Community-Associated Methicillin-Resistant *Staphylococcus aureus*

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Historically, infection with strains of methicillin-resistant *Staphylococcus aureus* (MRSA), which are usually multidrug-resistant, has been acquired by persons in hospitals, nursing homes, and other health care institutions. These infections are known as health care–associated MRSA infections. Community-associated MRSA (CA-MRSA) infection, which bears significant similarities to and differences from health care–associated MRSA infection, appears to be on the rise and has been described in several well-defined populations, such as children, incarcerated persons, Alaskan Natives, Native Americans, Pacific Islanders, sports participants, and military personnel. CA-MRSA infection has caused severe morbidity and death in otherwise healthy persons. Proven, reproducible strategies and programs for preventing the emergence and spread of CA-MRSA are lacking. Further surveillance and epidemiological and clinical studies on CA-MRSA infections are necessary for documenting the extent of the problem and for developing and evaluating effective prevention and control efforts.

Staphylococcus aureus is a common bacterium that causes a wide variety of infections, ranging from mild skin and soft-tissue infections to serious infections, such as sepsis and toxic shock syndrome, that can be fatal. Health care–associated methicillin-resistant *S. aureus* (HA-MRSA) infections have been recognized since the 1960s and are generally resistant to multiple antimicrobial drugs; until recently, HA-MRSA have been effectively susceptible only to vancomycin and now are also susceptible to linezolid and daptomycin, drugs approved in 2000 and 2003 for serious staphylococcal disease. More than 50% of infections caused by *S. aureus* in intensive care units and >40% of *S. aureus* infections outside the intensive care unit are MRSA infections [1].

As early as the 1980s, *S. aureus* strains were resistant to semisynthetic penicillins but were not multiply resistant to other important anti-staphylococcal drugs appeared in Australia and elsewhere. These infections have remained relatively infrequent until the past several years, when community-associated MRSA (CA-MRSA) infection appears to have increased in incidence, causing outbreaks in several well-defined populations, such as children, incarcerated persons, and participants in team sports, and causing sporadic infections.

CA-MRSA differs from HA-MRSA in several important ways (table 1). These include the lack of traditional risk factors associated with MRSA among patients, a susceptibility pattern with resistance to fewer classes of antimicrobial drugs, and the inclusion of specific virulence factors. CA-MRSA strains typically carry the Panton-Valentine leukocidin genes, which produce cytotoxins that can cause tissue necrosis and leukocyte destruction and are associated with community-associated staphylococcal skin infections and necrotizing pneumonia [3]. CA-MRSA strains currently circulating can also be distinguished, to a certain extent, by molecular typing methods such as PFGE and multilocus sequence typing. It appears that a few strains of *S. aureus* are responsible for much of the CA-MRSA disease being seen currently in the United States [4]. The current distinction between CA-MRSA and HA-MRSA is anticipated to blur if CA-MRSA begins to be transmitted in health care settings and displaces HA-MRSA. CA-MRSA outbreaks and some persistent transmission

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Clinical Infectious Diseases 2005; 41:S269–72

1058-4838/2005/4104S4-0010

Table 1. Comparison of community-associated and health care–associated methicillin-resistant *Staphylococcus aureus* (MRSA).

Characteristic	Community-associated MRSA	Health care–associated MRSA
Susceptibility,[a] drug		
Chloramphenicol	Usually susceptible	Frequently resistant
Clindamycin[b]	Usually susceptible	Frequently resistant
Erythromycin	Usually resistant	Usually resistant
Fluoroquinolone	Geographic variability	Usually resistant
TMP-SMZ	Usually susceptible	Usually susceptible
SCC *mec* type	IV	II
Lineage	USA 300, USA 400	USA 100, USA 200
Toxin-producing	More	Fewer
Panton-Valentine leukocidin–producing	Common	Rare
Health care exposure	Less frequent	More frequent

NOTE. SCC, staphylococcal chromosome cassette; TMP-SMZ, trimethoprim-sulfamethoxazole.

[a] Susceptibility is based on in vitro testing and Clinical and Laboratory Standards Institute break points [2]. A finding of susceptibility does not necessarily make the drug an appropriate treatment choice.

[b] See comment on inducible resistance in the main text.

cases have been identified in several population groups and specific settings:

Alaska Natives. In communities largely made up of Alaska Natives, there have been outbreaks of CA-MRSA skin infections associated with prior antibiotic use [5, 6].

