

Implementing a real-time PCR assay for rapid surveillance of MRSA

By David Persing, MD, PhD, and Ellen Jo Baron, PhD

Most healthcare institutions in the United States have been watching an ominous trend of escalating proportions of methicillin-resistant *Staphylococcus aureus* infections. According to the Centers for Disease Control and Prevention, more people in the United States die annually from MRSA (estimated 18,650 deaths) than from AIDS (roughly 16,000 deaths).¹

In addition to loss of life, MRSA costs the American healthcare system over \$ 2.5 billion in non-reimbursable costs.² In terms of the healthcare setting, MRSA infection rates have increased over the past three decades — in 1974, MRSA accounted for 2% of staph infections; in 2004 the number rose to 63%.³

In healthcare environments, MRSA is spread from patients who already have an MRSA infection or who are colonized with the bacterium but do not have any symptoms. The harmful pathogen is passed to other patients through hand-to-hand contact or by touching contaminated surfaces such as bed rails or telephones.

Many institutions have begun selective testing of some patients believed to be at higher risk. Several commercial

chromogenic agar plates have been developed to culture nasal swabs for active surveillance of MRSA. Even with the most rapid culture turnaround time, however, results from cultures are not available for at least 18 hours after inoculation of the medium. Such results could reach the unit more than a day after a colonized patient has been sharing a room with a non-colonized patient.

Moving the non-colonized patient into another room at this point can be a social and public-relations nightmare for patients, their families, and hospital administrators. The alternative, instituting barrier precautions pre-emptively on all patients until their MRSA status is known, is costly and problematic; despite the success of this strategy in controlling MRSA in Denmark and the Netherlands, not all healthcare institutions in the United States have that capacity.

Selective testing of patients based on some risk assessment has been shown to detect less than 85% of the colonized patients in a hospital⁴; and the elaborate admission interview required to determine who might be at risk is counterproductive, disliked by nursing staff, and slows

down admissions. Even less effective is passive surveillance, in which MRSA carrying patients are discovered and isolated only if cultures sent to the clinical laboratory yield MRSA. This approach fails to identify 70% of truly colonized patients.⁵

As MRSA outbreaks are widely reported in the news media, the public's fears are increasing, putting pressure on policymakers to address the issue. Already five states have enacted legislation mandating surveillance of MRSA for high-risk units in a hospital, and 31 states have reporting requirements.

Many hospitals are now implementing systems that use fully integrated real-time PCR technology, in most cases for the purpose of implementing rapid MRSA surveillance as part of their overall infection-control program. Major advantages of such a system is a MRSA test available in cartridge form with (1) its ability to process and deliver results in less than one hour, enabling physicians to take the appropriate precautions before the pathogen has the opportunity to spread, and (2) its moderate complexity, allowing a non-clinical laboratory scientist to perform the test.

The new technology combines on-board sample preparation with real-time PCR amplification and detection functions for fully integrated and automated nucleic-acid analysis. Training to use a moderate complexity test is easy, and less experienced workers can perform such tests with minimal hands-on time. With a random-access system, a new sample can be added at any time. In many laboratories, the combination of ease of use and random access translates into 24/7 access to MRSA results.

Nearly 450 U.S. hospitals (and over 900 worldwide) to date have chosen to deploy this technology, and laboratory technicians and technologists have voiced their satisfaction with the simplicity of the system's workflow and its proven results.

Leaders at sites that have implemented the MRSA assay have been able to reduce infection rates and cut healthcare-associated costs while improving patient care.

How are hospitals using rapid testing technology?

"The patients with the highest risk of MRSA infection are those who undergo invasive surgeries making it a serious concern for our orthopedic hospital" says Maureen Spencer, RN, MEd, CIC infection-control manager at New England Baptist Hospital in Boston. "Following invasive orthopedic surgical procedures, post-operative surgical wounds are vulnerable to infection — particularly bone infections which are among the toughest to treat.



"We were one of the first sites in the United States to implement a pre-screening program for all surgical patients for MRSA. When selecting a pre-screening program, time to result is a huge factor. It is critical that patients know their MRSA status before they leave their surgical consult in order to initiate a topical decolonization protocol and allow the surgeon to adjust the surgical antibiotic prophylaxis. Using the MRSA assay and the system, we proactively screen all surgical patients for MRSA at least two weeks prior to their procedure. If they are colonized with staph, doctors place the patients on a five-day decolonization protocol and conduct a second screening for MRSA before admission to the hospital for surgery. The goal is to reduce the introduction of MRSA into the hospital by ensuring patients are MRSA-free before they are admitted.

"Our data is showing that pre-screening surgical patients for MRSA lowers infection rates, creating a win-win situation for the hospital and patients. Since implementing the first PCR test in July of 2006 and moving to the MRSA test in early 2007, our hospital saw MRSA infection rates drop nearly 60%; from 0.46% to 0.18% in 2007 and decreasing further to 0.11% in 2008. This has helped the hospital decrease its orthopedic surgery hospital-acquired infection rates to 0.3% which is five times lower than the average national rate of 1.5%."

