High Prevalence of Methicillin-Resistant *Staphylococcus aureus* in Emergency Department Skin and Soft Tissue Infections

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Study objective: We sought to determine the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) among emergency department (ED) patients with skin and soft tissue infections, identify demographic and clinical variables associated with MRSA, and characterize MRSA by antimicrobial susceptibility and genotype.

Methods: This was a prospective observational study involving a convenience sample of patients who presented with skin and soft tissue infections to a single urban public hospital ED in California. Nares and infection site cultures were obtained. A health and lifestyle questionnaire was administered, and predictor variables independently associated with MRSA were determined by multivariate logistic regression. All *S aureus* isolates underwent antibiotic susceptibility testing. Eighty-five MRSA isolates underwent genotyping by pulsed field gel electrophoresis, staphylococcal chromosomal cassette *mec* (SCC*mec*) typing, and testing for Panton-Valentine leukocidin genes.

Results: Of 137 subjects, 18% were homeless, 28% injected illicit drugs, 63% presented with a deep or superficial abscess, and 26% required admission for the infection. MRSA was present in 51% of infection site cultures. Of 119 *S aureus* isolates (from infection site and nares), 89 (75%) were MRSA. Antimicrobial susceptibility among MRSA isolates was trimethoprim/sulfamethoxazole 100%, clindamycin 94%, tetracycline 86%, and levofloxacin 57%. Among predictor variables independently associated with MRSA infection, the strongest was infection type being furuncle (odds ratio 28.6). Seventy-six percent of MRSA cases fit the clinical definition of community associated. Ninety-nine percent of MRSA isolates possessed the SCC*mec* IV allele (typical of community-associated MRSA), 94.1% possessed Panton-Valentine leukocidin genes, and 87.1% belonged to a single clonal group (ST8:S).

Conclusion: In this urban ED population, MRSA is a major pathogen in skin and soft tissue infections. Although studies from other practice settings are needed, MRSA should be considered when empiric antibiotic therapy is selected for such infections. [Ann Emerg Med. 2005;45:311-320.]

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INTRODUCTION

Background

Methicillin-resistant *Staphylococcus aureus* (MRSA) has been recognized as a nosocomial pathogen since the 1960s. Cases of MRSA infection presenting from the community were first described in the early 1980s. However, until recently, the majority of such cases were associated with known risk factors for MRSA, particularly recent contact with a health care facility.[1] From an epidemiologic perspective, such cases were believed to represent temporary circulation into the community of a nosocomial strain.

In the mid 1990s, reports began to appear in the United States, particularly among children, of community-associated MRSA infection, defined as occurring in patients without identifiable risk factors.[2,3] Although most were relatively minor skin and soft tissue infections, deaths were soon described after treatment failure with β-lactam antibiotics.[4]

Recent studies, involving genetic typing and antimicrobial susceptibility testing of community-associated MRSA, seem to confirm that strains are spread within the community and are

Editor's Capsule Summary

What is already known on this topic

Methicillin-resistant *Staphylococcus aureus* (MRSA) has long been recognized as a pathogen, but has recently emerged as a community-acquired organism.

What question this study addressed

A convenience sample of 137 patients at an urban California hospital emergency department (ED) with skin and soft tissue infections were cultured, and clinical data collected.

What this study adds to our knowledge

MRSA was found in 51% of all culturable skin and soft tissue infections in this ED, and most appeared to be community associated. Infections classified as furunculosis were more likely to be due to MRSA.

How this might change clinical practice

In communities with a high prevalence of MRSA, β-lactam antibiotics such as cephalexin may no longer be the most appropriate empiric therapy for skin and soft tissue infections; others such as trimethoprim/sulfamethoxazole, clindamycin, or vancomycin may be more appropriate.

Research we'd like to see

Because the prevalence of MRSA appears to vary widely, similar studies in a variety of geographic settings would be useful. Outcome studies to determine the association of in vitro resistance to clinical failure would also be useful, because it is not clear that treating MRSA skin and soft tissue infections with β-lactam antibiotics is necessarily associated with poor outcome.

genetically and phenotypically distinct from hospital-associated MRSA.[5,6] The *mec*A gene codes for *S aureus* methicillin resistance. In community-associated MRSA, *mec*A is carried within a genetic element called staphylococcal chromosomal cassette *mec* (SCC*mec*) type IV, which is distinct from the SCC*mec* (types I, II, and III) typically found in hospital-associated MRSA. Compared with hospital-associated MRSA, community-associated MRSA tends to be susceptible to a broader array of antibiotics. Furthermore, community-associated MRSA may be more virulent than typical hospital-associated MRSA. Many community-associated MRSA strains have been found to carry genes for Panton-Valentine leukocidin, a virulence factor that is associated with skin and soft tissue infections and necrotizing pneumonia.[5-8]

