting ID/ASP Professionals: Preventing Burnout in an Era of Doing More with Less
- Developing and Using your Antibiogram
- Antimicrobial Stewardship in Challenging Environments
- How to Interpret and Apply Data from in vitro Studies to Patient Care
- How to Win Friends and Influence Outpatient Antibiotic Use
- Tales from the Trenches: Difficult Stewardship Challenges from our Community
- Evolution of PK/PD: Impact on Contemporary Therapeutics
- Combination Therapy for Serious Infections: S. aureus
- Combination Therapy for Serious Infections: Gram negative infections
- Demystifying two-sample and Bayesian AUC methods
- Implementing the 2020 Vancomycin Guidelines
- A Public Health Crisis: Advances in Vaccines
- A Public Health Crisis: Vaccine Mythbusters
- Antimicrobial Stewardship in Special Populations: Pediatrics
- Antimicrobial Stewardship in Special Populations: Adults with Cystic Fibrosis
- A New Era in HIV Management: Real Life Challenges in HIV Therapy
- A New Era in HIV Management: New Therapies, New Problems
- COVID-19: Public Health and Clinical Challenges
- COVID-19: Treatment Challenges, Access & Impact since COVID-19 Outbreak
- Emerging and Difficult to Treat Infections: *Candida auris*
- Emerging and Difficult to Treat Infections: Nontuberculous Mycobacteria
- What did you miss at the other ID Meetings

Employing Rapid Diagnostics and Diagnostic Stewardship for Managing Gram-Negative Infections

Continuing Education Activity

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Learning Objectives:
At the end of this article, learners will be able to:

1. Differentiate between the available rapid diagnostic technologies for identification and susceptibility testing of Gram-negative organisms within the bloodstream.
2. Explain diagnostic stewardship strategies used to appropriately employ the use of different rapid diagnostic technologies for Gram-negative bloodstream infections.
3. Discuss the impact of merging antimicrobial stewardship efforts with rapid diagnostic technology to optimize treatment for Gram-negative bloodstream infections.

Introduction
Antimicrobial resistance is a global threat of continued, increasing concern that has been associated with prolonged hospitalizations, increased morbidity and mortality, and escalating healthcare-related costs.1,2 In recent years, the presence of extended-spectrum beta-lactamases (ESBL) and carbapenem resistance in Gram-negative pathogens have brought clinical challenges.3-5 In fact, the Antibiotic Resistance Threats Report from the Centers for Disease Control and Prevention (CDC) lists several relatively common Gram-negative pathogens as top threats, including carbapenem-resistant Acinetobacter, carbapenem-resistant Enterobacteriaceae, and drug-resistant Neisseria gonorrhoeae as urgent threats and ESBL-producing Enterobacteriaceae and multidrug-resistant (MDR) Pseudomonas aeruginosa as serious threats.1 In response to these global threats, the Infectious Diseases Society of America (IDSA) released treatment guidelines for the management of resistant Gram-negative bacterial infections.6

While defining therapies for these difficult-to-treat infections is important, it is equally important to obtain timely culture and susceptibility results, especially when resistance is suspected. In one study by Kang and

colleagues, patients with antibiotic-resistant Gram-negative bacteria who received appropriate initial therapy had a 27.4% mortality rate versus 38.4% in those inadequately treated initially (p=0.049).7 In a study examining patients with Pseudomonas aeruginosa bacteremia, delays in starting effective antimicrobial therapy were independently associated with increased mortality (43.4% vs. 27.7%).8
Culture and susceptibility results are also important for appropriate de-escalation. In a study by Teshome and colleagues, a review of 7,118 adults revealed that each additional day of exposure to any antipseudomonal beta-lactams resulted in a 4% hazard risk increase for new resistance development (95% CI 1.04-10.5).2 Each additional day of cefepime, meropenem, and piperacillin-tazobactam resulted in 8%, 2%, and 8% increased risk of new resistance, respectively. Similarly, a study from Singh and colleagues revealed that patients had significantly higher rates of resistance and superinfection with mean antibiotic durations of exposure of 10 days versus 3 days (35% vs. 15%, p=0.0017).9
The purpose of this review is to discuss available rapid diagnostic technology (RDT), diagnostic stewardship, and the importance of merging antimicrobial stewardship efforts with these rapid diagnostic strategies for Gram-negative infections.

