

## ORIGINAL ARTICLE

## Methicillin-Resistant *S. aureus* Infections among Patients in the Emergency Department

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## ABSTRACT

**BACKGROUND**

Methicillin-resistant *Staphylococcus aureus* (MRSA) is increasingly recognized in infections among persons in the community without established risk factors for MRSA.

**METHODS**

We enrolled adult patients with acute, purulent skin and soft-tissue infections presenting to 11 university-affiliated emergency departments during the month of August 2004. Cultures were obtained, and clinical information was collected. Available *S. aureus* isolates were characterized by antimicrobial-susceptibility testing, pulsed-field gel electrophoresis, and detection of toxin genes. On MRSA isolates, we performed typing of the staphylococcal cassette chromosome *mec* (SCC*mec*), the genetic element that carries the *mecA* gene encoding methicillin resistance.

**RESULTS**

*S. aureus* was isolated from 320 of 422 patients with skin and soft-tissue infections (76 percent). The prevalence of MRSA was 59 percent overall and ranged from 15 to 74 percent. Pulsed-field type USA300 isolates accounted for 97 percent of MRSA isolates; 74 percent of these were a single strain (USA300-0114). SCC*mec* type IV and the Panton-Valentine leukocidin toxin gene were detected in 98 percent of MRSA isolates. Other toxin genes were detected rarely. Among the MRSA isolates, 95 percent were susceptible to clindamycin, 6 percent to erythromycin, 60 percent to fluoroquinolones, 100 percent to rifampin and trimethoprim-sulfamethoxazole, and 92 percent to tetracycline. Antibiotic therapy was not concordant with the results of susceptibility testing in 100 of 175 patients with MRSA infection who received antibiotics (57 percent). Among methicillin-susceptible *S. aureus* isolates, 31 percent were USA300 and 42 percent contained *pvl* genes.

**CONCLUSIONS**

MRSA is the most common identifiable cause of skin and soft-tissue infections among patients presenting to emergency departments in 11 U.S. cities. When antimicrobial therapy is indicated for the treatment of skin and soft-tissue infections, clinicians should consider obtaining cultures and modifying empirical therapy to provide MRSA coverage.

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**M**ETHICILLIN-RESISTANT *STAPHYLOCOCCUS aureus* (MRSA) emerged in the 1960s as a cause of infection among patients exposed to the bacteria in health care settings.<sup>1</sup> More recently, MRSA infections have been reported among persons without such exposure (community-associated MRSA).<sup>2,3</sup> Community-associated outbreaks of MRSA infection have occurred among prisoners, intravenous-drug users, athletes, military trainees, and men who have sex with men.<sup>4-6</sup> Community-associated MRSA has primarily been described as a cause of skin and soft-tissue infections, but it has also been associated with sepsis and necrotizing pneumonia.<sup>7-9</sup> As compared with health care-associated MRSA isolates, community-associated MRSA isolates tend to be resistant to fewer antibiotics, to produce different toxins,<sup>10</sup> and to have different types of the gene complex known as staphylococcal cassette chromosome *mec* (SCC*mec*); this complex contains the *mecA* gene that confers methicillin resistance.<sup>10</sup> Pulsed-field gel electrophoresis (PFGE) and other methods have identified a small number of molecular types that have accounted for most community-associated MRSA isolates characterized in the United States.<sup>11</sup>

Some institutions have a high prevalence of MRSA isolated from patients with sporadic skin and soft-tissue infections that are not associated with an outbreak.<sup>12,13</sup> However, data are limited regarding the prevalence of MRSA as a cause of skin and soft-tissue infections among patients in several communities throughout the United States and the *S. aureus* isolates associated with these infections. Therefore, we determined the prevalence of MRSA as a cause of skin infections among adult patients presenting to emergency departments in several geographically diverse, metropolitan areas in the United States. We also determined the bacteriologic characteristics of *S. aureus* isolated from skin and soft-tissue infections and evaluated factors potentially associated with MRSA infections of skin and soft tissue.

