

# For Bloodstream Infections, Rapid Molecular Testing Improves Patient Outcomes and Lowers Costs

Bloodstream infections are a potentially deadly scenario for healthcare facilities. They can be caused by a wide range of pathogens, making testing difficult. But they also require urgent treatment — patients with sepsis, for example, face a 7.6% increase in risk of death for each hour that optimal treatment is delayed.<sup>1</sup> Finally, these infections are increasingly associated with the antibiotic resistance crisis.

One of the biggest obstacles to improving the diagnosis of bloodstream infections is how long it takes to receive clinically actionable results. After blood cultures come back positive, clinical lab teams perform conventional ID and susceptibility testing that can take two to four days to generate useful information about the pathogen species and any relevant drug resistance. That's simply too much of a delay to contribute meaningfully to treatment selection. Consequently, patients with positive blood cultures are often given unnecessary antibiotics, or are relegated to empiric therapy that often isn't as effective as a more targeted treatment.

Rapid molecular testing has made it possible to dramatically accelerate time to results for bloodstream infection cases. Studies, conducted at institutions ranging from large academic medical centers to small community hospitals, have demonstrated that the ability to get bloodstream infection results as much as two days earlier enables medical teams to take patients off the wrong treatments and put them on more effective treatments sooner. That two-day difference alone has a measurable impact on shortening hospital stays, reducing readmission rates, and lowering overall healthcare costs.

## Rapid Diagnostics

Two tests designed for the VERIGENE® System — the VERIGENE® Gram-Positive Blood Culture (BC-GP) Test and the VERIGENE® Gram-Negative Blood Culture (BC-GN) Test — have been cited in dozens of peer-reviewed publications showing how faster results improve patient care. The VERIGENE System functions as a supplement to the initial blood cultures routinely run in hospitals. Once a blood culture shows positive results, clinical laboratorians deploy the VERIGENE rapid molecular testing platform, which identifies genus, species, and genetic resistance markers directly from positive blood culture bottles in just 2.5 hours.

The VERIGENE BC-GP Test detects up to 13 Gram-positive bacteria, while the VERIGENE BC-GN Test can identify up to nine

Gram-negative bacteria. Both tests also detect several markers of antibiotic resistance. These tests together detect 90% to 95% of what causes Gram-positive and Gram-negative bloodstream infections.

Results from these tests can be used with the local antibiogram to guide treatment selection, based on the pathogen identified as well as drug-resistance profiles. Just as importantly, they can be used to recommend no treatment. For example, Gram-positive bacteria are a common source of contamination during blood draws; they lead to a number of positive blood cultures that are not clinically relevant. In facilities without rapid testing, physicians typically treat these patients with antibiotics, contributing to the antibiotic resistance epidemic. Rapid results from VERIGENE bloodstream infection tests can quickly highlight contaminants, making it possible to avoid unnecessary use of antibiotics.

## Patient Outcomes

VERIGENE tests for bloodstream infection cases are widely used in clinical laboratories and have been covered in a large number of studies. The impact of these tests on reducing hospital stay durations and guiding treatment selection more quickly has been well documented.

One particularly impressive study came from a team at Children's Hospital Los Angeles and the University of Southern California. The effort represented a five-year analysis of the VERIGENE BC-GP Test on more than 1,600 samples since the test was implemented in 2013.<sup>2</sup>

Of the samples tested, the VERIGENE panel detected one or more targets in 1,520 of them, or nearly 93%. Almost 5% of the total cultures were ones where the test correctly detected no targets because the pathogen present was not included in the panel. "Of the 1,636 positive blood cultures with [VERIGENE] results, there was 99.8% [positive percent agreement (PPA)] compared to conventional methods for identification to genus and 94.3% PPA to species level," the authors reported in their publication.

The team also analyzed resistance marker results from the test, comparing them to data from conventional antimicrobial susceptibility testing. MRSA, MRSE, and vancomycin-resistant *Enterococcus faecium* all had PPA of 100%. The authors concluded that the test "demonstrated excellent performance and clinicians can confidently de-escalate antimicrobial therapy in the absence of

*mecA* and *vanA/B* gene.” They also noted the importance of using “a highly accurate and trustworthy test” since these results play such an important role in guiding patient care. As the authors report, “This study demonstrates the suitability and dependability of using genotypic resistance detection to accurately forecast phenotypic resistance in patients with staphylococcal or enterococcal bacteremia.”

In another study performed across multiple Scripps Health sites, including community hospitals in San Diego, pharmacists found that the VERIGENE BC-GN Test was an important component for antimicrobial stewardship efforts to reduce the unnecessary use of heavy-duty antibiotics.<sup>3</sup> More than 1,000 patients were included in the study, half diagnosed with the VERIGENE test and half using conventional methods. The use of antipseudomonal antibiotics decreased and the use of more targeted antibiotics increased substantially for patients tested with rapid molecular diagnostics. Having more information to guide treatment sooner led to demonstrably shorter stays in the ICU.

In one final example, pharmacy and clinical lab experts from the Cleveland Clinic evaluated the VERIGENE BC-GN Test, comparing 421 patients treated after test implementation to 456 patients treated with conventional testing.<sup>4</sup> With rapid diagnostics, physicians were able to get patients on the correct antimicrobial treatment or take them off ineffective therapies nearly 16 hours sooner. These patients also saw shorter hospital stays; on average they were released about two days, or 20%, earlier than patients who did not get rapid testing.