Rapid Diagnostics for Gram-negative Bloodstream Infections
Today, many hospitals are employing RDTs in their facilities. In fact, the market value for RDTs is projected to increase to over $2.85 billion by 2025.10 Additionally, with the increasing concern of multidrug-resistant pathogens, narrowing of broad-spectrum empiric therapy against Gram-negative organisms as quickly as possible is imperative to slow this spread. There are currently seven companies that have platforms designed to rapidly detect and identify Gram-negative pathogens in the blood. Table 1 provides a summary of the systems available in the United States.

The technologies primarily utilize single and multiplex polymerase chain reaction (PCR, mPCR) to rapidly identify bacteria and/or resistance mechanisms by detecting specific DNA and/or protein sequences. Traditionally, PCR utilizes two primers (one set) to detect either an organism or a resistance mechanism in a single run by detecting and amplifying a target piece of DNA. Currently, most RDTs employ the use of mPCR techniques, meaning that more than one set of primers is used to detect and identify both organisms and resistance in the same run. Conversely, matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) utilizes mass spectrometry to identify proteins within bacterial species that identify the organisms directly and indirectly from blood samples.11 This technology compares the observed protein spectrum to a database of expected protein spectrums and provides a numerical value (from 1 to 3) of confidence in identifying the organism. The higher the number, the higher the confidence that the observed and expected spectrums are aligned.

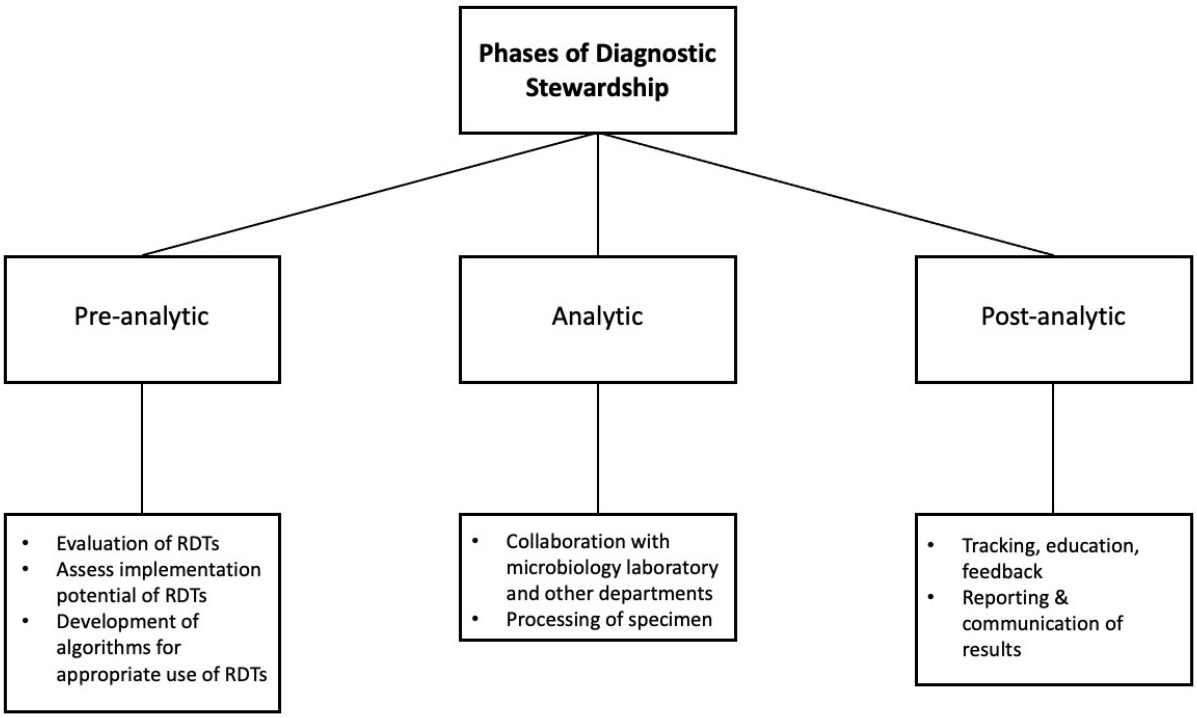
The technologies that utilize mPCR techniques include Accelerate PhenoTM (Accelerate Diagnostics), BioFire® FilmArray® (BioFire Diagnostics), ePlex® BCID-GN (GenMarkDx), GNR Traffic Light® PNA FISH® (OpGen), T2Bacteria (T2 Biosystems®), and Verigene® (Luminex). These RDTs specifically target 16s ribosomal RNA, while the VitekMS (bioMérieux, Inc.) targets bacterial protein sequences to identify species.12 Accelerate PhenoTM and GNR Traffic Light® PNA FISH®, while considered mPCR technology, utilize fluorescence-labeled nucleic acid probes to identify RNA sequences.12 Additionally, all the mentioned tests can identify organisms directly from blood cultures (positive cultures and whole blood) except for Verigene® and VitekMS. With most of the systems utilizing mPCR technology, it may be difficult for clinicians to determine which system would be the most useful in their practice. Identifying strengths and weaknesses of each system can help determine which system(s) to employ (Table 2).

