

Staphylococcus aureus Colonization Among Household Contacts of Patients With Skin Infections: Risk Factors, Strain Discordance, and Complex Ecology

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Background. The USA300 methicillin resistant *Staphylococcus aureus* (MRSA) genetic background has rapidly emerged as the predominant cause of community-associated *S. aureus* infections in the U.S. However, epidemiologic characteristics of *S. aureus* household transmission are poorly understood.

Methods. We performed a cross-sectional study of adults and children with *S. aureus* skin infections and their household contacts in Los Angeles and Chicago. Subjects were surveyed for *S. aureus* colonization of the nares, oropharynx, and inguinal region and risk factors for *S. aureus* disease. All isolates underwent genetic typing.

Results. We enrolled 1162 persons (350 index patients and 812 household members). The most common infection isolate characteristic was ST8/SCCmec IV, PVL+ MRSA (USA300) (53%). *S. aureus* colonized 40% (137/350) of index patients and 50% (405/812) of household contacts. A nares-only survey would have missed 48% of *S. aureus* and 51% of MRSA colonized persons. Sixty-five percent of households had >1 *S. aureus* genetic background identified and 26% of MRSA isolates in household contacts were discordant with the index patients' infecting MRSA strain type. Factors independently associated ($P < .05$) with the index strain type colonizing household contacts were recent skin infection, recent cephalosporin use, and USA300 genetic background.

Conclusions. In our study population, USA300 MRSA appeared more transmissible among household members compared with other *S. aureus* genetic backgrounds. Strain distribution was complex; >1 *S. aureus* genetic background was present in many households. *S. aureus* decolonization strategies may need to address extra-nasal colonization and the consequences of eradicating *S. aureus* genetic backgrounds infrequently associated with infection.

The emergence of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections in the late 1990s [1] has resulted in a dramatic shift in

the epidemiology of *S. aureus* infections. In the United States, the predominant CA-MRSA clone, USA300 MRSA, has become the most common cause of community-associated skin infection [2] and an endemic pathogen in many hospitals [3–5]. Data suggest that CA-MRSA infections have high attack rates in household contacts after an initial CA-MRSA infection occurs [6, 7].

In contrast to healthcare-associated (HA)–MRSA strain types, which have circulated in the healthcare setting for more than 40 years and rarely spread outside the hospital [8–10], there is evidence that CA-MRSA strain types frequently spread from person

Received 1 September 2011; accepted 19 January 2012; electronically published 3 April 2012.

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Clinical Infectious Diseases 2012;54(11):1523–35

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DOI: 10.1093/cid/cis213

Table 1. Demographics, Clinical Factors, and Bivariate Analysis of Risk Factors Associated With Colonization of the Index Patient by the Index Patient's Infecting Strain Type

Variable	All, n = 350 (%)	Colonized With Infecting Strain, n = 41 (%)	Not Colonized With Infecting Strain, n = 309 (%)	OR	95% CI	P Value
Site						
Chicago	177 (51)	22 (53)	155 (50)	1.15	.60, 2.21	.67
Los Angeles	173 (49)	19 (46)	154 (50)
Demographics						
Gender						
Female	180 (51)	26 (63)	154 (50)	1.75	.89, 3.42	.11
Male	170 (49)	15 (37)	155 (50)
Age						
Older adult (>65 yr)	15 (4)	2 (5)	13 (4)	1.30	.27, 6.22	.74
Adult (19–65 yr)	180 (51)	19 (46)	161 (52)	Ref
Child (5–18 yr)	55 (16)	8 (20)	47 (15)	1.44	.59, 3.50	.42
Younger child (<5 yr)	100 (29)	12 (29)	88 (28)	1.16	.54, 2.49	.71
Ethnicity						
African-American	177 (51)	24 (58)	153 (50)	1.20	.34, 4.32	.78
Caucasian	26 (7)	3 (7)	23 (7)	Ref
Hispanic	121 (35)	12 (29)	109 (35)	0.84	.22, 3.23	.81
Other/mixed/unknown	26 (7)	2 (5)	24 (8)	0.64	.10, 4.18	.64
Clinical factors						
Charlson comorbidity score						
Mean ± SD	1 ± 2	1 ± 2	1 ± 2	0.92	.78, 1.08	.30
Median (range)	0 (0–14)	0 (0–12)	0 (0–14)
Comorbidities						
Diabetes	57 (16)	5 (12)	52 (17)	0.69	.26, 1.83	.45
HIV infection	14 (5)	0 (0)	14 (14)	NA	NA	.39
In the past 12 mo:						
Had a previous skin infection	217 (62)	23 (56)	194 (63)	0.76	.39, 1.46	.41
Undergone major surgery	88 (25)	12 (29)	76 (24)	1.27	.62, 2.61	.52
Received dialysis	8 (2)	0 (0)	8 (3)	NA	NA	.60
Hospitalized	172 (49)	18 (44)	154 (50)	0.79	.41, 1.52	.48
Days of hospitalization						
Mean ± SD	4 ± 18	3 ± 8	4 ± 19	0.99	.97, 1.02	.82
Median (range)	0 (0–320)	0 (0–39)	0 (0–320)
Any antibiotic exposure	237 (67)	24 (59)	213 (69)	0.64	.33, 1.24	.18
Use of clindamycin	35 (10)	7 (18)	28 (9)	2.07	.86, 5.09	.16
Use of TMP-SMX	37 (11)	3 (8)	34 (11)	0.65	.19, 2.18	.78
Use of cephalexin	17 (5)	2 (5)	15 (5)	1.02	.23, 4.65	.99
Use of immunosuppressant medications	70 (20)	9 (23)	61 (20)	1.15	.52, 2.57	.72
Spent time living in a skilled nursing facility, rehabilitation center, or other type of group facility	8 (2)	2 (5)	6 (2)	2.68	.52, 13.74	.23
Epidemiologic factors						
Household density						
Mean ± SD	1.96 ± 1.08	1.94 ± 0.93	1.96 ± 1.10	0.99	.73, 1.35	.94
Median (range)	1.73 (0.40–9.0)	1.66 (0.667–4.0)	2.0 (0.40–9.0)
Homelessness in the past 12 mo	14 (4)	3 (7)	11 (3)	2.14	.57, 8.01	.22
Cuts/scratches in the 30 d prior to index infection	143 (41)	19 (46)	124 (40)	1.29	.67, 2.48	.50
Skin rash in the 90 d prior to index infection	60 (18)	14 (36)	46 (16)	2.97	1.44, 6.17	.002^a
Pets in the home, currently	156 (45)	15 (38)	141 (46)	0.702	.36, 1.38	.32

Table 1 continued.

