Characterization of Nasal and Blood Culture Isolates of Methicillin-Resistant *Staphylococcus aureus* from Patients in United States Hospitals

Fred C. Tenover,[a] Isabella A. Tickler,[a] Richard V. Goering,[b] Barry N. Kreiswirth,[c] José R. Mediavilla,[c] and David H. Persing[a] for the MRSA Consortium

Cepheid, Sunnyvale, California, USA[a]; Creighton University, Omaha, Nebraska, USA[b]; and University of Medicine and Dentistry of New Jersey, Public Health Research Institute, Newark, New Jersey, USA[c]

A total of 299 nares and 194 blood isolates of methicillin-resistant *Staphylococcus aureus* (MRSA), each recovered from a unique patient, were collected from 23 U.S. hospitals from May 2009 to March 2010. All isolates underwent *spa* and staphylococcal cassette chromosome *mec* element (SCC*mec*) typing and antimicrobial susceptibility testing; a subset of 84 isolates was typed by pulsed-field gel electrophoresis (PFGE) using SmaI. Seventy-six *spa* types were observed among the isolates. Overall, for nasal isolates, *spa* type t002-SCC*mec* type II (USA100) was the most common strain type (37% of isolates), while among blood isolates, *spa* type t008-SCC*mec* type IV (USA300) was the most common (39%). However, the proportion of all USA100 and USA300 isolates varied by United States census region. Nasal isolates were more resistant to tobramycin and clindamycin than blood isolates (55.9% and 48.8% of isolates versus 36.6% and 39.7%, respectively; for both, $P < 0.05$). The USA300 isolates were largely resistant to fluoroquinolones. High-level mupirocin resistance was low among all *spa* types (<5%). SCC*mec* types III and VIII, which are rare in the United States, were observed along with several unusual PFGE types, including CMRSA9, EMRSA15, and the PFGE profile associated with sequence type 239 (ST239) isolates. Typing data from this convenience sample suggest that in U.S. hospitalized patients, USA100 isolates of multiple *spa* types, while still common in the nares, have been replaced by USA300 isolates as the predominant MRSA strain type in positive blood cultures.

Methicillin-resistant *Staphylococcus aureus* (MRSA) isolates continue to be a global cause of both health care- and community-associated infections (12, 20, 24). Multiple clones of MRSA have been recognized and are circulating worldwide, although strains of clonal complex 5 (CC5) and CC8 are the largest and most diverse (16, 39). Population-based studies of invasive MRSA infections in the United States by using the Centers for Disease Control and Prevention's Active Bacterial Core Surveillance (ABCs) system indicate that pulsed-field gel electrophoresis (PFGE) type USA100 (multilocus sequence type 5 [ST5], CC5) is the predominant strain type observed, although these and other studies indicate that USA300 isolates (ST8, CC8) are increasing in frequency as a cause of health care-associated bacteremia (29, 30, 32, 42). Similarly, a population-based study of nasal colonization of noninstitutionalized persons in the United States (i.e., those not in hospitals, other health care facilities, prisons, or other institutions) also showed that USA100 was the most common MRSA strain type observed (22, 47). However, over the 4-year study period (2001 to 2004), there was a significant increase in the proportion of individuals harboring USA300 isolates in their nares (22). In addition, more recent data indicate that USA300 isolates are becoming a common cause of nasal carriage among U.S. hospitalized patients, especially in the southern United States (17), and continue to be a significant cause of community-acquired skin infections (35) and skin disease in long-term care facilities (45). A model of invasive MRSA infections reported by D'Agata et al. indicated that MRSA isolates of PFGE type (PFT) USA300 were likely to increase in frequency in the United States and replace USA100 isolates as the most common cause of invasive MRSA infections in the future (11). Such isolates were hypothesized in the model, based on published literature, to show increased viru-

lence relative to USA100 strains and required both enhanced hand washing and active surveillance for control.

Although PFGE has been the gold standard for typing of MRSA in the United States for many years (34) and a protocol for PFGE typing was established in 2003 for use in European laboratories (36), strain typing based on DNA sequence analysis of the repeated units of the staphylococcal protein A gene (i.e., *spa* typing) is now used much more commonly around the world for epidemiologic studies of MRSA (21, 24, 26). However, there are relatively few studies of the distribution of MRSA *spa* types among U.S. isolates, which makes comparisons of MRSA strain types in the United States to those in other countries, such as the most recent European MRSA surveillance data (24), difficult.

