Risk Factors for Community-Associated Methicillin-Resistant
Staphylococcus aureus Infections in an Outbreak of
Disease among Military Trainees in San Diego,
California, in 2002†

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An outbreak of community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) skin infections was observed in a population of U.S. military trainees in the summer of 2002. A questionnaire was developed and administered to 206 trainees, 22 of whom had MRSA infections. Factors associated with infection were described by multivariable logistic regression modeling and included having a roommate in training with a prior skin infection (odds ratio [OR] = 3.44) or having a family member or friend who worked in a health care setting (OR = 2.79). Previous antibiotic use, hospitalization, or health problems were not associated with MRSA infection. This outbreak of MRSA skin infections in an otherwise-healthy, well-defined, military population provided an opportunity to describe risk factors for CA-MRSA which may help focus prevention efforts in this and other communities.

Mounting evidence has confirmed that methicillin-resistant Staphylococcus aureus (MRSA), once based almost exclusively in health care facilities, is emerging as a community-based pathogen. Recent reports indicate that the prevalence of community-associated MRSA (CA-MRSA) infections is increasing (1, 4, 14, 17, 18, 22, 26), but even more concerning are the recent, numerous CA-MRSA outbreaks in groups of young, healthy individuals with no direct ties to health care facilities and none of the typical risk factors for infection (6–10, 15, 16, 20, 24).

Among the risk factors for CA-MRSA infection identified in previous investigations are prior antibiotic use, prior hospitalization, close contact with an MRSA-infected or -colonized individual, injection drug use, and underlying illnesses (3, 5, 11, 27–29, 31). As CA-MRSA infections continue to become more widespread, additional investigation into the risk factors for infection will be vital to the development and implementation of effective prevention and control measures. In this investigation, we examined potential risk factors for CA-MRSA infection in a population of military trainees.

MATERIALS AND METHODS

Population. Young, healthy males who were enrolled in a 26-week, physically demanding military training program comprised the population for this investigation. During the course of the program, trainees lived and worked closely together and rarely left the training facility. As a result of this closed environment, trainees experienced relatively uniform exposures. Due to their frequent contact with sand, boats, equipment, and seawater during their training regimen, trainees historically experienced a high occurrence of skin abrasions (L. Garsha, U.S. Navy, San Diego, Calif., personal communication, Sept. 2002).

Outbreak identification. The first MRSA case was identified by the presence of cellulitis and a positive wound culture on 2 August 2002. Between 2 August and 28 October 2002 (12 weeks), a total of 34 MRSA skin infections were confirmed (Fig. 1). Four of those infections occurred in trainees that had experienced a previous MRSA infection during this same 12-week period, and these were identified as repeat infections. The incidence of MRSA skin infection during this period was calculated as 9.5 cases per 1,000 person-weeks. This was considered markedly higher than the baseline rate of cellulitis in this population, estimated at 3 cases per 1,000 person-weeks (L. Garsha, personal communication).

Laboratory methods. Staphylococcal isolates from binasal swab specimens and wound cultures were sent to the Department of Defense Center for Deployment Health Research, San Diego, Calif., for additional molecular epidemiology analysis.

Clinical isolates were confirmed to be S. aureus by colony morphology, Gram stain, positive MRSA latex agglutination (Oxoid), and positive tube coagulase tests. In addition, a multiplex PCR was used to detect the mecA and meca genes to confirm identification of MRSA isolates (21).

The susceptibilities of these MRSA isolates to different antibiotics were determined by the broth microdilution method following the recommendations of the National Committee for Clinical Laboratory Standards guidelines (23). Penicillin, trimethoprim-sulfamethoxazole, levofloxacin, clindamycin, erythromycin, ceftriaxone, rifampin, tetracycline, and vancomycin were tested. Additional resistance determinations for mupirocin and oxacillin were performed with the E-test (AB Biodisk, Solna, Sweden) method. Resistance to oxacillin was defined as an MIC of ≥4 μg/ml. S. aureus ATCC 25921 and S. aureus ATCC 33500 were used as control strains susceptible and resistant to mupirocin, respectively.

Clinical isolates were further evaluated by molecular methods for the presence of the Panton-Valentine leukocidin (PVL) gene, and sequence type (ST) was determined using the multilocus sequence typing method (12, 13, 19, 21).