Variable	All, n = 350 (%)	Colonized With Infecting Strain, n = 41 (%)	Not Colonized With Infecting Strain, n = 309 (%)	OR	95% CI	P Value
Incarceration in the past 12 mo	9 (4)	0 (0)	9 (5)	-	-	.60
Illicit drug use in the past 12 mo	34 (10)	1 (2)	33 (11)	0.21	.03, 1.57	.15
>1 sexual partner in the past 12 mo	25 (12)	3 (12)	22 (12)	1.02	.29, 3.70	.99
In the past 3 mo:						
Showered at least once a day	39 (12)	4 (11)	35 (12)	0.91	.30, 2.71	.99
Shared make-up with others	20 (7)	2 (5)	18 (7)	0.76	.17, 3.42	.99
Shared bar soap with others	193 (57)	25 (63)	168 (56)	1.32	.67, 2.60	.42
Shared clothes with others with washing	21 (6)	3 (7)	18 (6)	1.25	.35, 4.44	.73
Shared towels with others	157 (46)	21 (51)	136 (45)	1.30	.67, 2.49	.43
Wore clothes more than once without washing	166 (49)	23 (58)	143 (47)	1.48	.76, 2.87	.25
Hand-washing frequency after using the bathroom						
Mean \pm SD	2.6 \pm 0.78	2.6 \pm 0.80	2.6 \pm 0.78	1.01	.66, 1.54	.97
Median (range)	3 (0–3)	3 (0–3)	3 (0–3)			
Household cleaning scale ^b						
Mean \pm SD	16 \pm 8	17 \pm 8	16 \pm 8	1.18	.62, 2.20	.61
Median (range)	18 (0–35)	18 (0–33)	18 (0–35)			
Use of a gym	27 (14)	5 (14)	22 (9)	1.56	.55, 4.42	.38
Participation in contact sports	83 (24)	11 (27)	72 (23)	1.21	.58, 2.53	.62
Goes to day care	25 (19)	1 (7)	24 (21)	0.27	.03, 2.19	.30
Use of public facilities ^c	76 (22)	12 (29)	64 (21)	1.58	.77, 3.27	.21
Strain-specific factors						
Infecting strain type categorization by the CDC case definition						
CA-MRSA	111 (32)	15 (37)	96 (31)	1.28	.65, 2.53	.92
HA-MRSA	122 (35)	17 (42)	105 (34)	Ref		
CA-MSSA	45 (13)	3 (7)	42 (14)	0.50	.15, 1.70	.29
HA-MSSA	72 (20)	6 (15)	66 (21)	0.63	.26, 1.56	.28
ST8-MRSA-Mec IV-PVL strain type	186 (53)	29 (71)	157 (51)	2.33	1.15, 4.75	.02
PVL presence	266 (76)	33 (81)	233 (75)	0.74	.33, 1.67	.56
SCCmec type IV	220 (63)	30 (73)	190 (62)	1.71	.82, 3.54	.17
Other household members colonized with the infection strain type	81 (23)	21 (51)	60 (19)	4.36	2.22, 8.55	<.001^d

Statistically significant relationships are bolded; NA indicates cannot be calculated due to zero cell.

Abbreviations: CA-MRSA, community-associated methicillin-resistant *Staphylococcus aureus*; CA-MSSA, community-associated methicillin-susceptible *S. aureus*; CDC, Centers for Disease Control and Prevention; CI, confidence interval; HA-MRSA, healthcare-associated methicillin-resistant *S. aureus*; HA-MSSA, healthcare-associated methicillin-susceptible *S. aureus*; HIV, human immunodeficiency virus; OR, odds ratio; PVL, Pantone-Valentine leukocidin; Ref, reference group; SD, standard deviation; TMP-SMX, trimethoprim-sulfamethoxazole.

^a Variable significant in multivariable analysis (OR, 2.9 [1.4–6.2]; $P = .006$).

^b Household cleaning is a measure of the frequency of cleaning for common household items, with higher values representing more frequent cleaning.

^c Use of public facilities is defined as use of a publicly available gym, locker room, shower, swimming pool, sauna, or Jacuzzi.

^d Variable significant in multivariable analysis (OR, 4.3 [2.1–8.6]; $P < .001$).

to person in households [11–14]. Although transmission of HA-MRSA may occur in part via asymptomatic carriers [8], less is known about MRSA and methicillin-susceptible *S. aureus* (MSSA) dissemination in community settings. Previous investigations of MRSA spread in households have been limited by relatively small sample size [15–21], lack of

geographic diversity [16, 19–22], focus on HA-MRSA [23, 24], nares-only surveillance [17, 19, 20, 22, 25, 26], or lack of distinction among *S. aureus* genetic backgrounds at the molecular level [23].

Recent investigations suggest nares-only screening may underestimate *S. aureus* colonization prevalence because *S. aureus*

has been found to colonize oropharyngeal [27–29] and inguinal areas [30–32] in persons irrespective of nasal colonization. Additionally, although USA300 MRSA is the most common genetic background causing CA-*S. aureus* skin infection [2], MRSA nasal colonization remains uncommon in the general population (<5%) [33].

