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Staphylococcus aureus Colonization and Strain Type at Various Body Sites among Patients with a Closed Abscess and Uninfected Controls at U.S. Emergency Departments

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Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is a prevalent cause of skin and soft tissue infections (SSTI), but the association between CA-MRSA colonization and infection remains uncertain. We studied the carriage frequency at several body sites and the diversity of *S. aureus* strains from patients with and without SSTI. Specimens from the nares, throat, rectum, and groin of case subjects with a closed skin abscess (i.e., without drainage) and matched control subjects without a skin infection ($n = 147$ each) presenting to 10 U.S. emergency departments were cultured using broth enrichment; wound specimens were cultured from abscess cases. Methicillin resistance testing and *spa* typing were performed for all *S. aureus* isolates. *S. aureus* was found in 85/147 (57.8%) of abscesses; 49 isolates were MRSA, and 36 were methicillin-susceptible *S. aureus* (MSSA). MRSA colonization was more common among cases (59/147; 40.1%) than among controls (27/147; 18.4%) overall ($P < 0.001$) and at each body site; no differences were observed for MSSA. *S. aureus*-infected subjects were usually (75/85) colonized with the infecting strain; among MRSA-infected subjects, this was most common in the groin. The CC8 lineage accounted for most of both infecting and colonizing isolates, although more than 16 distinct strains were identified. Nearly all MRSA infections were inferred to be USA300. There was more diversity among colonizing than infecting isolates and among those isolated from controls versus cases. CC8 *S. aureus* is a common colonizer of persons with and without skin infections. Detection of *S. aureus* colonization, and especially MRSA, may be enhanced by extranasal site culture.

Staphylococcus aureus frequently causes invasive and life-threatening infections. While historically common in patients with significant health care exposure, community-associated methicillin-resistant *S. aureus* (CA-MRSA) has emerged as an important cause of disease (1). CA-MRSA is the most common cause of skin and soft tissue infections (SSTI) among people presenting to emergency departments (EDs) in much of the United States, most of which are caused by a single MRSA strain, pulsed-field type USA300 (2). *S. aureus* colonization with methicillin-susceptible *S. aureus* (MSSA) is common in the general population, especially in the anterior nares (3). Studies of MRSA pathogenesis in health care settings have demonstrated that nasal colonization typically precedes and is a risk factor for infection (4); therefore, prevention strategies in health care often involve decolonization, especially before invasive surgical procedures (5).

Despite the increasing prevalence of CA-MRSA infections, nasal colonization with MRSA has been infrequently detected during CA-MRSA outbreaks or in nationally representative prevalence surveys (6, 7). One possible explanation for this observation is that CA-MRSA strains might preferentially colonize at nonnasal body sites. The throat and groin have been implicated as important sites of *S. aureus* and MRSA colonization among certain patient populations (8, 9), and other studies have suggested that colonization patterns of CA-MRSA strains may be distinct from those of health care-associated MRSA strains (10, 11). The epidemiology of community-associated *S. aureus* colonization and its role in subsequent infection are not well characterized in the United States. Insight into the prevalence of colonization at various body sites and strain diversity among infected and uninfected persons will inform the design of rational prevention strategies.

We investigated the best sites for detecting colonization with community-associated *S. aureus* and the dynamics of *S. aureus* colonization among patients presenting with or without a closed (i.e., intact, nondraining) abscess at 10 U.S. EDs. Isolates recovered from wounds, nares, throat, groin, and perirectal region were characterized by antimicrobial susceptibility and strain type, and infecting and colonizing isolates from individual subjects were compared.

MATERIALS AND METHODS

In order to limit confounding of the colonization by contamination from draining wounds, only patients with closed skin infections were selected for study. Consenting patients aged 18 years and older presenting at 10 EMERGEncy ID Net EDs between 2010 and 2012 (12) with a closed skin

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abscess with purulent material available for culture after incision and drainage were enrolled as case subjects; patients presenting to the same ED with minor trauma or noninfectious illness within 24 h of a case patient and whose age was within 5 years of the matched abscess case were consented and enrolled as control subjects. All site institutional review boards approved the study.

Those with a perirectal abscess, with major trauma or critical illness, residing in a nursing home or long-term-care facility, currently taking antibiotics, or currently imprisoned were excluded from the study. In total, 147 abscess cases and 147 control subjects were enrolled.

