Quicker, Simpler Tests Sought for MRSA Screening

Identifying colonized patients prior to or during hospitalization helps contain resistant bacteria.

BY BETSY BATES
Los Angeles Bureau

Researchers at the Mayo Clinic and elsewhere are racing to develop rapid-detection tests for *Staphylococcus aureus*, both to better tailor appropriate antibiotic prescribing and to halt the galloping spread of methicillin-resistant strains of the bacteria.

"There are many companies now developing rapid tests," Betsy McCaughey, Ph.D., said in an interview.

Among the contenders are Innovative Biosensors Inc. in College Park, Md., which is using light-based technology developed at the Massachusetts Institute of Technology; Cepheid, a Sunnyvale, Calif.–based company about to introduce another genetic-based rapid test; and 3M, which has "waded deep into this territory," said Dr. McCaughey, director of the New York City–based nonprofit Committee to Reduce Infection Deaths.

Progress has been keenest in identifying colonized patients prior to or during hospitalization to help reduce the spread of resistant bacteria.

At the University of Maryland Medical Center in Baltimore, for example, patients considered at risk for methicillin-resistant *S. aureus* (MRSA) can be screened in 2 hours with a polymerase chain reaction (PCR) DNA test developed by Becton, Dickinson & Co., rather than waiting 24-48 hours to get an answer by culturing for the bacteria.

All intensive care unit patients are being screened at admission, on a weekly basis, and on discharge so that infected patients can be identified and treated with appropriate isolation and contact precautions, said Richard Venezia, Ph.D., professor of pathology and director of clinical microbiology at the university.

"This is the first of a generation of tests that are going to be using 'within-the-tube' closed systems," based on either DNA or immunology, that represent a major technological advance in the way risky bacteria are identified, Dr. Venezia said.

The tests do not require complex interpretation nor the level of training or sophisticated precautions against cross-contamination that were necessary with previous PCR procedures developed in research laboratories.

The new tests are currently confined to hospital or community laboratories, but Dr. Venezia said that they will almost certainly be available for bedside or community office practices within 5 years.

At the Mayo Clinic in Rochester, Minn., two swab-based PCR tests are being developed, one to signal the presence of *S. aureus* and the other to identify MRSA, Dr. Mark Pittelkow, professor of dermatology, said in an interview.

S. aureus is rapidly overcoming streptococcus as the bacteria of concern, Dr. Pittelkow said.

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DR. PITTELKOW

The Mayo tests, to be marketed by Roche Pharmaceuticals, use a specially designed swab that does not wick samples in the same way as a cotton-tipped swab. For now, it still requires laboratory technicians to transfer material from the applicator to a plate for analysis, but the technology is heading toward a self-contained swab similar to those used for rapid strep tests in physicians' offices.

The Becton, Dickinson & Co. test, available since early 2006, is approved only for detecting colonization, not to guide antibiotic choices in individual patients. It requires laboratories to make an initial investment of more than $20,000 for a real-time PCR cycler, plus $20-$30 for each test performed. The equipment, however, can be used to perform other cutting-edge tests for detection of influenza, respiratory syncytial virus, and vancomycin-resistant enterococci, Dr. Venezia said.

Rapid, practical, easy-to-perform tests for *S. aureus* will become even more necessary for hospitals, because the Centers for Medicare and Medicaid Services has proposed that Medicare diagnosis-related group reimbursements for nosocomial infections be stopped.

The advent of such restrictions on payments for hospital-acquired illnesses might lead some institutions to universally test patients on admission and throughout their stays. Treatment of an MRSA infection can run as much as $36,000, said Barbara Kalavik, director of worldwide public relations for Becton, Dickinson & Co.

Just who pays for the tests is still a matter of contention.

When a physician orders a test to pinpoint the best antibiotic to treat a patient, the cost can be charged to the patient or insurance. Who will bear the cost of screening hospital patients is less clear, Ms. Kalavik said.

"Most hospitals absorb the cost of these programs," she said, but "starting Jan. 1, 2007, new CPT codes have been instituted that allow for hospitals to be reimbursed approximately $49 for screening outpatients" for MRSA. ■

Pneumonia Caused by MRSA Can Have Rapid, Deadly Course

Be alert for severe cases of community-acquired pneumonia that might be caused by methicillin-resistant *Staphylococcus aureus*, the Centers for Disease Control and Prevention advised.