To better understand the spread of USA300 MRSA and other *S. aureus* strain types in households, we studied *S. aureus* colonization in patients with skin infections and among their household members in 2 large US cities.

METHODS

We performed a cross-sectional investigation of children and adults with *S. aureus* skin infection and their household members. Patients were enrolled from Harbor-UCLA Medical Center in Torrance, California, and the University of Chicago Medical Center in Chicago, Illinois, from August 2008 to June 2010. Each center's clinical microbiology laboratory was screened daily for new skin cultures growing *S. aureus*. Both inpatients and outpatients were eligible. *S. aureus* was identified by standard techniques (Vitek 2, bioMérieux). Patients were eligible for participation if they (1) had the culture taken from a skin infection, (2) were willing to provide informed consent, (3) had >1 household member who would participate, and (4) resided within 25 miles of the site's medical center. Patients who lived in a group living facility or were homeless were ineligible. Infected patients were designated as "index patients." This study was approved by each site's institutional review board.

Home Visit

Consenting patients agreed to have a home visit within 21 days of enrollment during which all participating household members or their parent or guardian provided informed consent. Research personnel administered a standardized questionnaire on MRSA risk factors based on previously developed surveys of known or hypothesized CA-MRSA and MRSA risk factors [8, 13, 30, 34–43]. Survey questions for this study were refined using cognitive interviewing [44].

To assess *S. aureus* colonization, research personnel obtained separate cultures from the nares and oropharynx from subjects using a dry rayon-tip applicator (CultureSwab, BD Diagnostic Systems). Inguinal cultures were obtained by the subject or their parent/guardian in private after being provided detailed instructions.

Cultures for Colonization

After collection, swabs were transported promptly to the site's research laboratory and enriched in trypticase soy broth with 7% sodium chloride overnight at 37°C. The culture broth was plated onto BBL CHROMagar *S. aureus* media (BD Diagnostic Systems) and incubated for 24 hours at 37°C. Isolates were

confirmed as *S. aureus* by positive catalase and StaphAureux tests (Remel).

Molecular Characterization of Isolates and Definition of Isolate Relatedness

Speciation of all *S. aureus* infection and colonization isolates was confirmed at the University of Chicago MRSA Research Laboratory. Genomic DNA was extracted from each isolate using the Qiagen DNeasy Blood and Tissue Kit following manufacturer's instructions and modified by incubation with lysostaphin in resuspension buffer (at 37°C for 30 minutes) to facilitate *S. aureus* lysis [45]. *Staphylococcus aureus* speciation was confirmed using a polymerase chain reaction (PCR) assay specific for *spa* (encoding Protein A). *Staphylococcus aureus* isolates were characterized by multilocus sequence typing (MLST) [46] to determine the genetic background and by typing of the SCCmec element, the mobile genetic element that carries *mecA* [47]. SCCmec typing was performed by PCR as described [48], with type assignments using published guidelines [47]. Detection of genes encoding the Panton-Valentine leukocidin (PVL) was performed as described [49].

Two *S. aureus* isolates were considered indistinguishable if they shared the same MLST and SCCmec type and were concordant with respect to the presence or absence of the PVL genetic determinants. Based on a previous investigation demonstrating that ST8/PVL+/SCCmec IV is highly concordant with USA300 MRSA genetic background assessed by pulsed-field gel electrophoresis (M. David et al, unpublished data), isolates with these characteristics were categorized as USA300 MRSA.

Chart Abstraction and Criteria for CA *S. aureus*

We reviewed medical records of index patients using a standardized chart abstraction instrument that quantified recent hospitalizations, prior *S. aureus* infections, and comorbidities using a standard index [50]. We used the Centers for Disease Control and Prevention's Active Bacterial Core surveillance case definition to classify each infection as CA or HA [51].

Statistical Analyses

Data were analyzed using SAS software (version 9.1.3; SAS Institute). Colonizing isolates that were indistinguishable from the index infection were considered the outcome of interest for the data analysis. Bivariate analysis was performed using χ^2 or Fisher exact test, as appropriate. Multivariate modeling procedures [52] were performed to predict colonization of the index patient with their infecting strain type. Similar procedures accounting for clustering of household members were used to predict colonization of household members with the index patients' infecting strain type. All variables with a *P* value $\leq .10$ in the bivariate analysis were included in a multivariate logistic regression analysis. Backward elimination was performed using

Table 2. Comparison of Index Infection Strains, Index Colonizing Strains, and Household Member Colonizing Strains Circulating in Households

MRSA or MSSA	ST Type	SCCmec Type	PVL	Index Infecting Strain Type, n = 350 (%)	Index Colonizing Strain Type, n = 215 (%)	Household Member Colonizing Strain Type, n = 594 (%)	P Value ^a
MRSA	8	IV	+	186 (53)	57 (27)	178 (30)	<.001
MRSA	8	IV	+	8 (2)	3 (1)	6 (1)	.18
MRSA	8	IV	-	9 (3)	0 (0)	5 (1)	.02
MRSA	5	IV	-	3 (1)	3 (1)	3 (1)	.99
MRSA	5	II	-	3 (1)	6 (3)	8 (1)	.30
MRSA	239	III	+	6 (2)	7 (3)	7 (1)	.99
MRSA	1	IV	+	1 (1)	0 (0)	3 (1)	.99
MRSA	30	IV	+	1 (1)	0 (0)	3 (1)	.99
MRSA	Misc ^b	Varied	Varied	16 (3)	15 (7)	28 (4)	.59
MSSA	8	None	+	27 (8)	9 (4)	27 (5)	.03
MSSA	8	None	-	5 (1)	3 (1)	22 (4)	.11
MSSA	5	None	-	6 (2)	23 (11)	42 (7)	<.001
MSSA	15	None	-	3 (1)	3 (1)	33 (6)	.001
MSSA	30	None	-	5 (1)	13 (6)	47 (8)	<.001
MSSA	45	None	-	2 (1)	12 (6)	33 (6)	<.001
MSSA	72	None	-	1 (1)	9 (4)	20 (3)	<.001
MSSA	1	None	+	5 (1)	0 (0)	0 (0)	<.001
MSSA	188	None	-	4 (1)	6 (3)	12 (2)	.22
MSSA	Misc ^b	None	Varied	59 (17)	46 (21)	117 (20)	.22

Abbreviations: Misc, miscellaneous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*; PVL, Panton-Valentine leukocidin; SCCmec type, staphylococcal cassette chromosome mec type; ST type, sequence type by multilocus strain typing.