Accordingly, the goals of this study were to (i) determine the *spa* types of MRSA strains that colonize the nares and invade the bloodstream of patients in U.S. hospitals, (ii) translate the *spa* types of the MRSA strains into PFGE types, either by parallel testing of the isolates or by prediction of the PFGE types using information available both from the Ridom Spaserver website and published studies, (iii) compare the MRSA strain typing data from this survey to previous U.S. data from the National Health and Nutri-

tion Examination Survey (NHANES) (22, 47), the ABCs data for invasive MRSA isolates (30, 32), and recent European surveillance data (24), and (iv) determine if there are differences in the antimicrobial susceptibility patterns of the MRSA strains isolated from nasal and blood cultures.

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MATERIALS AND METHODS

Bacterial isolates. A total of 493 MRSA isolates (299 nares isolates and 194 blood isolates), collected from 10 to 20 unique patients (but without specific selection criteria) from 23 U.S. laboratories from May 2009 to March 2010 were studied. All isolates were deidentified prior to shipment so that they could not be linked to specific patients. The isolates were confirmed at Cepheid as MRSA by broth microdilution susceptibility testing using oxacillin (see below), Gram stain, catalase, and coagulase testing and by additional biochemical testing when necessary (3).

Antimicrobial susceptibility testing. Antimicrobial susceptibility testing was performed using the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method (9). Mueller-Hinton broth was obtained from Becton Dickinson (Sparks, MD), and cation concentrations were adjusted following CLSI guidelines (9). After inoculation, MIC trays were incubated at 35°C in ambient air for 18 to 24 h. Antimicrobial agent powders were obtained from Sigma-Aldrich (St. Louis, MO) or directly from the antimicrobial agent manufacturers. Microdilution wells containing daptomycin were supplemented with calcium to a final concentration of 50 μg/ml as described by CLSI, and wells containing oxacillin were supplemented with NaCl to a final concentration of 2% (9, 48). Selected isolates with borderline-susceptible results to linezolid and daptomycin were tested using Etest strips (bioMérieux, Durham, NC) as described by the manufacturer. Testing was performed on Mueller-Hinton agar plates obtained from Remel (Lenexa, KS) and interpreted as previously described (49). Tigecycline interpretive criteria were those established for staphylococci by the U.S. Food and Drug Administration, i.e., ≤0.5 μg/ml indicating susceptibility (no intermediate or resistant breakpoints were defined) (http://www.accessdata.fda.gov/drugsatfda_docs/label/2005/021821lbl.pdf, accessed on 8 September 2011). Quality control strains included *S. aureus* ATCC 29213 and *Enterococcus faecalis* ATCC 29212 (10). Mueller-Hinton plates with Etest strips were incubated in ambient air at 35°C for 24 h. A subset of the combined MIC results for nasal and blood isolates, along with data on mechanisms of aminoglycoside resistance (not discussed here), have been published previously (48).

Strain typing methods. Isolates underwent *spa* (44) and SCC*mec* typing (7) and were tested for genes encoding Panton-Valentine leucocidin (PVL) (41), arginine catabolic metabolic element (ACME) (15), and the high-level mupirocin resistance gene, *mupA* (1). A subset of 84 isolates representing common *spa* types and all isolates with unusual or rare *spa* types, were typed by pulsed-field gel electrophoresis using SmaI as previously described (20). *spa* types were assigned to PFGE types (PFTs) based on parallel testing of isolates with both methods, data from the Ridom SpaServer website (http://spaserver2.ridom.de/spaserver/query, accessed 1 June, 2011), and published literature (20, 21). Strains with the same *spa* type and antibiograms, particularly those that were from the same laboratory, were not typed by PFGE. Simpson's index of diversity was calculated using programs available at http://darwin.phyloviz.net/ComparingPartitions/index.php?link=Tool.

Minimum spanning tree analysis. Cluster analysis of *spa* sequences was performed using the *spa* typing plug-in tool of the BioNumerics software program (version 6.5; Applied Maths, Ghent, Belgium). The analysis compares and aligns sequences via an algorithm based on potential tandem *spa* repeat duplications, substitutions, and indels (the DSI model) (4). A minimum spanning tree (MST) was generated from the similarity matrix with the root node assigned to the *spa* sequence type with the greatest number of related types. The default software parameters were

used for analysis with a bin distance of 1.0%. Thus, the distance between *spa* types of 99% to 100% similarity was 0, 98% to 99% similarity was assigned a distance of 1, etc., on the MST. For cluster analysis, only *spa* types separated by an MST distance of ≤2 (i.e., if they were ≥97% similar) were considered closely related and assigned to the same cluster.