Clinical and epidemiological data were collected by study coordinators using a brief questionnaire at the time colonization specimens were obtained. This included demographics (age, gender, race, and ethnicity), clinical information (presenting complaint, presence of comorbidities such as diabetes, HIV infection, chronic skin conditions, history of skin infections, history of antibiotic use, or dialysis), and behavioral factors, such as participation in contact sports or recent use of gym equipment, hot tubs, and saunas, which could contribute to nasal or skin colonization.

Skin swabs for case subjects and control subjects were obtained separately from the anterior nares, throat, rectum, and groin using commercially prepared sterile collection devices (e.g., Culturette II [Becton Dickinson, Sparks MD]); purulent material was collected from cases subsequent to skin swab collection. All swabs were stored at 4°C for up to 5 days prior to overnight shipment for culture.

Swabs were inoculated into Trypticase soy broth containing 6.5% NaCl, incubated overnight at 35°C, and then subcultured onto mannitol salt agar (MSA). Gold or yellow colonies present at 24 or 48 h were subcultured onto blood agar, and *S. aureus* was identified by colony morphology and Staphaurex latex agglutination (Remel, Lenexa, KS). Methicillin resistance was determined using cefoxitin disk diffusion (13).

Isolates were characterized by PCR for LukS-PV, *tst* (14), *sea*, *seb*, and SCC*mec* type (15). *spa* type was determined by sequencing the polymorphic X region of the staphylococcal protein A gene (*spa*) (16, 17). For each subject, isolates were considered to be the same strain if there was no more than one difference in the *spa* sequence, provided that the toxin and SCC*mec* data were concordant.

DNA lysates were prepared using an NaOH heat lysis procedure (18). PCR and sequencing of *spa* used primers spa-1113f (5′-TAAAGACGAT CCTTCGGTGAGC-3′) and SPA-1514r (5′-CAGCAGTAGTGCCGTTT GCTT-3′), essentially as described previously (16). Sequences were imported into BioNumerics version 5.1 (Applied Maths Inc., Austin, TX, USA) and analyzed using the spa plug-in software synchronized with the SeqNet/Ridom spa server (www.seqnet.org). Since *spa* type is largely concordant with multilocus sequence type clonal complexes (CC), *spa* types were assigned to multilocus sequence typing (MLST)-based CC groups based on 100% association.

Pulsed-field gel electrophoresis (PFGE) types of CC8 isolates were inferred based on SCC*mec* types and toxin profiles: SCC*mec* IVa isolates were inferred to be USA300, *sea*- and *seb*-negative isolates with SCC*mec* IV (not IVa) were inferred to be USA500, and isolates positive for *sea* or *seb* that were SCC*mec* IV (not IVa) were inferred to be Archaic/Iberian. CC8 MSSA isolates were inferred to be USA300 if they were Panton-Valentine leukocidin (PVL) positive and CC8-other if they were PVL negative. CC5 MRSA isolates were inferred based on SCC*mec* type to be USA100 (SCC*mec*II) or USA800 (not SCC*mec*II); CC5 MSSA isolates were inferred to be USA800 (19).

Data were analyzed with SAS version 9.2. Proportions were tested using the Mantel-Haenszel chi-square or Fisher exact test, where appropriate. A P value of <0.05 was defined as statistically significant, and 95% confidence intervals were reported.

RESULTS

Questionnaire data were available for 145/147 cases and controls. The average age among both cases and controls was 38 years (median, 36; range, 18 to 82). Enrollment varied across sites, ranging from a low of 4 case-control pairs to a high of 22 (median, 15). Comorbidities such as diabetes, cancer, eczema, chronic liver failure, and chronic renal failure were similar. Compared to controls, cases were more often male and were more likely to have a history of prior MRSA and a recent skin lesion (Table 1). There was variation across sites in the proportion of infections due to MRSA (range, 20.0 to 50.0%) and MSSA (range, 13.3 to 46.2%) and in colonization sites for *S. aureus* in general, but there were no clear geographic patterns of either infection or colonization among cases or controls (not shown).