^a P value represents the proportion of the given strain type causing infection versus the proportion causing colonization in index and household members.

^b "Miscellaneous" strain types represent 106 other *S. aureus* strain types with different genotypes circulating in households.

the likelihood ratio test to identify the optimal model for the risk factors associated with colonization of the index patient. Backward elimination was performed using the Score test to find the best model of risk factors associated with colonization of household members. Models were examined for goodness of fit using the Hosmer-Lemeshow test. All variables were considered significant at the $\alpha = .05$ level.

RESULTS

We screened 2097 patients with *S. aureus* skin infections and successfully contacted 877 by telephone or inpatient visits. Of these, 710/877 patients (80%) were eligible; among eligible patients, 502/710 (71%) verbally agreed to participate. Household visits were completed among 356 (71%) of those who agreed to participate. The remaining 146 households either never scheduled a household visit or were not present when research personnel arrived at the home. We enrolled 179 households in Los Angeles and 177 households in Chicago. Six households in Los Angeles were excluded from analysis because the patient was discharged to a long-term care facility (n = 1), unable to schedule a study visit (n = 1), or the index isolate was

not confirmed as *S. aureus* during molecular characterization (n = 4).

Characteristics of Index Patients and Epidemiologic Case Definitions

Among the 350 households, the mean household size comprised 5.3 members (5.3 in Los Angeles and 5.4 in Chicago) and the mean number of household members enrolled was 3.4 (3.3 in Los Angeles and 3.5 in Chicago). Demographic, clinical, and behavioral characteristics of the 350 index patients are presented in Table 1. By epidemiologic categorization, 111 (32%) patients had CA-MRSA, 122 (35%) had HA-MRSA, 45 (13%) had CA-MSSA, and 72 (20%) had HA-MSSA infections (Table 1). Location of infection was head and neck in 16% (56/350), trunk in 16% (57/350), arm in 18% (63/350), buttocks/genitals in 19% (66/350), and leg in 38% (132/350). Of note, 18 patients (5%) had skin infections in >2 anatomic locations.

Strain Types of Isolates Infecting Index Patients

Among infecting isolates of index patients, the majority (233, 67%) were MRSA, 117 (33%) were MSSA, and 266 (76%) were PVL+. Among the 233 MRSA isolates, 220 (94.5%) contained SCCmec type IV, 6 (2.5%) contained SCCmec type II, 6 (2.5%)

Table 3. Comparison of *Staphylococcus aureus* Body Colonization by Epidemiologic Infection Type

Colonization Site	Index Patients					P Value	Household Members					P Value
	All, n = 350 (%)	CA-MRSA, n = 111 (%)	HA-MRSA, n = 122 (%)	CA-MSSA, n = 45 (%)	HA-MSSA, n = 72 (%)		All, n = 812 (%)	CA-MRSA, n = 268 (%)	HA-MRSA, n = 258 (%)	CA-MSSA, n = 100 (%)	HA-MSSA, n = 186 (%)	
Any body site												
Any <i>S. aureus</i>	137 (40)	45 (41)	40 (33)	18 (40)	34 (47)	.007	405 (50)	134 (50)	125 (49)	45 (45)	101 (54)	<.001
MSSA	86 (25)	27 (24)	17 (14)	15 (33)	27 (40)	.13	267 (33)	86 (32)	73 (28)	29 (29)	79 (42)	<.001
MRSA	62 (18)	21 (19)	27 (22)	3 (7)	11 (15)	<.001	177 (22)	61 (23)	61 (24)	22 (22)	33 (17)	<.001
Nasal												
Any <i>S. aureus</i>	75 (22)	23 (21)	20 (16)	11 (24)	21 (30)	.21	205 (25)	61 (23)	68 (26)	25 (25)	51 (28)	<.001
MSSA	47 (14)	15 (14)	5 (4)	10 (22)	17 (24)	.06	116 (14)	35 (13)	34 (13)	11 (11)	15 (8)	.002
MRSA	28 (8)	8 (7)	15 (12)	1 (2)	4 (6)	.001	89 (11)	26 (10)	34 (13)	14 (14)	36 (20)	.007
Oropharynx												
Any <i>S. aureus</i>	64 (19)	23 (21)	19 (16)	8 (18)	14 (19)	.049	236 (30)	81 (31)	72 (28)	22 (22)	61 (34)	<.001
MSSA	36 (11)	12 (11)	6 (5)	7 (16)	11 (15)	.41	160 (20)	55 (21)	42 (16)	13 (13)	50 (28)	<.001
MRSA	28 (8)	11 (10)	13 (11)	1 (2)	3 (4)	.002	76 (10)	26 (10)	30 (12)	11 (11)	11 (6)	<.001
Inguinal region												
Any <i>S. aureus</i>	76 (22)	18 (16)	28 (23)	7 (17)	23 (32)	.005	154 (19)	53 (20)	50 (19)	18 (18)	33 (18)	<.001
MSSA	41 (12)	10 (9)	11 (9)	5 (12)	15 (21)	.18	77 (10)	26 (10)	21 (8)	11 (11)	19 (10)	.11
MRSA	35 (10)	8 (7)	17 (14)	2 (5)	8 (11)	.004	77 (10)	27 (10)	29 (11)	7 (7)	14 (8)	<.001
Colonization at >1 body site												
Any <i>S. aureus</i>	63 (18)	16 (14)	20 (16)	7 (16)	20 (28)	.67	150 (18)	50 (18)	48 (18)	14 (14)	38 (20)	<.001
MSSA	42 (12)	12 (11)	8 (7)	6 (13)	16 (22)	.13	107 (13)	36 (13)	27 (10)	11 (11)	33 (18)	.003
MRSA	31 (9)	7 (6)	16 (13)	1 (2)	7 (10)	.002	75 (9)	22 (8)	29 (11)	9 (9)	15 (8)	.007
Nonnasal												
Any <i>S. aureus</i>	117 (34)	37 (33)	37 (31)	14 (31)	29 (41)	.007	332 (41)	115 (44)	100 (39)	34 (34)	83 (44)	<.001
MSSA	69 (20)	21 (19)	15 (12)	11 (24)	22 (31)	.20	217 (27)	75 (28)	56 (22)	23 (23)	75 (40)	<.001
MRSA	52 (15)	17 (15)	23 (19)	3 (7)	9 (13)	<.001	133 (16)	47 (18)	48 (19)	15 (15)	23 (12)	<.001
Nasal only												
Any <i>S. aureus</i>	20 (6)	8 (8)	3 (2)	2 (9)	5 (7)	.42	73 (9)	19 (7)	25 (10)	11 (11)	18 (10)	.14
MSSA	13 (4)	5 (5)	0 (0)	2 (9)	4 (6)	.15	37 (5)	11 (4)	13 (5)	5 (5)	11 (6)	.26
MRSA	7 (2)	3 (3)	3 (3)	0 (0)	1 (1)	.57	36 (4)	8 (3)	12 (5)	6 (6)	7 (4)	.41
Oropharynx only												
Any <i>S. aureus</i>	24 (6)	13 (12)	5 (5)	4 (9)	2 (3)	.009	125 (15)	47 (17)	34 (13)	11 (11)	33 (18)	<.001
MSSA	13 (4)	6 (6)	2 (2)	3 (7)	2 (3)	.35	92 (11)	33 (12)	23 (9)	7 (7)	29 (16)	<.001
MRSA	11 (2)	7 (6)	3 (3)	1 (2)	0 (0)	.08	33 (4)	14 (5)	11 (4)	4 (4)	4 (2)	.03