## METHODS

We conducted a prospective prevalence study involving adult patients with skin and soft-tissue infections who presented to hospitals in the EMERGENCY ID Net, a network of university-affiliated emergency departments in 11 U.S. cities: Albuquerque; Atlanta; Charlotte, N.C.; Kansas City, Mo.; Los An-

geles; Minneapolis; New Orleans; New York; Philadelphia; Phoenix, Ariz.; and Portland, Oreg. These departments had a combined approximate total of 900,000 visits per year.<sup>14</sup> The study was approved by the institutional review board at each site.

Patients 18 years of age or older presenting in August 2004 with purulent skin and soft-tissue infections of less than one week's duration (excluding perirectal abscesses) were enrolled in the study. Consent was obtained in writing at eight sites and orally with provision of an information sheet at three sites. Information on demographic characteristics, clinical presentation, potential risk factors for MRSA infection, and treatments provided was collected by emergency department physicians using standardized forms. Management decisions were made on an individual basis by physicians in the emergency department. Follow-up data were obtained by telephone approximately two to three weeks after enrollment.

Specimens were obtained from the single largest area of infection with the use of sterile Dacron swabs and were processed and cultured at hospital laboratories according to standard techniques.<sup>15</sup> Each laboratory determined the antimicrobial susceptibility of *S. aureus* isolates to the panel of agents routinely tested at that laboratory.<sup>16</sup> Available *S. aureus* isolates were forwarded to the Centers for Disease Control and Prevention (CDC) for further characterization. The inducibility of clindamycin resistance was determined by the D-zone disk-diffusion test.<sup>17</sup> The presence of genes for staphylococcal enterotoxins A through E and H, toxic shock syndrome toxin 1 (TSST-1), and Panton-Valentine leukocidin (*pvl*) and the type of SCC*mec* were determined by the polymerase chain reaction. All isolates were typed by PFGE with the use of *Sma*I restriction endonuclease. Additional methods are described in detail in the Supplementary Appendix (available with the full text of this article at [www.nejm.org](http://www.nejm.org)).

Descriptive statistics were used to summarize the characteristics of the patients and the prevalence of MRSA. To identify potential risk factors for MRSA infection among patients with skin and soft-tissue infections, we calculated adjusted odds ratios and 95 percent confidence intervals. Variables associated with MRSA infection in bivariate analyses were explored further with the use of multivariate logistic regression.

Audits of emergency department and laboratory logs for patients with a discharge diagnosis of ab-

cess, cellulitis, or wound infection were conducted at all study sites (except Atlanta) to determine the proportion of patients meeting eligibility criteria who were enrolled in the study. Demographic and clinical characteristics of enrolled patients were compared with those of unenrolled patients.

## RESULTS

A total of 422 patients with skin and soft-tissue infections were enrolled. The median age was 39 years (range, 18 to 79; interquartile range, 28 to 47), and 62 percent were men. Race or ethnic group was determined by the clinicians: 49 percent of patients were non-Hispanic blacks, 25 percent were non-Hispanic whites, 22 percent were Hispanic, and 4 percent belonged to other groups. Infections were located on the upper extremities in 29 percent of patients, lower extremities in 27 percent, torso in 17 percent, perineum in 14 percent, and head and neck in 13 percent. Infections were classified as an abscess in 81 percent of patients, an infected wound in 11 percent, and as cellulitis with purulent exudate in 8 percent.

*S. aureus* was isolated from skin and soft-tissue infections in 320 patients (76 percent); 249 of the *S. aureus* isolates (78 percent) were MRSA. MRSA was isolated from 59 percent of patients (Table 1).

The prevalence of MRSA ranged from 15 to 74 percent, and MRSA was the most common identifiable cause of skin and soft-tissue infections in 10 of 11 emergency departments. MRSA was isolated from 61 percent of abscesses, 53 percent of purulent wounds, and 47 percent of cases of cellulitis with purulent exudate. Other organisms isolated from 1 percent or more of infections included 71 isolates of methicillin-susceptible *S. aureus* (MSSA) (17 percent); 30 isolates of streptococcus species (7 percent) including 6 group B streptococcus, 2 group A streptococcus, 3 non-group A and non-group B  $\beta$ -hemolytic streptococcus, 4 anaerobic or microaerophilic streptococcus, and 15 viridans group streptococcus; 12 isolates of coagulase-negative staphylococci (3 percent); and 6 isolates of *Proteus mirabilis* (1 percent). Cultures from 31 patients were polymicrobial; 10 of these patients had MRSA. No microorganism was isolated from 38 patients (9 percent).