TABLE 1 Characteristics of subjects with or without closed skin infection

Characteristic	Cases ($n = 145$)		Controls ($n = 145$)		95% confidence interval
	No.	%	No.	%	
Gender					
Male	85	58.6	69	44.8	0.98, 2.49
Female	60	41.4	76	52.4	0.40, 1.02
Race/ethnicity					
White	72	49.7	77	50.0	0.55, 1.39
Black	63	43.4	56	36.4	0.08, 1.96
Asian	2	1.4	3	1.9	0.08, 4.52
American Indian	5	3.4	4	2.6	0.31, 5.36
Hispanic	27	18.6	30	19.5	0.49, 1.57
Risk factor					
History of comorbidity	53	36.6	40	26.0	0.92, 2.49
Diabetes	12	8.3	16	10.4	0.32, 1.61
Chronic liver failure	1	0.7	0	0.0	0.03, 78.1
Chronic renal failure	0	0.0	1	0.6	0.03, 78.1
Cancer	0	0.0	1	0.6	0.03, 78.1
Eczema	9	6.2	5	3.2	0.60, 6.23
Any history of prior MRSA	15	10.3	3	1.9	1.66, 23.9
Recent skin lesion (past 6 mo)	46	31.7	12	7.8	2.62, 10.6

***S. aureus* carriage by body site.** *S. aureus* was cultured from the abscesses of 85 (57.8%) case subjects, including 49 with MRSA (33.3%) and 36 (24.5%) with MSSA infections (Table 2). Case subjects were more likely than control subjects to be colonized with *S. aureus* ($P < 0.001$), a difference driven largely by their higher MRSA colonization prevalence ($P < 0.001$). MSSA colonization was not significantly different between case and control subjects (Table 2).

The distribution of MRSA colonization was similar among case and control subjects at each of the body sites sampled, but it was significantly more common among case subjects than among control subjects overall (40.8% versus 18.4%; $P < 0.001$) and at each body site (Table 2). Case subjects were significantly more likely than control subjects to be MRSA colonized at multiple body sites; most case subjects carried MRSA at two or three sites, while MRSA was recovered from a single site in most MRSA-colonized control subjects (Table 2).

There was no difference in the distribution or prevalence of MSSA colonization between case and control subjects overall or by body site. Most MSSA-colonized case and control subjects were positive at one or two sites (Table 2). Case subjects were significantly more likely to be colonized with MSSA in the throat than in the groin or rectum, and control subjects were more likely to be colonized in the throat than at any other site (data not shown).

TABLE 2 *Staphylococcus aureus* colonization by body site among subjects with and without a closed skin infection

Colonization	*S. aureus* colonization								MRSA colonization							
	Case subjects					Control subjects ($n = 147$)			Case subjects					Control subjects ($n = 147$)		
	All ($n = 147$)		MRSA-positive infection ($n = 49$)	MSSA-positive infection ($n = 36$)	*S. aureus*-negative infection ($n = 62$)				All ($n = 147$)		MRSA-positive infection ($n = 49$)	MSSA-positive infection ($n = 36$)	*S. aureus*-negative infection ($n = 62$)			
	No.	%	No.	No.	No.	No.	%		No.	%	No.	No.	No.	No.	%	
Colonized at any site[a]	119	81.0	47	95.9	32	88.9	40	64.5	96	65.3	59	40.1	46	93.9	3	8.3	10	16.1	27	18.4	76	51.7	14	28.6	31	86.1	31	50.0	77	52.4
By site																														
Nose	78	53.1	38	77.6	24	66.7	16	25.8	57	38.8	37	25.2	33	67.3	1	2.8	3	4.8	14	9.5	41	27.9	5	10.2	23	63.9	13	21.0	43	29.3
Groin	75	51.0	38	77.6	23	63.9	14	22.6	35	23.8	42	28.6	37	75.5	2	5.6	3	4.8	8	5.4	33	22.4	1	2.0	21	58.3	11	17.7	27	18.4
Rectum	63	42.9	33	67.3	20	55.6	10	16.1	34	23.1	36	24.5	31	63.3	2	5.6	3	4.8	11	7.5	28	19.0	2	4.1	19	52.8	7	11.3	24	16.3
Throat	85	57.8	32	65.3	23	63.9	30	48.4	79	53.7	32	21.8	24	49.0	1	2.8	7	11.3	13	8.8	54	36.7	9	18.4	22	61.1	23	37.1	67	45.6
No. of sites																														
4	27	18.4	18	36.7	7	19.4	2	3.2	14	9.5	13	8.8	13	26.5	0	0.0	0	0.0	0	0.0	8	5.4	0	0.0	6	16.7	2	3.2	11	7.5
3	32	21.8	13	26.5	13	36.1	6	9.7	20	13.6	16	10.9	13	26.5	1	2.8	2	3.23	7	4.8	16	10.9	0	0.0	12	33.3	4	6.5	14	9.5
2	37	25.2	14	28.6	11	30.6	12	19.4	27	18.4	17	11.6	14	28.6	1	2.8	2	3.23	5	3.4	24	16.3	3	6.1	12	33.3	9	14.5	23	15.6
1	23	15.6	2	4.1	1	2.8	20	32.3	35	23.8	13	8.8	6	12.2	1	2.8	6	9.68	15	10.2	28	19.0	11	22.4	1	2.8	16	25.8	29	19.7

[a] Twenty-six patients had both MRSA and MSSA colonization.

