MRSA USA300 at Alaska Native Medical Center, Anchorage, Alaska, USA, 2000–2006

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To determine whether methicillin-resistant Staphylococcus aureus (MRSA) USA300 commonly caused infections among Alaska Natives, we examined clinical MRSA isolates from the Alaska Native Medical Center, Anchorage, during 2000–2006. Among Anchorage-region residents, USA300 was a minor constituent among MRSA isolates in 2000–2003 (11/68, 16%); by 2006, USA300 was the exclusive genotype identified (10/10).

Methicillin-resistant Staphylococcus aureus (MRSA) isolates, once concentrated among patients who had contact with the health care environment, have become epidemic among otherwise healthy populations in the United States. In the 48 contiguous states, community-associated MRSA skin and soft tissue infections (SSTIs) are predominantly caused by strain USA300 (1). In contrast, in 1996, 2000, and 2004–2006, in rural southwestern Alaska, we found that USA300 was rarely isolated, although community-associated MRSA SSTIs were common. Instead, sequence type (ST) 1, the type of USA400 isolates, was more common (2), as others have found in northern Canada (3). We wondered whether, over time, USA300 might replace USA400 among Alaska Natives as it has elsewhere in North America (4,5).

To investigate this possibility, we conducted surveillance at the Alaska Native Medical Center (ANMC). ANMC is the primary hospital for Alaska Natives residing in the Anchorage area and the statewide referral hospital for the Alaska Tribal Health System.

The Study

During 2000–2003, 695 clinical MRSA isolates were obtained by the Clinical Microbiology Laboratory of ANMC. A convenience sample of 567 isolates was collected and termed the retrospective collection. This collection was stratified by year of isolation and by 3 geographic regions of Alaska in which patients resided: 1) the Anchorage region (Anchorage, the Mat-Su region, and the Aleutian Islands); 2) the region of southwestern Alaska previously studied (2); and 3) all other regions. A randomly selected sample of 163 (28.7%) of the 567 isolates, stratified by year of isolation, was chosen for genotyping, including 20% of the isolates from Anchorage-region residents, 20% from residents of southwestern Alaska, and all isolates from residents of other regions (Table 1).

The prospective collection collected in 2004–2006 consisted of the first 5 clinical MRSA isolates obtained each month by the ANMC Clinical Microbiology Laboratory from different patients. Although 177 MRSA isolates had been collected, 2 were not available, and 2 lacked the mecA gene by PCR, leaving 173 isolates for further study. Genotyping was carried out on a random sample of 20% of isolates from this collection, stratified by year of isolation from the Anchorage-region patients, and on samples from all patients from all other regions (Table 1).

Clinical and demographic information was collected about the patients comprising the retrospective and prospective isolate groups. Site of care was recorded only for the prospective collection. Active surveillance for MRSA was not performed at ANMC during 2000–2006.

Isolates were genotyped by multilocus sequence typing (MLST), and clonal complexes (CCs) were assigned to closely related sequence types as described (6,7). Staphylococcal cassette chromosome mec (SCCmec) typing was performed (8), and the presence of Panton-Valentine leukocidin (PVL) genetic determinants was assessed as described (9). Additionally, to clarify the relationship between ST and typing by pulsed-field gel electrophoresis (PFGE), a random sample of strains that were ST8 and ST1 were tested by PFGE as described (10). Control strains were USA300-LAC for USA300 and strain 649, a clinical strain identical to MW2 by PFGE, for USA400. Antimicrobial drug susceptibilities were determined by using automated testing (bioMérieux Vitek, Durham, NC, USA). The D-zone test for inducible clindamycin resistance was performed for isolates resistant to erythromycin and susceptible to clindamycin by single-agent testing (11). Results were compared by χ² or Fisher exact tests using Stata version 11 (StataCorp LP, College Station, TX, USA).

The patients in the 20% Anchorage-region retrospective sample (n = 68), in the 20% retrospective sample from the region of southwestern Alaska (n = 33), and in the 20% Anchorage-region prospective sample (n = 29) did not differ significantly by demographic characteristics from the larger sampled groups (data not shown). Isolates in the combined
Table 1. Overview of patient characteristics from retrospective (2000–2003) and prospective (2004–2006) collections from Alaska Native Medical Center, Anchorage, Alaska, USA, by location of patient residence*