Table 3 continued.

Colonization Site	Index Patients					Household Members					
	All, n = 350 (%)	CA-MRSA, n = 111 (%)	HA-MRSA, n = 122 (%)	CA-MSSA, n = 45 (%)	HA-MSSA, n = 72 (%)	All, n = 812 (%)	CA-MRSA, n = 268 (%)	HA-MRSA, n = 258 (%)	CA-MSSA, n = 100 (%)	HA-MSSA, n = 186 (%)	P Value
Inguinal region only											
Any <i>S. aureus</i>	30 (8)	8 (8)	17 (14)	3 (7)	7 (10)	57 (7)	18 (6)	18 (7)	9 (9)	12 (6)	.23
MSSA	18 (4)	4 (4)	0 (0)	2 (5)	5 (7)	31 (4)	9 (3)	10 (4)	6 (6)	6 (3)	.65
MRSA	12 (4)	4 (4)	17 (14)	1 (2)	2 (3)	26 (3)	9 (3)	8 (3)	3 (3)	6 (3)	.36

P values represent comparisons between groups within a given row. P values < .05 signify that 1 group has a proportion that was statistically significantly different from other groups.

Abbreviations: CA-MRSA, community-associated methicillin-resistant *Staphylococcus aureus*; CA-MSSA, community-associated methicillin-susceptible *S. aureus*; HA-MRSA, healthcare-associated methicillin-resistant *S. aureus*; HA-MSSA, healthcare-associated methicillin-susceptible *S. aureus*.

contained SCCmec type III, and 1 (0.5%) contained an un-typeable SCCmec element. Among the infecting index subjects' isolates, 230 (66%) were ST8 and 186 (53%) were USA300 MRSA. The genetic background of index patients' isolates is summarized in Table 2.

Colonization Among Index Patients

Among index patients, 137/350 (40%) were colonized with *S. aureus*. Nasal colonization was present in 75 (22%) patients, oropharyngeal colonization in 64 (19%), and inguinal colonization in 76 (22%). Nonnasal colonization was found in 34% (117/350) of subjects, while 6% (24/350) were colonized only in the oropharynx and 8% (30/350) only in the inguinal region (Table 3). Including their infecting strain, 71% (247/350) of index patients had 1 *S. aureus* strain type, 24% (84/350) had 2 strain types, and 5% (19/350) had 3 strain types isolated from their body.

Among index patients, 12% (41/350) had >1 colonizing strain types concordant with their infecting isolate and 27% (96/350) were colonized with an *S. aureus* strain type discordant from their infecting isolate. Among index patients infected with MRSA, 14% (32/233) carried a concordant strain type and 25% (57/233) carried a discordant *S. aureus* strain type. Of these 57 discordant *S. aureus* strain types, 28% (16/57) were discordant MRSA strain types. Among those infected with an MSSA strain, 8% (9/117) carried a concordant strain type and 39% (46/117) carried a discordant *S. aureus* strain type. Of these 46 discordant *S. aureus* strain types, 72% (33/46) were colonized with other MSSA strain types. Among patients infected with USA300 MRSA, concordant carriage occurred in 16% (29/186) and 23% (43/186) carried a discordant *S. aureus* strain type. Of these 43 discordant strain types, 23% (10/43) were non-USA300 MRSA strain types.

Factors associated with colonization with the infecting strain type in bivariate analysis are described in Table 1. In the multivariable model, independent predictors of colonization with the infecting strain type were skin rash in the prior 90 days (odds ratio [OR], 2.9 [1.4–6.2]; $P = .006$) and having ≥ 1 household members colonized with the infection strain type (OR, 4.3 [2.1–8.6]; $P < .001$).