When evaluated by cause of infection, 49 (33.3%) case patients had MRSA-positive infections, 36 (24.5%) had MSSA-positive infections, and *S. aureus* was not recovered from 62 (42.2%); other causes of infection were not investigated. Among case subjects without *S. aureus* infection, the rate of *S. aureus* colonization was significantly lower than among those with MRSA infections (64.5% versus 95.9%; $P < 0.001$) or MSSA infections (64.5% versus 88.9%; $P = 0.009$) (Table 2). The colonization distribution among patients with non-*S. aureus* skin infection was very similar to that among control subjects, and colonization rates among these groups were generally lower than among patients with *S. aureus* infection. Case subjects with either MRSA- or MSSA-positive infections were more likely to be colonized at multiple body sites, while case subjects with non-*S. aureus* infection and control subjects were more likely to be colonized at one body site (Table 2).

Case subjects with MRSA-positive infections were significantly more likely to be colonized with MRSA, overall and at each body site, than any other group ($P < 0.001$). The groin, followed by the nose and rectum, was the body site most likely to be MRSA colonized among those with MRSA-positive infections. Among controls and case patients without *S. aureus* infection, respiratory sites (nares and throat) demonstrated the highest MRSA colonization rates. Case subjects with MSSA infections or non-*S. aureus* infections, as well as control subjects, had low MRSA colonization rates and were most likely to be colonized at only one body site, while those with MRSA infections were most likely to be colonized at multiple body sites. MRSA colonization among control subjects was generally higher overall and by site than that among patients with non-MRSA infections (Table 2).

Overall, case subjects with MSSA infections were significantly more likely to be colonized with MSSA than any other group ($P < 0.001$). Case subjects with MSSA infections were significantly more likely to be colonized with MSSA at each site than those with MRSA infections ($P < 0.001$) and infections not caused by *S. aureus* ($P < 0.001$ for nose, groin, and rectum; $P = 0.02$ for throat). Compared to controls, MSSA colonization among MSSA-infected subjects was higher for the nose, groin, and rectum ($P < 0.001$), but MSSA throat colonization was not significantly different. Case subjects with MSSA infections were more likely to be colonized at multiple body sites, while other groups were most often colonized with MSSA at only one body site (Table 2).

Strain types. Sampling of four sites for colonization (nares, throat, groin, and rectum) plus the infection site for cases yielded 597 *S. aureus* isolates, including 243 MRSA and 354 MSSA isolates, from 294 patients. Although more than 16 distinct *S. aureus* clonal complexes were identified, the CC8 lineage was most common (321/597; 53.8% overall), accounting for 82.3% of infecting isolates and nearly half (48.5%) of all colonizing isolates recovered. Overall, 274/597 (45.9%) isolates were PVL positive, including 218/243 (89.7%) MRSA and 56/354 (15.8%) MSSA. The majority of CC8 isolates were inferred to be CC8-300 (85.3%), especially among MRSA isolates (97.4%) (Table 3), and nearly all (96.8%) were PVL positive. Among MSSA isolates, the CC8 lineage was divided between CC8-300 and CC8-other. CC5 was the next most common *S. aureus* strain identified in this study, accounting for 11.6% of isolates. CC5 was an uncommon cause of infection ($n = 1$) but was a frequent MSSA colonizing strain. All CC5 MSSA isolates ($n = 62$) were inferred to correspond to USA800, but most CC5 MRSA isolates ($n = 5$; 71.4%) carried SCC*mec*II and were inferred to be USA100.

