**ABSTRACT**

**Objective:** Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA), which is caused primarily by the Canadian methicillin-resistant *Staphylococcus aureus*-10 (CMRSA-10) strain (also known as the USA300 strain) has emerged rapidly in the United States and is now emerging in Canada. We assessed the prevalence, risk factors, microbiological characteristics and outcomes of CA-MRSA in patients with purulent skin and soft tissue infections (SSTIs) presenting to emergency departments (EDs) in the Greater Toronto Area.

**Methods:** Patients with *Staphylococcus aureus* SSTIs who presented to 7 EDs between Mar. 1 and Jun. 30, 2007, were eligible for inclusion in this study. Antimicrobial susceptibilities and molecular characteristics of MRSA strains were identified. Demographic, risk factor and clinical data were collected through telephone interviews.

**Results:** MRSA was isolated from 58 (19%) of 299 eligible patients. CMRSA-10 was identified at 6 of the 7 study sites and accounted for 29 (50%) of all cases of MRSA. Telephone interviews were completed for 161 of the eligible patients. Individuals with CMRSA-10 were younger (median 34 v. 63 yr, p = 0.002), less likely to report recent antibiotic use (22% v. 67%, p = 0.046) or health care–related risk factors (33% v. 72%, p = 0.097) and more likely to report community-related risk factors (56% v. 6%, p = 0.008) than patients with other MRSA strains. CMRSA-10 SSTIs were treated with incision and drainage (1 patient), antibiotic therapy (3 patients) or both (5 patients), and all resolved. CMRSA-10 isolates were susceptible to clindamycin, tetracycline and trimethoprim-sulfamethoxazole.

**Conclusion:** CA-MRSA is a significant cause of SSTIs in the Greater Toronto Area, and can affect patients without known community-related risk factors. The changing epidemiology of CA-MRSA necessitates further surveillance to inform prevention strategies and empiric treatment guidelines.

**Keywords:** *Staphylococcus aureus*, methicillin resistance, community-associated infections, risk factors, skin diseases and infections, soft tissue infections

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**RÉSUMÉ**

**Objectif :** L’infection à *Staphylococcus aureus* résistant à la méthicilline d’origine communautaire (SARM-C), qui est attribuable principalement à la souche canadienne du *Staphylococcus aureus* résistant à la méthicilline-10 (SARM10), également connu sous le nom de souche USA300, a connu une éclosion rapide aux États-Unis et est en train d’émerger au Canada. Nous avons évalué la prévalence, les facteurs de risque, les caractéristiques microbiologiques et le
INTRODUCTION

In the past, methicillin-resistant Staphylococcus aureus (MRSA) was almost exclusively a nosocomial pathogen. Over the last decade, it has emerged in community settings causing skin and soft tissue infections (SSTIs), necrotizing pneumonia, necrotizing fasciitis and sepsis. In the United States, community-associated MRSA (CA-MRSA) was first observed in marginalized populations and, in general, under conditions of close physical contact, overcrowding and poor hygiene. Now, CA-MRSA is reported as the most common cause of purulent SSTIs in many centres in the United States. Recent reports from various centres in the United States have shown that Staphylococcus aureus (S. aureus) accounts for nearly 75% of these infections, with CA-MRSA strains predominating.

CA-MRSA is emerging in Canada. Outbreaks of CA-MRSA have been described in at-risk populations in recent years and there have been anecdotal reports of MRSA infection in individuals without risk factors. The hospital-based Canadian Nosocomial Surveillance Program reported that 15% of MRSA infections in 2006 were acquired in the community, but this program only surveys inpatients. Broader population surveillance has been identified as a priority to increase our understanding of CA-MRSA in Canada.

