Stop Infections

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into six sections, with two focused on preventing infection from the specific organisms *C. difficile* and methicillin-resistant *Staphylococcus aureus*.

The document's other four sections address the device- and procedure-associated health care–acquired infections that Medicare stopped reimbursing hospitals for on Oct. 1, 2008: central line–associated bloodstream infection, ventilator-associated pneumonia, catheter-associated urinary tract infection, and surgical site infection.

The recommendations are prioritized, starting with minimum basic practices that should be adopted by all acute care hospitals, followed by special approaches considered appropriate for use in locations and/or populations within hospitals when infections are not controlled using the basic practices.

"This whole approach, of which *C. difficile* is a major part, is an attempt to help hospitals delve through the barrage of different recommendations in this area and come up with a practical, easy-to-handle approach," Dr. Classen said at the meeting. ■

The full text of the compendium is available at www.journals.uchicago.edu/toc/iche/2008/29/s1.

Rapid Test Flags Staph. aureus *And Methicillin Susceptibility*

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — A single-use bacteriophage amplification test kit was able to both accurately identify *Staphylococcus aureus* and determine whether it was methicillin sensitive or resistant within 5 hours in a study of clinical bacteremia isolates.

The findings suggest that it is possible to slash the diagnostic time for bacteremia—from 2-3 days to 5 hours—and obtain rapid results that will guide treatment and prevent overuse of broad-spectrum antibiotics, Dr. J. Drew Smith said in an interview during his poster presentation at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

The new bacteriophage amplification test 'is flexible with respect to read times, allowing it to be adapted to a variety of testing and reporting schedules.'

The test, made by MicroPhage Inc., uses bacteriophage amplification technology, which detects proteins produced by viruses that are selected to amplify in response to *S. aureus*. Blood culture samples are mixed in two separate tubes and placed in an incubator for 5 hours. The tubes are removed and six drops of each sample are applied to dipstick-type detectors similar to those used in home pregnancy tests. One tube determines whether or not the sample contains *S. aureus*; the other determines whether the bacteria are antibiotic resistant or susceptible, said Dr. Smith, director of research and development at MicroPhage.

In a panel of 120 *S. aureus* clinical isolates and 120 closely related nonpathogenic coagulase-negative staphylococci, the identity test for *S. aureus* had a sensitivity of 93% and a specificity of 96%. Among the strains identified as *S. aureus*, methicillin susceptibility was determined with 99% sensitivity and 99% specificity. Only 1.8% of samples were falsely identified as methicillin-resistant *S. aureus* (MRSA) and no samples were falsely identified as methicillin sensitive (MSSA), Dr. Smith and his associates reported.

Current polymerase chain reaction (PCR) technology allows for rapid detection of MRSA but doesn't accurately determine susceptibility. With the bacteriophage test, a result indicating MSSA allows for the patient to be safely switched from empiric vancomycin to nafcillin or another conventional β-lactam antibiotic, which are more effective against *S. aureus* than is vancomycin and can reduce mortality by 30%-50% if the organism is susceptible. The PCR test gives too many false positives for MSSA in order to be used for this purpose, Dr. Smith explained in the interview.

Bacteriophage amplification also could be used to screen patients for MRSA carriage. In a separate study presented in another poster, nasal swabs collected from preoperative and ICU patients were streaked on agar plates for MRSA detection. The swabs were transferred to MicroPhage tubes, incubated for 7-24 hours, and read in the same way as was done for the bacteremia test. This time, 32 samples were read at 7 and 24 hours and 77 were read at 12-18 hours and again at 18-24 hours. (More time is needed for nasal swabs than blood cultures because fewer bacteria are present, Dr. Smith explained.)

Sensitivity for detecting MRSA nasal carriage was 33% at 7 hours, 92% at 12-18 hours, and 100% at 18-24 hours. Specificity was 100% at 7 hours and 98% at 12-18 and 18-24 hours. Positive predictive value was 100% at 7 hours and 88% by 18-24 hours; negative predictive value rose from 94% at 7 hours to 100% at 18-24 hours.

Lab personnel were trained to use the test in less than half an hour, and it required no specialized or dedicated equipment. Moreover, "the test is flexible with respect to read times, allowing it to be adapted to a variety of testing and reporting schedules," the investigators said.

MicroPhage is hoping to market both uses for the technology to community hospitals and to offer the nasal tests to outpatient settings such as nursing homes or surgicenters. Clinical testing will begin in early 2009, and the company hopes to obtain licensure by early 2010, Dr. Smith said. ■

C. difficile Epidemic Still Poses Clinical Challenges

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — Rates of *Clostridium difficile* diarrhea have declined in Quebec since the 2003-2004 outbreak of a new highly transmissible and lethal strain, but infectious disease experts do not believe this means that the disease has peaked in North America.