In addition to strengths and weaknesses of the platforms, two groups have used the Desirability of Outcome Ranking Management of Antimicrobial Therapy (DOOR-MAT) methodology either to supplement RDT or to compare multiple RDTs to optimize appropriate therapy for treating bloodstream infections (BSI).13,14 First, Wilson and colleagues used this specific adaptation of DOOR methodology to compare traditional organism identification and susceptibility testing against RDTs.13 The authors noted that in patients with Escherichia coli or Klebsiella pneumoniae bacteremia where there were low rates of beta-lactam resistance, empiric beta-lactam therapy was broader than necessary and that RDTs have the potential to reduce overtreatment while still providing effective therapy. In a second evaluation, Claeys and colleagues used this DOOR-MAT methodology to compare two RDTs, specifically in patients with bloodstream infections.14 The authors concluded that while both Verigene® and ePlex® BCID had high agreement with on-panel targets, ePlex® BCID was able to identify more organisms. Furthermore, they concluded that DOOR-MAT may be useful to compare RDT systems and enhance clinical interpretation. Importantly, this study identified future directions to expand DOOR-MAT to incorporate resistance detection, as well as comparisons between other RDTs.

Incorporating Diagnostic Stewardship

Within the last two decades, the number of clinical laboratory tests available for patient care has increased to over 3,000.15 Due to the complexity and volume of tests available for Gram-negative infections, diagnostic stewardship is essential. Diagnostic stewardship (DS) is defined by the World Health Organization as "coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions".16 DS can also be defined as the "right test, right patient, right time"17 and is recommended by the 2016 IDSA and Society of Healthcare Epidemiology of America Stewardship Guidelines,18 CDC Core Elements of Hospital Antibiotic Stewardship Programs,19 and by the Society of Infectious Diseases Pharmacists.20

Figure 1. Diagnostic Stewardship Phases



DS occurs in three phases: preanalytic, analytic, and postanalytic (Figure 1).21 The preanalytic phase includes the evaluation of a RDT and its potential for implementation for the individual institution. The sensitivity, specificity, and predictive values for each RDT as well as the prevalence of resistant Gram-negative pathogens should be considered in the preanalytic phase. An evaluation of the pathogens identified in the previous year can guide the assessment of appropriateness of a RDT.22 As an example, if an institution tends to have more common and susceptible pathogens, a RDT that detects markers of resistance may be of less value.

This preanalytic phase should also include development of clinician guidance for when and how to order the test appropriately.17,21 Clinical decision support and testing algorithms can provide timely recommendations and guidance for providers. These algorithms may describe criteria for use, criteria for specimen rejection, prior authorization, and cost information.17 Additionally, reflex and cascade approaches to diagnostics can benefit this phase.

The analytic or processing phase requires substantial collaboration with the clinical microbiology laboratory. The analytic phase includes each step of the laboratory workflow of collecting the specimen, receiving the specimen, processing the specimen, and storage/transport.16 The workload, staffing hours, and cost should be considered17,21 as RDTs vary in hands-on time, space, and required skill.22 RDTs likely have their greatest benefit in the analytic phase. By significantly reducing the time to results, patients can be escalated or de-escalated to appropriate antimicrobial therapy more quickly than with traditional methods.12,17,23 Additionally, with greater numbers of laboratories becoming centralized, these potential delays should be weighed with the benefits of the RDT.12 Despite potential delays, an evaluation of two community hospitals that utilized a centralized laboratory demonstrated reduction in time to therapy modification from 75 to 30 hours ($p<0.001$).24