## Healthcare Costs

Beyond the clear improvement in patient outcomes, evaluations of rapid molecular testing have also shown that VERIGENE blood culture tests can significantly reduce overall healthcare costs.

One study came from Blount Memorial Hospital in Maryville, Tenn. The non-teaching community hospital adopted the VERIGENE BC-GP Test in an attempt to reduce the two- to four-day turnaround time that was standard with conventional blood culture testing.<sup>5</sup> The facility typically runs about 900 blood cultures each year.

For this evaluation, Clinical Pharmacy Specialist Brad Crane compared a three-month period of using the rapid assay to the same three-month period from the prior year. The Blount Memorial team saw many of the same patient care benefits as other facilities, including shorter times for getting on the right treatment and a 40% reduction in the length of ICU stays. But Crane also investigated financial implications. In the three-month pilot period, antibiotic expenditures went down by \$11,000 and overall hospital costs were reduced by \$159,000 — changes that could be directly attributed to the implementation of rapid testing. For this small hospital, Crane calculated the annual estimated savings to be more than \$600,000, even after factoring in the additional cost of the rapid diagnostics.

## Conclusion

The studies cited here represent just a small fraction of the total number of published evaluations featuring VERIGENE blood culture tests. Collectively, they demonstrate that a reliable, rapid molecular diagnostics approach to testing bloodstream infections delivers noticeable improvements in patient outcomes and reductions in healthcare expenditures. Thanks to faster pathogen identification and antibiotic resistance results, medical teams can get patients on the right treatments faster, reducing hospital stays as well as unnecessary antibiotic use.

Many of these studies were performed in conjunction with antimicrobial stewardship programs. These important efforts to rein in the spread of antibiotic resistance also benefit from getting accurate, trustworthy information sooner. Rapid testing can inform isolation protocols and other precautions taken with sick patients, and makes it possible to de-escalate antibiotic interventions based on robust evidence.

VERIGENE blood culture tests are a compelling option for clinical labs at large academic medical centers, small community hospitals, and everything in between.

### Snapshot: VERIGENE Tests in Action

Several recent publications and posters help to illustrate the use of VERIGENE bloodstream infection tests. Here’s a sampling of highlights.

#### **Impact of Rapid Identification of Positive Blood Cultures Using the VERIGENE System on Antibiotic Prescriptions: A Prospective Study of Community-onset Bacteremia in a Tertiary Hospital in Japan**

Scientists from the National Center for Global Health and Medicine in Tokyo performed a prospective study of 177 patients with community-onset bacteremia to understand the effects on antibiotic prescriptions when rapid testing was available.<sup>6</sup> The team found that VERIGENE test results were reliable and accurate — both for species identification and for detecting antimicrobial resistance — and that getting rapid answers changed the selection of antibiotic in 27.6% of cases.

The VERIGENE System reduced time to results by more than 2.5 days compared to conventional tests.

#### **Validation of an Antimicrobial Stewardship Driven VERIGENE Blood-Culture Gram-Negative Treatment Algorithm to Improve Appropriateness of Antibiotics**

Pharmacists at the University of Maryland formulated an antibiotic treatment algorithm for antimicrobial stewardship based on rapid diagnostics for Gram-negative bacteremia and evaluated its utility in this study of 188 patients with the VERIGENE Blood Culture Gram-Negative test.<sup>7</sup> Results showed that the algorithm would have increased the number of patients receiving appropriate antibiotic therapy by more than 10%: 88.4% would have been treated appropriately with rapid diagnostics compared to 78.1% with conventional tests. Much of that change would have occurred through evidence-based de-escalation of treatment.

## Snapshot: VERIGENE Tests in Action

### Impact of the VERIGENE Rapid Diagnostic Blood Test as an Antibiotic Stewardship Tool Amongst Hospitalized Patients in a Community Healthcare System

Pharmacy clinicians at community hospitals in Florida teamed up to review the effects of rapid diagnostic testing on how quickly patients were prescribed antibiotics and how long the course of treatment lasted.<sup>8</sup> They studied more than 400 patients across 10 hospitals, about half with and half without diagnostic testing using the VERIGENE blood culture nucleic acid test for Gram-positive and Gram-negative pathogens and contaminants. The authors found that mean time to receive appropriate antibiotics was 18 hours faster for patients who got VERIGENE testing, a reduction of about 30%. Other metrics improved as well: VERIGENE-tested patients had much shorter durations of antibiotics for contaminants, lower readmission rates 30 days after treatment, and fewer cases of *C. difficile* infections.

### Efficiency of the VERIGENE Blood Culture System on Time to Infection Control Barrier Precautions in Bacteremic Patients with Multi-Drug Resistant Organisms

This poster from clinicians at Drexel University and Hahnemann University Hospital in Philadelphia reported the results of a study evaluating how quickly infection control barrier precautions can be implemented for patients with multi-drug-resistant (MDR) infections.<sup>9</sup> They compared response with and without rapid diagnostic testing, using the VERIGENE Blood Culture Tests. After studying nearly 60 cases, the team found that diagnostic testing with VERIGENE allowed them to reduce the average response time from nearly 29 hours to a little more than four hours. This means a full extra day of better protection for people around infected patients, with “potential implications for improved efforts to reduce the spread and transmission of healthcare associated MDR infections,” the authors conclude.

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