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Dissemination of Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Clones in Northern Norway: Sequence Types 8 and 80 Predominate

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Increasing frequencies of community-acquired methicillin-resistant *Staphylcoccus aureus* (MRSA) strain isolation have been reported from many countries. The overall prevalence of MRSA in Norway is still very low. MRSA isolates ($n = 67$) detected between 1995 and 2003 in northern Norway were analyzed by pulsed-field gel electrophoresis, multilocus sequence typing, and staphylococcal cassette chromosome *mec* (SCC*mec*) typing. Sixty-seven isolates were associated with 13 different sequence types. Two successful MRSA clones predominated. Sequence type 8 (ST8) (40%) and ST80 (19%) containing SCC*mec* type IV were detected in hospitals and communities in different geographic regions during a 7-year period. In general, there was a low level of antimicrobial resistance. Only 26% of the isolates were multiresistant. International epidemic clones were detected. The frequent findings of SCC*mec* type IV (91%) along with heterogeneous genetic backgrounds suggest a horizontal spread of SCC*mec* type IV among staphylococcal strains in parallel with the clonal spread of successful MRSA strains.

Methicillin resistance in staphylococci is mediated by acquisition of staphylococcal cassette chromosome *mec* (SCC*mec*), which integrates in a site-specific manner into the chromosome (23). Methicillin-resistant *Staphylococcus aureus* (MRSA) has become a worldwide problem. The prevalence of MRSA varies widely between countries. Its prevalence is consistently higher in the United States, Japan, and Southern Europe than in other countries; more than 30% of individuals in these countries are infected, compared with less than 2% in Scandinavia, The Netherlands, and Switzerland (10, 34). Recent reports suggest that community-acquired MRSA (CA-MRSA) infections in healthy persons without the known risk factors for MRSA infection are increasing in frequency (7, 20, 33). In Europe, the extracellular product Panton-Valentine leukocidin (PVL) has been associated with severe necrotizing pneumonia and community-associated staphylococcal skin infections, such as furunculosis (11, 16).

Infections with MRSA have been notifiable in Norway since 1995, but colonization without infection is not notifiable. The overall prevalence of MRSA is still very low in Norway. In 2003 there was an increase in the number of reported cases: 216 cases compared to 142, 122, and 67 in the three previous years. Only 0.3% of *S. aureus* isolates in blood cultures were identified as MRSA in 2002 according to the Norwegian surveillance system NORM (28). In Norway, about 50% of the MRSA isolates are imported from various countries. The remainders are termed "Norwegian" strains and are presumed to be of domestic origin, with no apparent connection with recent travel abroad (4, 28, 38). Reports from Norway documenting the clonality of MRSA isolates are scarce, and we do not know much about the distribution of CA-MRSA and hospital-acquired MRSA.

The aim of this study was to define the MRSA clonal types and their molecular epidemiology over time in northern Norway by different molecular typing techniques, including SCC*mec* typing, pulsed-field gel electrophoresis (PFGE), and multilocus sequence typing (MLST).

MATERIALS AND METHODS

Setting and bacterial strains. Northern Norway consists of three counties (Nordland, Troms, and Finnmark), with 11 hospitals and a total population of 460,000 inhabitants. From these counties, a total of 143 MRSA isolates were reported to and identified at the University Hospital of North Norway, Tromsø, Norway, in the period from 1995 to 2003. Sixty-seven out of the 143 MRSA strains were selected for this study based on the following criteria: only one MRSA isolate from each patient was included, and only one isolate from each verified and known outbreak was included; i.e., strains from the same outbreak, but with one band difference in PFGE banding pattern, were included. Samples from nonresidents of the region and patients with a recent history of hospitalization abroad (i.e., within 1 year, based on clinical information given by the physician in charge) were excluded from the study.

Fifty out of 67 strains were from outpatients without any known link to health care facilities, and 17 strains were from hospitalized patients at five different hospitals. Seven out of 67 isolates were from nursing home residents, and they were grouped as nonhospital/outpatient samples. Both clinical and screening samples were included. The study included only two invasive isolates, while the remaining 65 isolates were recovered from wound secretions ($n = 31$), abscesses ($n = 8$), nasal swab screenings ($n = 14$), and other sites ($n = 12$). The 14 nasal swab samples were taken in association with the screening of hospital patients ($n = 4$), nursing home residents ($n = 5$), and hospital and nursing home staff ($n =$

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5). Seven of the 14 nasal swab samples were from nonhospital individuals/outpatients (staff, $n = 2$; patients, $n = 5$), and seven of the 14 nasal swab samples were from the hospital (hospital staff, $n = 3$; hospital patients, $n = 4$).