A total of 218 MRSA isolates (88 percent) and 55 MSSA isolates (77 percent) from 10 emergency departments were sent to the CDC for genetic and phenotypic characterization. The pulsed-field types of 216 of the MRSA isolates (99 percent) tested were characteristic of community-associated MRSA: 212 were type USA300, 2 were type USA400, and 2 were type USA1000.<sup>11,18</sup> Of 212 MRSA isolates

**Table 1. Bacterial Isolates from Purulent Skin and Soft-Tissue Infections in 11 U.S. Emergency Departments.\***

| Site             | No. of Patients Enrolled<br>(N=422) | MRSA<br>(N=249) <sup>†</sup> | MSSA<br>(N=71) | Other Bacteria<br>(N=64) <sup>‡</sup> | No Bacterial Growth<br>(N=38) |
|------------------|-------------------------------------|------------------------------|----------------|---------------------------------------|-------------------------------|
|                  |                                     |                              |                | number (percent)                      |                               |
| Albuquerque      | 42                                  | 25 (60)                      | 10 (24)        | 3 (7)                                 | 4 (10)                        |
| Atlanta          | 32                                  | 23 (72)                      | 4 (12)         | 3 (9)                                 | 2 (6)                         |
| Charlotte, N.C.  | 25                                  | 17 (68)                      | 0              | 4 (16)                                | 4 (16)                        |
| Kansas City, Mo. | 58                                  | 43 (74)                      | 6 (10)         | 4 (7)                                 | 5 (9)                         |
| Los Angeles      | 47                                  | 24 (51)                      | 6 (13)         | 8 (17)                                | 9 (19)                        |
| Minneapolis      | 28                                  | 11 (39)                      | 4 (14)         | 9 (32)                                | 4 (14)                        |
| New Orleans      | 69                                  | 46 (67)                      | 11 (16)        | 9 (13)                                | 3 (4)                         |
| New York         | 20                                  | 3 (15)                       | 8 (40)         | 5 (25)                                | 4 (20)                        |
| Philadelphia     | 58                                  | 32 (55)                      | 12 (21)        | 12 (21)                               | 2 (3)                         |
| Phoenix, Ariz.   | 30                                  | 18 (60)                      | 8 (27)         | 4 (13)                                | 0                             |
| Portland, Oreg.  | 13                                  | 7 (54)                       | 2 (15)         | 3 (23)                                | 1 (8)                         |

\* A total of 31 cultures, including 10 cultures from which MRSA was isolated, were polymicrobial. Because of rounding, percentages may not total 100. MSSA denotes methicillin-resistant *Staphylococcus aureus*.

<sup>†</sup> P<0.001 for the test for homogeneity of MRSA prevalence across sites.

<sup>‡</sup> Other bacteria isolated were as follows: MSSA (17 percent), streptococcus species (7 percent), coagulase-negative staphylococci (3 percent), and *Proteus mirabilis* (1 percent).

characterized as type USA300, 156 (74 percent) had a single pulsed-field pattern (strain USA300-0114). SCC $_{mec}$  type IV, characteristic of community-associated MRSA,<sup>19</sup> was found in 214 (98 percent) of the MRSA isolates, and *pvl* toxin genes were present in 213 (98 percent). Genes for staphylococcal enterotoxins A, B, C, D, E, and H and TSST-1 were identified in five or fewer MRSA isolates. Eight *S. aureus* isolates collected at the Atlanta site in April 2005 were similar to other study isolates with regard to PFGE and toxin characteristics.

USA300 was also the most common pulsed-field type among MSSA isolates, accounting for 17 of 55 MSSA isolates (31 percent) sent to the CDC. Among these type USA300 isolates, 8 (47 percent) had a pulsed-field pattern closely related to that of the MRSA strain USA300-0114. In addition, *pvl* genes were detected in 23 MSSA isolates (42 percent), including 17 (100 percent) of the isolates characterized as USA300.