Statistical methods. Fisher's exact test was used to compare the rates of resistance between nasal and blood isolates.

RESULTS

Typing results. The *spa* types (using Ridom nomenclature) and associated SCC*mec* types for the 299 nares isolates and 194 blood isolates are shown in Table 1. (The eGenomics *spa* types corresponding to the Ridom *spa* types are listed in Table S1 in the supplemental material.) Among blood isolates, *spa* type t008-SCC*mec* IV (which showed PFT USA300 patterns) was the most common strain type observed (n = 76), followed by t002-SCC*mec* II (which showed PFT USA100 patterns) (n = 43). Overall, the *spa* types of blood isolates associated with USA300 (n = 93) encompassed 48% of the isolates and were more common than those associated with USA100 (n = 69, 36% of isolates). In addition, there were eight *spa* type t064-SCC*mec* IV isolates of PFT USA500 and two isolates (*spa* types t008 and t197) that were PFT CMRSA9 (Canadian nomenclature [21]), both of which carried SCC*mec* VIII. These two isolates were from two different cities in Florida. Two isolates of *spa* type t037-SCC*mec* III demonstrating PFTs consistent with ST239 were isolated from California and Indiana, and one *spa* type t020-SCC*mec* IV isolate of PFT EMRSA15 was detected from California. Among blood isolates, the proportion of *spa* types corresponding to USA100 and USA300 varied by U.S. census region (Fig. 1). USA300 was the most common PFT in the Middle Atlantic (data from 4 laboratories), South Atlantic (data from 5 laboratories), Pacific (data from 7 laboratories), and West South Central (data from 1 laboratory) regions, while USA100 strains were the predominant type in New England (data from 2 laboratories), East North Central (data from 2 laboratories), West North Central (data from 1 laboratory), and Mountain (data from 1 laboratory) regions. No data from the East South Central region were available.

Among nasal isolates, *spa* type t002-SCC*mec* II (USA100) was the most common strain type (n = 110), followed by t008-SCC*mec* IV (USA300) (n = 60), t002-SCC*mec* IV (n = 12) (USA800), and t064-SCC*mec* IV (n = 8) (USA500). Overall, strains with the PFT USA100, which encompassed 29 unique *spa* types, were most common (n = 178), encompassing 60% of the isolates. The second most common PFT among nasal isolates was USA300 (n = 75, 25% of isolates). One t008-SCC*mec* VIII isolate from California (PFT CMRSA9) and two t037-SCC*mec* III isolates (with PFT ST239 from Washington and California), as well as a t032-SCC*mec* IV (EMRSA15) isolate from Illinois, were also observed among nasal isolates. For nasal isolates, the USA100 PFT was predominant in each of the census regions (data not shown).

Three *spa* types—t002, t062, and t088—were shared among USA100 and USA800 isolates. The isolates were assigned to PFT USA100 or USA800 (both of which are typically in multilocus sequence typing [MLST] type CC5) primarily based on the PFGE banding pattern but also with consideration of the SCC*mec* type (SCC*mec* II is usually present in USA100 and SCC*mec* IV is usually present in USA800). The antibiograms of the isolate were also considered and in each case were consistent with either USA800 (i.e., susceptible to tobramycin, clindamycin, and ciprofloxacin)

TABLE 1 *spa*, SCC*mec*, and pulsed-field gel electrophoresis types of study isolates[a]