For reference, the *mecA*-negative strain *S. aureus* NCTC 8325 and the SCC*mec*-positive strains *S. aureus* NCTC 10442, *S. aureus* N315, and *S. aureus* 85/2082 (21) were included in all analyzes. Five international MRSA clones (Iberian clone, Brazilian clone, pediatric clone, New York/Japan clone, and Hungarian clone) were included in the PFGE analyzes. The collection and analyzes of data were approved by the regional committee for medical research ethics and by the Norwegian social science data services.

Bacterial identification. All isolates were identified by positive Gram stain, the presence of catalase, and the presence of clumping factor (bound coagulase) by Staphaurex Plus* (Murex Biotech, Dartford, England). All strains were tested for the presence of the *mecA* gene and nuclease (*nuc*) gene by a multiplex *mec*/*nuc* PCR (6, 31).

Susceptibility testing. Antimicrobial susceptibility testing was performed using disk diffusion and breakpoints according to the Norwegian Working Group on Antibiotics (5) for ciprofloxacin (10 μg), doxycycline (30 μg), gentamicin (30 μg), trimethoprim-sulfamethoxazole (8 μg), fusidic acid (50 μg), rifampin (5 μg), streptomycin (30 μg), chloramphenicol (30 μg), and kanamycin (30 μg). The medium used for disk diffusion was the paper disk methods medium (PDM; AB Biodisk, Stockholm, Sweden). The NCCLS uses wider ranges when defining their breakpoint values, resulting in fewer isolates being classified as resistant. The Norwegian Working Group on Antibiotics set its breakpoints close to that of the native (often susceptible) bacterial population (24). Susceptibility to arbekacin (30 μg; Eiken Chemical Ltd., Japan) was determined by disk diffusion on Mueller-Hinton agar with an inoculum at a McFarland standard of 0.5. No NCCLS breakpoint for arbekacin exists, but the same zone diameters as for gentamicin were used for interpretation: for resistance, ≤ 13 mm; for intermediate susceptibility, 14 to 17 mm; and for susceptibility, ≥ 18 mm. MICs of oxacillin, linezolid, and mupirocin were determined by Etest (AB Biodisk, Solna, Sweden) according to NCCLS interpretive standards (27). Susceptibility to vancomycin was tested by a vancomycin agar screen (36). Detection of inducible clindamycin resistance was performed according to the standard NCCLS disk diffusion test using unsupplemented Mueller-Hinton agar and 15-μg erythromycin disks and 2-μg clindamycin disks as described by Fiebelkorn et al. (15).

Beta-lactamase. Production of beta-lactamase was tested with nitrocefin disks (Oxoid, Basingstoke, United Kingdom) according to the instructions of the manufacturer.

PFGE. Chromosomal DNA was prepared and SmaI digestion and PFGE were performed as described previously (19). The PFGE gels were analyzed both visually according to the method of Tenover et al. (35) and by GelCompar II software version 2.5 (Applied Maths, Kortrijk, Belgium). The PFGE types were defined on the basis of the DNA banding patterns in accordance with the criteria of Tenover et al. (35) for bacterial strain typing.

SCC*mec* complex. The SCC*mec* types were determined by PCR typing of the *mec* and *ccr* gene complexes as described previously (19, 21). All strains were tested for the presence of IS*1272* and type IV SCC*mec* with the primers and PCR described in the work of Okuma et al. (29).

Southern blot hybridization. Southern blot transfer of PFGE SmaI-digested genomic DNA to a positively charged nitrocellulose membrane (Roche, Mannheim Germany), *ccrAB* probe labeling, and Southern blot hybridization were carried out as described previously (19).

DNA sequencing. PCR products were purified with the EXO/SAP (shrimp alkaline phosphatase and exonuclease I) PCR product presequencing kit (USB Corporation, Ohio). Heterogeneity in the *ccrA* and *-B* genes was identified by bidirectional DNA sequencing as described by Hanssen et al. (19).