The postanalytic phase includes reporting and communication of results to clinicians.21 The postanalytic phase can be affected by selective reporting of sensitivity results and templated comments.21 Templated comments were evaluated in a three-arm study by Banerjee and colleagues. Patients with positive blood cultures (n=617) were randomized into standard blood culture processes, rapid mPCR (BioFire® FilmArray®) with templated comments, or rapid mPCR with templated comments and real time intervention by an antimicrobial stewardship team. For Gram-negative organisms, these templated comments included information about carbapenemase production, resistance to beta-lactams, recommendations for precautions, and recommendations to consult infectious diseases. These comments led to decreased treatment of contaminants ($p=0.015$) and a reduction in use of piperacillin-tazobactam ($p=0.01$). Outcomes were further improved with intervention by the antimicrobial stewardship program.25 Institutions should also consider methods of communication such as alerts of results by phone, how results are reported into the electronic medical record, and the impact of real-time clinical decision support surveillance software. Critical results should be prioritized, and considerations should be made for who will be contacted during the day and overnight.

Merging Rapid Diagnostics and Diagnostic Stewardship for Gram-Negative Bloodstream Infections

Combining RDTs and DS is essential to help conserve antimicrobials, however, antimicrobial stewardship programs need to ensure proper education of the RDTs available to apply the results effectively and economically.26 While RDTs allow providers the ability to quickly identify the offending pathogen, they also require the employment of DS to know which test to order, when, and how to correctly interpret the results.

RDT allows providers to apply results towards patient care sooner and help provide more effective care by changing, broadening, or narrowing therapy, but only when used appropriately and to its full potential.

Although not as commonly seen among BSIs, many of the errors in healthcare settings that lead to increased costs with no value are related to duplication of testing or misinterpretation of results. In a survey of infectious diseases physicians (n=700), 67.5% of respondents felt that testing is becoming too complex for non-infectious diseases providers, and 79% felt stewardship should be implemented for costly or complex diagnostics.27 In order to optimize RDTs and each phase of DS, a multidisciplinary Diagnostic Stewardship Committee is recommended. Members of this committee may include professionals from the departments of clinical microbiology, information technology, medical staff, and pharmacy.28 Similar to an Antimicrobial Stewardship Committee, this group can evaluate the diagnostic needs and value of a RDT at an individual institution while considering laboratory workflow and cost.20 This committee can also track appropriateness of tests and provide education and feedback.15,17

One role for a Diagnostic Stewardship Committee is to assess the value of an individual RDT for an institution and provide guidance on incorporation of DS and antimicrobial stewardship intervention. While the initial and ongoing costs of the test need to be considered, justification for a RDT can be evaluated with other outcomes such as reduced hospital length of stay and overall costs. Without antimicrobial stewardship, a RDT only has an estimated 41% chance of being cost effective.29 Two studies by Perez and colleagues demonstrated clinical and economical outcomes with the implementation of a RDT for Gram-negative BSI. In an evaluation of MALDI-TOF, time to optimal antibiotics was reduced by 46 hours ($p=0.004$) compared to traditional methods; hospital length of stay was decreased from 11.9 to 9.3 days ($p=0.01$); and hospital costs were lowered significantly ($p=0.009$).30 A follow up study by Perez and colleagues compared patients with resistant Gram-negative BSI before and after implementation of MALDI-TOF and antimicrobial stewardship interventions. Time to effective and optimal antibiotic therapy were significantly reduced ($p<0.001$). Hospital length of stay was reduced from 23.3 days to 15.3 days ($p=0.0001$), and ICU length of stay was reduced from 16 to 10.7 days ($p=0.008$). This study also demonstrated lower mortality in the intervention group (21% vs 8.9%, $p=0.01$), and the RDT intervention was a predictor of survival after multivariate logistic regression. Average hospital costs per patient were also decreased, resulting in an annualized cost savings estimated at $2.4 million ($p=0.002$).31 Additionally, a large meta-analysis reviewing the effect of stewardship on overall BSIs showed that in the presence of stewardship programs, there was a decrease in mortality for these patients (OR 0.64; 95% CI, 0.51–0.79).23

Clinician education and feedback from a Diagnostic Stewardship Committee is beneficial as RDTs increase in sensitivity and complexity. Education for providers may include a description of the RDT, indications for the test and alternatives, sensitivity and risk for contaminants, benefits and disadvantages, time to result, and guidance for antimicrobial therapy.32 In a survey of 156 physicians after implementation of mPCR (BioFire® FilmArray®) at one institution, only 60% reported that they adjusted antibiotics based on the results from the RDT, and correct interpretation of results ranged from 52-86%.33 In a study of RDTs in pediatric patients with positive blood cultures, unsolicited intervention on the results of a RDT was associated with improved antibiotic selection and high satisfaction rates (4.8/5) by providers.34 Implementing a new culture on antimicrobial prescribing in the setting of RDTs that incorporates handshake stewardship can be done if the stewardship team forms rapport with providers and provides education while making recommendations.35-38 This aligns with the findings that passive stewardship education (e.g., presentations and conferences) is not as

effective at altering prescribing patterns as active education (e.g., patient-specific education, education combined with audit and feedback).39