PFGE type	Blood		Nares	
	spa type-SCC*mec* (*n*)[b]	Total no. of isolates (194)	*spa* type-SCC*mec* (*n*)	Total no. of isolates (299)
USA100	t002-II (43), t002-NT (1), t045-II (4), t062-II (1), t062-IV (1), t067-II (1), t088-II (1), t214-II (1), t242-II (9), t242-NT (1), t688-II (1), t985-II (1), t1062-II (1), t2358-II (1), t2666-II (1), t6778-II (1)	69	t002-II (110), t002-NT (5), t010-II (1), t045-II (5), t062-II (1), t067-II (4), t071-II (1), t088-II (3), t105-II (3), t105-NT (4), t242-II (15), t242-NT (5), t509-II (2), t535-II (1), t539-II (2), t548-II (1), t548-NT (1), t570-II (1), t586-II (1), t837-II (1), t895-II (1), t1220-II (1), t1567-II (1), t2666-II (1), t3557-II (1), t3558-II (1), t4371-II (1), t4916-II (1), t4963-II (1), t5081-II (1), t-6778-II (1)	178
USA200	None observed	0	t021-IV (1)	1
USA300	t008-IV (76), t008-NT (2), t024-IV (1), t051-IV (1), t304-IV (2), t334-IV (1), t622-IV (1), t648-IV (1), t1617-IV (1), t2743-IV (2), t3908-IV (1), t4069-IV (2), t4229-IV (1), t6774-IV (1)	93	t008-IV (60), t008-NT (3), t024-IV (3), t190-IV (1), t211-IV (1), t334-II (1), t622-IV (1), t681-IV (1), t951-IV (1), t1779-IV (1), t6127-IV (1), t6774-IV (1)	75
USA400	t127-IV (1)	1	t1178-IV (1)	1
USA500	t064-IV (8)	8	t064-IV (8); t451-IV (1)	9
USA700	None observed	0	t148-IV (1), t148-NT (1)	2
USA800	t002-IV (3), t062-IV (1), t1265-IV (1)	5	t002-IV (12), t088-IV (3), t111-IV (1), t306-IV (1), t1265-IV (2), t5213-IV (1)	20
USA1000	t216-IV (1)	1	t216-IV (1), t316-IV (1), t437-IV (1), t976-NT (1)	4
CMRSA9	t008-VIII (1), t197-VIII (1)	2	t008-VIII (1)	1
EMRSA15	t020-IV (1)	1	t032-IV (1)	1
ST239-associated pattern	t037-III (2)	2	t037-III (2)	2
Unnamed[c]	Unnamed-II (1), unnamed-IV (1), t189-IV (1), t668-II (5), t6770-II (2), t6771-IV (1), t6775-II (1)	12	Unnamed-II (1), unnamed-IV (2), t450-II (1), t579-II (1)	5

[a] PFGE types were determined directly for 84 isolates, including all unusual *spa* types, and on representative isolates of clusters of similar isolates (same *spa* type and antibiograms) from the same laboratory.
[b] NT, not typeable.
[c] These PFGE profiles have not been described previously.

or USA100 (i.e., resistant to those antimicrobial agents) (34). Most of the *spa* t008-SCC*mec* IV strains (whether from blood or nasal cultures) were positive by PCR for the genes encoding PVL and ACME, consistent with USA300 strains (14, 34, 46). Only three non-USA300 isolates, including one *spa* t064-SCC*mec* IV-USA500 blood isolate and two nasal isolates with SCC*mec* IV but novel *spa* and PFGE types, were positive for both PVL and ACME. ACME (but not PVL) was also present in six *spa* t242-USA100 nasal isolates.

Index of diversity and minimum spanning tree. Simpson's index of diversity was 0.792 for *spa* typing and 0.637 for PFGE typing, confirming the greater diversity recognized by *spa* typing. A minimum spanning tree was constructed for all 493 isolates in order to visualize the relationships among the *spa* types (Fig. 2). Two major clusters were observed. The first is a cluster of CC5-related *spa* types corresponding primarily to PFTs USA100 and USA800. There are seven potential *spa* type founders listed in the two black circles on the left of the figure. The program could not identify a unique founder strain. This large cluster contains strains of SCC*mec* types II and IV. The CC8 cluster on the right contains multiple PFTs, including USA300, USA500, and CMRSA9, most of which contain SCC*mec* IV; however, the CMRSA9 strains (*spa* type t008) contain SCC*mec* VIII, as noted previously. Two isolates of *spa* types t6127 and t631 (indicated by arrows in the center of

the figure) demonstrated PFGE profiles similar to USA300 but did not cluster with the other USA300 isolates among the CC8 strains. Other *spa* types showed minimal clustering. The overall clustering of the *spa* types is consistent with previously published data (21).

