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RISK FACTORS FOR COMMUNITY-ACQUIRED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (CAMRSA) INFECTIONS IN MILITARY TRAINEES: REVIEW OF AN OUTBREAK IN SAN DIEGO, CALIFORNIA, 2002

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**Risk Factors for Community-Acquired Methicillin-Resistant *Staphylococcus aureus* (CAMRSA) Infections in Military Trainees:
Review of an Outbreak in San Diego, California, 2002**

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ABSTRACT

An outbreak of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) skin infections was observed in a population of US military trainees in the summer of 2002. A questionnaire was developed and administered to 209 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 healthcare 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.

INTRODUCTION

15 Mounting evidence has confirmed that methicillin-resistant *Staphylococcus aureus*
(MRSA), once based almost exclusively in healthcare facilities, is emerging as a community-
based pathogen. Recent reports indicate that the prevalence of community-acquired MRSA (CA-
MRSA) infections is increasing (1, 4, 14, 17, 18, 22, 24), but even more concerning are the
recent, numerous CA-MRSA outbreaks in groups of young, healthy individuals with no direct
20 ties to healthcare facilities and none of the typical risk factors for infection (6-10, 15, 16, 20, 23).

 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, 25-27, 29). As CA-MRSA
infections continue to become more widespread, additional investigation into the risk factors for
25 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

30 **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,
35 trainees historically experienced a high occurrence of skin abrasions (Dr. Larry Garsha, US
Navy, San Diego, Calif, September 2002, personal communication).

Outbreak identification. The first MRSA case was identified by the presence of cellulitis and a positive wound culture on August 2, 2002. Between August 2, 2002 and October 28, 2002 (12 weeks), a total of 34 MRSA infections were confirmed (figure 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 infection during this period was calculated as 9.5 cases per 1000 person-weeks. This was considered markedly higher than the baseline rate of cellulitis in this population, estimated at 3 cases per 1000 person-weeks (Dr. Larry Garsha, US Navy, San Diego, September 2002, personal communication).

Laboratory methods. Staphylococcal isolates from nasal swab specimens and wound cultures were sent to the Department of Defense Center for Deployment Health Research, San Diego, Calif, to provide additional molecular epidemiology for the outbreak. Clinical isolates were examined for the presence of the *mecA* gene, Panton-Valentine leukocidin (PVL) gene, and sequence type (ST) based on the method of multi-locus sequence typing (MLST) (12, 13, 19, 21).

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

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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 209 military trainees, representing approximately 70% of the available military trainee population, in October 2002.

65 Data captured by the survey included demographic characteristics, medical characteristics, including prior antibiotic use, prior hospitalizations, medications, and 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
70 any members of their crew had been treated for a skin infection, whether they had a family member or friend who worked in a healthcare 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.

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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, collinearity among variables was assessed. A manual backward stepwise logistic regression was conducted, with variables
80 considered for inclusion in the model if initial significance was characterized by p values < 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 p
< 0.05 or otherwise identified as possible confounders. Results were reported as odds ratios
85 (ORs) and 95% confidence intervals (CIs) calculated for variables associated with MRSA
infection. SAS® software (Version 8.0, SAS Institute, Cary, NC) was used for analyses.

RESULTS

Based on testing of nasal swab specimens and wound cultures, military trainees were
90 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
tested positive for MRSA were classified as MRSA colonized. Trainees who did not have a skin
infection and whose nasal swab specimen did not test positive for MRSA were classified as
95 MRSA negative. Of the 209 military trainees surveyed, 10.5% (n=22) were MRSA infected,
3.3% (n=7) were MRSA colonized, and 86.1% (n=180) were MRSA negative. Due to the small
number, the 7 MRSA colonized cases were not included in further analyses.

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,
100 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
105 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 healthcare 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 the odds of becoming infected with MRSA compared with trainees who did not report having a roommate with a skin infection (OR = 3.44; 95% CI, 1.34-8.85). Trainees who reported having a family member or friend who worked in a healthcare setting had 2.8 times the odds of becoming infected with MRSA compared with trainees who did not report such ties to the healthcare field (OR = 2.79; 95% CI, 1.09-7.15) (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 compared with those who did not report such environmental tobacco exposure (OR = 0.26; 95% CI, 0.07-0.94).

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 MLST.