Ultimately, none of the available RDTs can entirely replace traditional microbiology methodology. Due to the limited spectrum and sensitivity of the available assays, RDTs may not be appropriate if the pathogen is "off-panel" or if the BSI is polymicrobial. Additionally, no RDTs are rapid enough yet to prevent the initial use of empiric antibiotics.40 The establishment of a DS Committee can provide guidance to optimize the use of RDTs and effectively combine this technology with antimicrobial stewardship efforts.

Conclusions

These RDTs provide decreased mortality and length of stay, as well as improved time to effective therapy.23 However, they should not be used alone.18,41 Employment of RDTs need to be combined with DS as part of the antimicrobial stewardship team's responsibilities or as a responsibility for a Diagnostic Stewardship Committee. Additionally, education surrounding interpreting RDTs is essential for providers to understand the utility of the technology and appropriately respond to the results. While RDTs are still evolving, they provide us with a much-needed improvement in time to identify offending pathogens and resistance mechanisms. This allows antimicrobials to be tailored sooner, thereby optimizing therapy and improving patient outcomes.

Table 1. Comparison of Rapid Diagnostic Technology for Detecting Gram-negative Bacteria in the Blood[42-51]

Test	Accelerate Pheno™	BioFire® FilmArray®	ePlex® BCID-GN	GNR Traffic Light® PNA FISH®	T2Bacteria	Verigene ®	VitekMS
Manufacturer	Accelerate Diagnostics	BioFire Diagnostics	GenMarkDx	OpGen	T2 Biosystems®	Luminex	bioMérieux, Inc.
Detection method	Fluorescence-labeled nucleic acid probes	mPCR	mPCR	Fluorescence-labeled nucleic acid probes	mPCR	mPCR	Mass spectrometry
Detection target	16s ribosomal RNA	16s ribosomal RNA	16s ribosomal RNA	16s ribosomal RNA	16s ribosomal RNA	16s ribosomal RNA	Protein
Direct from blood	Yes	Yes	Yes	Yes	No*	No	No
# of pathogens detected	12	10 (BCID) 14 (BCID2)	21	3	3	9	Dependent on database
# of resistance mechanisms detected	Provides phenotypic interpretation of MICs	1 (BCID) 7 (BCID2)	7	n/a	Not currently available[Ÿ]	6	n/a
Sensitivity	94.5%-99.4%	90-99%	99%	84.2%	95%	97.1%	90%
Specificity	99.1%-100%	97-99.8%	96%	90.9%	98%	99.5%	100%
Turnaround time	ID: 2 hours MICs: 7 hours	1 hour	1.5 hours	1.5 hours	3-5 hours	2-3 hours	0.1-0.5 hours

mPCR = multiplex polymerase chain reaction; ID = identification; MIC = minimum inhibitory concentration

[Ÿ]resistance panel is currently available for research use only in the U.S.

*can run sample directly from whole blood

Table 2. Clinical Comparison of Gram-negative Bloodstream Infection Rapid Diagnostic Technology[11,12,50,51]

Test	Strengths	Weaknesses
Accelerate Pheno™	• Provides phenotypic susceptibility results	• Direct from positive blood culture results • Moderate turnaround time for organism identification
BioFire® FilmArray®	• Tied for largest resistance panel size • Updated panel is second largest for detecting organisms • Individual sample runs • Fastest turnaround time for organism identification	• Direct from positive blood culture results • Polymicrobial samples • Microorganisms with low rates of differences in ribosomal protein sequences
ePlex® BCID-GN	• Largest panel size for detecting organisms • Tied for largest resistance panel size • Quick turnaround time	• Direct from positive blood culture results
GNR Traffic Light® PNA FISH®	• Individual sample runs • Quick turnaround time	• Direct from positive blood culture results • Limited number of pathogens targeted • No resistance markers tested
T2Bacteria Panel	• Direct from whole blood results	• Limited number of pathogens targeted • No resistance markers tested* • Longest turnaround time for organism identification
Verigene®	• Individual sample runs	• Direct from bacterial colony results • Polymicrobial samples • Microorganisms with low rates of differences in ribosomal protein sequences
VitekMS	• Improved identification accuracy over traditional techniques • Can batch samples • Extensive identification of organisms	• Direct from bacterial colony results • Direct from positive blood culture results • No resistance markers tested • Quality of reference database • Microorganisms with complex cell wall composition • Microorganisms with low rates of differences in ribosomal protein sequences • Anaerobe identification to the species level • Polymicrobial samples

