Altered Bacteriophages May Curb Hospital MRSA

BY BRUCE JANCIN
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LISBON — MRSA, you may have met your match.

Immobilized bacteriophages offer a novel solution to the relentlessly growing problem of hospital-acquired infection with methicillin-resistant *Staphylococcus aureus*, Michael Mattey, Ph.D., said at the 12th International Congress on Infectious Diseases.

Bacteriophages are highly effective bacteria killers. Until recently, however, their use in medical settings has been impractical because in nature these viruses are effective only in water.

That hurdle has now been overcome. A British biotech company, Blaze Venture Technologies, has developed a stabilized bacteriophage that's immobilized on cosmetic-grade, 10-micrometer nylon beads. These are naturally occurring bacteriophage isolates selective for MRSA that have been altered so they can withstand dehydration.

When a powder of the microscopic phage-coated beads is poured into standard medical cleaning products used to wipe down hospital surfaces, MRSA is killed on contact. Better yet, after the cleanser has dried, the phages left behind remain active for 2 weeks at room temperature, preventing reintroduction of MRSA on treated wards, explained Dr. Mattey, a Blaze employee who also is at the University of Strathclyde, Glasgow, which holds a general patent on bacteriophage-immobilization technology.

Wiping down hospital surfaces with cleaning solutions that contain phage-coated beads kills MRSA on contact.

DR. MATTEY

Current approaches to the MRSA problem entail treating infected patients with drugs to which the bacteria remain sensitive. That applies pressure to breed further resistance, with eventual loss of antibiotic effectiveness. In contrast, the strategy underlying immobilized bacteriophages involves reversal of antibiotic resistance through selective control aimed at taking away the MRSA strains' evolutionary advantage.

"Really, the whole idea is, 'Let's breed better bacteria,' " he said in an interview. The prevalence of MRSA among *S. aureus* strains is increasing at about 3.5% annually in hospitals in the United States and Europe.

"So if you got rid of 3.5% of the [bacterial] parents with MRSA, you would stabilize things. And if you got rid of more than 3.5%, you'd reverse the MRSA problem," Dr. Mattey said at the meeting sponsored by the International Society for Infectious Diseases. Indeed, mathematical models indicate that with a 6% annual kill rate of MRSA, the prevalence of resistant strains would drop from 60% to essentially zero in a 25-year period.

Immobilized MRSA-hunting bacteriophages are attractive not only as an additive for cleaning solutions, but also for hand cleansers, impregnated wipes, and sprays. The Blaze cleaning products are currently undergoing testing to establish their safety. Dr. Mattey expects European agency approval for use in hospitals in 2-3 years.

MRSA will be the initial target of the bacteriophage-enhanced medical cleaning products simply because MRSA is such an important problem. But bacteriophage isolates selective for virtually any antibiotic-resistant bacteria can be developed. And it takes only about 36 hours to culture bacteriophages that will counter new mutant MRSA strains—versus a decade to develop a new antibiotic.

Blaze initially is moving into the medical cleaning market because of the pressing need coupled with the fact that the regulatory bar is set relatively low, with only a demonstration of product safety required. But company scientists have other irons in the fire.

The same phage technology has been used to develop a 10-minute MRSA-screening device as an alternative to conventional MRSA testing, which requires culturing patient swabs for several days. Early detection and containment of MRSA outbreaks has the potential to dramatically reduce nosocomial infection rates. The company is gearing up for field trials of the point-of-care device through two U.K. National Health Service trusts.

In addition to MRSA, the sensor can be used to detect a wide range of other problem bacteria by using cards coated with bacteriophages selective for that particular organism.

Blaze also is developing therapeutic applications for the stabilized bacteriophages. Surgical suture material impregnated with immobilized phage has been "very successful" at preventing serious wound infections in animal studies, according to Dr. Mattey.

In addition, Blaze scientists have conducted positive proof-of-concept animal studies involving injection of phage-bearing 5-micrometer nylon beads for treatment of septicemia.

"In human studies, we won't be injecting nylon beads. We'll use the sort of polymers used in biodegradable sutures that break down in a week or two," the biologist said. ■

Urban Hospital Sees High Rate Of Treatment Failure for MRSA

BY DOUG BRUNK
San Diego Bureau

SAN FRANCISCO — A quarter of adult patients who completed the recommended initial therapy for methicillin-resistant *Staphylococcus aureus* infection experienced clinical failure, results from an urban hospital study showed.