Computer analyses and sequence accession numbers. The *ccrAB* nucleotide sequences and deduced amino acid sequences were edited by using the Chromas software (version 2.21) and aligned using the BioEdit sequence alignment editor (v5.0.9) (18). Nucleotide sequences were compared to sequences in GenBank, and protein sequences were compared to nonredundant GenBank coding sequence translations, by using the BLASTN, BLASTP, and BLASTX local alignment search tools (3).

MLST. Chromosomal DNA was extracted using the GenoM-48 robotic workstation (GenoVision, Oslo, Norway) and the protocol MagAttract DNA tissue. MLST was performed according to the protocol of Enright et al. (12) with a few modifications of the PCR master mix. The PCRs were carried out in a final volume of 25 μl containing 25 ng of chromosomal DNA, 0.025 μg of each primer (except for tpi_up and tpi_dn, of which 0.25 μg was added), 0.2 mM deoxynucleoside triphosphate (Invitrogen, Carlsbad, CA), 0.5 U Platinum *Taq* DNA polymerase (Invitrogen), 2.5 μl 10× buffer, and 1.5 mM $MgCl_2$ (both supplied with Platinum *Taq* polymerase). The amplified products were purified using the GFX96 PCR purification kit (Amersham Biosciences, Buckinghamshire, United Kingdom), followed by sequencing reactions performed using the Big Dye Terminator v3.1 cycle sequencing kit (Applied Biosystems). Unincorporated dye terminators were removed from the extension products by isopropanol precipitation as described in the ABI Prism BigDye Terminator cycle sequencing ready reaction kit protocol (Applied Biosystems). Sequences of both strands were analyzed using an ABI Prism 3100 DNA genetic analyzer (Applied Biosystems). The sequencing primers were the same as in the initial PCR amplification.

Nucleotide sequence accession numbers. *ccr* sequences were submitted to the EMBL/GenBank database and assigned accession numbers AY669512, AY254749, AY254756, and AY254758.

TABLE 1. Antibiograms for the 67 MRSA strains used in this study by disk diffusion, Etest, and vancomycin screen

Test	Antimicrobial agent	No. of strains (%)		
		Susceptible	Intermediate	Resistant
Disk diffusion	Ciprofloxacin	13 (19.4)	45 (67.2)	9 (13.4)
	Clindamycin	59 (88.1)	1 (1.5)	7 (10.4)
	Doxycycline	49 (73.1)	5 (7.5)	13 (19.4)
	Erythromycin	45 (67.2)		22 (32.8)
	Fusidic acid	35 (52.2)		32 (47.8)
	Gentamicin	64 (95.5)		3 (4.5)
	Kanamycin	42 (62.7)		25 (37.3)
	Streptomycin	51 (76.1)		16 (23.9)
	Arbekacin	67 (100)		
	Chloramphenicol	62 (92.5)		5 (7.5)
	Rifampin	65 (97.0)		2 (3.0)
	Trimetoprim-sulfamethoxazole	65 (97.0)	2 (3.0)	
Etest	Oxacillin	1[a] (1.5)		66 (98.5)
	Linezolid	66 (98.5)	1 (1.5)	
	Mupirocin	67 (100)		
Vancomycin screen	Vancomycin	67 (100)		

[a] This strain tested positive for *mecA* by PCR and was therefore considered MRSA.

RESULTS

Methicillin resistance and *mecA*. Sixty-six strains were resistant to oxacillin, while one strain had an oxacillin MIC of 1 μg/ml. All 67 strains tested positive for the presence of the *mecA* gene by PCR and were therefore considered MRSA isolates (Table 1). There was a 98.5% correlation between phenotypical expression of oxacillin resistance (oxacillin MIC) and the presence of the *mecA* gene. Forty-four isolates had oxacillin MICs of <96 μg/ml, while 23 isolates had an oxacillin MIC of ≥96 μg/ml.

Genetic relationship. Among 66 *S. aureus* strains, 15 PFGE profiles were obtained (Fig. 1; Table 2). One strain was not PFGE typeable, and it was not included in the PFGE analysis. A major PFGE type, F, was detected among 26 isolates with 19 different subtypes. Isolates with PFGE type F were characterized by sequence type 8 (ST8) and SCC*mec* type IV (ST8-IV) (Fig. 1, left), whereas isolates of PFGE types M and N were characterized by ST80 and SCC*mec* type IV (Fig. 1, right). The strains N315 and 85/2082 and the Brazilian clone, Hungarian clone, and Iberian clone did not show any relationship to any of the clinical isolates in this study. NCTC 8325 showed a two-band difference from isolates with PFGE patterns F1 and ST8-IV. They were considered closely related (Fig. 1, left). MRSA strain NCTC 10442 (ST250-I) showed a four-band dif-

