ORIGINAL ARTICLE BACTERIOLOGY

Body site colonization in patients with community-associated methicillin-resistant *Staphylococcus aureus* and other types of *S. aureus* skin infections

E. S. Yang[1,2], J. Tan[1], S. Eells[1], G. Rieg[1,2], G. Tagudar[1] and L. G. Miller[1,2]

1) *Division of Infectious Diseases and Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance and* 2) *David Geffen School of Medicine at the University of California, Los Angeles, CA, USA*

Abstract

Efforts to control spread of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) are often based on eradication of colonization. However, the role of nasal and non-nasal colonization in the pathogenesis of these infections remains poorly understood. Patients with acute *S. aureus* skin and soft tissue infection (SSTI) were prospectively enrolled. Each subject's nasal, axillary, inguinal and rectal areas were swabbed for *S. aureus* and epidemiological risk factors were surveyed. Among the 117 patients enrolled, there were 99 patients who had an SSTI and for whom data could be analysed. Sixty-five patients had a CA-MRSA SSTI. Among these patients, MRSA colonization in the nares, axilla, inguinal area and rectum was 25, 6, 11 and 13%, respectively, and 37% overall were MRSA colonized. Most (96%) MRSA colonization was detected using nose and inguinal screening alone. Non-nasal colonization was 25% among CA-MRSA patients, but only 6% among patients with CA-methicillin-susceptible *S. aureus* (MSSA) or healthcare-associated MRSA or MSSA. These findings suggest that colonization patterns in CA-MRSA infection are distinct from those in non-CA-MRSA *S. aureus* infections. The relatively high prevalence of non-nasal colonization may play a key role in CA-MRSA transmission and acquisition of infection.

Keywords: Colonization, MRSA, skin infection, *Staphylococcus aureus*
Original Submission: 13 August 2008; **Revised Submission:** 13 November 2008; **Accepted:** 14 November 2008
Editor: F. Allerberger
Article published online: 18 August 2009
Clin Microbiol Infect 2010; **16:** 425–431
10.1111/j.1469-0691.2009.02836.x

Corresponding author and reprint requests: L. G. Miller, Division of Infectious Diseases, Harbor-UCLA Medical Center, 1000 W. Carson St Box 466, Torrance, CA 90502, USA
E-mail: lgmiller@ucla.edu

Introduction

Over the past decade, community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections have emerged in persons without traditional MRSA risk factors. Previous studies on the pathogenesis and spread of MRSA have demonstrated that colonization with MRSA is a critical risk factor for subsequent healthcare-associated MRSA infection [1], but to date there are very few data on patients with CA-MRSA.

Staphylococcus aureus colonization is most consistently identified in humans in the anterior nares. However, recent studies of patients with CA-MRSA infection in outbreaks have shown a significant number of infected patients without colonization at that site [2,3]. Understanding body site colonization in patients with CA-MRSA infection may be of critical importance. For example, interventions to eradicate colonization and prevent CA-MRSA infection often target non-nasal sites, yet there are few data on non-nasal colonization among patients with CA-MRSA.

We hypothesized that patients with CA-MRSA skin infections might be colonized at body site locations other than the anterior nares. This hypothesis is supported by previous studies that have shown CA-MRSA spread via sexual contact in both a heterosexual couple and men who have sex with men [4,5]. We examined the prevalence of MRSA colonization at four body sites to elucidate further the relationship between MRSA colonization and infection in patients with CA-MRSA and other types of *S. aureus* skin infections.

Materials and Methods

From February 2005 to October 2007, we enrolled patients with acute *S. aureus* skin infections from two clinical sources:

(i) a 400-bed tertiary care county hospital (Harbor-UCLA Medical Center) and (ii) outpatients at the human immunodeficiency virus (HIV) clinic associated with this medical centre. Inpatients were identified (on all days when a clinical investigator was available) by screening of the clinical microbiology laboratory for new cultures positive for *S. aureus* from a wound source. We attempted to enrol all patients with acute *S. aureus* skin and soft tissue infections (SSTIs) requiring hospitalization. Patients were eligible if: (i) the culture was positive for *S. aureus*, identified by a rapid *S. aureus*-specific latex agglutination test (Staphaurex; Remel, Lenexa, KS, USA), (ii) the patient was still hospitalized, and (iii) the culture had been taken within 72 h of admission. Patients with both methicillin-sensitive and methicillin-resistant *S. aureus* were included, because patients were enrolled before antibiotic susceptibility testing had been carried out. HIV-infected outpatients were eligible if: (i) they had a clinical condition consistent with a *S. aureus* infection, and (ii) a culture could be obtained from the patient. Outpatients were offered a small financial incentive to participate in the survey and colonization site sampling portions of the study.