Household Contacts' Colonization

Among the 826 household members, 14 declined the body colonization swabs. Demographics and comorbidities of the 812 household contacts are summarized in Table 4. Of note, 24% (197/812) of household members reported a skin infection in the prior 12 months and 50% (405/812) were colonized with *S. aureus*. Colonization site data are provided in Table 3. Overall, 33% (267/812) of household members were colonized with MSSA and 22% (177/812) with MRSA. Forty-one percent (333/812) were colonized with 1 strain

Table 4. Bivariate Analysis of Risk Factors Associated With an Index Patient's Infecting Strain Colonizing a Household Member in at Least 1 Body Site

Variable	All, n = 812 (%)	Colonized With Index Infection Strain, n = 111 (%)	Not Colonized With Index Infection Strain, n = 701 (%)	OR	95% CI	P value
Site						
Chicago	422 (52)	54 (49)	368 (53)	0.99	.94, 1.04	.63
Los Angeles	390 (48)	57 (51)	333 (48)
Demographics						
Gender						
Female	510 (63)	63 (57)	447 (65)	0.96	.92, 1.01	.13
Male	294 (37)	48 (43)	246 (36)
Age						
Older adult (>65 yr)	36 (4)	5 (5)	31 (5)	1.01	.90, 1.13	.85
Adult (19–65 yr)	492 (61)	67 (60)	425 (61)	Ref
Child (5–18 yr)	175 (22)	27 (24)	148 (21)	1.02	.95, 1.08	.59
Younger child (<5 yr)	109 (13)	12 (11)	97 (14)	0.97	.91, 1.03	.33
Ethnicity						
African-American	412 (51)	53 (48)	359 (51)	1.06	.97, 1.16	.18
Caucasian	48 (6)	3 (3)	45 (6)	Ref
Hispanic	300 (37)	50 (45)	250 (36)	1.11	1.001, 1.22	.03
Other/mixed/unknown	52 (6)	5 (5)	47 (7)	1.02	.91, 1.14	.69
Clinical factors						
Charlson comorbidity score						
Mean ± SD	0 ± 1	0 ± 1	0 ± 1	0.98	.96, 1.00	.16
Median (range)	0 (0–7)	0 (0–6)	0 (0–7)
Comorbidities						
Diabetes	71 (9)	9 (8)	62 (9)	0.99	.91, 1.07	.73
HIV infection	8 (2)	1 (1)	7 (2)	0.99	.82, 1.19	.91
In the past 12 mo						
Had a previous skin infection	197 (25)	45 (41)	152 (23)	1.12	1.04, 1.19	<.001^a
Undergone major surgery	59 (7)	4 (4)	55 (8)	0.94	.87, 1.01	.07
Received dialysis	1 (0.12)	0 (0)	1 (0.14)	NA	NA	.99
Hospitalized	101 (13)	15 (14)	86 (13)	1.01	.93, 1.08	.88
Days of hospitalization						
Mean ± SD	0.5 ± 2	0.5 ± 2	0.5 ± 2	1.00	.98, 1.01	.93
Median (range)	0 (0–30)	0 (0–21)	0 (0–30)
Any antibiotic exposure						
Use of clindamycin	12 (2)	4 (4)	8 (1)	1.22	.89, 1.67	.22
Use of TMP-SMX	11 (1)	4 (4)	7 (1)	1.23	.96, 1.58	.09
Use of cephalexin	15 (2)	7 (6)	8 (1)	1.39	1.06, 1.78	.02^b
Use of immunosuppressant medications	78 (10)	14 (13)	64 (9)	1.04	.95, 1.14	.42
Spent time living in a skilled nursing facility, rehabilitation center, or other type of group facility	19 (2)	2 (2)	17 (3)	0.95	.84, 1.07	.41
Epidemiologic factors						
Household density						
Mean ± SD	2.0 ± 0.98	2.2 ± 0.92	2.0 ± 0.98	1.01	.99, 1.04	.33
Median (range)	2.0 (0.33–6.0)	2.2 (0.71–6.0)	2.0 (0.33–6.0)
Homelessness in the past 12 mo	40 (5)	5 (5)	35 (5)	0.99	.89, 1.11	.99
Cuts/scratches in the 30 d prior to index infection	308 (38)	51 (46)	257 (37)	1.05	.99, 1.11	.07
Skin rash in the 90 d prior to index infection	87 (11)	18 (17)	69 (10)	1.09	.99, 1.18	.06
Pets in the home currently	339 (42)	47 (43)	292 (42)	1.01	.95, 1.06	.83

Table 4 continued.