MRSA susceptibilities were as follows: 100 percent were susceptible to trimethoprim-sulfamethoxazole (217 of 217) and to rifampin (186 of 186); 95 percent were susceptible to clindamycin (215 of 226), 92 percent to tetracycline (207 of 226), 60 percent to fluoroquinolones (106 of 176), and 6 percent to erythromycin (13 of 226). Although the proportion of all *S. aureus* isolates (MRSA and MSSA) that were resistant to clindamycin was less than 15 percent at 10 of the study sites, 6 of 10 *S. aureus* isolates from New York City (60 percent) were resistant to clindamycin. Among the isolates that were sent to the CDC, 11 of 218 MRSA isolates (5 percent) and 7 of 55 MSSA isolates (13 percent) were not susceptible to clindamycin, including 4 (2 percent) MRSA isolates and 5 (9 percent) MSSA isolates with inducible clindamycin resistance detected by an antimicrobial-susceptibility D-zone disk-diffusion test. Sixty-six patients with MRSA infections (27 percent) had one or more established risk factors for health care-associated MRSA; these included 43 patients who had been hospitalized within the past year, 28 with a history of MRSA infection, 2 who resided in a long-term care facility, and 1 who was undergoing dialysis. Isolates from 55 of these patients were evaluated at the CDC, and 54 (98 percent) had pulsed-field types characteristic of community-associated MRSA.

Features associated with the isolation of MRSA as compared with the isolation of any other bac-

teria (Table 2) included antibiotic use in the month before enrollment, the presence of an abscess or a lesion attributed to a spider bite at enrollment, history of MRSA infection, and a recent history of close contact with someone with a similar skin infection. The presence of an underlying illness and characterization as belonging to the "other" category of race or ethnic background were negatively associated with the isolation of MRSA. In multivariate logistic-regression analyses, all these factors were associated with MRSA infection, with the exception of the presence of an abscess (Table 3). Black race was independently associated with MRSA infection. Controlling for study site did not affect the association between any of these factors and MRSA infection. Among 64 patients with none of these factors, 31 (48 percent) were infected with MRSA. The only factor that was significantly associated with isolation of MRSA, as compared with MSSA, was the presence of abscess at enrollment (odds ratio, 2.3; 95 percent confidence interval, 1.2 to 4.4).

Complete information about treatment was available for 406 of the 422 patients (96 percent). Of these, 79 (19 percent) were treated with incision and drainage alone, 39 (10 percent) received antibiotics alone, 267 (66 percent) were treated with both incision and drainage and antibiotics, and 21 (5 percent) neither underwent incision and drainage nor received antibiotics. Of 400 patients for whom information about the outcome was available, 59 (15 percent) were admitted to the hospital. An antistaphylococcal penicillin or cephalosporin was given to 198 of 311 patients who received antibiotics (64 percent). In 100 of 175 MRSA infections for which antibiotic treatment was provided (57 percent), antibiotic therapy was not concordant with the results of susceptibility testing.

Of the 422 patients, 248 (59 percent) were contacted for follow-up 15 to 21 days (median, 17) after their visit to the emergency department, and 238 (96 percent) of those patients who were contacted for follow-up reported that their infection had resolved or improved. There were no significant differences in the outcome between patients infected with MRSA and those infected with other bacteria or between patients in whom the infecting MRSA isolate was resistant and those in whom the isolate was susceptible to the prescribed antibiotic. Baseline characteristics were similar for patients with and those without follow-up information.

**Table 2. Potential Risk Factors for Infection with MRSA, as Compared with Other Bacteria, in Patients with Purulent Skin and Soft-Tissue Infections in 11 U.S. Emergency Departments.\***