Patients were excluded from the study if: (i) *S. aureus* had been previously isolated from the patient during the current hospitalization; (ii) the patient had already been enrolled in the study; or (iii) the subject had previously refused to participate in the study. Study staff approached all eligible patients, described the study, and attempted to complete the informed consent process. The study design was approved by the Institutional Review Board at Harbor-UCLA Medical Center.

Data collection

A standardized questionnaire was administered to all consenting patients. This questionnaire used items from a previous investigation of CA-MRSA risk factors [6], and surveyed subjects about exposures previously associated with healthcare-associated (HA)-MRSA infection [1,7] or with CA-MRSA infection [4,8–12]. We also collected information about clinical and demographic factors using a standardized abstraction instrument described previously [6]. These included age, gender, race/ethnicity, level of education, hospitalization in the past 12 months, body site of *S. aureus* infection, comorbidities (Charlson Co-morbidity Index), HIV infection, number of visits (if any) to healthcare providers for *S. aureus* prior to admission, and duration of symptoms prior to admission. A study physician confirmed that the subject was diagnosed with a skin infection and swabs were taken from the infected site and nasal, axillary, inguinal and rectal areas. Swabs were then analysed for the presence of methicillin-resistant or methicillin-susceptible *S. aureus* using standard microbiological techniques and enrichment-selective media for *S. aureus* and MRSA.

Case definitions

Antimicrobial susceptibility was determined using the VITEK system (BioMerieux USA, Durham, NC, USA), according to NCCLS protocols; isolates resistant to oxacillin were considered MRSA; isolates susceptible to oxacillin were considered methicillin-susceptible *S. aureus* (MSSA).

Subjects were considered to have CA infection if the culture specimen was not from a surgical site and if, in the past 12 months, the subject (i) had not resided in a long-term care facility, such as a nursing home; (ii) had no indwelling devices, such as an intravenous catheter; (iii) had not visited an infusion clinic; and (iv) had not received peritoneal or haemodialysis. Any subjects who did not fulfil these criteria were classified as having HA infection. This definition is consistent with the CDC and Prevention's ABC criteria, as previously described [6,13]. These criteria allowed categorization of all cases as CA-MRSA, CA-MSSA, HA-MRSA or HA-MSSA. Colonization was defined as the presence of the same type of organism that caused infection (either MRSA or MSSA) colonizing a non-infected body site.

Data analysis

The dataset of risk factors associated with MRSA colonization among patients with CA-MRSA SSTIs was managed using SAS (version 9.1.3; SAS Institute, Cary, NC, USA). Bivariate analysis was used to compare 16 variables (Table 2) hypothesized *a priori* to be associated with MRSA colonization among patients with CA-MRSA SSTIs. Bivariate analysis was assessed using odds ratios and the associated p-values. All variables with a p-value ≤ 0.20 in the bivariate analyses were included in a multivariate logistic regression analysis. Multicolinearity was assessed for all models using a macro developed for use with the SAS system. Multivariate analysis was conducted to assess variables associated with MRSA colonization. Backwards elimination was performed using the Likelihood Ratio test to find the best model. Models were examined for goodness of fit using the Hosmer–Lemeshow statistic. All variables were considered significant at the $\alpha = 0.05$ level.

Results

One hundred and seventeen patients were enrolled in this investigation. Some were later excluded from analysis for the following reasons: six patients' cultures were determined to be coagulase-negative *Staphylococcus* upon further testing; six agreed to enrol but then refused all colonization swabs; and

six patients' cultures were determined not to be associated with a SSTI. Among the 99 patients with a SSTI included in the analysis, 65 were determined to have CA-MRSA, 22 had CA-MSSA, six had HA-MRSA, and six had HA-MSSA. Eight (8%) patients were enrolled as outpatients from the HIV clinic. Ninety-three (94%) of the patients presented to medical care primarily for a SSTI. The demographics for patients in each of the four groups are summarized in Table 1. Among patients with CA-MRSA SSTIs, the mean age was 39 years, and 76% were male. The demographics of patients with CA-MRSA are summarized in Table 2.