In Wooster, OH, Gail Woosley, manager of Lab Services for Wooster Community Hospital says, "The goal of our infection-control program is to lower healthcare-acquired infection rates and improve patient care by delivering physicians the test results they need as quickly as possible. In my 33 years in the field, it is not often that I am impressed by some of the new technology being made available, but this system really impressed me. Relative to other lab equipment, the new system technology is affordable, even for a small institution. If you have a device that can save you money in terms of patient time in the hospital, supplies used during their hospital stay, and the health of the patient, its value is not measurable.

"We find that technology to be very useful in three patient population groups.

- The first group includes individuals that are having any type of surgery where a foreign body will remain within the patient such as joint replacement or hernia repairs.
- Our second and largest group includes those coming to us from another healthcare facility. These people are screened upon admission and then placed in the appropriate room with the appropriate precautions. The rapid turnaround time allows us to identify which patients are colonized, enabling us to place that at-risk patient in isolation in order to curb the spread of the infection. Traditional turnaround time prevented us from taking these measures which were necessary

because we still have semiprivate rooms in our institution.

- Our final group includes those individuals that have been admitted patients in our facility but return for re-admission. If this happens within 45 days from discharge, we test upon readmission."

In Stockton, CA, Richard Wong, administrative director of Pathology and Clinical Laboratory for Dameron Hospital, says, "We have been at the forefront in the San Joaquin Valley with regard to active surveillance on multidrug-resistant organisms since the 1987 implementation of its first screening program.

"Technology has allowed us to expand and improve on our infection-control methods as the nationwide threat of hospital-acquired infections grows. The MRSA test delivers the fastest time to result available today, making it an ideal technology for our critical initiative, allowing us to reduce hospital-acquired infection rates and provide the highest standards of patient safety.

On average, our hospital runs about 480 MRSA tests per month with plans to increase as we move towards universal screening of all patients who enter the site. Of importance, we have found the MRSA assay is 100% sensitive compared to culture-based tests."

More recently tests approved for the system we use include a combined test for *S aureus* (usually methicillin sensitive) and MRSA in blood cultures from patients with suspected sepsis, and a similar test for direct detection of both organisms in skin and soft-tissue infections. Both tests deliver results in less than one hour and their results can be used in real-time to guide optimal treatment or management decisions. Other tests in development that are relevant to infection control include a test for VRE, *Clostridium difficile*, and multidrug-resistant tuberculosis. It is becoming increasingly clear that the medical value of rapidly available, actionable results provided by the new technology can be an important ally in the "search-and-destroy" strategy being adopted by more and more hospitals. □

David Persing, MD, PhD, is the executive VP and chief medical and technology officer for Cepheid. **Ellen Jo Baron, PhD**, is director of Medical Affairs for Cepheid. The systems and tests for which Cepheid is well-known are its GeneXpert System and its accompanying MRSA/*S Aureus* test.

References

1. Klevens RM, Morrison MA, Nadle J, et al. Invasive Methicillin-Resistant *Staphylococcus aureus* Infections in the United States. *JAMA*. 2007;298:1763-1771.
2. The Centers for Disease Control and Prevention. <http://www.cdc.gov/mrsa/>. Accessed October, 17, 2007.
3. The Centers for Disease Control and Prevention. <http://www.cdc.gov/mrsa/>. Accessed October 3, 2007.
4. Robiscek A, Beaumont JL, Paule SM, et al. 2008. Universal Surveillance for Methicillin-Resistant *Staphylococcus aureus* *Annals Intern Med*. 148:409-419.
5. Bootsma MC, Diekmann O, Bonten MJ. Controlling methicillin-resistant *Staphylococcus aureus*: Quantifying the effects of interventions and rapid diagnostic testing. *PNAS*. 103:5

MLO's Continuing Education Test is available online only. Print out and mail a copy with your check, or use the new online CE test and convenient online payment feature available through the auspices of Northern Illinois University. Go to www.mlo-online.com and look under CE Tests.

PETRI PLATE STREAKING SYSTEM



The ISOPLATER® Petri plate streaking machine reduces costs and boosts productivity by automatically loading, streaking and stacking up to 180 pre-inoculated Petri dishes per hour. Standardized streaks in four successive quadrants maximize isolation and yield consistent results. Operation occurs in a contained negative pressure area and exhaust air is HEPA-filtered to protect personnel. To get automated results, reduce costs and improve your workflow with the ISOPLATER®, contact:

Vista Technology Inc.
8432-45 St., Edmonton, Alberta, Canada T6B 2N6
Phone: 780-468-0020 Fax: 780-465-9732
Toll-free: 888-468-0020 Email: MLO2008@vistatechnology.com



Vista Technology Inc.