| Risk Factor  | MRSA<br>(N=249)          | Other Bacteria<br>(N=135) | Odds Ratio<br>(95% CI)† |
|--|--------------------------|---------------------------|-------------------------|
|  | <i>no./total no. (%)</i> |                           |                         |
| Race or ethnic group                                     |                          |                           |                         |
| Non-Hispanic white                                       | 61/247 (25)              | 37/135 (27)               | 1.0‡                    |
| Non-Hispanic black                                       | 134/247 (54)             | 53/135 (39)               | 1.6 (0.9–2.6)           |
| Hispanic   | 48/247 (19)              | 36/135 (27)               | 0.8 (0.4–1.5)           |
| Other  | 4/247 (2)                | 9/135 (7)                 | 0.3 (0.1–0.9)§          |
| Intravenous-drug user                                    | 26/244 (11)              | 11/135 (8)                | 1.3 (0.6–3.0)           |
| Taken any antibiotic in past mo                          | 84/245 (34)              | 24/134 (18)               | 2.4 (1.4–4.1)§          |
| Taking antibiotic for the infection                      | 61/244 (25)              | 24/134 (18)               | 1.5 (0.9–2.7)           |
| Prison or jail in past yr                                | 53/244 (22)              | 19/135 (14)               | 1.7 (0.9–3.1)           |
| Competitive sports involving contact in past mo          | 21/246 (9)               | 8/135 (6)                 | 1.5 (0.6–3.8)           |
| Homeless in past yr                                      | 40/246 (16)              | 17/135 (13)               | 1.3 (0.7–2.6)           |
| Abscess  | 203/243 (84)             | 97/131 (74)               | 1.8 (1.0–3.1)§          |
| Spontaneous infection (no apparent precipitating factor) | 100/248 (40)             | 49/135 (36)               | 1.2 (0.8–1.9)           |
| Reported spider bite                                     | 71/248 (29)              | 17/135 (13)               | 2.8 (1.5–5.3)§          |
| Underlying illness                                       | 25/249 (10)              | 34/135 (25)               | 0.3 (0.2–0.6)§          |
| HIV infection  | 11/249 (4)               | 4/135 (3)                 | 1.5 (0.5–4.9)           |
| History of MRSA infection                                | 28/242 (12)              | 5/132 (4)                 | 3.3 (1.2–10.1)§         |
| Hospitalized in past yr                                  | 43/247 (17)              | 32/135 (24)               | 0.7 (0.4–1.2)           |
| Resident in long-term care facility                      | 2/244 (1)                | 2/134 (1)                 | 0.6 (0.0–7.6)           |
| Health care worker                                       | 17/244 (7)               | 5/135 (4)                 | 1.9 (0.7–6.9)           |
| Homosexual male contact                                  | 7/132 (5)                | 5/79 (6)                  | 0.8 (0.2–3.4)           |
| Close contact with person with similar infection         | 43/245 (18)              | 8/135 (6)                 | 3.4 (1.5–8.1)§          |
| Household contact with MRSA infection                    | 15/245 (6)               | 3/131 (2)                 | 2.8 (0.8–15.2)          |
| Household contact with health care exposure¶             | 46/249 (18)              | 30/135 (22)               | 0.8 (0.5–1.4)           |
| Household contact with jail exposure                     | 42/243 (17)              | 15/131 (11)               | 1.6 (0.8–3.2)           |
| Household contact with intravenous-drug use              | 27/245 (11)              | 11/133 (8)                | 1.4 (0.6–3.1)           |

\* CI denotes confidence interval, and HIV human immunodeficiency virus.

† Missing data were excluded in these calculations. Information regarding race was missing for two patients.

‡ This group served as the reference group for other race variables.

§ P<0.05.

¶ This category includes hospitalization or residence in a long-term care facility in past year, employment as a health care worker, receipt of dialysis, or presence of an indwelling catheter or tube.

Case-finding audits revealed that approximately 42 percent of eligible patients were enrolled. As compared with enrolled patients, unenrolled patients were similar in terms of age (mean, 38 years; range, 18 to 82), sex (63 percent were male), and race or ethnic group (57 percent were white non-Hispanic or Hispanic, 39 percent were black, and 4 percent were in other groups). MRSA was isolated in 135 of 236 eligible but unenrolled patients

from whom wound cultures were obtained (57 percent).

## DISCUSSION

MRSA has emerged as the most common identifiable cause of skin and soft-tissue infections in several metropolitan areas across the United States. Although more than 80 percent of patients with

skin and soft-tissue infections associated with MRSA in this study received empirical antimicrobial therapy for their infection, the infecting isolate was resistant to the agent prescribed for 57 percent of these patients. This finding suggests a need to reconsider empirical antimicrobial choices for skin and soft-tissue infections in areas where MRSA is prevalent in the community.

