# Rapid Diagnostic Technology to Aid in Identification of Organisms Causing Bloodstream Infection

## Kimberly C. Claeys, PharmD, BCPS

* There is an increasing armamentarium of tools to allow clinicians to rapidly identify organisms present in blood cultures hours to days sooner than traditional microbiological techniques (Table 1).
* Integrating these rapid diagnostic tests (RDTs) into routine clinical practice, along with active antimicrobial stewardship involvement, has been shown to improve patient outcomes, including:
  + Decreased time to optimal therapy
  + Decrease hospital length of stay
  + Decrease incidence of C. difficile infection
  + Decreased all-cause mortality

## Table 1: Rapid Diagnostic Tests used in Clinical Practice

|  |  |  |  |
| --- | --- | --- | --- |
| **Technology** | **Organisms** | **Resistance Markers** | **Turn-around Time\*** |
| **Peptide Nucleic Acid Fluorescence In Situ Hybridization (PNA FISH®)** | *S. aureus vs CoNS*  *E. faecalis vs other Enterococcus spp.* | mecA | 0.3-1.5 hrs |
| *E. coli vs K. pneumoniae vs P. aeruginosa* |
| *C. albicans/parapislosis vs C. tropicalis vs C. glabrata/krusei* |
| **Matrix-assisted laser desorption ionization time-of-flight mass spectrometry**  **(MALDI-TOF MS)** | Large database of bacteria and yeast | N/A | 0.2 hrs |
| **Nucleic acid microarray (Verigene BCID)** | *Staphylococcus spp., Streptococcus spp., E. faecalis, E. faecium, Listeria spp.* | mecA, vanA, vanB | 2.5 hrs |
| *E. coli, K pneumoniae, K. oxytoca, P. aeruginosa, Acinetobacter spp., Proteus spp., Citrobacter spp., Enterobacter spp.* | KPC, NDM, CTX-M, VIM, IMP, OXA |
| **Multiplex PCR (BioFire BCID)** | *Staphylococci; Streptococci; Enterococcus; Listeria;* | mecA, vanA, vanB, KPC | 1 hr |
| *A. baumannii, H. influenza, N. meningitides, P. aeruginosa, Enterobacter cloacae, E. coli, K. oxytoca, K. pneumoniae, Proteus spp., S. marcescens* |
| *C. albicans, C. glabrata, C. krusei, C. parapsilosis, C. tropicalis* |
| **Fluorescence In Situ Hybridization and digital microscopy (Accelerate PhenoTest)** | *S. aureus/S. lugdenensis/CoNS, Streptococcus spp., E. faecium/faecalis* | None, detects phenotypic resistance (S/I/R) | 1.5 – 7 hrs |
| *E. coli , K. pneumoniae, Citrobacter spp., Proteus spp., Enterobacter spp. Serratia marcescens, P. aeruginosa, A. baumannii* |
| *C. albicans/glabrata* |

*\*Time from Gram-stain result*

* Collaboration between the Clinical Microbiology Laboratory, Infectious Diseases physicians, and Antimicrobial Stewardship pharmacists is key to successfully integrating the above RDTs
* Typical workflow integrating RDT results includes:
* If you plan on incorporating a treatment algorithm based on RDT results, important to consider local susceptibility patterns and best available evidence
  + Review facility antibiograms to help determine drugs of choice
  + Determine baseline susceptibility rate your institution if comfortable with (i.e. 90% versus 95% of organisms susceptible according to last updated antibiogram)
  + For uncommon organisms/resistance (i.e. KPC-producing Enterobacteriaceae) review peer-review literature for optimal therapy decisions
  + Important to educate clinicians about how to interpret results from RDT and how to apply treatment algorithm
  + For certain combinations of antimicrobials and organism it may be prudent to validate algorithm recommendations before widespread use (i.e. CTX-M negative E. coli or Klebsiella spp. and phenotypic resistance to ceftriaxone)
  + Update algorithm recommendations as needed (i.e. based on new susceptibility data or literature)
* Treatment algorithm recommendations should not supersede clinical judgment and individual patient case scenarios (i.e. previous antibiotic exposure, antibiotic allergies, immune function, etc.).
* If patient is clinical responding to current therapy and algorithm recommends broader therapy, it may not be necessary to broaden.

## Example Verigene RDT Treatment Algorithms

## Example BioFire RDT Treatment Algorithms

## References:

1. Avdic E, Carroll KC. The role of the microbiology laboratory in antimicrobial stewardship programs. Infect Dis Clin North Am. 2014 Jun;28(2):215–35.
2. Bookstaver PB, Nimmich EB, Smith TJ, Justo JA, Kohn J, Hammer KL, et al. Cumulative Effect of an Antimicrobial Stewardship and Rapid Diagnostic Testing Bundle on Early Streamlining of Antimicrobial Therapy in Gram-Negative Bloodstream Infections. Antimicrob Agents Chemother. 2017;61(9).
3. Claeys KC, Schlaffer KE, Heil EL, Leekha S, Johnson JK. Validation of an Antimicrobial Stewardship-Driven Verigene Blood-Culture Gram-Negative Treatment Algorithm to Improve Appropriateness of Antibiotics. Open Forum Infect Dis. 2018 Oct;5(10):ofy233.
4. Donner LM, Campbell WS, Lyden E, Van Schooneveld TC. Assessment of Rapid-Blood-Culture-Identification Result Interpretation and Antibiotic Prescribing Practices. J Clin Microbiol. 2017;55(5):1496–507.
5. Messacar K, Parker SK, Todd JK, Dominguez SR. Implementation of Rapid Molecular Infectious Disease Diagnostics: the Role of Diagnostic and Antimicrobial Stewardship. J Clin Microbiol. 2017;55(3):715–23.
6. Rivard KR, Athans V, Lam SW, Gordon SM, Procop GW, Richter SS, et al. Impact of antimicrobial stewardship and rapid microarray testing on patients with Gram-negative bacteremia. Eur J Clin Microbiol Infect Dis. 2017 Oct;36(10):1879–87.
7. Schooneveld TV, Bergman S, Fey P, Rupp M. Recommendations Regarding Use of Rapid Blood Pathogen Identification Panel Data. <https://www.nebraskamed.com/sites/default/files/documents/for-providers/asp/biofire-recs.pdf>
8. Seddon MM, Bookstaver PB, Justo JA, Kohn J, Rac H, Haggard E, et al. Role of Early De-escalation of Antimicrobial Therapy on Risk of Clostridioides difficile Infection following Enterobacteriaceae Bloodstream Infections. Clin Infect Dis. 2018 Oct 12;
9. Timbrook TT, Morton JB, McConeghy KW, Caffrey AR, Mylonakis E, LaPlante KL. The Effect of Molecular Rapid Diagnostic Testing on Clinical Outcomes in Bloodstream Infections: A Systematic Review and Meta-analysis. Clin Infect Dis. 2017 Jan 1;64(1):15–23.