In Canada the rise of CA-MRSA is primarily due to the epidemic strain Canadian methicillin-resistant Staphylococcus aureus-10 (CMRSA-10) (equivalent to USA300 in the United States). CMRSA-10 has unique microbiological properties relative to hospital-associated MRSA strains including the presence of the staphylococcal chromosomal cassette mec (SCCmec) type IV, the frequent presence of Panton–Valentine leukocidin (PVL) genetic determinant and increased susceptibility to non-β-lactam antibiotics. As the strain primarily responsible for the rapid emergence of CA-MRSA, CMRSA-10 can be used to monitor the changing epidemiology of MRSA and to develop CA-MRSA prevention and treatment strategies.

The goal of this study is to determine the current prevalence, associated risk factors, microbiological characteristics and treatment outcomes of CA-MRSA in patients with purulent SSTIs presenting to emergency departments (EDs) in the Greater Toronto Area.

METHODS

Study population

This study was conducted between Mar. 1 and Jun. 30, 2007, in the ED of 7 hospitals in the Greater Toronto Area (combined volume of 350 000 patient visits annually). The 7 hospitals serve a variety of patient populations and include adult inner-city hospitals (hospitals 1, 2 and 3), a pediatric referral centre (hospital 4), an urban academic hospital near the city core (hospital 5), and community hospitals providing both pediatric and adult emergency care (hospitals 6 and 7).

The triage nurse at each centre informed all eligible patients presenting with SSTIs that they would be contacted by telephone and asked to consent to participate in the study if eligible. Study information brochures containing investigator contact information and posters were placed at each site.

Emergency physicians were asked to swab the single largest area of infection of each patient with a purulent
SSTI. During the study period, patients were managed according to usual practice at the discretion of the treating physician. The ED charts at 1 participating hospital were reviewed for the entire study period to assess the proportion of SSTI patients from whom wound swabs were collected.

**Patient enrolment process**

Eligible participants were identified based on the microbiological classification of cultures obtained from wound swabs. Only patients with *S. aureus*-positive cultures obtained in the ED were eligible for inclusion. Following the identification of *S. aureus*, each laboratory forwarded the patient demographics and contact information to study staff, who telephoned patients for consent to participate.

**Patient interviews**

With the exception of age and sex, patient information for this study was obtained by standardized telephone interviews. Patients with laboratory-confirmed *S. aureus* infections were contacted at least 2 weeks after their ED visit. Trained interviewers made 15 attempts to reach each patient on different days and times, including evenings and weekends. The study questionnaire addressed demographics, clinical presentation including predisposing skin breaks, risk factors for community- and hospital-associated MRSA infections, treatment and outcome. The specific risk factors included in the questionnaire are detailed in Table 1. Patients were also asked if they could recall receiving advice from ED staff about preventing the spread of skin infections.

Consenting patients with MRSA were also contacted at least 3 months after their index visit and asked about the outcome of their initial infection, recurrent infections and transmission to household or family members. Patients who were initially contacted 75 days or more after their visit to the ED were not contacted again for follow-up at 3 months.

This study was conducted in compliance with the Personal Health Information Protection Act and was approved by the research ethics board at each hospital.

**Laboratory methods**

The laboratories at participating sites identified *S. aureus* from wound specimens using conventional methodologies, including colony morphology, gram stain morphology, catalase test, Pastorex Staph Plus latex agglutination (Bio-Rad Laboratories) and tube coagulase test.

Based on the individual laboratory’s standard protocols, methicillin susceptibility was determined using 1 or more of the following methods: oxacillin screen plates (Mueller-Hinton agar with 4% sodium chloride