Outbreak intervention. During the course of the outbreak, trainees and staff had their noses cultured several times to identify potential sources of MRSA carriage in this population. In addition, several measures were implemented in the trainee population to reduce the spread of infection. All trainees were required to apply mupirocin to their noses and to bathe with an antimicrobial...
Skin cleanser on three separate occasions. In addition, the barracks were routinely disinfected with a 5% bleach solution.

Postoutbreak survey. As part of the outbreak investigation, a postoutbreak survey was developed to describe potential risk factors for CA-MRSA infection in this population. An optically scannable questionnaire was administered to 206 military trainees, representing approximately 70% of the available military trainee population, in October 2002.

Data captured by the survey included demographic characteristics and medical characteristics, including prior antibiotic use, prior hospitalizations, medications, allergies, and past medical history. Past medical history included questions about prior skin conditions. Trainees were also asked to provide information about dietary supplement use, tobacco and alcohol use, travel history, whether their roommate had been treated for a skin infection, whether any members of their crew had been treated for a skin infection, whether they had a family member or friend who worked in a health care setting, and whether they had a family member who had recently been hospitalized or had an outpatient procedure.

Self-reported data on prior hospitalizations, prior antibiotic use, and medication allergies were verified by medical records.

Statistical analyses. After descriptive investigation of population characteristics, analyses were performed to assess the significance of associations between the outcome (MRSA infection) and demographic and exposure variables. Using regression diagnostics, colinearity among variables was assessed. A manual backward stepwise logistic regression was conducted, with variables considered for inclusion in the model if initial significance was characterized by P values of <0.15 from the univariate analysis. All covariates were investigated as possible confounders prior to removing them from further modeling. Multivariable logistic regression modeling was performed; the reduced model included only those variables with significance characterized by a P value of <0.05 or otherwise identified as possible confounders. Results were reported as odds ratios (ORs) and 95% confidence intervals (CIs) calculated for variables associated with MRSA infection. SAS software (version 8.0; SAS Institute, Cary, N.C.) was used for analyses.

This research was conducted in compliance with all applicable federal regulations governing the protection of human subjects in research.

RESULTS

Based on testing of nasal swab specimens and wound cultures, military trainees were classified as MRSA infected, MRSA colonized, or MRSA negative. Trainees who had a skin infection and tested positive for MRSA by wound culture of the infected area were classified as MRSA infected. Trainees who did not have a skin infection but whose nasal swab specimen did not test positive for MRSA were classified as MRSA negative. Of the 206 military trainees surveyed, 10.7% (n = 22) were MRSA infected, 1.9% (n = 4) were MRSA colonized, and 87.4% (n = 180) were MRSA negative. Due to the small number, data from the four MRSA-colonized individuals were not included in further statistical analyses, although the complete laboratory testing battery was performed on the isolates.

Questionnaire data for the remaining 202 trainees indicated that 77.2% were Caucasian, 67.4% were younger than 25 years old, 32.2% reported antibiotic use within the past 12 months, 16.8% reported a hospitalization within the past 24 months, 6.5% reported current dietary supplement use, 43.1% reported any tobacco use, and 46.5% reported current alcohol use (Table 1).

The variables identified through univariate analyses as being significantly associated with MRSA infection included antibiotic use within the 12 months prior to training (P = 0.123), dietary supplement use prior to training (P = 0.110), having a roommate in training with a prior skin infection (P = 0.003), having a family member or friend who worked in a health care setting (P = 0.013), and having a parent or member of the household who smoked during the trainee’s childhood (P = 0.007). Two variables were identified in the reduced logistic regression model as having a significant positive association with MRSA infection. Military trainees who reported having a roommate in training with a prior skin infection had 3.4 times higher odds of becoming infected with MRSA than trainees who did not report having a roommate with a skin infection (OR = 3.44; 95% CI, 1.34 to 8.85). Trainees who reported having a family member or friend who worked in a health care setting had 2.8 times higher odds of becoming infected with MRSA than trainees who did not report such ties to the health care field (OR = 2.79; 95% CI, 1.09 to 7.15) (Table 1). Conversely, having a parent or other household member who smoked during the trainee’s childhood was negatively associated with MRSA infection; trainees who reported this appeared less likely to develop an MRSA infection than those
who did not report such environmental tobacco exposure (OR = 0.26; 95% CI, 0.07 to 0.94).

**Laboratory results.** Staphylococcal isolates from all 22 MRSA-infected individuals tested positive for the mecA and PVL genes. In addition, all 22 isolates were identified as ST8 by multilocus sequence typing. Three of the four isolates from MRSA-colonized individuals were also identified as ST8, while the remaining isolate was identified as ST30. Antibiotic susceptibility testing showed resistance of all isolates to oxacillin, penicillin, erythromycin, and ceftriaxone. The isolates were susceptible to all other antibiotics tested.