Importance

Despite the well-documented emergence of community-associated MRSA in the United States, evidence about its importance in emergency department (ED) patients remains indirect. The prevalence of MRSA colonization in the community has ranged from 0.2% to 2.8% in recent US studies,[9] with the highest rates seen among the poor and in urban populations where injection drug use is common.[10,11] Most recent reports of community-associated MRSA infection have concerned clustered outbreaks, such as within isolated Native American communities, within prisons, and among athletes who share equipment.[12-16] In these settings, as much as 55% to 80% of *S aureus* infections were due to community-associated MRSA. In a study of all *S aureus* isolates at 12 medical center laboratories in Minnesota during 2000, 12% were community-associated MRSA, and 75% of community-associated MRSA isolates were from skin and soft tissue infections.[6] How many of these were ED cases was not reported. There has been no published study that prospectively examines the importance of community-associated MRSA in the ED setting.

Goals of This Investigation

We sought to investigate the prevalence of MRSA colonization and infection in ED patients with community-acquired skin and soft tissue infections and to identify demographic and clinical variables associated with MRSA in our population. Antimicrobial susceptibility testing and genotyping were performed to assess the relatedness among MRSA strains and determine whether they were likely health care or community associated.

METHODS

Study Design

This was a prospective case series involving a convenience sample of patients with skin and soft tissue infections.

Setting

The study was conducted in the ED of an urban county teaching hospital located in northern California. The annual ED census is approximately 75,000 visits. The study was approved by the medical center institutional review board.

Selection of Participants

Patients were prospectively enrolled when research assistants or study authors were available in the ED (approximately 80 hours per week), from October 2003 through February 2004. Research assistants identified all patients whose chief complaint was consistent with skin or soft tissue infection. In addition, treating physicians were asked to notify the research assistants or study authors when a skin or soft tissue infection was encountered. Patients were eligible for enrollment if the treating physician determined they had any of the following types of skin or soft tissue infection: cellulitis, necrotizing soft tissue infection, wound infection, ulcer, septic bursitis, or abscess (including furuncle/boil/superficial skin abscess, paronychia, hordeolum, pilonidal abscess, and hydradenitis). Odontogenic infections and Bartholin gland abscesses were excluded. Patients

could be enrolled only once. Children were excluded. Written informed consent to participate was required.

Data Collection and Processing

A health history and lifestyle questionnaire (see Appendix E1, available at http://www.mosby.com/AnnEmergMed) was administered to all subjects by research assistants or study authors. The questionnaire included a detailed assessment of antibiotic use, drug use habits, and housing history. Infection type was determined by the treating physician. Clinical data such as vital signs, antibiotic therapy, and whether the patient was hospitalized were taken from the patient's medical record. Detailed outcome information, such as response to antibiotics and return visits, was not collected.

At initial enrollment in the ED, cultures were obtained from the anterior nares for *S aureus* and from the infection site for any bacterial pathogen. In cases of pure cellulitis (without abscess or evident skin break), no infection site culture was obtained. Blood cultures were obtained at the discretion of the treating physician for subjects who were admitted to the hospital.

Nares and infection site cultures were taken with sterile Dacron swabs. Specimens were transported and processed using standardized methods.[17] All wound specimens were Gram-stained and cultured for common pathogens, including *S aureus*, β-hemolytic streptococci, enterococci, and facultatively anaerobic Gram-negative bacilli. Nares specimens were examined for *S aureus* only. A maximum of 2 MRSA isolates per patient (1 nares plus 1 infection site isolate) were included in the study.

S aureus was identified by colony morphology, slide and tube coagulase tests, catalase tests,[17] and MicroScan Pos Combo 20 multibiochemical substrate panels (MicroScan, Dade Behring, Inc., West Sacramento, CA) by following the manufacturer's recommendations.

Minimum inhibitory concentrations were determined by broth microdilution using cation-adjusted Mueller-Hinton broth according to the manufacturer's instructions (MicroScan). Minimum inhibitory concentration breakpoints and quality-control protocols were used according to standards established by the National Committee on Clinical Laboratory Standards.[18,19] Inducible resistance to clindamycin was determined by the Kirby-Bauer disc diffusion "D" test.[20] All MRSA strains were examined for intermediate-level resistance to vancomycin and vancomycin heteroresistance.[21-23]

All available infection-site MRSA isolates (2 were discarded before genotyping) and the first 17 nares MRSA isolates underwent genotyping by pulsed-field gel electrophoresis using a *Sma*I restriction endonuclease.[24] Isolates were scored as described by Tenover et al.[25] Isolates with a pulsed-field gel electrophoresis pattern that differed by fewer than 6 bands were classified as a pulsed-field gel electrophoresis group. Sequence types[26] and multilocus restriction fragment types[24] were determined by comparison with databases from previous studies.[8,16,27] The 4 major allotypes of the methicillin resistance gene (SCC*mec*) were detected by multiplex polymerase chain reaction.[28] Panton-Valentine leukocidin genes were detected by coamplification of *lukS-PV* and *lukF-PV*-genes.[8,29]