Antimicrobial susceptibility testing. The results of antimicrobial susceptibility testing are shown in Table 2. Nasal MRSA isolates were more resistant to levofloxacin (81.3% versus 76.8%; $P < 0.01$) and tobramycin (55.9% versus 36.6%; $P < 0.001$) and showed more inducible clindamycin resistance (i.e., were D-zone test positive) than blood isolates (67.6% versus 48.5%; $P < 0.001$). Constitutive clindamycin resistance, although higher among nasal isolates, was of borderline significance ($P = 0.052$). These figures likely reflect the predominance of USA100 strains among the nasal isolates. However, 65.7% of t008-IV isolates (USA300-like) were ciprofloxacin resistant. High-level mupirocin resistance was low among MRSA isolates from both specimen types (3.3% for nasal isolates and 5.2% for blood isolates); all mupirocin-resistant isolates were positive for *mupA*. *spa* types associated with USA100 strains displayed antimicrobial resistance patterns typical of USA100, including resistance to erythromycin (98%), tobramycin (87%), clindamycin (both constitutive and inducible, 97%), and fluoroquinolones (both ciprofloxacin and levofloxacin resistance proportions were >98% resistant, whereas moxifloxacin resistance was 93%). USA300 strains, traditionally resistant only to
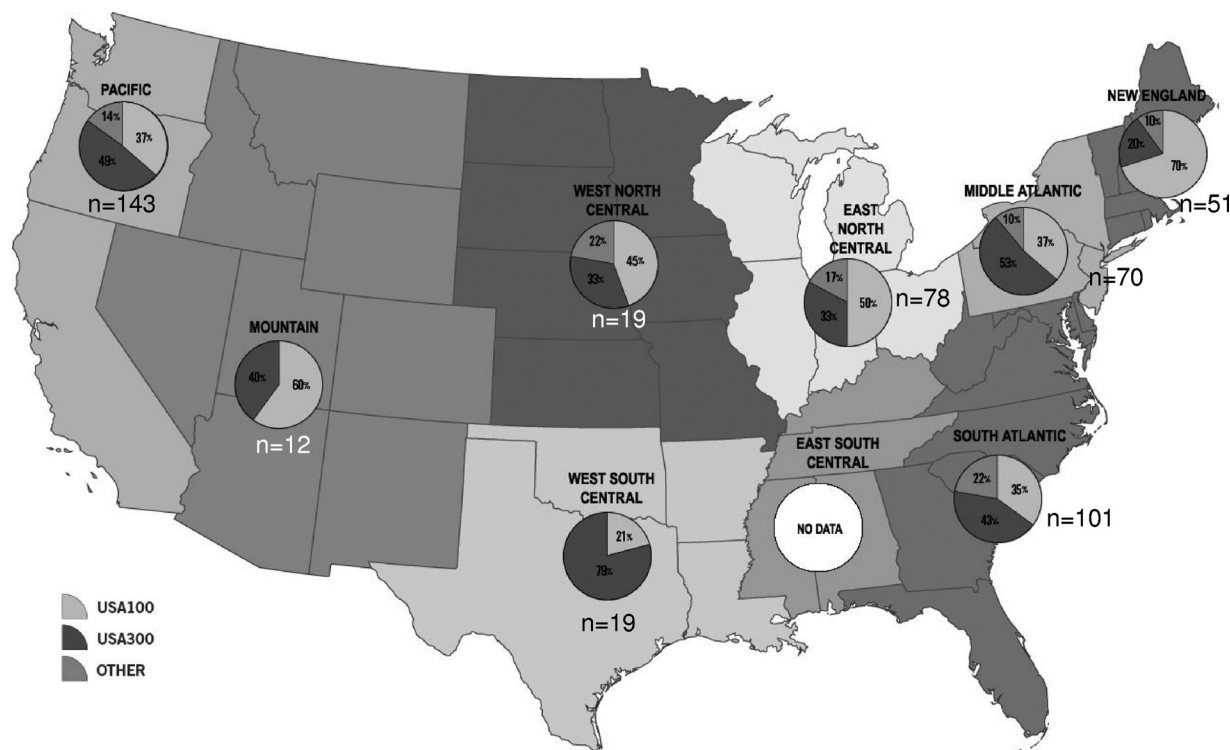
FIG 1 Proportions of USA100, USA300, and other pulsed-field types from blood culture isolates delineated by U.S. census region. The percentages of USA100 isolates are indicated in light gray, the percentages of USA300 isolates are indicated in dark gray, and other pulsed-field types are indicated in the intermediate gray color. The numbers of isolates obtained from each region are also shown.