Colonization

Among patients with a CA-MRSA SSTI, 37% (24/65) were found to be MRSA colonized (Fig. 1a). Twenty-five percent of patients (16/65) were colonized in the nares, 6% (4/65) in the axilla, 17% (11/64) in the inguinal area, and 13% (7/54) in the rectal area. Among those CA-MRSA-infected patients who were MRSA colonized, 96% (23/24) could be identified using a combination of nasal and inguinal screening alone. Of patients with CA-MSSA, HA-MRSA and HA-MSSA, only 6% (2/34) had colonization outside the nasal area (Fig. 1b–d).

TABLE 1. Demographic information concerning all patients with skin and soft tissue infections

Variable	All patients *n* = 99 (%)	CA-MRSA SSTI *n* = 65 (%)	CA-MSSA SSTI *n* = 22 (%)	HA-MRSA *n* = 6 (%)	HA-MSSA *n* = 6 (%)	p-value
Age, mean ± SD	40 ± 12	39 ± 12	46 ± 12	40 ± 20	37 ± 10	0.07
Gender male	75 (76)	49 (75)	17 (77)	4 (67)	5 (83)	0.94
Ethnicity						
Caucasian	37 (37)	32 (49)	3 (14)	1 (17)	1 (17)	0.03
African–American	20 (20)	12 (19)	4 (18)	2 (33)	2 (33)	
Hispanic	36 (36)	18 (28)	13 (59)	2 (33)	3 (50)	
Other	6 (6)	3 (5)	2 (9)	1 (17)	0 (0)	

CA, community-associated; HA, healthcare associated; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*; SSTI, skin and soft tissue infection.
p-values represent comparisons amongst the four patient groups (CA-MRSA, CA-MSSA, HA-MRSA, HA-MSSA) were made via *t*-test or Fisher's exact test, as appropriate.

TABLE 2. Demographic and clinical characteristics of subjects with CA-MRSA skin and soft tissue infections

Variable	All patients *n* = 65 (%)	MRSA colonization *n* = 24 (%)	No MRSA colonization *n* = 41 (%)	OR	95% CI	p-value
Demographic variables						
Age, mean ± SD	39 ± 12	40 ± 13	40 ± 12	0.99	0.95–1.04	0.67
Gender male	49 (75)	21 (89)	28 (68)	3.3	0.82–12.9	0.08
Ethnicity						
Caucasian	32 (49)	13 (54)	19 (46)	Ref	–	–
African–American	12 (19)	5 (21)	7 (17)	1.04	0.27–4.02	0.95
Hispanic	18 (28)	5 (21)	13 (32)	0.56	0.16–1.9	0.37
Other	3 (5)	1 (4)	2 (5)	0.73	0.06–8.9	0.81
Education						
College graduate	10 (16)	4 (10)	4 (10)	Ref	–	–
High school graduate	40 (62)	15 (63)	25 (61)	0.4	0.10–1.7	0.21
Did not graduate high school	15 (23)	3 (13)	12 (29)	0.17	0.03–0.99	0.05
Clinical						
Charlston comorbidity score						
Mean ± SD	1.7 ± 2.5	2.6 ± 2.9	1.2 ± 2.0	1.3	1.02–1.5	0.03
HIV positive	14 (21)	9 (38)	5 (12)	4.3	1.2–15.1	0.02
In the last 12 months						
Previous MRSA infection	21 (32)	11 (46)	10 (24)	2.6	0.89–7.7	0.07
Use of antibiotics	27 (42)	10 (42)	17 (42)	2.0	0.60–6.6	0.99
Hospitalization	14 (22)	7 (29)	7 (17)	1.4	0.56–3.3	0.25
Incarceration	18 (28)	7 (29)	11 (27)	1.1	0.37–3.4	0.84
Intravenous drug use	13 (20)	5 (21)	8 (20)	1.1	0.31–3.8	0.99
Snort/sniff drugs	11 (17)	7 (29	4 (10)	3.8	0.98–14.7	0.08
Any drug use	23 (35)	12 (50)	11 (27)	2.7	0.95–7.8	0.06
≥2 sexual partners	14 (22)	3 (13)	11 (27)	0.39	0.10–1.6	0.18
Homelessness	21 (32)	6 (25)	15 (37)	0.61	0.22–1.7	0.34
In the past 30 days						
Contact with person who had a skin infection	8 (12)	1 (4)	7 (17)	0.21	0.02–1.8	0.24

CA, community-associated; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*; ref, referent group.