Our findings are consistent with the dramatic trend of increasing reports of outbreaks and increased prevalence of community-associated MRSA during the past few years. MRSA was uncommon in community-acquired skin and soft-tissue infections before 2000 and accounted for only 3 percent of staphylococcal isolates submitted to Minnesota laboratories in 2000.<sup>20</sup> Between 2001 and 2004, the prevalence of MRSA among patients with skin and soft-tissue infections at our Los Angeles institution increased from 29 percent to 64 percent.<sup>13</sup>

Virtually all (99 percent) MRSA strains isolated from skin and soft-tissue infections in this study had pulsed-field types characteristic of community-associated MRSA, even though more than 25 percent of patients had established risk factors for health care-associated MRSA. A single pulsed-field type (USA300) accounted for 97 percent of MRSA isolates and 31 percent of MSSA isolates. A single strain (USA300-0114) associated with previously reported community outbreaks<sup>5</sup> accounted for 72 percent of MRSA isolates, and a closely related strain was the single most common MSSA strain identified. Pulsed-field type USA300 has been linked to community-associated MRSA outbreaks throughout the country<sup>5,11</sup> and represents the leading cause of community-associated MRSA in single-center prevalence studies.<sup>12,21</sup> USA300 has rapidly replaced other pulsed-field types to become predominant among centers that have conducted longitudinal studies.<sup>22</sup> Our finding of the genetic similarity of MRSA and MSSA isolates from community-associated infections is consistent with previous reports.<sup>7,8,21,23</sup> This similarity suggests the acquisition of SCC*mec* by *S. aureus* strains established in the community or the loss of SCC*mec* by community-associated MRSA strains. The predominance of isolates from one genetic background may be related to virulence or transmissibility factors that confer unusual fitness.

Ninety-eight percent of MRSA isolates and more than 40 percent of MSSA isolates in our study contained *pvl* genes; these findings are

**Table 3. Results of Multivariate Logistic-Regression Analyses to Identify Potential Risk Factors for MRSA Infection.\***

| Characteristic  | Adjusted Odds Ratio (95% CI)* |
|---|-------------------------------|
| Race  |                               |
| Non-Hispanic white  | 1.0†                          |
| Non-Hispanic black  | 1.9 (1.1–3.4)                 |
| Other   | 0.3 (0.1–1.0)                 |
| Use of any antibiotic in past mo (vs. no use)                           | 2.4 (1.3–4.3)                 |
| Reported spider bite (vs. other cause of infection)                     | 3.0 (1.6–5.7)                 |
| Underlying illness (vs. no underlying infection)                        | 0.3 (0.2–0.6)                 |
| History of MRSA infection (vs. absence of such history)                 | 3.4 (1.1–10)                  |
| Close contact with person with similar infection (vs. no close contact) | 3.8 (1.6–9.3)                 |

\* Estimates were adjusted for all other variables in the table. CI denotes confidence interval.

† This group served as the reference group for other race variables.

consistent with other recent reports.<sup>24,25</sup> *S. aureus* strains containing *pvl* genes have been associated with spontaneous skin and soft-tissue infections and necrotizing pneumonia; however, the role of *pvl* toxin in the pathogenesis of *S. aureus* skin and soft-tissue infections has not been fully elucidated.<sup>26</sup>

Most patients in our study were treated with  $\beta$ -lactam agents such as cephalexin and dicloxacillin, to which MRSA isolates are not susceptible. Although we had limited follow-up information, we found no association between patients' outcomes and the susceptibility of the pathogen to the prescribed antimicrobial agents. This absence of an association, which is consistent with previous reports,<sup>3,27</sup> suggests that most simple skin abscesses, even when caused by MRSA, can be cured with adequate drainage alone. Nonetheless, when antibiotics are clinically indicated and MRSA is prevalent in the community, it is difficult to justify empirical use of agents known to be inactive against MRSA. The susceptibility of a given pathogen to prescribed antimicrobial agents may be more likely to affect the outcome among patients with cellulitis or purulent wounds. Unfortunately, there were insufficient numbers of these patients with follow-up information in our study to assess this relationship. Although we identified several clinical and epidemiologic factors associated with MRSA infection, it does not appear that the presence or absence of these factors would be useful to guide decisions about the

use of empirical antibiotics. Most patients without MRSA had at least one of these factors, and almost half of those without any of these factors were found to have MRSA.