Primary Data Analysis

Isolation of *S aureus* from the nares was considered colonization, and isolation from the infection site was considered infection. Community-associated MRSA was defined clinically as occurring in community-dwelling persons without the following established risk factors for health care–associated MRSA: hospitalization or surgery within the previous year, residence in a nursing facility, dialysis, and presence of an indwelling vascular or bladder catheter.[6]

All questionnaire data, bacteriology data, and genetic data were entered into a FileMaker Pro6 database (Filemaker Inc., Santa Clara, CA). Prevalence and 95% confidence intervals (CIs) were calculated using standard equations.[30] Predictor variables associated with MRSA infection or colonization were determined by univariate analysis. Twenty-seven demographic and clinical variables were assessed in the univariate analysis. Selection of these variables for analysis was based on previous literature. Factors found by univariate analysis to be associated with MRSA, with elevated odds ratios (ORs) and significance ($P<.1$), were entered into stepwise logistic regression to identify significant independent associations. ORs were evaluated using the Cochran-Mantel-Haenszel test. Logistic regression model fit was evaluated by the likelihood ratio test. Generation of ORs, significance testing, and logistic regression testing were performed by SAS statistical software (version 9, SAS Institute, Inc., Cary, NC).

RESULTS

During a 5-month period, 137 patients were enrolled. Seven patients declined to participate. Infection types consisted of 66 deep abscesses, 20 superficial skin abscesses (furuncles), 18 cases of pure cellulitis, and 32 cases of other infection types such as ulcer and wound infection. Infections were located as follows: lower extremity, 66; upper extremity, 38; and head, neck, or trunk, 32.

Selected demographic and clinical characteristics of subjects are presented in Table 1. There were no hemodialysis patients or patients with indwelling catheters. There were no deaths.

Culture results are summarized in the Figure. The majority (71%) of nares cultures were negative for *S aureus*. Of the 40 nares *S aureus* isolates, 28 (70.0%; 95% CI 55.8% to 84.2%) were MRSA. Eighteen patients with pure cellulitis had only nares cultures taken; 5 (27.8%) of these grew *S aureus*, of which 3 were MRSA. Of 119 infection-site cultures, 79 (66.4%) grew *S aureus*, of which 61 (77%; 95% CI 68.0% to 86.5%) were MRSA. Thus, MRSA was isolated from 51.3% (95% CI 42.3% to 60.2%) of infection-site cultures. Other pathogens frequently isolated from infection-site cultures included streptococcal species (12) and *Proteus* species (5). Twelve infections were polymicrobial, 2 of which grew MRSA, and 3 grew methicillin-susceptible *S aureus*. Blood cultures, obtained from 4 subjects,

were all sterile. Overall (nares plus infection-site cultures), 74.8% (95% CI 67.0% to 82.6%) of *S aureus* isolates were MRSA. Sixty-eight subjects (49.6%; 95% CI 41.3% to 58.0%) were either colonized or infected with MRSA.

In the 119 subjects with both nares and infection-site cultures, 62 (52.1%) were concordant (defined as MRSA/MRSA, methicillin-susceptible *S aureus*/methicillin-susceptible *S aureus*, or negative/negative or other pathogen). Among 61 subjects with MRSA isolated from the infection site, 21 (34.4%; 95% CI 22.5% to 46.3%) were colonized with MRSA, whereas among 18 subjects with methicillin-susceptible *S aureus* infections, 5 (28%) were colonized with methicillin-susceptible *S aureus*. Of the 31 subjects with *S aureus* recovered from both sites, 26 (84%) were concordant for methicillin susceptibility. Of 21 subjects with MRSA present in the nares and infection site, genetic typing of the nares isolate occurred in 12. All 12 of these subjects had genetically identical clones in both sites.

Antibiotic susceptibility among staphylococcal isolates is summarized in Table 2. All 89 MRSA isolates were susceptible to vancomycin and trimethoprim/sulfamethoxazole. There were no cases of intermediate or heteroresistant vancomycin resistance. Of the 84 (94.3%) MRSA isolates susceptible to clindamycin by standard testing, 2 exhibited inducible clindamycin resistance. Eighty-four percent of MRSA isolates were susceptible to tetracycline (a surrogate for doxycycline susceptibility). Only 56.8% of MRSA isolates were fully susceptible to levofloxacin; 28.4% exhibited intermediate sensitivity, and 14.8% were fully resistant. Of the 47 patients with MRSA infection who were treated with antibiotics, 37 (78.7%) were initially prescribed a β-lactam, to which it was resistant.

Demographic and clinical variables associated with MRSA colonization or infection (termed MRSA predictor variables), as identified by univariate analysis, are presented in Table 3. Predictor variables independently associated with MRSA, as identified by multivariate logistic regression analysis, are presented in Table 4. In the multivariate model, white race and furuncle were associated with both MRSA colonization and infection, whereas homelessness and a recent history of multiple abscesses were associated only with colonization. Factors not associated with MRSA were age, income, incarceration history, hospitalization history, injection drug use status and frequency, injection drug use hygiene habits, known MRSA contact, antibiotic use history, skin disease history, and HIV status.