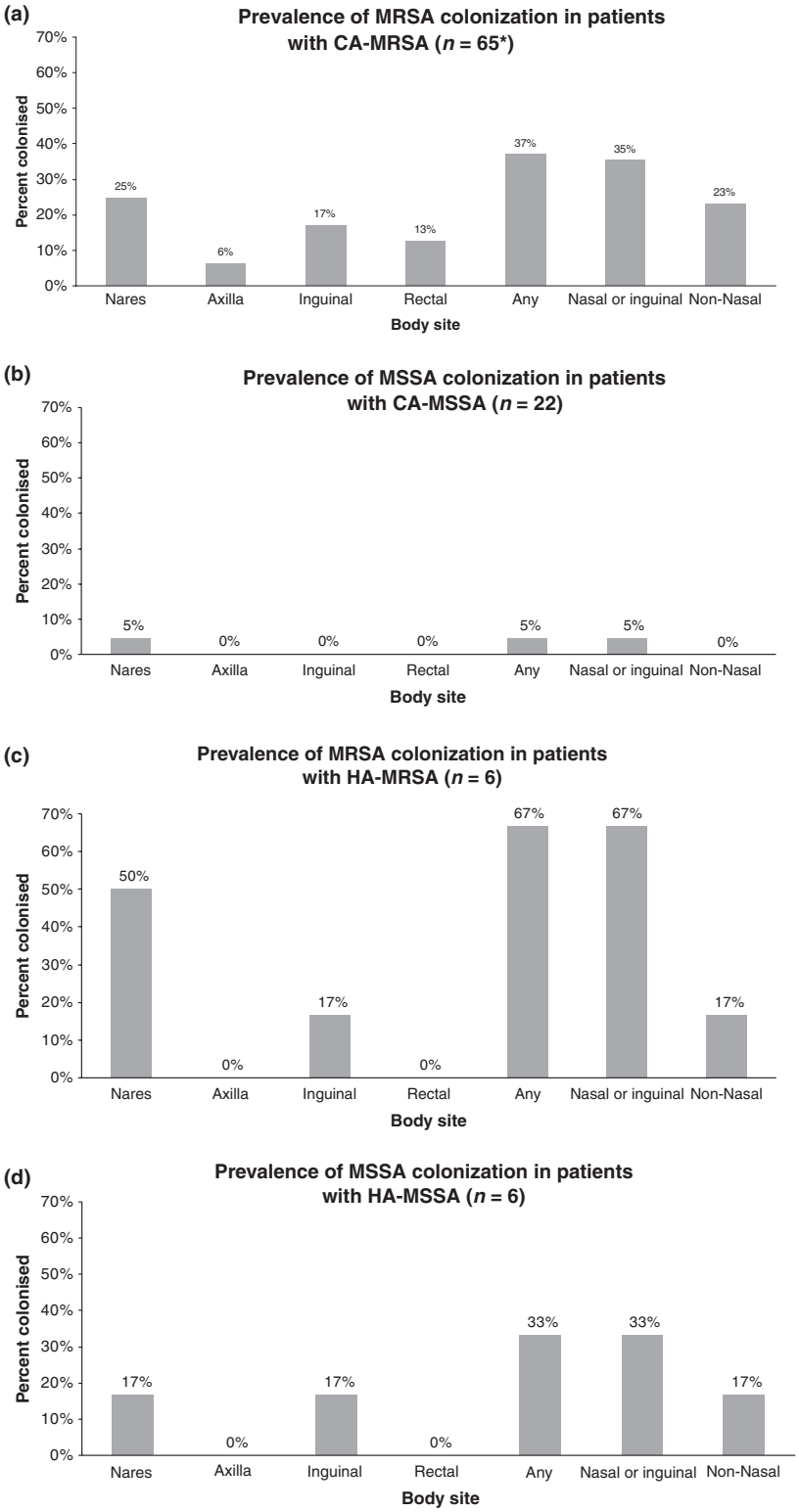

FIG. 1. Prevalence of *Staphylococcus aureus* colonization in patients with skin or soft tissue infection. The bar graph height indicates the percentage colonized out of the total number of patients with each type of infection (CA-MRSA, CA-MSSA, HA-MRSA, or HA-MSSA). Nineteen patients refused rectal swabbing (nine with CA-MRSA and three each with HA-MRSA, CA-MSSA, and HA-MSSA). One patient (in the CA-MRSA group) refused inguinal swabbing. CA, community-associated; HA, healthcare-associated; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*.