Variable	All, n = 812 (%)	Colonized With Index Infection Strain, n = 111 (%)	Not Colonized With Index Infection Strain, n = 701 (%)	OR	95% CI	P value
Incarceration in the past 12 mo	21 (3)	3 (4)	18 (3)	1.02	.87, 1.19	.86
Illicit drug use in the past 12 mo	66 (11)	11 (14)	55 (11)	1.05	.96, 1.15	.26
>1 sexual partner in the past 12 mo	73 (12)	9 (12)	64 (12)	0.99	.92, 1.07	.80
In the past 3 mo						
Showered at least once a day	131 (16)	23 (21)	108 (16)	1.04	.97, 1.11	.32
Shared make-up with others	88 (12)	13 (13)	75 (11)	1.01	.93, 1.10	.82
Shared bar soap with others	496 (63)	67 (63)	429 (63)	1.00	.95, 1.05	.96
Shared clothes with others without washing	51 (6)	8 (7)	43 (6)	1.03	.94, 1.13	.53
Shared towels with others	389 (48)	55 (50)	334 (48)	1.02	.97, 1.07	.42
Wore clothes more than once without washing	400 (50)	58 (53)	342 (49)	1.02	.97, 1.07	.42
Hand-washing frequency after using the bathroom						
Mean ± SD	2.7 ± 0.62	2.7 ± 0.76	2.8 ± 0.60	0.97	.92, 1.01	.20
Median (range)	3 (0–3)	3 (0–3)	3 (0–3)
Household cleaning scale ^c						
Mean ± SD	17 ± 7	17 ± 8	17 ± 7	0.99	.99, 1.00	.17
Median (range)	18 (0–34)	18 (0–29)	18 (0–34)
Use of a gym	87 (12)	10 (10)	77 (12)	0.98	.92, 1.05	.59
Participation in contact sports	201 (25)	33 (30)	168 (24)	1.04	.98, 1.10	.23
Goes to day care	30 (16)	3 (10)	27 (17)	0.92	.82, 1.02	.10
Use of public facilities ^d	224 (28)	32 (29)	192 (28)	1.00	.96, 1.06	.86
Strain Specific Factors						
Infecting strain categorization by the CDC case definition						
CA-MRSA	268 (33)	39 (35)	229 (33)	0.95	.88, 1.01	.12
HA-MRSA	258 (32)	52 (47)	206 (29)	Ref
CA-MSSA	100 (12)	8 (7)	92 (13)	0.89	.82, .97	.008
HA-MSSA	186 (23)	12 (11)	174 (25)	0.88	.82, .94	.003
ST8-IV-PVL infection strain type	442 (54)	87 (78)	355 (51)	1.13	1.08, 1.19	<.001^e
PVL presence	622 (77)	95 (86)	527 (75)	1.07	1.01, 1.13	.03
SCCmec type IV	503 (62)	89 (80)	414 (59)	1.10	1.05, 1.16	<.001

Statistically significant relationships are bolded; NA indicates cannot be calculated due to zero cell.

Abbreviations: CA-MRSA, community-associated methicillin-resistant *Staphylococcus aureus*; CA-MSSA, community-associated methicillin-susceptible *S. aureus*; CDC, Centers for Disease Control and Prevention; CI, confidence interval; HA-MRSA, healthcare-associated methicillin-resistant *S. aureus*; HA-MSSA, healthcare-associated methicillin-susceptible *S. aureus*; HIV, human immunodeficiency virus; OR, odds ratio; PVL, Panton-Valentine leukocidin; Ref, reference group; SCCmec type, staphylococcal cassette chromosome mec type; TMP-SMX, trimethoprim-sulfamethoxazole.

^a Variable significant in multivariable analysis (OR, 2.01 [1.31–3.08]; $P = .001$).

^b Variable significant in multivariable analysis (OR, 3.5 [1.3–9.5]; $P = .01$).

^c Household cleaning is a measure of the frequency of cleaning for common household items with higher values representing more frequent cleaning.

^d Use of public facilities is defined as use of a publicly available gym, locker room, shower, swimming pool, sauna, or Jacuzzi.

^e Variable significant in multivariable analysis (OR, 3.0 [1.7–5.3]; $P = .0002$).

type, 8% (63/812) with 2 strain types, and 1% (9/812) with 3 strain types.

Colonizing Strain Types of Household Contacts

Of the 350 households, the presence of >1 *S. aureus* strain circulating among household contacts was common. Including the index patient's infecting isolate, 35% (123/350) of

households had a single strain type identified, 33% (117/350) had 2 strain types, 20% (40/350) had 3 strain types, 7% (24/350) had 4 strain types, and 5% (16/350) had ≥5 strain types identified.

The genetic backgrounds of *S. aureus* identified among household members are summarized in Table 2. The most common genetic background was USA300 MRSA, which

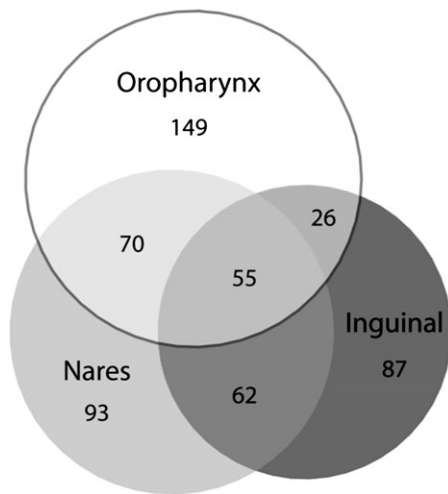


Figure 1. Overlap of nares, oropharynx, and inguinal colonization among the 542 *Staphylococcus aureus*-colonized subjects from our total population of 1162 persons of households of persons with a recent *S. aureus* skin infection. Each circle size is proportional to the amount of *S. aureus* detected at that given anatomic site. Of note, nares-only surveys would have missed 48% of *S. aureus*-colonized persons.

represented 30% of isolates. USA300 MRSA was found to colonize 16% of CA-MRSA, 20% of HA-MRSA, 16% of CA-MSSA, and 12% of HA-MSSA household members.

Fourteen percent (111/812) of household members had at least 1 colonizing strain type concordant with the index patient's infecting isolate and 39% (317/812) of their colonizing isolate types were discordant. In households with an index MRSA infection, 17% (91/526) of contacts carried a concordant strain type compared with 7% (20/286) among household contacts of an MSSA index infection and 20% (87/442) of households with a USA300 MRSA index infection.

For household contacts, bivariate associations between hypothesized risk factors for colonization and strain type concordant with the index patient's infecting strain type are described in Table 4. In multivariable analysis, significant predictors of strain type concordant with the index patient's infecting strain type included previous skin infection (OR, 2.01 [1.31–3.08]; $P = .001$), cephalixin use in the past 12 months (OR, 3.5 [1.3–9.5]; $P = .01$), and the index patient having a USA300 infection strain type (OR, 3.0 [1.7–5.3]; $P < .001$).

DISCUSSION

Our investigation of 350 households with *S. aureus* infection in Los Angeles and Chicago comprising 1162 persons demonstrated the prevalence of *S. aureus* colonization among index patients and their household members is high, yet colonizing

strain types are surprisingly diverse, complex, and frequently not concordant with the infecting isolate.