Of the 68 patients colonized or infected with MRSA, 52 (76%) fit the clinical definition for community-associated MRSA. Of the 16 patients not meeting the definition, hospitalization in the previous year constituted the sole health care–associated MRSA risk factor in 13 patients. Three patients resided in a skilled nursing facility, all of whom also had been hospitalized in the previous year.

Of the 85 MRSA isolates that underwent genotyping, 84 (98.8%) possessed the SCC*mec* IV allele (which is associated with community-associated MRSA worldwide[31]). Only 1 isolate (ST5:D) possessed the SCC*mec* II allele (associated with nosocomial acquisition). Eighty (94.1%) MRSA isolates possessed Panton-Valentine leukocidin exotoxin genes. Six genotypes were identified in total. A single clonal group (ST8:S) accounted for 74 (87.1%) of the MRSA isolates. All isolates belonging to ST8:S, ST1:K (n=3), ST8:C (n=2), and ST30:Z (n=1) were Panton-Valentine leukocidin–positive, whereas ST59:P (n=4) and ST5:D (n=1) did not carry Panton-Valentine leukocidin genes.

Table 1. Selected demographic and clinical characteristics of study subjects.

Characteristic (N=137)	Subjects, No. (%)
Sex	
Male	93 (67.9)
Female	44 (32.1)
Age, y	
18–29	22 (16.1)
30–39	42 (30.7)
40–49	41 (29.9)
50–59	22 (16.1)
>60	10 (7.3)
Race	
Black	60 (44.8)
White	36 (26.9)
Hispanic	26 (19.4)
Asian/Pacific Islander	11 (8.2)
Native American	1 (0.8)
Income/y	
<$10,000	95 (69.9)
>$10,000	41 (30.1)
Housing history	
Ever homeless	53 (38.7)
Currently homeless	24 (17.5)
Resided in SNF in previous 12 mo	3 (2.2)
Incarcerated in previous 12 mo	37 (27.0)
Health history	
Known MRSA contact	42 (30.7)
IDU, ever	50 (63.5)
IDU in previous 12 mo	38 (27.7)
Known HIV	4 (2.9)
IDDM	9 (6.6)
Ever hospitalized	102 (75.0)
Hospitalized in previous 12 mo	37 (27.0)
Visited ED in previous 12 mo	86 (62.8)
>2 ED visits in previous 12 mo	32 (23.8)
Abscess in previous 12 mo	51 (37.2)
>2 Abscesses in previous 12 mo	20 (14.6)
Antibiotics in previous 12 mo	52 (38.0)
Clinical presentation and course	
Fever (≥37.3°C [≥99.1°F])	34 (24.8)
Received antibiotics	91 (66.4)
Admitted	36 (26.3)
Infection type	
Pure cellulitis	18 (13.1)
Deep abscess	66 (48.2)
Furuncle	20 (14.6)
Ulcer	14 (10.2)
Wound infection	10 (7.3)
Other	9 (6.6)

SNF, Skilled nursing facility; *IDU,* injection drug use; *IDDM,* insulin-dependent diabetes mellitus.

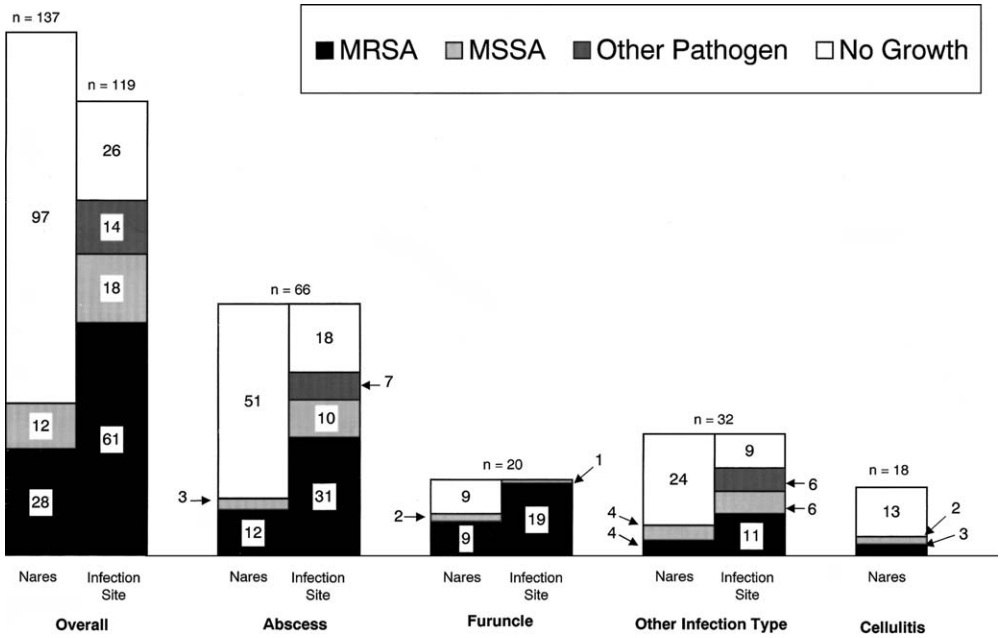

Figure. Summary of culture results, overall and by infection type. *MSSA*, Methicillin-susceptible *S aureus*.