β-lactam and macrolide agents (34), showed increased resistance to tobramycin (36.6%) and fluoroquinolones (64% resistant to ciprofloxacin and 58% resistant to levofloxacin, although only 21.5% were resistant to moxifloxacin). There were no significant differences between the antibiograms of the same *spa* types from nares and blood sources, with the exception of clindamycin resistance, which was significantly different for USA100 isolates from the nares (12%) versus those from blood cultures (8%, $P = 0.003$) (data not shown). No daptomycin resistance or linezolid nonsusceptible phenotypes were observed among the isolates.

DISCUSSION

In 2003, McDougal et al. described a system of nomenclature for PFGE typing of *S. aureus* strains (the USA types) to help clarify the epidemiologic spread of MRSA strains in the United States (34). Subsequently, most reports describing the MRSA strains that either colonized or caused invasive infections among individuals in the United States have used the USA nomenclature to report strain types (29, 30, 32). The MRSA strain type USA300, which initially was seen primarily as a cause of community-associated skin and soft tissue infections (18), has now been reported from invasive infections in the United States and in many countries around the world (2, 19, 23, 29, 31, 40, 43, 46, 50).

Although PFGE typing continues to be of value for epidemiologic studies of MRSA strains (32), *spa* typing data, often reported in conjunction with SCC*mec* typing data, are used with increasing frequency around the world for MRSA strain identification (20, 24). In this study, we used *spa* typing as our primary method of strain identification and then translated the *spa* types into PFGE types to allow comparisons with prior U.S. data sets.

Data from NHANES surveys of nasal colonization in 2001 through 2004 indicated that MRSA isolates of PFT USA100 were the most common colonizers of individuals in community settings (i.e., persons not in health care centers, prisons, or other institutions) (22), although the proportion of USA300 isolates increased in frequency during the 2003-2004 time period compared to 2001-2002 (22, 47). The *spa* typing data from our convenience sample when translated to PFGE types, suggest that USA100 is still the predominant strain type in the nares of U.S. patients. However, in our study, USA100 isolates, which represented 53.2% of the 1,984 isolates in a CDC ABCs study of invasive isolates from 2005-2006, (32), have been replaced by USA300 isolates as the predominant type among MRSA strains isolated from positive blood cultures. In contrast, USA300 isolates represented only 31.4% of the isolates in the ABCs study, which included isolates collected from 48 hospitals in eight metropolitan areas across the United States. The change in strain type from USA100 to USA300 among invasive isolates in the present study was predicted by the mathematical models developed by D'Agata et al. (11) but was not apparent in all census regions across the United States (although data from three regions were limited to a single laboratory). The shift was observed in the West South Central region, where USA300 has been recognized for many years, particularly in children (6, 28), and in the Middle Atlantic and South Atlantic regions, where increasing rates of USA300 colonization have been observed (Fig. 1) (17). A recent report on MRSA strain types from 43 U.S. medical centers by Richter et al. (38) shows a larger proportion of USA100 than USA300 isolates among blood isolates nationwide, even though, overall, there were over 3 times
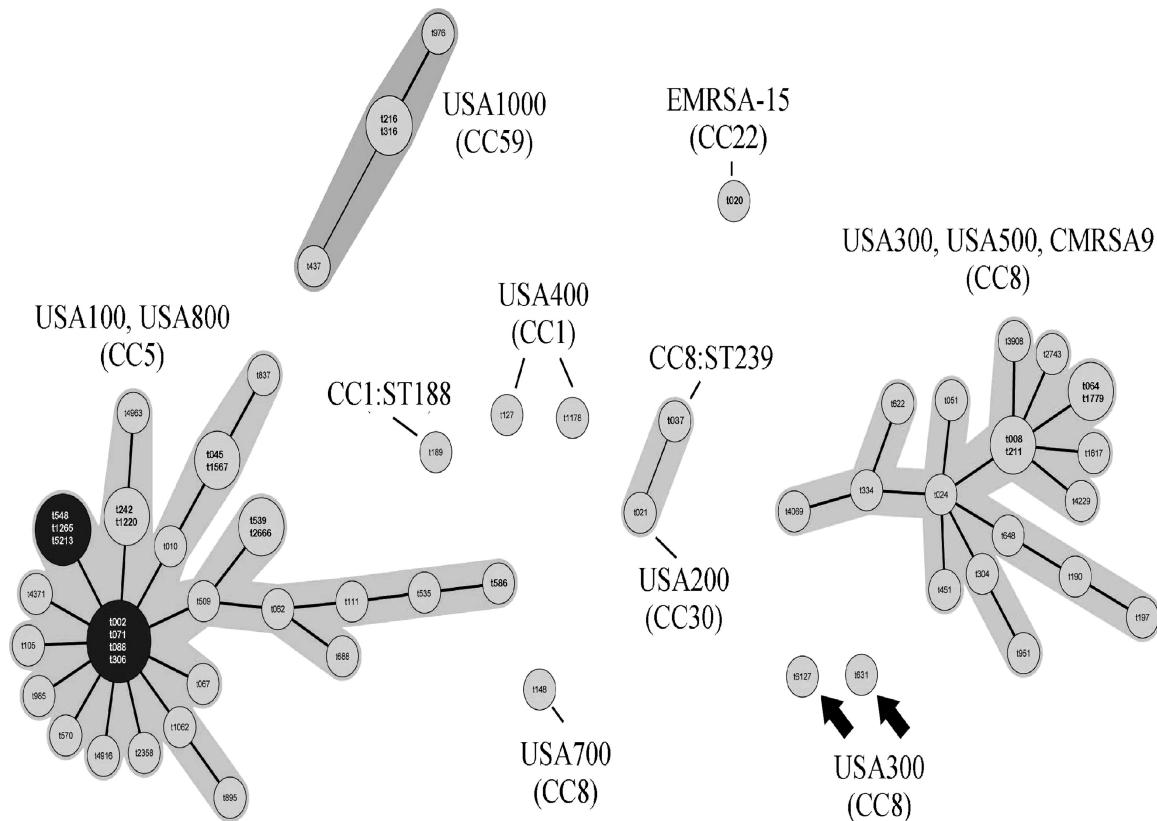
FIG 2 Minimum spanning tree of *spa* typing data. PFTs and MLST clonal complexes are listed based on the Ridom SpaServer website (http://spaserver2.ridom .de/spaserver/query, accessed 1 June 2011). There is no PFT defined for the ST188 strain. Founder *spa* types are indicated in black circles. No founder could be assigned for the CC8 cluster. Arrows indicate two unique USA300 isolates (*spa* types t6127 and t631) which fell outside the CC8 cluster.