TABLE 3 *Staphylococcus aureus* strain type by body site colonized among subjects with and without closed skin infections

Methicillin resistance and CC	Associated *spa* type(s) by rank (no. of types observed)[a]	Case subjects					Control subjects				Colonizing isolate total	Overall isolate total
		Abscess	Groin	Nose	Rectum	Throat	Groin	Nose	Rectum	Throat		
		No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
MRSA												
CC8-300	t008, t024, t121, t1578, t068 (9)[b]	48 (98)	41 (97.6)	35 (94.6)	34 (91.9)	27 (84.4)	6 (75)	11 (78.6)	8 (72.7)	11 (84.6)	173 (89.2)	221 (90.9)
CC5	t242, t002, t5923 (3)	0 (0)	0 (0)	0 (0)	0 (0)	3 (9.4)	1 (12.5)	1 (7.1)	2 (18.2)	0 (0)	7 (3.6)	7 (2.9)
CC8-500	t008 (1)	1 (2)	0 (0)	1 (2.7)	1 (2.7)	1 (3.1)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1.5)	4 (1.6)
CC59	t316, t976, (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.1)	1 (12.5)	1 (7.1)	0 (0)	1 (7.7)	4 (2.1)	4 (1.6)
CC8-Iberian	t064 (1)	0 (0)	0 (0)	1 (2.7)	0 (0)	0 (0)	0 (0)	1 (7.1)	0 (0)	0 (0)	2 (1.0)	2 (0.8)
CC97	t267 (1)	0 (0)	1 (2.4)	0 (0)	1 (2.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (1.0)	2 (0.8)
CC30	t017 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9.1)	0 (0)	1 (0.5)	1 (0.4)
All other	t1579, t559 (2)	0 (0)	0 (0)	0 (0)	1 (2.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7.7)	2 (1.0)	2 (0.8)
Total	19 distinct spa types	49	42	37	37[c]	32	8	14	11	13	194	243
MSSA												
CC5	t002, t548, t688, t1791, t1818 (14)	1 (2.8)	3 (8.8)	5 (12.2)	4 (14.3)	10 (18.5)	5 (18.5)	10 (23.3)	9 (37.5)	15 (22.4)	61 (19.2)	62 (17.5)
CC8-300	t008, t121, t304, unknown (4)	16 (44.4)	8 (23.5)	6 (14.6)	8 (28.6)	5 (9.3)	2 (7.4)	3 (7)	2 (8.3)	3 (4.5)	37 (11.6)	53 (15.0)
CC8-OTHER	t334, t008, t068, t701, t377 (11)	5 (13.9)	8 (23.5)	5 (12.2)	3 (10.7)	6 (11.1)	3 (11.1)	2 (4.7)	2 (8.3)	7 (10.4)	36 (11.3)	41 (11.6)
CC30	t021, t012, t8485, t685, t338 (13)	3(8.3)	1 (2.9)	3 (7.3)	1 (3.6)	1 (1.9)	1 (3.7)	8 (18.6)	1 (4.2)	10 (14.9)	26 (8.2)	29 (8.2)
CC45	t007, t050, t073, t330, t553 (12)	1 (2.8)	2 (5.9)	4 (9.8)	2 (7.1)	7 (13)	2 (7.4)	2 (4.7)	0 (0)	4 (6)	23 (7.2)	24 (6.8)
CC15	t084, t4454, t094, t4685, t091 (8)	0 (0)	1 (2.9)	3 (7.3)	0 (0)	5 (9.3)	0 (0)	4 (9.3)	2 (8.3)	7 (10.4)	22 (6.9)	22 (6.2)
CC188	t189, t7858 (2)	1 (2.8)	3 (8.8)	2 (4.9)	1 (3.6)	0 (0)	3 (11.1)	2 (4.7)	0 (0)	6 (9)	17 (5.3)	18 (5.1)
CC20	t164, t731, t996, unknown (4)	2 (5.6)	3 (8.8)	2 (4.9)	4 (14.3)	3 (5.6)	1 (3.7)	0 (0)	0 (0)	2 (3)	15 (4.7)	17 (4.8)
CC97	t359, t267, t521, t2297 (4)	2 (5.6)	0 (0)	2 (4.9)	1 (3.6)	5 (9.3)	2 (7.4)	0 (0)	2 (8.3)	1 (1.5)	13 (4.1)	15 (4.2)
CC12	t160, t888, t4176 (3)	1 (2.8)	2 (5.9)	2 (4.9)	1 (3.6)	3 (5.6)	0 (0)	2 (4.7)	1 (4.2)	0 (0)	11 (3.5)	12 (3.4)
All other[d]	t127, t571, t1614, t2465, t2700 (>20)	4 (11.1)	3 (8.8)	7 (17.1)	3 (10.7)	9 (16.7)	8 (29.6)	10 (23.3)	5 (20.8)	12 (17.9)	57 (17.9)	61 (17.2)
Total	>90 spa types	36	34[e]	41	28	54	27	43	24	67	318	354

[a] For MSSA, only the first five types are listed.
[b] These represent >5% of observed *spa* types.
[c] One patient had two MRSA strains at the rectal site.
[d] Includes 7 distinct CC plus seven *spa* types not associated with a CC.
[e] One patient had two MSSA strains at the groin site.