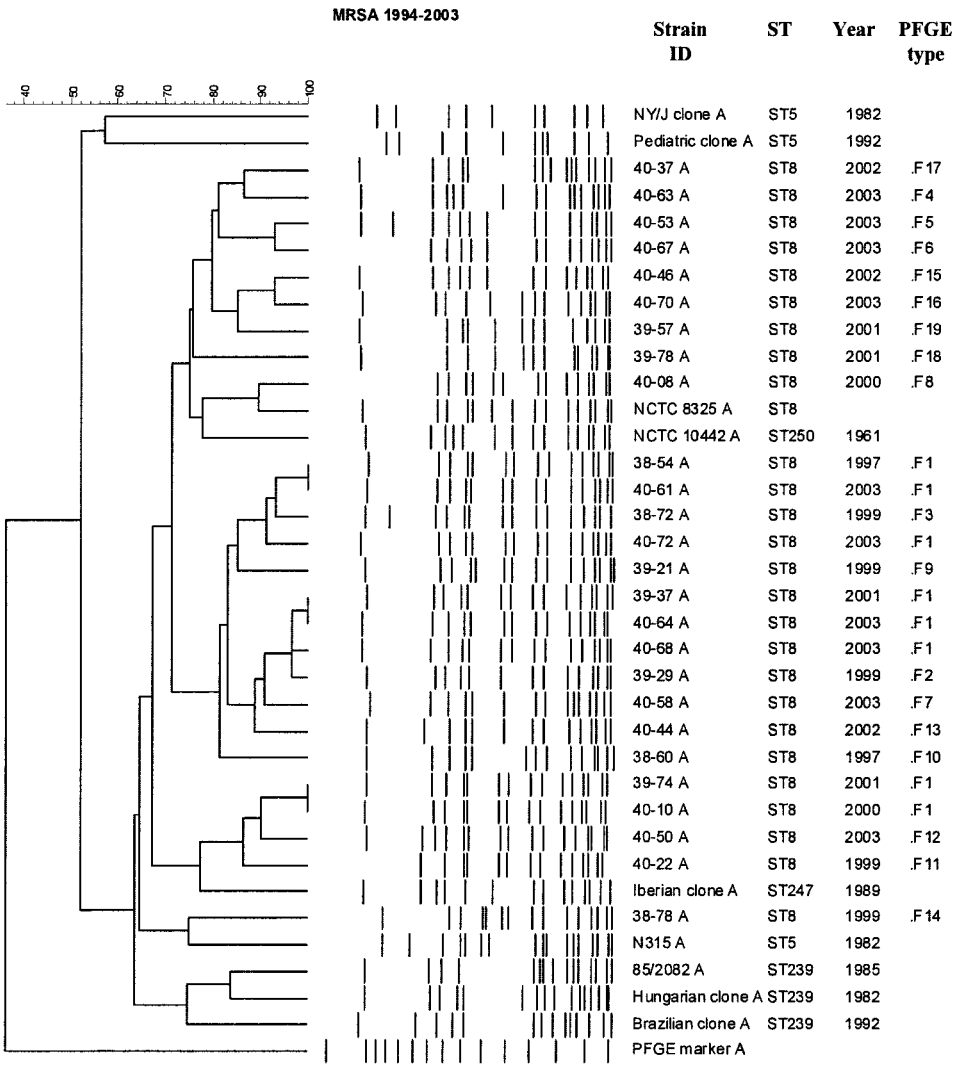

FIG. 1. PFGE dendrograms representing the genetic relatedness of 26 ST8-MRSA isolates (left) and 13 ST80-MRSA isolates (right). Included are also the five international MRSA clones (Brazilian, Hungarian, pediatric, Iberian, and New York/Japan clones) and the reference strains N315, NCTC 10442, 85/2082, and NCTC 8325. PFGE patterns were analyzed both visually and using GelCompar II version 2.5 (Applied Maths, Belgium). The Dice coefficient was calculated using a position tolerance of 1.5%, and the PFGE dendrograms were constructed using the unweighted pair group method with arithmetic means. Isolates that shared 95% similarity on the arithmetic mean dendrogram were considered to have the same PFGE type. The PFGE types were also defined on the basis of the DNA banding patterns by following the criteria of Tenover et al. (35) for bacterial strain typing. Strains differing by four to six fragments were considered to be subtypes of a given clonal type. The strain identifier, ST, year of isolation, and PFGE types are shown to the right. A low-range PFGE ladder (New England Biolabs, Beverly, MA) was used as the molecular size marker. The scale bar at the top of the dendrogram represents similarity.