TABLE 3. Multivariate analysis predicting MRSA colonization among patients with CA-MRSA skin and soft tissue infections (*n* = 65)

Variable	OR	95% CI	p-value
HIV status	5.8	1.5–22.3	0.01
Previous MRSA infection	3.6	1.1–11.8	0.03

CA, community-acquired; MRSA, methicillin-resistant *Staphylococcus aureus*.

Risk factors for MRSA colonization in adults

Among patients with CA-MRSA, HIV infection (OR 4.3, p 0.02) and greater comorbidities (OR 1.3, p 0.03) were associated with MRSA colonization (Table 2). Patients who did not graduate from high school were found to have a significantly lower prevalence of colonization (OR 0.17, p 0.05). Factors not associated with MRSA colonization included previous antibiotic exposure, hospitalization, incarceration, and drug use. Upon multivariate analysis (Table 3), HIV infection (OR 5.8, p 0.01) and history of MRSA infection in the past 12 months (OR 3.6, p 0.03) were both found to be independently associated with MRSA colonization.

Discussion

In a four-body-site survey, we detected MRSA colonization in patients with acute CA-MRSA infection in 40% of patients. Other notable findings include that non-nasal colonization was much more common in patients with CA-MRSA SSTIs compared with those with non-CA-MRSA *S. aureus* SSTIs. This proportion of CA-MRSA patients who were colonized is in contrast to the findings in HA-MRSA infections, in which the vast majority of patients are colonized at the time of infection [14]. The low number of patients with HA-MRSA infections who were MRSA colonized might have resulted from our patients being essentially outpatients with HA-MRSA, a group in which colonization prevalence is poorly understood. Nevertheless, the findings that MRSA colonization is more common in CA-MRSA than in HA-MRSA supports observational data of CA-MRSA pathogenesis, and may have clinical and pathogenetic significance. For example, during outbreaks, CA-MRSA infection has frequently been acquired via skin–skin or skin–fomite contact [2,9], suggesting that non-nasal CA-MRSA may be important in CA-MRSA acquisition or transmission. At a basic level, the genome of the USA300 subtype of CA-MRSA, the most common circulating strain of CA-MRSA nationwide and at our institution [7,18], may help facilitate this spread. USA300 strains commonly contain the arginine catabolic mobile element (ACME), which is believed to promote survival on human skin. ACME is uncommonly found in other strains of *S. aureus* [15].

Interestingly, almost all CA-MRSA-colonized patients (96%; 25/26) in this study could be identified using a combination of nasal and inguinal swabs (Fig. 1). Previous investigations [16], which have rarely focused on CA-MRSA, have found that *S. aureus* colonization is most common in the anterior nares. These findings suggest that CA-MRSA colonizes a more diverse array of body sites than non-CA-MRSA [17]. In our population, screening for colonization in the axilla and rectum in patients with CA-MRSA did not significantly increase sensitivity in detecting MRSA colonization. Although we did not screen for CA-MRSA colonization in the pharynx, other studies have suggested that the pharynx may be an additional site of CA-MRSA colonization [18].

In our population, colonization of patients with CA-MRSA infection appears to be different from that of patients infected with HA-MRSA, HA-MSSA or CA-MSSA, as 23% (15/65) of patients with CA-MRSA were MRSA-colonized in non-nasal areas. This contrasts with the 0% (0/22) of patients with CA-MSSA, 17% (1/6) of patients with HA-MRSA, and 17% (1/6) of patients with HA-MSSA who were colonized outside the nose.

Colonization studies often sample only one location on the body, usually the anterior nares. The adequacy of this screening technique has been questioned [19]. From our findings, it appears that screening only the anterior nares may be sufficient to detect most colonized patients who have healthcare-associated *S. aureus* and CA-MSSA infections. The low prevalence of colonization (1/22, 4.5%) among patients with CA-MSSA infection is surprising, and may be attributable to the frequent use of clindamycin for skin infections in our institution. Our colonization cultures were typically not obtained until 48–72 h after antibiotics had been started. Clindamycin, which has been demonstrated to be efficacious in nares decolonization [20], may have rendered some patients with acute *S. aureus* infection negative upon nasal sampling for colonization. The high prevalence of non-nasal colonization in patients with CA-MRSA suggests that decolonization regimens for patients with recurrent infections (the efficacy of which remains relatively unproven) should probably include body washes such as chlorhexidine or hexachlorophene, or diluted bleach baths [21].