| Table 1. Comparison of risk factors among enrolled patients with purulent skin and soft tissue infections caused by methicillin-susceptible *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* and the prototypical community-associated methicillin-resistant *Staphylococcus aureus* strain |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Risk factor                                      | No. (%) of patients | p value*  | No. (%) of patients | p value*  |
| Antibiotics in previous 3 months                  | MSSA, n = 134  | MRSA, n = 17  | CMRSA-10, n = 9  | Other MRSA strains, n = 18  |
| Known exposure to MRSA†                           | 38 (28)          | 14 (52)         | 0.02                     | 2 (22)          | 12 (67)         | 0.05                  |
| Direct health care–related risk factor‡           | 4 (3)            | 11 (41)         | < 0.001                  | 2 (22)          | 9 (50)          | 0.21                  |
| Indirect health care–related risk factor§         | 63 (47)          | 16 (59)         | 0.26                     | 3 (33)          | 13 (72)         | 0.10                  |
| Community risk factor¶                            | 59 (44)          | 9 (33)          | 0.31                     | 3 (33)          | 6 (33)          | 1.00                  |
| Travel to United States in previous year          | 35 (26)          | 7 (26)          | 0.95                     | 3 (33)          | 4 (22)          | 0.65                  |
| Chronic skin condition                            | 30 (22)          | 6 (22)          | 0.97                     | 1 (11)          | 5 (28)          | 0.63                  |

MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *Staphylococcus aureus*; CMRSA-10 = Canadian methicillin-resistant *Staphylococcus aureus*-10; *p* value* = Fisher exact 2 × 2 test for a difference in proportions (e.g., proportion of patients with MSSA versus the proportion of patients with MRSA who reported the risk factor).

†Known exposure to MRSA: patient or household/family member with history of MRSA colonization or infection.
‡Direct health care-related risk factor included any 1 of the following: health care worker/volunteer; admitted to hospital overnight or resident of a long-term care facility in previous year; receiving dialysis; urinary catheter; intravenous line; surgery in previous 6 months.
§Indirect health care–related risk factor included any 1 of the following: household or family member admitted to hospital overnight in previous year; household or family member is a health care worker; regular visit to long-term care facility in previous year.
¶Community risk factor included any 1 of the following: lived in shelter, military barracks, correctional facility or other group setting in the previous year; had regular contact with someone who lives in a shelter, is homeless, uses intravenous drugs, is HIV-positive, is a member of the gay/lesbian/bisexual community; participation in group or contact sports. (Other group settings reported by patients with MRSA included hostel, rehabilitation centre and subsidized housing, and by patients with MSSA included rooming house, foster home, palliative care centre and recreational and educational facilities).
and 6 μg/mL oxacillin) or cefoxitin disk diffusion and/or detection of penicillin-binding protein 2a (MRSA-Screen, Oxoid, Ltd.). MRSA isolates were forwarded to a central laboratory and susceptibilities were determined by broth microdilution using Clinical and Laboratory Standards Institute (CLSI) protocols. Published interpretative criteria were used to determine the susceptibility of fusidic acid and mupirocin, as CLSI breakpoints have not been established. Inducible clindamycin resistance was tested by double disk diffusion in accordance with the CLSI protocols.

Pulsed field gel electrophoresis was performed using the Canadian standardized Staphylococcus aureus protocol and classified by Canadian MRSA epidemic strain nomenclature. MRSA isolates were tested at a reference laboratory for the presence of PVL by polymerase chain reaction. SCCmec typing (I–IV) was conducted using a previously described multiplex polymerase chain reaction.

For our study, CA-MRSA was defined by isolating MRSA with the CMRSA-10 pulsed field gel electrophoresis pattern, which is consistent with the observation that this is the predominant clone associated with the emergence of CA-MRSA in Canada and the United States. The pulsed field gel electrophoresis pattern is currently the most useful microbiological determinant of CA-MRSA because other genetic determinants such as PVL have been detected in both methicillin-susceptible Staphylococcus aureus (MSSA) and other MRSA clones.

### Statistical analysis

Data were managed using EpiData (version 3.1, The EpiData Association) and analyzed using SAS statistical software (version 9.1, SAS Institute Inc.). Descriptive statistics were used to describe patient characteristics and the prevalence of MRSA in the study population. Demographics and risk factor frequencies were compared between patients grouped by methicillin susceptibility (MSSA compared with MRSA) and MRSA strain type (CMRSA-10 compared with other MRSA strains) using the χ² test, Fisher exact test and Student t test when appropriate.