LIMITATIONS

The most significant limitation of this study is the potential lack of external validity to other practice settings in terms of MRSA prevalence and MRSA predictor variables that were identified. The prevalence of MRSA in the community that our ED serves may be substantially higher than in other US communities. Although our study population was diverse in terms of age, ethnic background, and health status, it was typical of an urban public hospital in the high prevalence of injection drug use, homelessness, frequent ED users, and low-income status. Injection drug use and low socioeconomic status have been associated with MRSA in previous studies.[6,11,14,32] Deep or superficial abscesses accounted for 63% of skin and soft tissue infections, which may be higher than the proportion in other practice settings.

We did not attempt to separate clinically defined community-associated MRSA from hospital-associated MRSA before analysis of MRSA predictor variables, as has been done in other studies.[33,34] However, this study was designed to evaluate the clinically relevant issue for emergency physicians: predictors of MRSA infection among a cohort of ED patients with skin and soft tissue infections.

The analysis (univariate plus multivariate logistic regression) used to identify MRSA predictor variables may have included too many comparisons. The multivariate logistic regression model incorporated only statistically significant univariate associations from our relatively small, single ED sample. Therefore, predictor variables found to be associated with MRSA in this study may not be applicable to other ED populations.

We would like to point out the limitation inherent in our MRSA colonization data and, consequently, in our analysis of predictors of colonization. The MRSA colonization rate we report pertains to a selected population of patients, defined by presence of a skin or soft tissue infection. Therefore, predictor variables associated with MRSA colonization identified in this study may not apply to our overall ED population. On the other hand, the 29% *S aureus* colonization rate (MRSA plus methicillin-susceptible *S aureus*) we found is similar to that reported in unselected community populations,[9,35] which suggests that the colonization pattern in our study population may be fairly representative of our community as a whole.

There is potential for selection bias in a study of this type, which involves a convenience sample. Research assistants and treating physicians were not blinded to the study's purpose, to investigate the prevalence of MRSA. Although we strove to identify all eligible infections during the hours of enrollment, we do not have information about the total denominator of skin and soft tissue infections presenting to our ED during the months in which the study took place.

It is possible that significant misclassification of infection type occurred based on the research assistant's query of the treating physician. We suspect that some infections labeled as abscess (classified as deep abscess) were actually superficial skin abscesses, or furuncles. If more infections had been accurately classified as furuncle, the proportion associated with MRSA might have been somewhat lower, and the magnitude of the association with this infection type might have been smaller. Future studies should characterize infection type as precisely as possible, perhaps with the use of photography.

Table 2. Antibiotic susceptibility (%) among all staphylococcal isolates.

Antibiotic	MSSA (N=30)	MRSA (N=89)
Oxacillin	100	0
Erythromycin	57.7	3.6
Levofloxacin	96.6	56.8*
Tetracycline	96.6	85.7
Clindamycin	93.3	94.3†
TMP/SMX	100	100
Vancomycin	100	100

TMP/SMX, Trimethoprim/sulfamethoxazole.
*Of MRSA isolates, 28.1% (25 of 38 nonsusceptible isolates) exhibited intermediate susceptibility to levofloxacin.
†Two MRSA isolates initially susceptible to clindamycin by standard testing exhibited inducible clindamycin resistance.

DISCUSSION

This is the first study to report the prevalence of MRSA among exclusively ED patients presenting with skin and soft tissue infections. We found that MRSA was present in an alarming 49.6% of subjects and that 74.8% of all *S aureus* isolates were MRSA. Seventy-six percent of cases met a strict clinical definition of community-associated MRSA, and all but 1 MRSA isolate possessed the SCC*mec* IV allele, a genetic marker of community acquisition.[31] The findings of this study are consistent with the worldwide emergence of community-associated MRSA[10,36] and the increasing incidence of community-associated MRSA infections in California[16,27,37] and across the United States.[2,14,38]

Results of infection-site cultures in this study reflect the range of skin and soft tissue infections that were enrolled, including injection drug use–related and non–injection drug use–related abscesses, diabetic foot ulcers, and wound infections. The predominance of *S aureus*, followed by β-streptococcal and Gram-negative species, is similar to the findings in previous bacteriologic studies of such infections.[39-41] However, such a high proportion of MRSA (51% of infection site cultures; 77% of *S aureus* isolates) has to our knowledge never been reported in an unselected sample of community-acquired skin and soft tissue infections.