There are several limitations to this study. First, all of the patients were enrolled from a single medical centre, and therefore the results may not be generalizable to other populations. However, the patient population at Harbor-UCLA Medical Center has ethnic and socioeconomic diversity. Second, we did not enrol patients on a consecutive basis, because of limited availability of study personnel. However,

given the observational nature of the study, it is unlikely that selection bias significantly influenced our findings. Third, we relied on patient self-reporting to identify risk factors and associations. Patients may be less than forthcoming about risk factors such as incarceration, drug use or sexual contact. Nevertheless, in a previous investigation using this instrument, risk factors that may be considered socially undesirable were significantly associated with MRSA risk [6], suggesting that the survey has validity and limited bias. Fourth, we did not further characterize the *S. aureus* isolates. However, previous studies in this population at our institution have shown that >90% of CA-MRSA isolates are USA300 SCC*mec* Type IV-containing strains [22], the most commonly circulating CA-MRSA strain in the USA, whereas isolates of CA-MSSA are heterogeneous in terms of strain type [6].

A further limitation is that patients were not approached until they had received antibiotics, given that identification of *S. aureus* from a wound culture typically takes up to 1–2 days. However, prior systemic antibiotic therapy is unlikely to alter the results significantly, because most systemic antibiotics, with the exception of clindamycin, active against *S. aureus* are poor at eradicating colonization even after prolonged courses [23]. The investigation is also limited because it is cross-sectional, and does not distinguish between colonization leading to infection and colonization as a result of infection.

There are several strengths to the investigation. First, whereas virtually all other studies on MRSA colonization focus solely on the anterior nares, we screened for colonization at four different body sites, increasing the sensitivity of our assay. The traditional method of screening only the anterior nares identified only 67% (16/24) of CA-MRSA-colonized patients that were identified using four site screening (Fig. 1). This difference in sensitivity suggests that future investigations should probably include inguinal screening in addition to nasal screening for CA-MRSA colonization. Second, the investigation was performed prospectively, and patients were interviewed before the antibiotic susceptibility of the *S. aureus* isolate was known, reducing the likelihood of observer or recall bias. Third, we used a very rigorous definition of CA and HA infection. This definition is consistent with CDC definitions and can be accurately defined only by a combination of clinical information and information obtained from patient survey. Therefore, unlike categories of CA and HA derived from databases, our categorization of patients into CA and HA categories is very accurate.

In conclusion, we found that MRSA colonization in patients with acute CA-MRSA infection is present in less than half and that nearly all colonized patients can be identified using nasal and inguinal screening alone. We also found that, unlike CA-MRSA, non-nasal colonization among patients with HA-MRSA, CA-MSSA and HA-MSSA infections is uncommon. Longitudinal studies would further clarify the role of colonization in the pathogenesis of CA-MRSA and other categories of *S. aureus* infection. Furthermore, understanding the role that non-nasal colonization plays as a reservoir for CA-MRSA transmission and re-infection would help to determine the clinical significance of non-nasal colonization.

Acknowledgements

We would like to thank J. Perlroth Daar, M. Witt and S. Nichols and the Harbor-UCLA Medical Center General Clinical Research Center for their assistance with this investigation. We would also like to thank the patients and their families for participating in this investigation.

Transparency Declaration

Financial support was provided by GCRC Grant M01-RR00425 National Center for Research Resources. L.G.M.'s work was supported by a grant from the Center for Disease Control and Prevention (R01/CCR923419). All authors declare no potential conflicts of interest.