Although uncommon, community-acquired pneumonia (CAP) can be caused by methicillin-resistant *S. aureus* (MRSA). Such cases often affect young, otherwise healthy individuals and can be rapidly fatal. MRSA should be suspected in patients with severe pneumonia, especially during the influenza season, and in those with cavitary infiltrates. The index of suspicion for MRSA CAP should be particularly increased in those who have a history of MRSA skin infection or who have had close contact with MRSA-infected individuals, the CDC said (MMWR 2007;56:325-9).

During December 2006 to January 2007, 10 cases of severe MRSA CAP were reported to the CDC from Louisiana and Georgia. Patient ages ranged from 4 months to 48 years; eight were younger than 30 years. Five were female and five male. Six of the 10 patients died, including 4 children aged 8-14 years.

One patient had a history of chronic hepatitis C and hypertension, and two were current smokers. Four had documentation of recent MRSA skin and soft-tissue infection or were living with someone who did. In all 10 cases, influenzalike illness had been diagnosed prior to or concurrent with CAP. Six patients had laboratory-confirmed influenza. Of six for whom vaccination status was available, none had received influenza vaccine for the 2006-2007 season. Radiologic information, available for all 10 patients, showed unilobar infiltrates in 3 and multilobar infiltrates in 7. In three patients, MRSA was isolated from sputum only.

Particularly notable was the short period between any respiratory symptom onset and either death or recovery of MRSA from the patient: Respiratory symptoms began a median of 3 days (range 2-6 days) before collection of specimens that grew MRSA. Of the six patients who died, the median period from onset to death was 3.5 days (range 2-25 days); four of the six died within 4 days of symptom onset.

These short durations suggest that the influenza virus and the MRSA infections probably occurred concomitantly, the CDC noted.

—Miriam E. Tucker

Severity of CA-MRSA Pneumonia Linked to Panton-Valentine Toxin

BY KATE JOHNSON
Montreal Bureau

MONTREAL — The high mortality in community-acquired pneumonia caused by methicillin-resistant *Staphylococcus aureus* may be largely due to Panton-Valentine leukocidin toxin, said Dr. Ian Gould, consultant microbiologist at the University of Aberdeen (Scotland).

Thus, efforts to control the infection should probably focus on the toxin as well as the bacteria, Dr. Gould said at an international conference on community-acquired pneumonia. "Even if the antibiotics can kill the bug, the toxin's still there and that's what's doing the damage," he said in an interview at the meeting.

Panton-Valentine leukocidin (PVL) toxin is produced mostly by community-acquired, as opposed to hospital-acquired, strains of methicillin-resistant *S. aureus* (MRSA). And the prevalence is increasing, Dr. Gould said.

"Clearly, there have been big changes in the epidemiology of community-acquired MRSA, and now there are quite a few epidemic strains that produce PVL," he said. In fact, according to a recent report from the Centers for Disease Control, the majority of reported community-acquired MRSA infections are PVL-producing strains (MMWR 2007;56:325-9; see story at left.) Yet although most of these infections involve skin and soft tissue and are "relatively mild," according to Dr. Gould, "more and more commonly, we're seeing very severe respiratory disease." In the recent CDC report of 10 cases of MRSA-associated community acquired pneumonia (CAP), all isolates were positive for PVL toxin.

"This is an organism that causes severe pneumonia," said Dr. Coleman Rotstein, who also presented at the meeting, which was sponsored by the International Society of Chemotherapy. The key features of CAP caused by MRSA are empyema and necrotizing pneumonia, said Dr. Rotstein, professor of medicine at McMaster University, Hamilton, Ont.

He and other experts at the meeting agreed that treatment options are limited.

"When it comes to treatment, we are standing in the dark, with a case mortality in the published literature of around 75%," Dr. Gould said.

"For these new MRSA CAP etiologies, the present arsenal of antibiotics is unfortunately insufficient," said Dr. Ethan Rubenstein, who also presented at the meeting. He is professor and head of infectious diseases at the University of Manitoba, Winnipeg.

According to Dr. Gould, high-dose clindamycin or linezolid are good options not only for their antibacterial effects but also because of their potential ability to lower PVL production. IV immunoglobulin is also well recognized as an adjunct, he said. In addition, gentamicin is indicated for patients who are bacteremic.

"We haven't seen the end of this story by any means—this is a highly adaptable, rapidly developing organism," Dr. Gould said. "I have to say things are going to get worse here before they get better." ■