Native Americans. At an Indian Health Service facility in a rural midwestern Native American community, the proportion of MRSA isolates increased substantially from 1989 to 1997. Most MRSA infections (74%) were classified as community-acquired, and 89% were distinct from HA-MRSA, both by molecular typing and antimicrobial susceptibility pattern, with CA-MRSA isolates typically susceptible to non–β-lactam antimicrobial agents. Low socioeconomic status, crowded housing conditions, and limited access to health care contribute to the high background rate of skin infections in this population [7].

Pacific Islanders. In a survey of 4 health care facilities in Hawaii, between July 2001 and June 2003, 51% of patients infected with CA-MRSA were Pacific Islanders, who constitute 24% of that state's population [8].

Correctional facility inmates. In Georgia, California, and Texas, between 2001 and 2003, an increase in infections due to CA-MRSA among inmates in correctional facilities was associated with barriers to routine hygiene; with hindrance of access to medical care because of required copayments, inadequate supplies and staff for wound care, and frequent medical staff turnover; and with skin infections among inmates being attributed incorrectly to spider bites [9–11]. At these facilities and at a facility in Mississippi that had a prolonged outbreak, inmates' self-care of wounds and boils as well as sharing of personal items such as linens were associated with infection [12].

Competitive sports participants. Outbreaks of infection among participants in wrestling, football, and fencing have also been seen. In these outbreaks, 3 factors may have contributed to transmission: abrasions and lacerations associated with sport and the equipment, physical contact, and sharing of equipment [13–15]. In 2003, there was an outbreak of MRSA abscesses among members of a professional football team; all infections developed at turf abrasion sites. MRSA infection was significantly associated with the lineman position and a body mass index of >30. Antibiotic use among players was 10 times higher than among people of the same age and sex in the community. MRSA from another competing professional football team and from other community outbreaks had indistinguishable PFGE patterns; all carried the Panton-Valentine leukocidin toxin genes and the staphylococcal chromosome cassette (SCC) *mec* type IVa resistance gene cassette [4].

Military personnel. Among military recruits at a single training facility, there was a CA-MRSA outbreak from August to December 2002, with the monthly incidence of MRSA increasing from ⩾2 cases/1000 recruits before the outbreak period to 4.9–11 cases/1000 recruits during the outbreak period. Most patients did not have established risk factors for MRSA. In a prospective, observational study of soldiers during training, colonization with CA-MRSA (strains that were Panton-Valentine leukocidin toxin gene–positive) was associated with a significant risk of soft-tissue infection over an 8- to 10-week period [16, 17].

Other groups or individuals. During the 2003–2004 influenza season, through a combination of a survey of infectious disease physicians and reports from state and local health departments, 17 persons with influenza were reported with severe staphylococcal infection, and 15 of the infections were due to MRSA. All MRSA tested had a community-associated lineage. Among the 5 persons who died, 4 had infections due to MRSA [18]. Postpartum women, children (including neonates), injection drug users, and men who have sex with men have

reported CA-MRSA infections, sometimes in the context of an outbreak [19–23].

Although the origins of these strains of MRSA are obscure, their appearance and proliferation are likely attributable to several factors. The first factor is antimicrobial use generally, both appropriate and inappropriate, because this is what drives proliferation of resistance universally. Second, the strains contain an SCC (which contains the resistance gene against β-lactam antibiotics, known as *mec*A) that is smaller than the gene cassette found in HA-MRSA strains (SCC *mec* type II) and may be particularly efficient at transferring resistance among different bacteria. Third, the presence of virulence factors may make these strains more likely to cause disease.

The possibly rising incidence of MRSA infection outside of the health care setting has several implications for public health and clinical diagnosis and treatment. *S. aureus* is already a common cause of disease, and the appearance of new strains that are more resistant and virulent could signal increased incidence of disease. Many infections with *S. aureus* are treated with antimicrobial agents (e.g., cellulitis) or with incision and drainage (e.g., abscesses) without a specimen being taken for culture and susceptibility testing. Therefore, many infections are being and will be treated without information on antimicrobial susceptibility. Initiation of medical treatment without this information may result in inappropriate drug therapy (sometimes called "discordant therapy"), the use of less effective drugs for treatment, or the overuse of certain drugs if physicians assume that all infections have the CA-MRSA resistance pattern. Concerns have been raised regarding inducible clindamycin resistance that might emerge during treatment of CA-MRSA infection with this drug. Although data on the clinical implications of this resistance are few, some treatment failures have been associated with this mechanism of resistance [24]. Inducible resistance in vitro can be detected through disk-induction testing, often referred to as the "D-zone test" [25].