References

1. Mulligan ME, Murray-Leisure KA, Ribner BS *et al.* Methicillin-resistant *Staphylococcus aureus*: a consensus review of the microbiology, pathogenesis, and epidemiology with implications for prevention and management. *Am J Med* 1993; 94: 313–328.
2. Begier EM, Frenette K, Barret NL *et al.* A high-morbidity outbreak of methicillin-resistant *Staphylococcus aureus* among players on a college football team, facilitated by cosmetic body shaving and turf burns. *Clin Infect Dis* 2004; 39: 1446–1453.
3. Kazakova SV, Hageman JC, Matava M *et al.* A clone of methicillin-resistant *Staphylococcus aureus* among professional football players. *N Engl J Med* 2005; 352: 468–475.
4. Lee NE, Taylor MM, Bancroft E *et al.* Risk factors for community-associated methicillin-resistant *Staphylococcus aureus* skin infections among HIV-positive men who have sex with men. *Clin Infect Dis* 2005; 40: 1529–1534.
5. Cook HA, Furuya EY, Larson E, Vasquez G, Lowy FD. Heterosexual transmission of community-associated methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* 2007; 44: 410–413.
6. Miller LG, Perdreau F, Bayer AS *et al.* Clinical and epidemiologic characteristics cannot distinguish community-associated methicillin-resistant *Staphylococcus aureus* infection from methicillin-susceptible *S. aureus* infection: a prospective investigation. *Clin Infect Dis* 2007; 44: 471–482.

7. Graffunder EM, Venezia RA. Risk factors associated with nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection including previous use of antimicrobials. *J Antimicrob Chemother* 2002; 49: 999–1005.
8. Centers for Disease Control and Prevention. Outbreaks of community-associated methicillin-resistant *Staphylococcus aureus* skin infections – Los Angeles County, California, 2002–2003. *MMWR Morb Mortal Wkly Rep* 2003; 52: 88.
9. Centers for Disease Control and Prevention. Methicillin-resistant *Staphylococcus aureus* infections among competitive sports participants—Colorado, Indiana, Pennsylvania, Los Angeles County, 2000–2003. *MMWR Morb Mortal Wkly Rep* 2003; 52: 793–795.
10. Eady EA, Cove JH. Staphylococcal resistance revisited: community-acquired methicillin resistant *Staphylococcus aureus*—an emerging problem for the management of skin and soft tissue infections. *Curr Opin Infect Dis* 2003; 16: 103–124.
11. Chambers HF. The changing epidemiology of *Staphylococcus aureus*? *Emerg Infect Dis* 2001; 7: 178–182.
12. Salgado CD, Farr BM, Calfee DP. Community-acquired methicillin-resistant *Staphylococcus aureus*: a meta-analysis of prevalence and risk factors. *Clin Infect Dis* 2003; 36: 131–139.
13. Minnesota Department of Health. Community-associated methicillin-resistant *Staphylococcus aureus* in Minnesota. *Dis Control Newsl.* 2004; 32: 61–72
14. von Eiff C. Nasal carriage as a source of *Staphylococcus aureus* bacteremia. *N Engl J Med* 2001; 344: 11–16.
15. Diep BA, Gill SR, Chang RF *et al.* Complete genome sequence of USA300, an epidemic clone of community-acquired methicillin-resistant *Staphylococcus aureus*. *Lancet* 2006; 367: 731–739.
16. Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks. *Clin Microbiol Rev* 1997; 10: 505–520.
17. Williams RE. Healthy carriage of *Staphylococcus aureus*: its prevalence and importance. *Bacteriol Rev* 1963; 27: 56–71.
18. Ringberg H, Cathrine Petersson A, Walder M, Hugo Johansson PJ. The throat: an important site for MRSA colonization. *Scand J Infect Dis* 2006; 38: 888–893.
19. Rosenthal A, White D, Churilla S, Brodie S, Katz KC. Optimal surveillance culture sites for detection of methicillin-resistant *Staphylococcus aureus* in newborns. *J Clin Microbiol* 2006; 44: 4234–4236.
20. Strausbaugh LJ, Jacobson C, Sewell DL, Potter S, Ward TT. Antimicrobial therapy for methicillin-resistant *Staphylococcus aureus* colonization in residents and staff of a veterans affairs nursing home care unit. *Infect Control Hosp Epidemiol* 1992; 13: 151–159.
21. Kaplan SL. Treatment of community-associated methicillin-resistant *Staphylococcus aureus* infections. *Pediatr Infect Dis J* 2005; 24: 457–458.
22. Moran GJ, Krishnadasan A, Gorwitz RJ *et al.* Methicillin-resistant *S. aureus* infections among patients in the emergency department. *N Engl J Med* 2006; 355: 666–674.
23. Chang SC, Hsieh SM, Chen ML, Sheng WH, Chen YC. Oral fusidic acid fails to eradicate methicillin-resistant *Staphylococcus aureus* colonization and results in emergence of fusidic acid-resistant strains. *Diagn Microbiol Infect Dis* 2000; 36: 131–136.