"Personally, I'm a bit pessimistic. I think the property of this specific strain is such that it will persist for a long time," Dr. Jacques Pepin of the University of Sherbrooke (Que.), said at a press briefing during the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

Dr. Dale N. Gerding of Hines Veterans Affairs Hospital, Chicago, agrees. "Have we hit the peak of the epidemic yet? In the United States, I don't think we have."

The strain is now present in all 50 U.S. states and is largely responsible for the changing epidemiology of *C. difficile* infection (CDI), noted Dr. L. Clifford McDonald of the Centers for Disease Control and Prevention, who first reported the appearance of the strain in six U.S. states in 2005 (N. Engl. J. Med. 2005;353:2433-41.

Recent studies suggest that the strain is present in 30%-50% of U.S. isolates, but the lack of national surveillance data makes it difficult to monitor. It is estimated that in 2006 more than 500,000 total CDI cases resulted—directly or indirectly—in more than 15,000 deaths. "There is marked geographic variation in rates of cases and deaths. It's [affected] by the age of the population," Dr. McDonald said in a symposium held during the meeting.

Hospital survey data suggest that the rate of discharges with *C. difficile* listed as a diagnosis for short-stay patients rose from 30.7/100,000 population in 1996 to 77.3/100,000 in 2006, a slight decline from the 84.8/100,000 seen in 2005. National inpatient survey samples show a similar trend. There appears to be a slight leveling off, but it's far too soon to declare the epidemic over, Dr. McDonald said.

In a prospective study conducted at 12 Quebec hospitals, there were 1,703 CDI patients, with an incidence of 22.5 per 1,000 admissions and an 30-day attributable mortality rate of 6.9% (N. Engl. J. Med. 2005;353:2442-9).

The Quebec outbreak represented the first multihospital epidemic of a new strain of *C. difficile*. Since the peak years of 2003-2004, the incidence has yet to fall back to what it was before the outbreak. Before the strain arrived, death certificates listed about 100 deaths per year caused by *C. difficile*. That rose to about 700 deaths per year during the outbreak, and is now about 400. The population of Quebec is about 7 million, so an extrapolation to the United States would equal about 100,000 deaths, Dr. Pepin said.

"The new strain is not going to disappear. The proportion of cases caused by this strain has remained stable. It's possible to reduce the incidence, but I don't think we will ever get back to the incidence levels we had prior to that unless we have a vaccine," he said.

The current treatments of choice for *C. difficile*—vancomycin and metronidazole—have been used for 30 years, Dr. Gerding noted. Recent data suggest that metronidazole does not work as well as it used to, particularly in severely ill patients. But concern about the disease has led to increased research into antimicrobial agents as well as unconventional approaches such as toxin binders, monoclonal antibodies, and "biotherapeutic" treatments such as fecal transfusions.

"It's a desperate situation and we need new treatment approaches," he said.

Improvements in diagnostic testing will also be needed, said Dr. Lance R. Peterson, director of microbiology and infectious disease research at NorthShore University HealthSystem, Evanston, Ill., who also spoke at the symposium.

About 20% of all hospitalized patients have loose stools, most of which are not infected with *C. difficile*. Current enzyme immunoassays give rapid results, but their sensitivity is only about 70-80%, with a 3-5% false-positive rate. The error rates among the current tests have led to confusion in the literature regarding the epidemiology of the disease. The confusion includes controversy over whether proton pump inhibitors are related to *C. difficile* and whether some strains may not be related to antimicrobial use.

New molecular diagnostics include real-time polymerase chain reaction (PCR) tests, which can accurately detect 95%-98% of *C. difficile* infections within 2 hours. At least three companies are developing commercial versions of the test.

"We're starting to have a rapid test that's useful. … This will be imperative to understand the epidemiology of this changing emerging infection going forward," said Dr. Peterson, who also is professor of pathology and medicine at Northwestern University, Chicago.

The new emphasis on prevention of health care–acquired infections could make a difference, Dr. McDonald noted. The CDC is working with hospitals to prevent outbreaks by revising antimicrobial prescribing practices as well as environmental efforts, such as using gowns and enforcing hand-washing rules. "Data suggest that many more cases of CDI can be prevented than we currently realize. … It seems like it's something that will require a new way of doing business with regard to infection-control measures."

Dr. Pepin is on the advisory board for Acambis, which is developing a *C. difficile* vaccine. Dr. Gerding holds patents for the treatment and prevention of CDI licensed to ViroPharma Inc., and is a consultant for and/or holds research grants from several companies. Dr. Peterson has received research funding and/or consulting fees from several companies and the National Institutes of Health. Dr. McDonald reported having nothing to disclose. ■