ference from strains harboring PFGE patterns F1 and F4. The pediatric clone (ST5-IV) clustered with the strains containing ST5-IV and showed a three-band difference from strains with PFGE pattern G4. They were considered possibly related (data not shown). The New York/Japan clone (ST5-II) was considered possibly related to strains with PFGE pattern G4, showing a six-band difference (data not shown).

SCC*mec*. Sixty-one (91%) out of 67 isolates was of SCC*mec* type IV (Table 2). Two isolates were of SCC*mec* type I, two were of SCC*mec* type II, one isolate was of SCC*mec* type III, and one isolate was of SCC*mec* type IIIA. Three out of 67 strains were *ccrAB* PCR untypeable. Positive Southern blot hybridization with *ccrAB* probes, the *mec* complex PCR, and the IS*1272-mecA* PCR indicated that they were of SCC*mec* type III, IIIA, or IV. The *ccrA2* gene was sequenced in three ST8-IV isolates, three ST80-IV isolates, two ST5-IV isolates, and one ST12-IV isolate. The *ccrA2* gene in strains with ST80 (GenBank accession no. AY669512), ST5, and ST12 showed 100% identity to *ccrA2* in strain MR108 containing SCC*mec* type IVc (GenBank accession no. AB096217). *ccrA2* in ST8-IV MRSA strains (GenBank accession no. AY254749, AY254756, and AY254758) (19) showed 96% and 99% identity to *ccrA2* in strains N315 (SCC*mec* type II) (GenBank accession no. D86934) and MR108 (SCC*mec* type IVc) (GenBank accession no. AB096217), respectively. ST8-IV strains contained a local variant of the *ccrA2* gene.

MLST. MLST identified 13 STs among the 67 isolates (Table 2). No new STs were detected. Six STs were each repre-

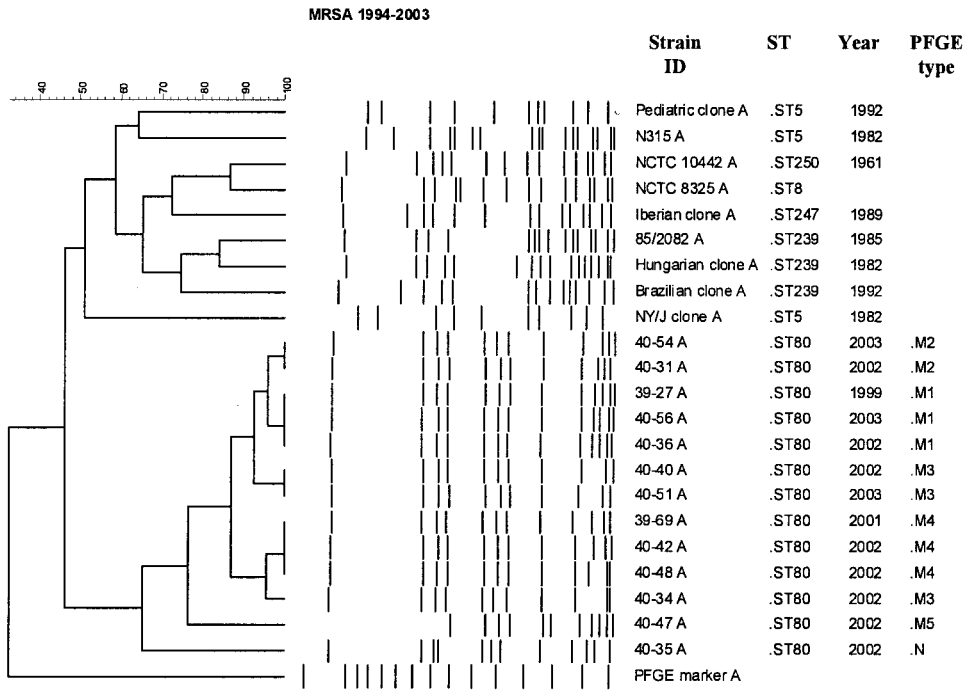

FIG. 1—*Continued*.