There was limited diversity (six clonal complexes) among MRSA isolates in this study. All MRSA isolates from infections belonged to CC8, and CC8-300 accounted for 98% of these. Although there was more diversity among colonizing MRSA, CC8-300 was the most common colonizing MRSA strain isolated from both case and control subjects (89.2%); other strains, including CC5 (3.6%), CC59 (2.1%), and CC8-500 (1.5%), were relatively uncommon (Table 3). The distribution of colonizing strains from control subjects was more diverse than that of colonizing strains from cases. Almost 20% of colonizing isolates from control subjects were non-CC8 strains, while more than 95% of colonizing isolates from case subjects were CC8.

MSSA strains demonstrated substantial diversity. More than 10 MSSA clonal complexes were identified, the most prevalent of which were CC5 and CC8-300. CC5 isolates were nearly twice as common as CC8-300 among colonizing MSSA, whereas CC8-300 MSSA caused most infections. As with MRSA, the distribution of colonizing MSSA strains was different between case and control subjects. Among cases, CC8-300 was the most common MSSA colonizer (17.2%), followed by CC5 and CC8-other (14% each), whereas CC5 was the most common MSSA type colonizing controls (24.2%), followed by CC30 (12.4%), CC8-other (8.7%), and CC15 (8.1%); CC8-300 accounted for only 6.2% of MSSA strains colonizing control subjects (Table 3). The distribution of strain types colonizing case subjects without *S. aureus* infection was similar to that for control subjects (not shown).

Site of colonization and strain distribution among *S. aureus*-infected subjects. Most often, *S. aureus*-infected subjects were colonized with the same strain isolated from the abscess (88.2% overall; 93.9% among MRSA and 80.6% among MSSA). Most subjects were colonized with only the infecting strain at one or more body sites (58.8%) or were colonized with the infecting strain plus a different strain (29.4%) (Table 4 and data not shown). Only six subjects with *S. aureus* skin infection were free from colonization at each of the four body sites sampled (7.1%), and only four were colonized only with a strain other than the infecting strain (4.7%). Fewer than 6% of *S. aureus*-infected subjects were colonized with the infecting strain plus additional strains. One MSSA-infected subject was not colonized with the

TABLE 4 Concordance of *Staphylococcus aureus* strains colonizing case subjects with *S. aureus*-positive closed skin infections

Infection (*n*) and site	Same strain		Different strain (MSSA)		Different strain (MRSA)		Not colonized	
	No.	%	No.	%	No.	%	No.	%
MRSA (49)								
Groin	37	75.5	1	2.0	0	0.0	11	22.4
Nose	32	65.3	5	10.2	1	2.0	11	22.4
Rectal[a]	31	63.3	2	4.1	1	2.0	16	32.7
Throat[a]	23	46.9	10	20.4	1	2.0	16	32.7
Any site	46	93.9	15	30.6	3	6.1	2	4.1
MSSA (36)								
Groin[a]	17	47.2	5	13.9	2	5.6	13	36.1
Nose	19	52.8	4	11.1	1	2.8	12	33.3
Rectal[a]	19	52.8	0	0.0	2	5.6	16	44.4
Throat	16	44.4	6	16.7	1	2.8	13	36.1
Any site	29	80.6	11	30.6	3	8.3	4	11.1

[a] More than one strain was recovered at this site.

infecting strain but was colonized with two MRSA strains and one additional MSSA strain.

Among subjects infected with MRSA, the groin was the most likely site to be colonized with the same strain, followed by the nose, rectum, and throat (Table 4). Only 4.1% of MRSA-infected patients were not colonized with *S. aureus* at any site, and 2.0% were colonized only with a strain other than the infecting strain. MSSA colonization was common among those infected with MRSA, as 20.4% carried an MSSA strain in addition to the infecting MRSA, but cocolonization with other MRSA strains was uncommon (4.1%).