Various antimicrobial agents, such as clindamycin, trimethoprim-sulfamethoxazole, and doxycycline, have been recommended for outpatient empirical treatment of community-associated skin and soft-tissue infections that may be attributable to MRSA.<sup>28-30</sup> More than 90 percent of MRSA isolates in our study were susceptible to each of these agents. Likewise, 100 percent of the MRSA isolates were susceptible to rifampin. Although resistance to rifampin monotherapy has occurred rapidly, the combination of rifampin plus trimethoprim-sulfamethoxazole has been shown to eradicate MRSA colonization and has been suggested for the treatment of MRSA infection in the community.<sup>31</sup> Resistance to macrolides and fluoroquinolones was prevalent among MRSA isolates in this and other studies.<sup>3,12,13</sup>

Although the prevalence of clindamycin resistance, including inducible resistance, was low overall, it varied geographically. Clindamycin has been used successfully in the treatment of infections with MRSA isolates possessing inducible resistance.<sup>29,32</sup> However, clinical treatment failures have also been reported.<sup>33</sup> Therefore, if clindamycin therapy is being considered, *S. aureus* isolates with the potential for inducible clindamycin resistance (i.e., isolates resistant to erythromycin but susceptible to clindamycin on initial testing) should be evaluated for inducible resistance by D-zone disk-diffusion testing.<sup>17</sup>

Patients with nonpurulent cellulitis were not included in our study. Previous studies have shown that a large proportion of cellulitis may be attributable to group A streptococcus.<sup>34</sup> In contrast, among infections characterized as cellulitis with purulent drainage in our study, MRSA was isolated from 47 percent and group A streptococcus was rarely isolated. Although generally susceptible in vitro to clindamycin, most group A streptococci are resistant to trimethoprim-sulfamethoxazole. To provide coverage for streptococcal infection, the use of clindamycin or a combination of a  $\beta$ -lactam plus trimethoprim-sulfamethoxazole may be preferable for nonpurulent cellulitis.

Optimal empirical therapy for severely ill hospitalized patients with complicated skin and soft-tissue infections has not been established; however, broad-spectrum intravenous therapy including an

agent such as vancomycin for MRSA coverage remains appropriate. One study reported that clindamycin therapy was successful in children with invasive community-associated MRSA infections.<sup>29</sup> In recent randomized clinical trials, newer agents with MRSA activity had efficacy similar (daptomycin and tigecycline) or superior (linezolid) to that of vancomycin for the treatment of complicated skin and soft-tissue infections or skin and soft-tissue infections associated with MRSA.<sup>35-37</sup>

As compared with patients with other bacterial infections of the skin, patients with MRSA infection were more likely to report a spider bite as the reason for their skin lesion, perhaps because of the propensity for MRSA strains circulating in the community to cause painful lesions in the absence of previous skin trauma. Thus, clinicians should consider the possibility of MRSA infection in patients who report spider bites. Eighteen percent of patients with skin and soft-tissue infections associated with MRSA reported close contact with a person who had a similar infection. This finding highlights the importance of educating patients about methods to prevent further transmission of infection, including keeping lesions covered with clean, dry bandages; practicing good hand hygiene; and avoiding the sharing of contaminated items.

The high prevalence of MRSA among patients with community-associated skin and soft-tissue infections has implications for hospital policies regarding infection control. Standard precautions (including the use of gowns and gloves by health care workers for contact with wound drainage) should be used for all patients. Contact precautions, which include the use of gowns and gloves for all contact with patients or their environment, have been recommended for patients in acute care inpatient facilities who are known to be infected or colonized with MRSA.<sup>38</sup> Our results suggest that strategies used for patients with confirmed MRSA infections should be considered for all patients with purulent skin and soft-tissue infections in areas with a high prevalence of MRSA.

In many U.S. cities, MRSA is now the most common pathogen isolated in the emergency department from patients with skin and soft-tissue infections. Clinicians should consider obtaining cultures from patients with skin and soft-tissue infections and modifying standard empirical therapy to provide MRSA coverage when antibiotics are indicated. Further studies are needed to

determine the extent of this infection in other locations, follow trends in antimicrobial susceptibility, and identify optimal therapy.

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#### APPENDIX

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