Direct comparison of our findings with other community-associated MRSA studies is difficult because we prospectively enrolled an unselected group of patients with skin and soft tissue infections, and we report the proportion of MRSA among all infection site cultures. In contrast, previous studies of community-associated MRSA have been mostly retrospective and have focused on cultures taken during an outbreak or from a known high-prevalence group. These studies usually report the proportion of MRSA among *S aureus* isolates only. Skin and soft tissue infections generally accounted for more than 80% of community-associated MRSA cases in these previous studies. Investigations of 2 MRSA outbreaks in Native American communities in the late 1990s found that 55% and 80% of staphylococcal infections were caused by MRSA.[14,15] A Japanese study, conducted in 1999 and 2000, of 229 *S aureus* isolates from a variety of skin infections in outpatients reported a 21% prevalence of MRSA.[42] Among children with community-onset *S aureus* infection and presenting to a single medical center in Texas in 2000, 44% of isolates were MRSA.[38] In a study of clinical *S aureus* isolates from San Francisco jail inmates, the proportion of MRSA increased from 29% in 1997 to 74% in 2002.[16] Similarly, surveillance cultures of draining skin lesions in Texas prison inmates revealed an increase in the proportion of MRSA, from 24% of *S aureus* isolates in 1998 to 66% in 2002.[43]

Our study is unique in obtaining nasal cultures in all participants. The 29% rate of *S aureus* nasal colonization in our study population is on par with that reported in community surveillance studies[9,35] and is lower than might be expected among patients with active skin infections. However, our finding that 70% of nasal *S aureus* isolates were MRSA, for an overall MRSA colonization rate of 20%, is unprecedented in a group of nonhospitalized, largely non–nursing facility patients. By contrast, a meta-analysis of contemporary community surveillance studies found a pooled MRSA colonization rate of only 1.3%.[9] The proportion of MRSA among nasal *S aureus* isolates in 833 homeless subjects in San Francisco in 1999 and 2000 was 12%, for an overall MRSA prevalence of 2.8%.[11]

Among the 18 subjects with pure cellulitis, the only clue to the infecting pathogen was nasal culture results. The overall *S aureus* colonization rate (28%) and proportion of MRSA (60%) were similar to that of subjects with suppurative infections. No conclusion about the etiology of cellulitis can be drawn from these data, but it is consistent with the concept that other pathogens besides *S aureus*, particularly group A streptococcus, are frequently responsible for cellulitis.[44]

Concordance between nares and wound cultures (52.1%) was substantial, despite the lower yield of nares cultures. Negative nares cultures among patients with documented *S aureus* infections may be partially explained by sampling error (false-negative nares cultures) or from the fact that *S aureus* sometimes colonizes the axilla and groin, providing an alternative reservoir for infection.[45] Remarkably, all 12 subjects who had MRSA in the nares and infection site, and both isolates were analyzed, possessed the identical clone in both sites. These results support the notion that nasal colonization with MRSA provides a major reservoir for infection.

Antimicrobial susceptibility patterns of MRSA isolates in this study are typical of community-associated MRSA from other recent reports.[6,14] All isolates demonstrated uniform resistance to oxacillin (a surrogate for methicillin), signifying lack of susceptibility to all β-lactam antibiotics, including cephalosporins. However, most were susceptible to a number of other non–β-lactam antibiotics, including 100% susceptible to trimethoprim/sulfamethoxazole and 85.7% susceptible to tetracycline. The 10% erythromycin susceptibility among our MRSA isolates is similar to that found in community-associated MRSA in Texas[33] but somewhat lower than what has been reported in community-associated MRSA isolates from the