A higher proportion of patients infected with MSSA than of those infected with MRSA were not *S. aureus* colonized at any site (11.1% versus 4.1%), and 2 patients (5.6%) were colonized only with a strain other than the infecting strain (one patient carried both an MRSA strain and two MSSA strains). Similar to the case for those infected with MRSA, colonization with both the infecting strain plus additional MSSA was common (22.2%), but cocolonization with the infecting MSSA strain plus an MRSA strain was not observed. MSSA-infected subjects were most likely to be colonized with the same strain in the nose or rectum, followed closely by the groin and throat (Table 4). For both MRSA- and MSSA-infected subjects, the throat was the most likely site to find colonization with a strain other than the infecting strain.

Since MRSA were represented almost entirely by a single strain (CC8-300), it was difficult to understand whether differences observed between MRSA and MSSA in this study were impacted by methicillin resistance or strain type. Therefore, we examined the colonization distribution of CC8-300 among MSSA-infected subjects to see if it was similar to that of MRSA. Indeed, when CC8-300 MSSA strains ($n = 16$) were examined independently of other MSSA strains, the groin and rectum were most commonly positive (each 50%), followed by the nose (37.5%) and throat (31.3%), whereas other MSSA strains were found more often in the nose (65%) than in the rectum or throat (55% each) or groin (45%) (data not shown).

DISCUSSION

While other studies have reported that nasal *S. aureus* isolates are often identical to strains that later cause clinical infection (20, 21), we found that among MRSA-infected subjects, the infecting strains were most likely to be detected in the groin. We would have missed 80 colonized subjects, or about 40% of the colonized population in our study, if only nasal swabs were assessed for colonization. For the purpose of general or active surveillance among persons without skin infections, respiratory sites might provide the best detection of MRSA colonization. However, if members of the population under surveillance have a skin infection, our data suggest that the groin would be the preferred single site for detecting MRSA colonization. Other recent studies have also implicated the groin and rectum as important sites of colonization with MRSA (22, 23).

We found higher *S. aureus* colonization rates among both cases and controls than others have reported. This is impacted in part by the inclusion of broth enrichment for culture and also by our culturing of specimens from 4 body sites per patient. If one considers only the nares, MSSA colonization rates among case and control subjects were similar (27.9% and 29.3%, respectively), and these rates were comparable to those found in other studies of community subjects that did not include broth enrichment cultures (7). Of note, a recent study among patients presenting to a single ED found much lower rates of MSSA nasal colonization among case patients than we found, even with the use of broth enrichment (22). In contrast, we found a higher rate of MRSA nasal carriage among control subjects (9.5%) than others have reported for subjects in the community (7, 22, 24) and those presenting to EDs with skin infections (22). MRSA nasal colonization in our study was much higher among cases (25.2%) than among controls (9.5%), a finding that has also been reported by others (22, 25).

The proportion of closed abscesses from which *S. aureus* was cultured (57.8%) and the proportions of infections due to MRSA and MSSA (33.3% and 24.5%, respectively) were similar in our study to those found in other recent U.S. studies (22, 26, 27) but were substantially lower than those found in previous studies conducted within this network of EDs, which found MRSA in 63% of patients presenting with an abscess (2). This might indicate that community-associated SSTI due to *S. aureus* is decreasing, perhaps due to increased awareness of this disease and more active measures to prevent infection in community settings.

Our data indicate that heavy colonization with *S. aureus*, defined as colonization at multiple body sites, correlates with *S. aureus* infection. Case subjects with infections due to MRSA or MSSA were significantly more likely to be colonized with the corresponding strain than those not infected with *S. aureus* and than controls. Since all of the case subjects in this study had closed skin infections, it is unlikely that the abscess was a source of colonization for other body sites. It is interesting that the rate of colonization with the infecting strain was higher in our study than in another recent study of patients presenting to EDs with a skin infection, in which both open and closed abscesses were examined (88.2% versus 58.4%) (22). This might suggest that *S. aureus* colonization precedes infection in community settings, as has been described for health care settings (4).

A limitation to this finding is that a patient history of infection with any *S. aureus* strain is unknown; enrolled subjects were asked

only about prior MRSA infection and prior skin lesions, and thus we do not know whether prior MSSA infection might have impacted colonization. Data collected from subjects during enrollment indicate that over 30% of case subjects reported a recent skin lesion and about 10% reported a history of MRSA. We found that 42.2% of case subjects with a closed skin abscess were not infected with *S. aureus*, and therefore these cases would be expected to impact *S. aureus* colonization during this study period. Furthermore, there was no significant difference in history of MRSA or reported skin lesions among MRSA-infected, MSSA-infected, and non-*S. aureus*-infected case subjects.