The most effective strategies for prevention of the emergence and spread of CA-MRSA remain to be established. Infection control as practiced in hospitals and long-term care facilities clearly would play a large role in health care and possibly other institutional settings. Strategies for the community would emphasize improving detection and appropriate treatment of infections and optimizing basic hygiene and wound care measures among groups at risk. The roles of additional measures, such as decolonization, are not established. In specific populations and circumstances, epidemiological data should focus prevention efforts.

Several surveillance projects are underway to better understand the burden of disease due to and risk for infection with CA-MRSA. Research on CA-MRSA has largely been based on isolates from clinical microbiology laboratories; therefore, the sample of isolates has been biased toward those collected from patients already in the health care system. The National Health and Nutrition Examination Survey, conducted by the Centers for Disease Control and Prevention (CDC)'s National Center for Health Statistics, has been collecting data on nasal carriage of *S. aureus* since 2001 to determine national prevalences of *S. aureus* and MRSA colonization. Information on potential risk factors for colonization is being collected through a questionnaire. This project will determine factors associated with MRSA colonization in the community setting, as well as any changes that occur over time [26].

State health departments and academic centers that participate in the Active Bacterial Core surveillance project of the CDC's Emerging Infections Program are collaborating with the CDC to develop a practical strategy for MRSA surveillance in the community. This project will measure the incidence and describe the epidemiological characteristics of invasive disease due to CA- and HA-MRSA in diverse geographic areas. The project will also describe the microbiological characteristics of the isolates collected. In addition, this project will expand the availability of staphylococcal strains to researchers through the National Institutes of Health (NIH)'s Network on Antimicrobial Resistance in *S. aureus* (NARSA) program [27].

The NARSA program is funded by the National Institute of Allergy and Infectious Diseases of the NIH and is designed to support and facilitate critical research efforts among clinical and basic scientists from the academic, industrial, and public health sectors regarding staphylococcal infection and disease. The isolates in the NARSA repository have proved to be valuable resources to investigators around the world for studies done to gain a better understanding of the mechanisms of resistance.

Surveillance for *S. aureus* needs to be improved so that the prevalence and geographic distribution of CA-MRSA is better defined and can be monitored for trends. This may include development of standardized methods for state-based surveillance, active population-based surveillance, use of existing data, periodic nasal colonization studies, and improved laboratory detection of MRSA to allow monitoring of trends in the microbiological characteristics of CA-MRSA. The appropriate management of CA-MRSA disease needs to be established in many public health and individual patient settings. This would include development of guidance for treatment and prevention in outbreak and institutional settings that describe when and what interventions are warranted, such as use of antisepsis, cohorting, or environmental disinfection. The Federal Bureau of Prisons has developed guidelines for correctional facilities [28].

Clinicians need improved guidance on diagnosis and treatment of CA-MRSA disease, including wound management, differential diagnosis of specific clinical presentations, culture and susceptibility testing, selection of empirical therapy for adults

and children with possible CA-MRSA disease, and when, if ever, to attempt decolonization and use antiseptic agents to prevent reinfection or transmission.

In summary, the epidemiology, clinical impact, microbiology, treatment, and prevention of CA-MRSA, although increasingly well understood, need further research and clarification. To have a substantial impact on the burden of CA-MRSA disease and to prevent increasing incidence, risk factors for development of CA-MRSA infection must be identified. Outcomes, including mortality and economic costs, need to be measured. The most effective and most cost-effective interventions remain to be proved. Ideally, a vaccine for all at-risk populations would be the most effective intervention, but one is unlikely to be developed in the near future. In the meantime, other interventions and the promotion of appropriate use of antimicrobial agents in communities need to be pursued.

Acknowledgments

I thank Rachel J. Gorwitz and Jeffrey C. Hageman, for help in manuscript preparation.

Potential conflicts of interest. J.T.W.: no conflicts.

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