*resistance marker testing currently available for research purposes in the US

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Instructions for Obtaining CE

The self-assessment quiz that can be found at the end of this article can be completed for 0.1 CEU of Continuing Pharmacy Education credit. The quiz may be completed online (http://madidtraining.org/newsletter/) at no cost for MAD-ID members. Non-members should print and mail the completed quiz, along with a $15.00 check made payable to MAD-ID to: MAD-ID, 537 Calico Retreat, Mt. Pleasant, SC 29464-2765. Your CE credit will be reported on CPE monitor within 4 weeks of receipt.

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Self-Assessment Questions

(To be completed online (http://mad-idtraining.org/newsletter/) or, in the case of non-MAD members, printed and mailed. You must achieve a grade of 80% of better to receive continuing education credit.)

1. A patient presents to the intensive care unit with presumed septic shock. Blood cultures are drawn and sent to the microbiology laboratory, and empiric antibiotics are initiated. Which rapid diagnostic test would yield the quickest identification of the offending organism? (Learning Objective 1)
   a. Accelerate Pheno™
   b. ePlex® BCID-GN
   c. T2Bacteria Panel
   d. Verigene®

2. The Antimicrobial Stewardship Committee is charged with investigating and recommending a rapid diagnostic technology for the microbiology laboratory to purchase that will aid in identifying as many Gram-negative organisms and resistance mechanisms as possible. Which of the following RDT is the most appropriate to recommend? (Learning Objective 1)
   a. ePlex® BCID-GN
   b. Verigene®
   c. BioFire® FilmArray®
   d. GNR Traffic Light® PNA FISH®

3. Which of the following statements appropriately describes a phase of diagnostic stewardship? (Learning Objective 2)
   a. An evaluation of the previous year's pathogens identified in blood cultures and their resistance mechanisms should occur in the analytic phase of diagnostic stewardship.
   b. A decrease in time to effective antimicrobial therapy attributed to rapid diagnostics would be represented in the preanalytic phase of diagnostic stewardship.
   c. Communication with clinicians in the form of templated comments or selective reporting would occur in the postanalytic phase of diagnostic stewardship.
   d. Decision support for ordering the appropriate rapid diagnostic test should be developed in the postanalytic phase of diagnostic stewardship.

4. Which of the following statements describes the importance of diagnostic stewardship? (Learning Objective 2)
   a. Rapid diagnostics are becoming more specific than traditional microbiology methods, allowing for higher rates of false positives in the setting of low pretest probability.
   b. Pathogens, mechanisms of resistance, laboratory workflow, and laboratory/pharmacist staffing hours vary by institution and are important considerations in selecting a rapid diagnostic test for implementation.
   c. The ability to efficiently modify an antibiotic regimen is only based on the time to results of the rapid diagnostic test.
   d. The selection of a rapid diagnostic test should focus exclusively on de-escalation, rather than escalation of antimicrobial therapy.

5. What is one way to incorporate diagnostic stewardship with antimicrobial stewardship in a facility that uses RDTs targeted toward Gram-negative bacilli bloodstream infections? (Learning Objective 3)
   a. Providing educational programs
   b. Stopping the duplication of testing
   c. Forming a diagnostic stewardship committee
   d. Adding best practice alerts (BPAs)

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Please provide your honest assessment of the value of this learning activity so that we can continue to improve our offerings.

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   - ☐ Pharmacist
   - ☐ Physician
   - ☐ Nurse
   - ☐ PA
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Criteria	Strongly agree (a)	Generally agree (b)	No Opinion (c)	Mildly disagree (d)	Strongly disagree (e)
2. The speaker(s) / author(s) adequately addressed the learning objectives	a	b	c	d	e
3. The speaker(s) / author(s) used an effective learning method	a	b	c	d	e
4. The content of the activity was relevant to my practice	a	b	c	d	e
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