### RESULTS

During the 4-month study period, S. aureus was isolated from 299 ED patients with purulent SSTIs (Fig. 1). Among these eligible patients, the overall prevalence of MRSA was 19% (58 of 299 isolates) and averaged 17% by study site (range 6%–26%). CMRSA-10 was the most common strain type comprising 29 (50%) of the 58 MRSA isolates overall and a median of 25% of MRSA isolates by study site (range 0%–85%) (Table 2). Of the remaining isolates, 14 were CMRSA-2, 5 were CMRSA-4, there was 1 isolate each of CMRSA-1, -5, -6, -7, -8 and -9, and there were 4 isolates with patterns other

![Fig. 1. Flow diagram detailing patient enrolment subsequent to the identification of Staphylococcus aureus (S. aureus) in samples from purulent skin and soft tissue infections (SSTIs) collected in the emergency department (ED).](https://www.cambridge.org/core/terms)
than CMRSA-1–10. The highest proportion of CMRSA-10 (85%) was in Hospital 1, an inner-city hospital with rare pediatric visits. The hospital with the lowest proportion of MRSA and no CMRSA-10 was Hospital 4, the pediatric referral hospital in the city centre. Based on review of ED charts at Hospital 1 during the study period, 99 (87%) of 114 patients with a SSTI presentation had a culture swab collected.

Age and sex distributions of eligible patients with MRSA were similar to those with MSSA (Table 3). Eligible patients with CMRSA-10 were significantly younger than patients with other MRSA strains \((p < 0.001)\).

A total of 161 patients (134 patients with MSSA and 27 patients with MRSA) could be contacted and consented to telephone interviews. Overall, interviewed patients were younger (mean age 45, standard deviation [SD] 25, yr v. 51, SD 24, yr; \(p = 0.045\)) and slightly less likely to be male (54% v. 64%; \(p = 0.08\)) than patients not enrolled.

Table 1 shows the characteristics of the 161 interviewed patients. Patients with MRSA were more likely to report antibiotic use in the previous 3 months (52% v. 28%, \(p = 0.020\)) and to have had known MRSA exposures (41% v. 3%, \(p < 0.001\)) but were similar to patients with MSSA in all other risk factors examined. In contrast, CMRSA-10 patients reported known community-related risk factors for MRSA more often than patients with other MRSA strains (56% v. 6%, \(p = 0.008\)), and health care–related risk factors or recent antibiotic use less often. Four of 9 patients with CMRSA-10 did not report any community-related risk factors. However, 2 of these 4 patients reported direct health care–related risk factors and 1 additional patient reported visiting a MRSA-colonized family member in hospital.

The clinical presentations, treatment and outcomes of the enrolled patients are detailed in Table 4. The 9 interviewed patients with CMRSA-10 SSTIs all had resolved or improved by the first interview at a median of 28 days after the visit to the ED. Of the 7 patients with CMRSA-10 who completed follow-up interviews, 4 reported recurrent skin infections that had since resolved with additional treatment. In contrast, 5 (28%) of 18 SSTIs due to other MRSA strains had not improved or resolved at the time of the first interview conducted at a median of 45 days after the ED visit. At the 3-month follow-up for the 9 patients with other MRSA strains, none had recurrent infections and only 1 patient, with a surgical site infection, reported their initial infection had not resolved or improved.

Only one-third (31%) of 161 interviewed patients recalled receiving advice about how to prevent the spread of skin infections. Most frequently, patients recalled being advised to practise hand hygiene (10%), keep the infection covered (9%), and avoid sharing personal items such as towels (3%).

All CMRSA-10 isolates contained SCCmec IVa and were positive for the PVL gene. There were 9 other MRSA isolates that contained the SCCmec IVc cassette of which 6 were also PVL positive. The remaining 17 of 29 (59%) of the isolates contained SCCmec II. Unlike other MRSA strains, all CMRSA-10 isolates were susceptible to trimethoprim-sulfamethoxazole, clindamycin, tetracycline, doxycycline, and gentamicin (Table 5).