sented by a single MRSA isolate only. ST8 and ST80 were the most frequent, and they were identified in 40% (27/67) and 19% (13/67) of the isolates, respectively. All MRSA isolates with ST80 were of SCC*mec* type IV. Two different SCC*mec* types were identified among ST8 isolates: ST8-I (one isolate) and ST8-IV (26 isolates). One ST5 isolate was associated with SCC*mec* type I, and four isolates of ST5 were associated with SCC*mec* type IV. They showed close relationship to four isolates containing ST125-IV on PFGE. The 67 strains were classified into seven clonal complexes (Table 2). Combining the ST and SCC*mec* type, we identified 15 clonal types, out of which clones ST8-IV, ST80-IV, ST45-IV, ST125-IV, and ST5-IV were each represented by four or more isolates. Of the 15 clonal types, only 1 was identical to one of the five pandemic MRSA clones. ST5-IV (pediatric clone) was represented by four isolates. Other international clones observed were ST45-IV (Western Europe, Scandinavia) (http://www.mlst.net) (n = 4) and ST8-IV (EMRSA-2, -6, and NY/V) (13) (n = 26); ST30-

TABLE 2. Molecular types and antibiotypes of 67 MRSA isolates recovered in northern Norway from 1995 to 2003

ST	MLST	CC[a]	SCC*mec* type	No. of isolates	Yr(s) of isolation	Antibiogram[b]	*ccr*[c] type	PFGE type[d]
5	1-4-1-4-12-1-10	5	I	1	2002	EDO	1	G4
5	1-4-1-4-12-1-10	5	IV	4	2001–2003	O, EO	2	G1-G3
8	3-3-1-1-4-4-3	8	IV	26[e]	1997–2003	FO	2	F1-F19
8	3-3-1-1-4-4-3	8	I	1	2003	FO	1	NT
12	1-3-1-8-11-5-11	12	IV	2	1995, 2002	CFO, O	2	H1-H2
22	7-6-1-5-8-8-6	22	IV	2	2002–2003	O	2	O
25	4-1-4-1-5-5-4	25	III	1	1998	O	3	K
30	2-2-2-2-6-3-2	30	IV	3	2001–2003	O	2	I1-I3
36	2-2-2-2-3-3-2	30	II	1	1996	CLEKO	2	J
39	2-2-2-2-2-2-2	30	IV	3	2003	KO, O	2	L1-L3
45	10-14-8-6-10-3-2	45	IV	4	1997–2003	FO, O	2	B1-B2, C, D
80	1-3-1-14-11-51-10	S	IV	13[f]	1999–2003	KSO	2	M1-M5, N
125	1-4-1-4-12-1-54	5	IV	4	2001–2002	CLEKSO, CLEKO, CKO	2	G1, G5-G7
225	1-4-1-4-12-25-10	5	II	1	2003	CLEKO	2	A1
254	3-32-1-1-4-4-3	8	IIIA	1	1997	EDKRSHOG	3	E

[a] CC, clonal complex; S, singleton not assigned to any clonal complex.
[b] C, ciprofloxacin; L, clindamycin; E, erythromycin; D, doxycycline; F, fusidic acid; K, kanamycin; S, streptomycin; H, chloramphenicol; O, oxacillin; G, gentamicin; R, rifampicin.
[c] *ccr*, cassette chromosome recombinase.
[d] NT, not typeable.
[e] Among the 26 ST8-MRSA-IV isolates, four of the isolates were from nasal swab samples, i.e., the nursing home staff (n = 2), the hospital staff (n = 1), and from a nursing home patient (n = 1).
[f] Among the ST80-MRSA-IV isolates, two isolates were from nasal swab samples. They were from a hospital patient and an outpatient.

IV and ST36-II (EMRSA-16) (13, 30), represented by three isolates and one isolate, respectively; and ST22-IV (EMRSA-15) (1, 12) and ST5-I (EMRSA-3), represented by two isolates and one isolate, respectively. ST225 and ST125 are both single-locus variants of ST5, and ST39-IV is a double-locus variant of ST239 (14) (Table 2).