Table 3. Univariate analysis of predictor variables.*

Predictor Variable	No. of Subjects	Colonized, No. (%)	Colonized, OR (95% CI)	Subjects, No.	Infected, No. (%)	Infected, OR (95% CI)
White	36	12 (33.3)	2.66 (1.11–6.37)†	29	21 (72.4)	3.28 (1.31–8.19)†
Nonwhite	101	16 (15.8)		90	40 (44.4)	
Black	60	7 (11.7)	0.35 (0.14–0.90)†	56	26 (46.4)	0.69 (0.34–1.43)
Nonblack	77	21 (27.3)		63	35 (55.6)	
Income >$10,000/y	42	8 (19.1)	0.88 (0.35–2.20)	33	16 (48.5)	0.86 (0.38–1.91)
Income <$10,000/y	95	20 (21.1)		86	45 (52.3)	
Ever homeless	53	16 (30.2)	2.59 (1.11–6.05)†	45	27 (60.0)	1.76 (0.83–3.74)
Never homeless	84	12 (14.3)		74	34 (46.0)	
Currently homeless	24	11 (45.8)	4.78 (1.84–12.41)†	23	17 (73.9)	3.35 (1.22–9.22)†
Not currently homeless	113	17 (15.0)		96	44 (45.8)	
Jail in past 12 mo	37	11 (29.7)	2.07 (0.86–4.97)	31	16 (51.6)	1.02 (0.45–2.31)
No jail in past 12 mo	100	17 (17.0)		88	45 (51.1)	
≥3 ED visits in previous 12 mo	32	13 (40.6)	4.11 (1.68–10.02)†	30	19 (63.3)	1.93 (0.83–4.53)
0–2 ED visits in previous 12 mo	105	15 (14.3)		89	42 (47.2)	
Hospitalized in past 12 mo	37	9 (24.3)	1.37 (0.56–3.38)	32	13 (40.6)	0.56 (0.24–1.27)
Not hospitalized in past 12 mo	100	19 (19.0)		87	48 (55.2)	
IDU in past 12 mo	38	9 (23.7)	1.31 (0.53–3.21)	33	15 (45.5)	0.72 (0.32–1.62)
No IDU in past 12 mo	99	19 (19.2)		86	46 (53.5)	
IDDM	9	1 (11.1)	0.49 (0.06–3.80)	7	1 (14.3)	0.14 (0.02–1.24)
Not IDDM	128	27 (21.1)		112	60 (53.6)	
Antibiotics in past 3 mo	52	14 (26.9)	1.87 (0.81–4.32)	44	27 (61.4)	1.92 (0.90–4.09)
No antibiotics in past 3 mo	85	14 (16.5)		75	34 (45.3)	
Abscess in previous 12 mo	51	16 (31.4)	2.82 (1.21–6.59)†	44	23 (52.3)	1.07 (0.51–2.25)
No abscesses in previous 12 mo	86	12 (14.0)		75	38 (50.7)	
≥3 Abscesses in past 12 mo	20	9 (45.0)	4.22 (1.54–11.57)†	20	9 (45.0)	0.74 (0.28–1.94)
0–2 Abscesses in past 12 mo	117	19 (16.2)		99	52 (52.5)	
Furuncle	20	9 (45.0)	4.22 (1.54–11.57)†	20	19 (95.0)	25.79 (3.32–200)†
Other infection type	117	19 (16.2)		99	42 (42.4)	

*All variables significantly associated with MRSA colonization or infection are presented, as well as selected variables not found to be significantly associated.
†Significant associations are marked with a dagger. Additional variables (not shown) that were not significantly associated with MRSA were: IDU hygiene habits, known MRSA contact, skin disease history, and HIV status.

upper Midwest.[6,14] Only 56.8% of MRSA isolates in this study were fully susceptible to levofloxacin, which is lower than in other studies that reported fluoroquinalone susceptibility among community-associated MRSA, where susceptibility to ciprofloxacin ranged from 79%[6] to 98%[14] to 100%.[15]

As in other studies of community-associated MRSA, most MRSA isolates were susceptible to clindamycin. In erythromycin-resistant clindamycin-susceptible strains, however, it is possible for inducible clindamycin resistance to develop during treatment.[46] Although the clinical significance of this phenomenon is debated,[47,48] treatment failures with clindamycin have been described in infections due to initially susceptible MRSA.[49,50] We found that among 84 initially erythromycin-resistant clindamycin-susceptible stains, 2 (2.4%) exhibited inducible clindamycin resistance, somewhat less than the 10% rate among community-associated MRSA isolates from children in Texas.[33]

Among 47 documented patients with MRSA infections receiving antibiotics in this study, an ineffective β-lactam was prescribed for 78.7%. Although the emergency physicians involved often treated simple abscesses with incision and drainage alone, when antibiotics seemed warranted, a β-lactam such as cephalexin was usually chosen. A major change in empiric antibiotic therapy for skin and soft tissue infections has been necessary in our ED. An agent that is active against community-associated MRSA is now recommended. In most cases, *S pyogenes* coverage is required as well. For oral therapy in moderate to severe infections, we use the combination of trimethoprim/sulfamethoxazole and cephalexin. Doxycycline alone is used for minor infections in adults. Given its cost, the risk of pseudomembranous colitis, and the risk of inducible resistance, use of clindamycin is generally limited to children, adults who are allergic to other agents, and parenteral therapy (combined with vancomycin).