**DISCUSSION**

CA-MRSA initially appeared in the United States as localized community outbreaks, but has since become widespread in community and health care settings. A
We observed that a substantial proportion of similar pattern is emerging in Canada with outbreaks in high-risk populations reported in some provinces.11-15 We observed that a substantial proportion of S. aureus isolates from purulent SSTI specimens obtained from 7 high-volume EDs in metropolitan Toronto were MRSA (19%). Moreover, CMRSA-10 accounted for 50% of these MRSA isolates and was identified at all but 1 of the study sites.

Although the majority of patients with CMRSA-10 had known community-related risk factors for CA-MRSA, some may have acquired this strain after contact with the health care system. In our patients, a report of hospital-associated risk factors did not rule out infection with CA-MRSA. The occurrence of CA-MRSA outside traditionally identified high-risk groups has implications with CA-MRSA. The occurrence of CA-MRSA outside hospital-associated risk factors did not rule out infection with the health care system. In our patients, a report of ARSA, some may have acquired this strain after contact with the health care system. In our patients, a report of hospital-associated risk factors did not rule out infection with CA-MRSA. The occurrence of CA-MRSA outside traditionally identified high-risk groups has implications with CA-MRSA. The occurrence of CA-MRSA outside hospital-associated risk factors did not rule out infection with the health care system. In our patients, a report of ARSA, some may have acquired this strain after contact with the health care system.

A large number of the patients in this study received both antibiotic therapy and incision and drainage as treatment for their SSTI. Several studies have demonstrated that incision and drainage without antibiotic therapy may be sufficient for minor SSTIs.29,30 The situations in which antibiotics are necessary for the resolution of SSTIs remain unclear. The need for antibiotic therapy is an important question, as overuse of these medications is a key contributing factor to the development of resistant organisms like MRSA. When antibiotics are indicated, knowledge of the antibiotic susceptibility patterns of circulating strains is essential. In settings where MRSA prevalence is low, empiric treatment with a β-lactam antibiotic with activity against S. aureus may be appropriate. In our city, the prevalence of methicillin-resistance in staphylococcal SSTIs was 19%, which may require physicians to reconsider their empiric therapy given the suggestion that a prevalence above 10%–15% warrants re-evaluation.1

Table 4. Comparison of clinical presentation, treatment and outcomes among enrolled patients with purulent skin and soft tissue infections caused by methicillin-susceptible Staphylococcus aureus, methicillin-resistant Staphylococcus aureus and the prototypical community-associated Staphylococcus aureus strain

<table>
<thead>
<tr>
<th>No. (%) of patients</th>
<th>No. (%) of patients</th>
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<tbody>
<tr>
<td>Clinical feature</td>
<td>MSSA, n=134</td>
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<tr>
<td>Clinical presentation</td>
<td>Skin break or injury preceded infection</td>
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<td></td>
<td>Febrile at emergency department presentation</td>
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<tr>
<td>Treatment</td>
<td>Incision and drainage alone</td>
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<tr>
<td></td>
<td>Antibiotics alone</td>
</tr>
<tr>
<td></td>
<td>Both incision and drainage and antibiotics</td>
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<tr>
<td></td>
<td>No treatment</td>
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<tr>
<td></td>
<td>Resolved/improved by time of initial interview</td>
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<tr>
<td></td>
<td>Recurrent infection before follow-up interview†</td>
</tr>
<tr>
<td></td>
<td>Transmission to family/household contacts before follow-up interview†</td>
</tr>
</tbody>
</table>

CMRSA-10 = Canadian methicillin-resistant Staphylococcus aureus-10; MRSA = methicillin-resistant Staphylococcus aureus; MSSA = methicillin-susceptible Staphylococcus aureus. Note: all isolates were susceptible to dalbavancin, daptomycin, linezolid, minocycline, tigecycline, quinupristin/dalfopristin, rifampin, and vancomycin.