In addition, among a subset of patients who had osteomyelitis, 46% relapsed.

"We have a high rate of failure of treating MRSA infections in this urban population, especially among people with bone infections," Dr. Julie Dombrowski said in an interview during a poster session at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy. "Even with appropriate standard-of-care treatment at this time, which is IV vancomycin for bone infection, we still are having failures. We need better antibiotics or different antibiotics."

The researchers reviewed the clinical data from 215 patients at San Francisco General Hospital who completed the recommended therapy for MRSA infections between 1998 and 2004.

Of the 215 patients, 54 (25%) had infections at more than one site. There were 81 cases of osteomyelitis (38%); 60 cases of bloodstream infections without endocarditis (28%); 45 cases of pneumonia (21%); 32 cases of endocarditis (15%); 23 joint infections (11%); 18 epidural abscesses (8%); 15 surgical wound infections (7%); and 1 case of meningitis (0.5%).

The most common comorbidities were diabetes (19%) and HIV (14%). About a third of patients (34%) were homeless, 46% reported they used injection drugs, and 26% reported they abused alcohol, said Dr. Dombrowski, of the department of medicine at the University of California, San Francisco.

She also reported that 53 patients (25%) failed initial antibiotic therapy. Vancomycin monotherapy was used in 159 of the patients (74%), whereas rifampin and gentamicin were the antibiotics used most commonly in combination with vancomycin (in 12% and 8% of cases, respectively.) Of the 81 patients who had osteomyelitis, 37 (46%) relapsed.

Bivariate analysis revealed that the following factors were associated with treatment failure: male gender, diabetes, injection drug use, ICU admission, admission to orthopedics, and pneumonia, endocarditis, or osteomyelitis.

Multivariate analysis of the data revealed that osteomyelitis was the only factor independently associated with treatment failure.

The degree of treatment failure seen in patients with osteomyelitis surprised Dr. Dombrowski. "I expected that we would have more failures among bone infections than other kinds of infections like endocarditis or pneumonia, but we were surprised that we weren't able to cure almost half of the bone infections," she said at the conference, which was sponsored by the American Society for Microbiology. ■

Detroit Center Finds CA-MRSA In 69% of Soft Tissue Infections

BY DOUG BRUNK
San Diego Bureau

SAN FRANCISCO — Methicillin resistance was noted in 69% of community-acquired soft tissue infections due to *Staphylococcus aureus* in a single-center study of hospitalized adults in Detroit.

Additionally, more than half of the community-acquired methicillin-resistant *Staphylococcus aureus* [MRSA] infections were associated with abscesses, Dr. Houssein Jahamy reported in a poster presented at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

MRSA was the etiologic agent in 136 (69%) of the 198 patients hospitalized with a soft tissue infection caused by *S. aureus* between Nov. 1, 2005 and June 1, 2006 at St. John Hospital and Medical Center in Detroit, reported Dr. Jahamy, a second-year infectious diseases fellow at the hospital. Abscesses were noted in 57% in the MRSA group and in 28% of those with methicillin-sensitive *S. aureus* infections.

"Right now we are seeing plenty of patients with community-acquired MRSA," Dr. Jahamy said in an interview. "Some show up at the hospital or clinic complaining of a spider bite." In most cases, the "spider bite" is a furuncle. "That's a big tip-off that they probably have community-acquired MRSA."

He and his associates reviewed the microbiology findings for all patients hospitalized with community-acquired soft tissue infections. They also collected information on demographics, comorbid conditions, type and location of initial lesion, and evidence of bloodstream invasion or other complications.

Compared with methicillin-susceptible *S. aureus* infections, those caused by MRSA were more likely to occur in women (77%) than in men (62%), in patients who did not have diabetes (73%) than in those with diabetes (60%), and in those who did not have a comorbidity (75%) than in those with comorbidities (65%). In line with findings that MRSA infections are more likely to be seen in patients with few comorbidities, MRSA-infected patients had shorter average hospital stays—6 days, compared with 8 days in those with methicillin-susceptible infections.

Dr. Jahamy and his coinvestigators observed no significant differences between the MRSA and methicillin-susceptible *S. aureus* groups in terms of history of spider bite (7% vs. 4%, respectively), infections that started as a furuncle (23% vs. 18%, respectively), or incidence of bloodstream invasion (6 vs. 9%, respectively).

Dr. Jahamy reported that he had no financial disclosures associated with the study. ■