**DISCUSSION**

The steady increase in reports of CA-MRSA outbreaks in young, healthy populations with no apparent risk factors for infection is concerning. With each outbreak, it is important to determine the possible risk factors for infection in order to focus prevention and control efforts.

This outbreak of CA-MRSA occurred in a young, healthy, and well-defined population of military trainees. During the course of their 26-week intense training regimen, these trainees lived and worked closely together. In this environment, a small number of initial MRSA cases quickly became noticed as an outbreak.

The control measures implemented within this military trainee population during the summer and fall of 2002 were apparently effective in stopping the MRSA outbreak. During its 12-week course, however, the affected population incurred a high cost from infections. At least six trainees were hospitalized due to their MRSA infection, and eight trainees were unable to complete their original training program and therefore had to restart. Although these hospitalization and lost-time rates were higher than would be expected for a healthy trainee population, the “voluntary drop” rate for this trainee population was actually much lower than expected. Only one trainee reported dropping the training program after his MRSA infection.

In this outbreak investigation, the major risk factor associated with MRSA infection was having a roommate during training who had a prior skin infection. This finding is consistent with data from previous studies that identified close contact with an MRSA-infected or -colonized individual as a risk factor for infection (11, 29). Another risk factor associated with MRSA infection in this outbreak was having a family member or friend who worked in a healthcare setting. This finding suggests that this CA-MRSA outbreak may have had indirect ties to health care facilities from trainees’ past contact with family and friends, a factor that has also been suggested in previous studies of MRSA infection (27). Finally, the statistical analyses identified having a parent or other household member who smoked during the trainee’s childhood as protective against MRSA infection. Although difficult to explain, one might speculate that childhood environmental tobacco smoke exposure is a surrogate for another factor(s), perhaps immunologic, that is protective against infection.

Note that none of these trainees had asthma or reactive airway disease; therefore, those exposed to environmental smoke as children may represent a subgroup with especially strong immune profiles (2).

From previous studies, it is important to note that other factors found associated with CA-MRSA infection, including past antibiotic use and prior hospitalization, were not found to be associated with MRSA infection in this present investigation. This implies that this population of otherwise healthy, strong, young adults may be different from other populations affected by MRSA.

The results of the laboratory testing of staphylococcal isolates conducted in this outbreak investigation were consistent with those of other CA-MRSA outbreaks. The isolates in this outbreak were primarily susceptible to the antibiotics tested, except for beta-lactams and erythromycin. This finding is consistent with antibiotic susceptibility patterns reported in previous CA-MRSA outbreaks. In addition, this finding contrasts sharply with the multidrug resistance patterns often observed with nosocomial MRSA infections (4, 6, 11, 16, 25, 29). The presence of the mecA gene in the 22 isolates is consistent with the finding of methicillin resistance among these pathogens (21). In addition, the PVL gene is a potential virulence factor that has been linked to other CA-MRSA infections (19, 30).
Finally, the identification of all 22 MRSA skin isolates as ST8 by multilocus sequence typing indicates that a single MRSA clone was transmitted in this outbreak. Community- and hospital-acquired MRSA outbreaks with ST8 have been identified previously within the United States (30).

The limitations of this study include the small sample size and the unique population. As a result, the findings of this investigation may not be generalizable. There are inherent limitations to the use of survey data, including recall and response biases. It may be notable that the 70% response rate was strong, and some survey data were confirmed via medical record review.

Despite limitations, this outbreak investigation included strengths that may contribute to our expanding understanding of CA-MRSA infections. Most notably, the outbreak occurred in a well-defined population of young, healthy, military trainees who experienced relatively uniform exposures in their environment. In this controlled setting, one may have more confidence that factors found to be associated with infection are true risk factors.

The control measures implemented during this outbreak may have helped reduce the transmission of MRSA between trainees who had close contact but were not roommates, such as trainees who were members of the same crew. However, the data suggest that control measures did not eliminate the risk of MRSA transmission between roommates. Targeting education, hygiene, and personal behaviors may be key to reducing the spread of MRSA among those with close physical contact in future outbreaks. Future studies may also explore the immunologic mechanisms that appear to make some otherwise healthy adults at higher risk for MRSA infections.

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REFERENCES