as many USA300 isolates recovered across all specimen types compared to USA100 isolates (1,137 versus 377, respectively). Given that five of nine U.S. census regions showed similar data in our convenience sample (where USA100 predominates), we do not believe that our data are necessarily in conflict with those reported by Richter et al. (38). Unfortunately, the data in the latter study were not reported by geographic region.

Recent data from European surveillance studies indicate that five *spa* types accounted for 48.1% of the invasive MRSA isolates collected from 450 hospitals in 26 countries (24). Epidemiologic data suggest that local spread of MRSA strains is accompanied by local evolution. The most common *spa* type in Europe, t032, corresponds to PFT EMRSA15 (ST22) SCC*mec* IV; however, only two such isolates were observed in our study. The next most common *spa* type, t008, is a conglomeration of multiple STs, including ST8 (which includes the PFT USA300), ST247, ST250, and ST254. Although isolates of PFT USA300 remain uncommon in European countries, there are other *spa* types with PFGE profiles that correspond to USA300 that were recognized (see below). The third and fourth most common *spa* types, t041 and t003, were not observed in our convenience sample. The fifth type, t002 (6.4% of isolates), including ST5 and ST231, encompasses the USA100 PFT (which is typically ST5). Other *spa* types that were among the top 20 in Europe (although all had <3% prevalence) that were also recognized among our U.S. isolates (and their most common predicted PFTs) include t067 (USA100), t037 (ST239), t024 (USA300), t190 (USA300), t045 (USA100), and t127 (USA400). The fact that there

is considerable diversity among the major *spa* types and PFTs in Europe and the United States supports the concept of local spread and microevolution of strains (24, 37).

USA300 isolates, as originally described by McDougal et al., were typically susceptible to fluoroquinolones, clindamycin, and tobramycin (34). In our more recent survey, isolates with *spa* types corresponding to USA300 (supported by the fact that they were positive for the presence of PVL and ACME genes) are now largely resistant to fluoroquinolones and showed emerging resistance to clindamycin and tobramycin. Resistance to fluoroquinolones, clindamycin, and tetracycline among USA300 isolates was reported both by Han et al. (25) and Diep et al. (13), while in a follow-up study, McDougal et al. reported resistance to fluoroquinolones, clindamycin, and gentamicin (33). The strains in the McDougal study reflected both the accumulation of chromosomal mutations (for fluoroquinolones) and plasmid-mediated resistance genes [including *ermA* and *aph(2″)-Ia/aac(6′)-Ie*]. The rise in tobramycin resistance observed among isolates from this study has been attributed to the widespread dissemination of the *ant(4′)-Ia* determinant in the United States (48). Taken together, these changes in susceptibility may have implications for the management of MRSA cases, especially in areas where USA300 isolates are common. Fortunately, high-level mupirocin resistance among all isolates has remained low among strains from U.S. hospitals despite greater emphasis on decolonization of MRSA-positive patients (5).