Our analysis of MRSA predictor variables differed from that in other community-associated MRSA studies.[11,33,34,51] It involved exclusively patients with skin and soft tissue infections and assessed the association of MRSA colonization or infection with numerous demographic and clinical features, including

Table 4. Results of multivariate logistic regression analysis: predictor variables independently associated with MRSA infection or colonization.*

MRSA/Predictor Variable	OR	95% CI
Colonized		
Furuncle	5.0	1.6–15.4
≥3 Abscesses in previous year	4.6	1.5–14.4
Currently homeless	3.8	1.3–10.8
White	2.9	1.1–7.9
Infected		
Furuncle	28.6	3.6–225.4
White	3.8	1.4–9.9

*Model fit for colonization: likelihood ratio χ^2=29.4, *df*=2, $P<.0001$. Model fit for infection: likelihood ratio χ^2=26.9, *df*=4, $P<.001$.

infection type. We identified several predictor variables that were independently associated with MRSA colonization and infection. The most striking finding was the strong association of furuncle (superficial skin abscess or boil) with presence of MRSA, both in nares and infection site cultures. This finding is consistent with previous reports describing the type of skin and soft tissue infections in community-associated MRSA outbreaks.[7,51,52] As noted by others, many patients presenting with a furuncle caused by MRSA complain of a spider bite.[12,53] Our study is the first to formally establish the very strong association between furunculosis and community-associated MRSA.

The association of white race with MRSA infection and colonization is difficult to explain and has not been observed in other studies, although one study found that community-associated MRSA was more common in blacks than Hispanic or white patients.[33] More plausible and valid is the finding that homelessness, frequent ED visits, and a history of multiple abscesses were associated with MRSA colonization. It is important to note, on the other hand, that recent hospitalization, recent antibiotic use, and injection drug use were not associated with MRSA in this study. One retrospective study did find an association between recent antibiotic use and community-associated MRSA infection.[51] In view of the high overall MRSA prevalence in our study population, the utility of predictor variables for identifying likely MRSA infection appears limited, with the likely exception of furunculosis.

The results of genetic typing support the contention that most MRSA in this ED population was community acquired and provide insight about the current epidemiology of community-associated MRSA in California and the United States. More than 98% of MRSA isolates in this study possessed the SCC*mec* IV allele. SCC*mec* IV is typical of community-associated MRSA worldwide and is now considered a putative marker for community acquisition.[10,31,54,55] In a recent study by Naimi et al,[6] in which MRSA isolates were defined on clinical grounds as community or health care associated, SCC*mec* IV occurred in 85% of community-associated MRSA versus 12% of health care–associated isolates.

Panton-Valentine leukocidin genes were found in 94% of MRSA isolates in our study. Panton-Valentine leukocidin, like SCC*mec* IV, is associated with community acquisition.[6,8] The Panton-Valentine leukocidin genes encode an exotoxin that confers virulence by creating pores in the leukocyte cell membrane.[5] It is associated with spontaneous skin and soft tissue infections, including furunculosis,[7,51,52] and with necrotizing pneumonia.[5,56] The strong association that we found between community-associated MRSA possessing Panton-Valentine leukocidin genes and furunculosis supports the notion that Panton-Valentine leukocidin is instrumental in the formation of so-called spontaneous primary skin infections.[51,52]

We found that 87% of MRSA isolates in this study were from a single Panton-Valentine leukocidin–positive clonal group, designated ST8:S. This clone, which had not been reported in San Francisco before 2000, appears to be responsible for the majority of recent MRSA infections in San Francisco and Los Angeles prisons[16] and for a substantial proportion of skin and soft tissue infections occurring throughout the San Francisco public health network since 2002.[8,27] ST8:S belongs to the same pulsed field type, termed USA 300,[57] as isolates causing outbreaks of skin and soft tissue infections among football players in Pennsylvania and California[13] and in prisons in Texas and the southeastern United States.[43] In contrast, the community-associated MRSA clone responsible for outbreaks among children and Native Americans in the upper midwestern United States[2,4,14] belongs to the USA 400 lineage, of which there were 2 (ST1:K) in our sample. The genetic data presented in this study, when linked with other studies on the molecular epidemiology of community-associated MRSA, support the notion that community-associated MRSA is spreading rapidly within and between communities. It has been suggested that the combination of Panton-Valentine leukocidin genes and SCC*mec* IV allele represents a "superadapted" *S aureus* phenotype poised to replace methicillin-susceptible *S aureus* in the community.[7,36]

In summary, MRSA is a major pathogen in skin and soft tissue infections in this urban ED population. Among predictor variables found to be associated with MRSA, furunculosis was by far the strongest. However, the utility of predictors for identifying likely MRSA infection may be limited, given such a high overall MRSA prevalence. Clinical and genotyping data confirm that the majority of MRSA in this study was community acquired. The predominance of a single clone that can be linked to recent outbreaks elsewhere in the United States suggests that community-associated MRSA is well adapted to spread. Community-associated MRSA is probably a common cause of skin and soft tissue infections in other EDs. When skin and soft tissue infections require antibiotic therapy, we recommend choosing an agent that is active against MRSA.

There is a need for further research along several lines: to establish the prevalence of MRSA in other geographic locations, perhaps through a network of participating EDs; to test interventions that might slow the emergence or interrupt the spread of community-associated MRSA within communities;[51]

to examine the role of newer antibiotics and topical agents in the treatment of MRSA infections and colonization; and to pursue development and testing of an *S aureus* vaccine.[58]

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