The distribution of strain types causing infection was similar to what has been previously reported. Our finding that the CC8-300 strain accounted for nearly all MRSA infections and a large proportion of the MSSA infections mirrored the findings of previous reports, although our use of an inferred algorithm in this study does not allow a direct strain-to-strain comparison (2, 22, 23). In contrast to the homogeneity among infecting MRSA strains, more than 10 different strain types were encountered among infecting MSSA strains. The vast majority of colonizing MRSA isolates were found to belong to strain CC8-300 (89%), including 92.5% from cases and 78.2% from controls. Among MSSA strains, CC5 was the dominant colonizing strain overall (19.2%) and among controls (24.2%), but CC8-300 was the most common colonizing strain among cases (17.2%) (Table 3).

A similar study examining subjects with acute CA-MRSA infection found that only 37% were colonized with MRSA in the nares, axilla, groin, and rectum, and rates at each of these sites and overall were substantially lower than we report (10). We found that MRSA-infected outpatients had much higher colonization rates; of the 49 MRSA-infected subjects in our study, 93.9% were also colonized with MRSA. We also found a much higher MSSA colonization rate at nasal as well as nonnasal sites among MSSA-infected subjects in our study, more than 10 times higher than what was reported by Yang et al. (10). ED patients in our study were not investigated to rule out previous health care exposures, and thus our cohort likely includes both community- and health care-associated infections, which may explain the higher rates. Also, we collected throat instead of axilla cultures, and throat carriage among MRSA-infected subjects in our study was high (49%) compared to axilla coverage in that study (6%).

Our study found higher rates of *S. aureus* colonization in the community than have been previously reported. A previous study found *S. aureus* (MRSA and MSSA) nasal colonization in 28.6% of people surveyed and MRSA colonization in 1.5% of people surveyed (7), whereas we detected *S. aureus* nasal colonization in 38.8% of controls and MRSA nasal colonization in 9.5%. This difference may be due to the fact that controls in our study were patients seeking care at EDs rather than the general public, or it may reflect an actual increase in MRSA colonization in the community or may be due to our use of broth enrichment to enhance recovery. In comparison, a recent single-institution ED-based study by Kumar et al. that examined colonization using broth enrichment reported that 4.6% of all control subjects were colonized with MRSA in the nares (22). Previous studies of colonizing MRSA strains demonstrated that USA100, followed distantly by USA800, was most commonly detected by nasal culture among persons in the community (7, 28). In contrast, we found USA300 MRSA to be more common than other strains in the nares and at all body sites of control subjects. A previous study examining MRSA nasal colonization among hospitalized patients found that 24% of MRSA nasal isolates were USA300 and that the proportion of USA300 increased from 2005 to 2007 (29).

The dominant MSSA nasal colonizing strains among controls in our study were CC5 (i.e., USA800) and CC30 (i.e., USA200 and USA1100), which were also the most common at all body sites among controls. Although comparable studies that include specific strain types for MSSA are uncommon, this distribution of strains is different from that observed by previous surveys of nasal colonization among the general population, which found that USA200 and USA600 predominated and USA800 was rare (7, 28).

The relatively high MRSA colonization prevalence observed here could be reflective of unrecognized health care exposures, although the overwhelming dominance by the CC8-300 strain provides some evidence against this possibility. This is also supported by a recent study which found relatively high rates of colonization with both MRSA and MSSA among household contacts of children with community-associated skin infection (30). Another limitation of this study is that findings may not be generalizable to all MRSA strains, since most were a single strain, USA300. However, this is the most common infecting strain among community-acquired SSTI, so it does help inform community epidemiology.

The question of whether colonization or infection occurs first among patients with community-associated MRSA infection persists. In health care settings, MRSA nasal colonization is a demonstrated risk factor for subsequent infection (5), but the progression of community-associated *S. aureus* infection may be different (31). In this study, only case patients with closed abscesses were investigated in an attempt to limit the potential for colonization due to wound contamination. Thus, we believe that these data present evidence that colonization, especially at multiple body sites, might precede infection based on the high rates of *S. aureus* colonization among case subjects infected with *S. aureus* compared to those with non-*S. aureus* infections and the control group. Our data also demonstrate that USA300 is a common colonizing strain, even among patients without skin infection, but extranasal colonization may be particularly important.

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