An interesting aspect of this study is the detection of several

TABLE 2 Activity of selected antimicrobial agents against recent isolates of MRSA from the U.S. hospitals

Drug	Nasal isolates				Blood isolates				
	MIC			% resistant	MIC			% resistant	P value[a]
	50%	90%	Range		50%	90%	Range		
Amikacin	8	32	≤1–>64	5.4	8	32	≤1–>64	2.1	>0.05
Ciprofloxacin	>8	>8	≤0.12–>8	83.6	>8	>8	≤0.12–>8	81.4	>0.05
Clindamycin (not induced)	0.25	>8	≤0.06–>8	48.8	0.125	>8	≤0.06–>8	39.7	0.052
Clindamycin (after induction)				67.6				48.5	<0.001
Daptomycin	1	1	0.25–1	0.0	1	1	0.5–2	1.5	>0.05
Erythromycin	>16	>16	0.25–>16	89.3	>16	>16	0.25–>16	88.1	>0.05
Gentamicin	0.5	1	≤0.12–>16	3.0	0.5	1	≤0.12–>16	4.1	>0.05
Levofloxacin	>8	>8	≤0.06–>8	81.3	4	>8	≤0.06–>8	76.8	<0.01
Linezolid	2	4	1–4	0.0	2	4	1–4	0.0	>0.05
Moxifloxacin	4	>4	≤0.03–>4	69.9	2	>4	≤0.03–>4	56.2	>0.05
Mupirocin	≤4	≤4	≤4–>512	3.3	≤4	8	≤4–>512	5.2	>0.05
Nitrofurantoin	16	16	4–>128	0.3	16	16	8–64	0.0	>0.05
Oxacillin	>32	>32	4–>32	100	16	>32	4–>32	100	>0.05
Tetracycline	≤0.25	0.5	≤0.25–>32	4.3	≤0.25	0.5	≤0.25–>32	4.6	>0.05
Tigecycline	0.125	0.25	0.016–0.5	0.0	0.125	0.25	0.06–0.5	0.0	>0.05
Tobramycin	>16	>16	0.25–≥16	55.9	1	>16	≤0.12–>16	36.6	<0.001
Trimethoprim-sulfamethoxazole	≤0.125/2.375	0.25/4.75	≤0.125/2.375–>16/304	5.4	<0.125/2.375	0.25/4.75	≤0.125/2.375–>16/304	6.2	>0.05
Vancomycin	0.5	1	0.25–1	0.0	0.5	1	0.5–2	0.0	>0.05

[a] P values determined using Fisher's exact test.

SCC*mec* types and PFTs which have been infrequently reported in the United States, including SCC*mec* type III and SCC*mec* type VIII and PFTs CMRSA9, EMRSA15, and the pattern associated with ST239. SCC*mec* III (in ST239 isolates of *spa* type t037) has been common in Europe for over a decade, but SCC*mec* type VIII is a more recent SCC*mec* type, which has emerged primarily in Canada in CMRSA9 isolates (27, 51). It is particularly interesting that one SCC*mec* VIII isolate was from California while the other was from Florida, suggesting that these are randomly imported cases that have not yet spread geographically. ST239 strains, although rare, have been reported previously from Florida (8).

In summary, the diversity of MRSA strain types in the United States continues to expand but varies by geographic region. The notable increase in the proportion of USA300 isolates causing invasive infections is of concern, since such strains have been predicted to be more virulent (11). *spa* types associated with USA300 strains have also become much more resistant to antimicrobial agents, particularly fluoroquinolones, although the reasons for this are unknown. In this study, *spa* typing demonstrated greater strain diversity than did PFGE typing (as reflected in the higher index of diversity for *spa* typing) and especially when used in conjunction with SCC*mec* data, facilitated the comparison of U.S. data to data sets from other countries. Knowledge of the *spa* types for USA100 and USA300 strains should facilitate the tracking of their spread internationally.

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