Our investigation yielded several notable findings. First, our data suggest that the USA300 MRSA genetic background appears to spread more easily in households than other genetic backgrounds. An index infection with the USA300 MRSA genetic background was an independent predictor of concordant strain type colonization in another household member. These findings may explain USA300 MRSA's emergence in communities [53, 54] and infection clusters in households, jails, military barracks, and sports teams [54–57]. Of note, USA300 MRSA was highly prevalent and found in ≥ 1 persons in 80% of households with an index HA-MRSA infection and 26% of households with an HA-MSSA infection.

Second, *S. aureus* colonization of household members was very common (50%) and higher than the 20%–35% prevalence of nasal colonization commonly cited [58–60]. These findings probably reflect that we surveyed 3 body sites and used enrichment broth culture. Similar to studies in other populations [29–32], assessing additional anatomic sites for *S. aureus* colonization revealed a higher prevalence of *S. aureus* colonization. Notably, a nares-only culture survey in our population of household contacts would have missed 48% of *S. aureus*-colonized persons (Figure 1) and 51% of MRSA-colonized persons. These findings suggest that development of successful decolonization regimens to prevent infection should consider agents that eradicate skin and oropharyngeal colonization.

Third, only 74% (91/122) of household contacts with MRSA colonization were colonized with the same MRSA genetic background as the index patient. The unexpectedly high prevalence of discordant MRSA genetic backgrounds colonizing contacts (26%) suggests that merely surveying for MRSA colonization in household contacts of persons with a skin infection would overestimate the spread of the index patients' MRSA clones within the household and that many households in our study had >1 *S. aureus* or even MRSA strain type circulating.

Fourth, *S. aureus* colonization among index patients (40%) was less common than among household contacts (50%). Households were visited on average 18 days after the infection culture was obtained. Thus, this finding probably reflects index patients' recent antibiotic treatment that may have eradicated *S. aureus* colonization.

Finally, our data demonstrate that the distribution of pathogenic strain types differs from that of strain types colonizing index patients and their household contacts. For example, USA300 MRSA genetic background caused 53% of infections but comprised just 29% of colonizing strain types ($P < .001$). Conversely, sequence type 30 MSSA caused just 1% of infections but was responsible for 7.4% of colonizing isolates. These findings suggest that some genetic backgrounds are

unlikely causes of disease and that others, such as USA300 MRSA, have high pathogenic potential. If true, decolonization strategies may need to be refocused to avoid inadvertently eliminating less pathogenic *S. aureus* strains and disrupting commensal flora. Alternatively, these findings may stem from decolonization of patients' infecting USA300 strain and subsequent recolonization with less pathogenic strains.

Compared with other investigations of household *S. aureus* spread, it should be noted that 3 European investigations and 1 American investigation found that all or all but 1 of the MRSA strain types colonizing household members were identical to those infecting the index patient [17, 18, 21, 24]. Perhaps this lack of strong concordance is due to the higher level of endemic MRSA colonization and the differences in the genetic backgrounds of prevalent MRSA clones that exist in the United States compared with many European countries. In the US study noted above, results may have differed from ours because the study was conducted before the emergence of CA-MRSA. Interestingly, 1 smaller US study conducted in an area of endemic CA-MRSA, like ours, found discordance in about half of isolates colonizing household members [19].

There are strengths to our study. First, to our knowledge, our investigation is the largest detailed survey of household contacts of patients with *S. aureus* skin infections. Unlike many previous investigations of household colonization that did not survey multiple body sites [17, 19, 20, 22, 23, 25, 26], we assessed 3 body sites for colonization and undertook a detailed epidemiologic survey. Second, our study was performed at 2 urban sites in the United States that have different racial and ethnic population distributions. Third, we performed genotyping of isolates. A previous large investigation of HA-MRSA spread to household contacts found that the rate of spread to contacts was 20% [23]. However, in the absence of strain typing, this number may be an overestimation. Furthermore, the purported risk factors for MRSA transmission in this prior investigation would be biased by the lack of strain typing. Finally, other previous investigations did not examine epidemiologic factors or were likely underpowered to detect significant relationships [15–21].

There are limitations to our study. First, our survey may not have detected some colonized individuals because some studies have found *S. aureus* colonization on the wrists, rectum, axilla, and vagina [30, 61, 62]. However, the yields of these additional sites may have been low [30, 61, 62]. Second, our study is cross sectional and could not determine directionality of strain transfer. Third, our population may not be representative of other populations. Study subjects came from populations of relatively low socioeconomic status in the United States where CA-MRSA infections are epidemic. Fourth, the number of comparisons and tests performed for statistical analyses may increase the likelihood of type 1 error.

In summary, we found that *S. aureus* colonization was very common among household contacts of persons with acute *S. aureus* infection. Given the strain type diversity among MSSA and MRSA isolates found in household members, development of successful household *S. aureus* screening and decolonization programs infections may not be a simple task. It is plausible that decolonization will eradicate less pathogenic strain types, leaving the person vulnerable to recolonization with more pathogenic strain types, such as USA300 MRSA. The complex nature of colonization we observed may prompt rethinking of MRSA prevention strategies. The implications of eliminating *S. aureus* strain types uncommonly associated with disease are unclear and require further study.

Notes

Acknowledgments. We thank Everly Macario, Mellie Badar, Ramiro Correa, Sallie Chui, and Grace Tagudar for assistance with survey development, collection of study data, and processing of laboratory specimens. We also thank the staff of the Clinical Microbiology Laboratory at Harbor-UCLA Medical Center for their assistance with specimen collection. Finally, we thank all of the patients and their families for their participation and for allowing us to visit their homes for this study.

Financial support. This work was supported by a grant from the National Institutes of Health (R01 AI067584-01A1).

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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