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 6 trainees were hospitalized due to their MRSA infection, and 8 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 1 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 with a prior skin infection. This finding is consistent with data from previous studies that identify close contact with an MRSA-infected or colonized individual as a risk factor for infection (11, 27). 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 healthcare facilities from trainees’ past contact with family and friends, a factor that has also been suggested in previous studies of MRSA infection (25). Finally, these 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 other

factor(s), perhaps immunologic, that are protective against infection. Note than 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).

It is important to note that other factors, that have been associated with CA-MRSA infection in previous studies of 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 are consistent with those of other CA-MRSA outbreaks. 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, 28). Finally, the identification of all 22 MRSA isolates as ST8 by MLST indicates that a single MRSA clone was present in this outbreak. Community- and hospital-acquired MRSA outbreaks with ST8 have been identified previously within the United States (28).

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 is 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
175 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,
180 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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Table 1. Characteristics of survey responders and associations with MRSA infection

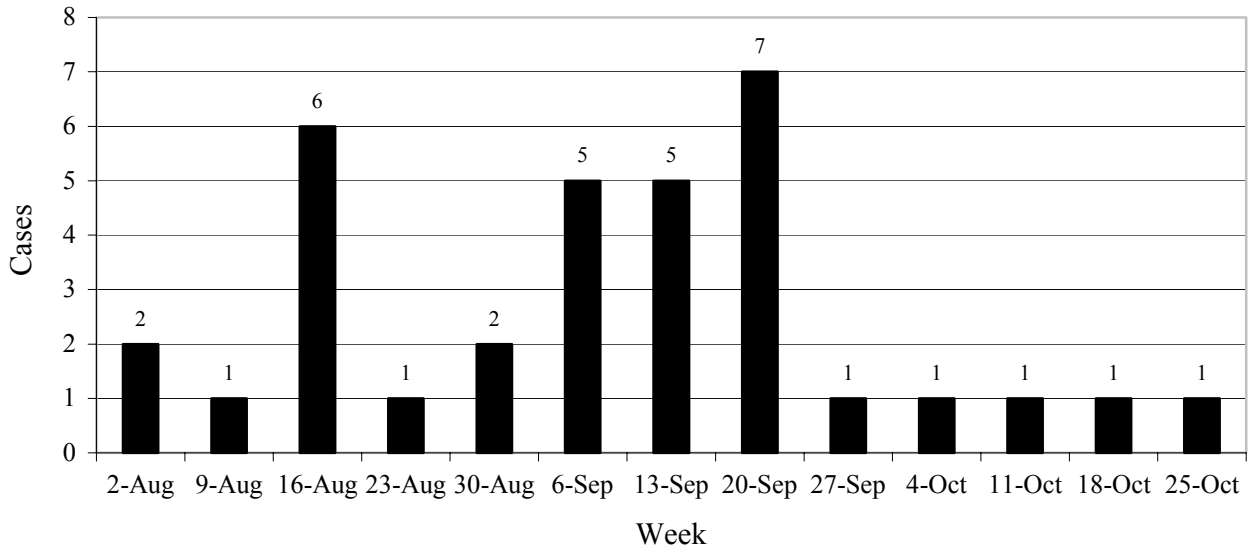
Variable	Total N		MRSA infected		OR*	CI*
	Number	%	Number	%		
Race/ethnicity					NSS	
Caucasian	156	77.2	17	77.3		
Other	46	22.8	5	22.7		
Age (y)					NSS	
<21	50	24.8	8	36.4		
21-25	86	42.6	7	31.8		
>25	66	32.7	7	31.8		
Antibiotic use within past 12 months	65	32.2	5	22.7	NSS	
Hospitalization within past 24 months	34	16.8	3	13.6	NSS	
Currently taking a dietary supplement	13	6.5	1	4.6	NSS	
Any past or current tobacco use	87	43.1	11	50	NSS	
Current alcohol use	94	46.5	10	45.5	NSS	
Having a roommate during training with a prior skin infection	49	24.3	11	50	3.44	1.34, 8.85
Having a family member or friend who worked in a healthcare setting	56	27.7	11	50	2.79	1.09, 7.15
Having a parent or member of the household who smoked during the respondent's childhood	77	38.1	3	13.6	0.26	0.07, 0.94

* Adjusted odds ratio (OR) and 95% confidence interval (CI) based on multivariable logistic regression modeling. NSS = not statistically significant.

Legend for figure

Figure 1. Number of MRSA cases in the military trainee population during each week of the 2002 outbreak.

Figure 1



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