Table 5. Frequency of antibiotic resistance among methicillin-resistant Staphylococcus aureus isolates causing purulent skin and soft tissue infections by strain type

<table>
<thead>
<tr>
<th>No. (%) of resistant isolates by type of MRSA strain</th>
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<tbody>
<tr>
<td>Antibiotic</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
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<tr>
<td>Clindamycin</td>
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<tr>
<td>Doxycycline</td>
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<tr>
<td>Erythromycin</td>
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<td>Fusidic acid</td>
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<td>Gentamicin</td>
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<tr>
<td>Mupirocin</td>
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<tr>
<td>Tetracycline</td>
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<tr>
<td>Trimethoprim/sulfamethoxazole</td>
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</tbody>
</table>

CMRSA-10 = Canadian methicillin-resistant Staphylococcus aureus-10; MRSA = methicillin-resistant Staphylococcus aureus.

†Denominators for follow-up interview (only MRSA patients contacted): 7 patients with CMRSA-10 and 9 patients with other MRSA strains.
All CMRSA-10 isolates in this study were susceptible to oral agents including clindamycin, trimethoprim-sulfamethoxazole, tetracycline and to parenteral agents including vancomycin and tigecycline. In patients with community-related risk factors and no health care-related risk factors for MRSA, these may be appropriate empiric choices when deemed necessary. In all other patients, the appropriate oral antibiotic choice is less clear since infections may be due to more antibiotic-resistant strains of MRSA.

Few patients in this study recalled receiving advice from ED staff about how to prevent the spread of skin infections. To limit or prevent the widespread dissemination of CMRSA-10 in Canada, additional patient education and other control efforts are needed. Patients with SSTIs should be advised to cover their wound, to not share personal items such as razors, towels or sports equipment, to launder their clothes and linens frequently, to wash sports equipment after use and to practise frequent hand hygiene. If community outbreaks of MRSA are suspected, public health authorities should be notified promptly.

Continued surveillance for MRSA in Canada, including strain typing, is warranted and EDs provide valuable sentinel sites. CA-MRSA strains can spread readily in the general population and may develop resistance to additional antimicrobial agents including clindamycin, mupirocin and tetracycline as recently reported in certain settings in the United States. Surveillance data are therefore needed to monitor the changing prevalence, epidemiology and susceptibility profiles of CA-MRSA strains in order to determine empiric treatment guidelines and prevention strategies.

Emergency departments are at the front line of clinical medicine and provide ideal settings for detecting and monitoring new disease trends. The creation of an emergency-based surveillance system in Canada would enable real-time monitoring of emerging infections, including CA-MRSA. A prospective cross-Canada study on CA-MRSA prevalence is currently being undertaken through a collaboration of this working group and the Canadian Association of Emergency Physicians-Research Consortium.

Limitations

The primary limitation of this study was the lack of overall SSTI denominator. Although an audit conducted at one hospital indicated that physicians swabbed the majority of eligible patients, these data were not available at all study sites, which prohibited the determination of the overall prevalence of MRSA and CA-MRSA in ED patients presenting with purulent SSTIs. Additionally, the estimates reported may have been influenced by patterns of specimen collection by different physicians at different sites. We were also unable to capture the number of patients presenting with SSTIs caused by non–S. aureus organisms. A second limitation was the low enrolment for the telephone interview among eligible persons. Future studies should include ED chart reviews to obtain data for nonresponders and patients with no fixed address when possible. Finally, the results of this study may not be applicable to other Canadian cities. Outbreaks of CA-MRSA have been more frequent in other parts of Canada and CMRSA-10 may be more pervasive in these communities. As the epidemiology of CA-MRSA is continually evolving, this study is reflective of the current situation in the Greater Toronto Area.

CONCLUSION

CA-MRSA is a significant cause of SSTIs in Toronto, and can affect patients without known community-related risk factors. Epidemiological risk factors may not distinguish between MSSA and MRSA or between CA-MRSA and hospital-associated MRSA. Despite extensive research conducted in this area, the most appropriate treatment for CA-MRSA remains unclear.

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REFERENCES


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