Antimicrobial susceptibility. Resistance to fusidic acid, erythromycin, and kanamycin was detected in 48%, 33%, and 37% of the isolates, respectively. Only a few of the isolates showed resistance to ciprofloxacin (13%), doxycycline (19%), streptomycin (24%), rifampin (3%), gentamicin (5%), clindamycin (10%), and chloramphenicol (8%) (Table 1). All isolates were susceptible to trimethoprim-sulfamethoxazole, mupirocin, arbekacin, and vancomycin (Table 1). Constitutive production of beta-lactamase was found in 84% of the isolates. Inducible clindamycin resistance was detected in 18% of the isolates. Of the 67 strains, 18 (26%) were multiresistant (i.e., resistant to three or more antibiotic groups in addition to beta-lactams). The strains were resistant to an average of 2.7 antibiotics.

All ST80-IV strains were resistant to aminoglycosides (kanamycin, streptomycin) and oxacillin. In most cases, erythromycin, clindamycin, fusidic acid, ciprofloxacin, and chloramphenicol resistance were linked to ST80-IV strains (Table 2). The resistance profile typical for ST8-IV was fusidic acid and oxacillin, which was observed in 17 (65%) out of 26 strains (Table 2).

DISCUSSION

In an attempt to determine the molecular epidemiology of MRSA strains in northern Norway from 1995 to 2003, 67 isolates were characterized by different molecular typing methods. The majority of isolates belonged to two predominant clones, i.e., ST8-IV and ST80-IV, whereas the remaining isolates showed great genetic diversity.

The most frequent MRSA clone in northern Norway was ST8-IV. This clone is represented by EMRSA-2 and -6 and has been identified in several European countries and the United States (2, 13). Chung et al. (8) reported ST8-IV as the second most frequent MRSA clone in Miami, FL. They called this clone the New York clone V, and the ST8 genetic background was proposed to represent the predicted ancestor of the very first European MRSA strain. This clone was multiresistant. This is in contrast to the results of our study, where only fusidic acid and oxacillin resistance was observed in 17 out of 26 ST8-IV isolates. ST8-MRSA clones are proposed to have emerged by multiple independent introductions of SCC*mec* into a successful ST8-methicillin-susceptible *S. aureus* (MSSA) clone (13). In our study, strains with ST8-IV were highly related, suggesting clonal expansion in northern Norway. However, variation in the resistance pattern and local variants of *ccrAB* sequences found in northern Norwegian ST8-IV strains suggest that they have evolved for some time separated from their origins and possibly acquired SCC*mec* from local staphylococcal strains (19).

The second most frequent MRSA clone was ST80, accounting for 19% of all MRSA isolates, indicating that strains with ST80-IV have established themselves outside hospitals in northern Norway between 1999 and 2003 and are probably emerging. Two of the ST80 strains were recovered from the same hospital, while the remaining 11 isolates were from outpatients. ST80 has been associated with the central European CA-MRSA isolates reported from France and Switzerland (39). Aires de Sousa et al. (2) described MRSA strains with ST80 in Greece. They all contained a distinct *spaA* type, SCC*mec* IV, and were resistant to oxacillin, erythromycin, and fusidic acid. Erythromycin and fusidic acid resistance was associated with ST80 in 9 out of 13 strains in our study, while kanamycin, streptomycin, and oxacillin resistance was observed in all 13 strains. Interestingly, the ST80 strains were resistant to an average of 4.1 antibiotics, in contrast to, e.g., ST8 strains, which were resistant to 1.6 antibiotics. PVL and SCC*mec* type IV are common among CA-MRSA isolates of ST80 (11, 16). In our study, the ST80-MRSA strains were not tested for the presence of PVL. It remains to be elucidated if PVL has contributed to the success of the ST80 MRSA strains. At present the origin of clone ST80-IV is not clear. It remains to be elucidated what has facilitated the spread of ST8 and ST80, if these STs are representative of the whole country, and if the numbers are increasing in the region. Today, it is unknown which clone(s) is responsible for the increase in the number of reported MRSA cases in 2003 in Norway. This is a subject for further studies.

In contrast to the MRSA isolates represented by the two dominant clones, the rest of the isolates were more genetically diverse. Twenty-eight out of 67 isolates (41.8%) represented STs with less than five isolates, and we considered them sporadic cases. Andersen et al. (4) reported that most cases of MRSA infection in Norway occur unexpectedly or sporadically and that the epidemic ends shortly afterward, e.g., within 1 month. Most sporadic cases of MRSA strains in northern Norway appear to be due to the continuous introduction of new international clones into the country or the establishment of new MRSA clones.

It is noteworthy that strains with ST80-IV, ST5-IV, and ST12-IV in this study contained *ccrA2* genes with 100% identity to *ccrA2* in SCC*mec* type IVc. According to Ito et al. (22), this is the first report of CA-MRSA associated with SCC*mec* type IVc.

The isolates in this study were generally susceptible to most of the antibiotics tested, apart from fusidic acid. Fusidic acid resistance was observed in 47.8% of the isolates. This has also been reported by Tveten et al. (37), who describe a specific clone of *S. aureus* with resistance to fusidic acid that causes impetigo bullosa in outpatients in Norway. Other studies indicate that the Norwegian MRSA types are similar to the old classical, sensitive MRSA types, often with a relatively low level of methicillin resistance (4). There was no correlation between antibiogram and SCC*mec* type in our study; i.e., multiresistance was observed both in strains containing SCC*mec* type IV and in strains harboring the other SCC*mec* types. We observed 24 isolates with SCC*mec* type IV that were resistant to three or more classes of antimicrobial agents. This is in accordance with other studies suggesting that some strains with SCC*mec* type IV and a high level of resistance have acquired resistance to non-beta-lactam antibiotics in order to be able to survive in the hospital environment (1) or through exposure to the antibiotics (29).

There was a high correlation between ST and PFGE type in

this study. Strain types that were grouped by MLST had similar PFGE profiles, whereas distinct MLST strain types had very different PFGE profiles. This has also been reported by others (13, 17).

In the present study, 61 out of 67 isolates (91%) containing SCC*mec* type IV were associated with nine different STs. All isolates containing SCC*mec* type IV belonged to 12 different PFGE types. It has been suggested that the relatively small SCC*mec* type IV strains may have an increased mobility compared with their larger SCC*mec* counterparts and therefore greater propensity for transfer to diverse *S. aureus* genetic backgrounds (1, 9, 11). There is a less intensive selective pressure outside hospitals, advantageous for SCC*mec* type IV, as SCC*mec* type IV gives a smaller fitness cost for the bacteria than SCC*mec* types I, II, and III (1). The presence of SCC*mec* type IV in distinct genetic backgrounds could represent either an independent acquisition event or horizontal gene transfer of the SCC*mec* element from one *S. aureus* strain to another (25, 30).

Seventy-four percent of the MRSA strains were isolated from persons in the community. According to our epidemiological information, they did not have any known link to health care facilities or known risk factors for the acquisition of MRSA. Most of the strains were associated with type IV SCC*mec* (91%), nonmultiresistance (74%), low levels of oxacillin resistance (oxacillin MIC, <96 μg/ml) (73%), and genetic diversity. These are all characteristic traits associated with CA-MRSA (29). However, the same clonal types (e.g., ST8-MRSA-IV and ST80-MRSA-IV) were observed in both hospitals and communities, and therefore it is impossible to decide where they originated. It is likely that some health care-associated MRSA cases were misclassified as community-associated MRSA cases and vice versa. The true site of acquisition of MRSA is rarely known with certainty (33). Our findings are consistent with community-acquired, rather than nosocomial, MRSA infection. Further studies among randomly selected healthy members of the community will probably give the answer if we have "true CA-MRSA" strains in northern Norway.

It is assumed that SCC*mec* type IV has repeatedly integrated into MSSA backgrounds (32) and that this element may be acquired from coagulase-negative staphylococci (26). The molecular typing performed in this study has shown that the ST8 isolates are closely related, so they could recently have diverged from a common ancestor, for example, by horizontal gene transfer of the SCC*mec* type IV to a local MSSA strain. MSSA NCTC 8325 showed a close relationship to the north Norwegian MRSA isolates. This illustrates the need for MLST analyzes of MSSA strains in Norway in order to say something about the origin of the MRSA strains.

We have shown that two successful MRSA clones predominate in northern Norway. The majority of strains are CA-MRSA and SCC*mec* type IV, and there is generally a low-level of antibiotic resistance. It remains a puzzle why such a large proportion of MRSA disease is caused by only two clonal types of bacteria, and it is unknown what factors determined the ease of transmission of these MRSA strains. The frequent findings of SCC*mec* type IV along with heterogeneous genetic backgrounds may indicate horizontal transfer of SCC*mec* IV among staphylococcal strains in northern Norway in parallel to the clonal spread of successful MRSA strains. Monitoring the geographic distribution of epidemic clones may contribute to our understanding of why certain MRSA clones are spreading between countries, whereas others are limited to a single country, city, or hospital.

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