| Characteristic                  | No. (%) samples | No. (%) samples | No. (%) samples |
|-------------------------------|-----------------|-----------------|-----------------|
| Anchorage region              | Retrospective   | Prospective     | Retrospective   | Prospective     | Retrospective   | Prospective     |
| n = 68                        | n = 29          | n = 33          | n = 23          | n = 62          | n = 9           |
| Sex                           | M               | F               | M               | F               | M               | F               |
| M                             | 34 (50)         | 34 (50)         | 22 (67)         | 11 (33)         | 41 (66)         | 21 (34)         |
| F                             | 10 (34)         | 19 (66)         | 12 (52)         | 11 (48)         | 7 (78)          | 2 (22)          |
| Age group, y                  |                 |                 |                 |                 |                 |                 |
| 0–2                           | 1 (2)           | 3 (10)          | 4 (12)          | 1 (4)           | 4 (7)           | 0               |
| 3–12                          | 7 (10)          | 2 (7)           | 4 (12)          | 6 (26)          | 4 (7)           | 0               |
| 13–20                         | 9 (13)          | 2 (7)           | 3 (9)           | 1 (4)           | 3 (5)           | 1 (11)          |
| 21–39                         | 24 (35)         | 10 (35)         | 11 (33)         | 7 (30)          | 7 (11)          | 0               |
| 40–59                         | 24 (35)         | 11 (38)         | 5 (15)          | 4 (17)          | 24 (39)         | 4 (44)          |
| >60                           | 3 (4)           | 1 (4)           | 6 (18)          | 4 (17)          | 20 (32)         | 4 (44)          |
| Clinical specimen             |                 |                 |                 |                 |                 |                 |
| Blood                         | 1 (2)           | 1 (4)           | 0               | 1 (4)           | 0               | 0               |
| Bone or joint                 | 1 (2)           | 0               | 0               | 1 (4)           | 1 (2)           | 1 (11)          |
| Respiratory tract             | 3 (4)           | 1 (4)           | 6 (18)          | 2 (9)           | 22 (36)         | 2 (22)          |
| Skin or soft tissue           | 56 (82)         | 25 (86)         | 26 (79)         | 15 (65)         | 33 (53)         | 3 (33)          |
| Urine                         | 1 (2)           | 1 (4)           | 0               | 1 (3)           | 4 (17)          | 4 (7)           |
| Other†                        | 6 (9)           | 1 (4)           | 1 (3)           | 4 (17)          | 4 (7)           | 3 (33)          |
| Unknown                       | 0               | 0               | 0               | 0               | 1 (2)           | 0               |
| Site of care (prospective only)|                 |                 |                 |                 |                 |                 |
| Inpatient                     | NA              | 2 (7)           | NA              | 11 (48)         | NA              | 5 (56)          |
| Outpatient                    | NA              | 27 (93)         | NA              | 12 (52)         | NA              | 4 (44)          |
| Emergency                     | NA              | 0               | NA              | 0               | NA              | 0               |
| *NA, not available.          |                 |                 |                 |                 |                 |                 |
| †Liver abscess, pleural fluid, tracheal culture after tracheostomy placement, surgical drain fluid culture, eye culture from eye with conjunctivitis, cultures from other eye specimens, culture from soft tissue of the neck, culture from ear with otitis media, and cultures from other ear specimens. | | | | | | |
Table 2. MRSA isolate characteristics, combined retrospective and prospective collection samples by region of patient residence, Alaska, USA, 2000–2006*†

| CC and ST | Anchorage region, n = 97 | Southwestern region, n = 56 | Other regions, n = 71 |
|-----------|--------------------------|-----------------------------|----------------------|
| CC1†      |                          |                             |                      |
| ST1       | 25 (26)                  | 43 (77)                     | 10 (14)              |
| CC5       |                          |                             |                      |
| ST5       | 11 (11)                  | 2 (4)                       | 16 (23)              |
| ST105     | 1 (1)                    | 2 (4)                       | 9 (13)               |
| ST225     | 0                        | 0                           | 1 (1)                |
| ST231     | 0                        | 1 (2)                       | 1 (1)                |
| CC8§      |                          |                             |                      |
| ST8       | 32 (33)                  | 2 (4)                       | 9 (13)               |
| CC30      |                          |                             |                      |
| ST30      | 14 (14)                  | 3 (5)                       | 16 (23)              |
| ST30slv   | 3 (3)                    | 2 (4)                       | 0                    |
| CC45      |                          |                             |                      |
| ST45      | 1 (1)                    | 0                           | 0                    |
| ST45slv   | 1 (1)                    | 0                           | 0                    |
| ST54      | 1 (1)                    | 0                           | 0                    |
| CC59      |                          |                             |                      |
| ST59      | 7 (7)                    | 1 (2)                       | 7 (10)               |
| ST969     | 0                        | 0                           | 2 (3)                |
| ST969slv  | 1 (1)                    | 0                           | 0                    |
| SCCmec type |                        |                             |                      |
| II        | 10 (10)                  | 4 (7)                       | 29 (41)              |
| IV        | 88 (91)                  | 52 (93)                     | 39 (55)              |
| c-2.5     | 1 (1)                    | 0                           | 3 (4)                |

*MRSA, methicillin-resistant Staphylococcus aureus; ST, sequence type; slv, single locus variant; SCCmec, staphylococcal cassette chromosome mec; PFGE, pulsed-field gel electrophoresis.
†Among 61 isolates genotyped from the prospective cohort, 18 were from inpatients (ST1 [n = 9], ST105 [n = 1], ST231 [n = 1], ST5 [n = 3], and ST8 [n = 4]), and 43 were from outpatients (ST1 [n = 14], ST105 [n = 1], ST30 [n = 2], ST30slv [n = 1], ST5 [n = 3], and ST8 [n = 22]).
‡CC1 has recently been changed to CC15 by the administrators of the MLST database.
§CC59 (100%) isolates were almost all susceptible to clindamycin. Also among these patients, CC8 (94%), CC30 (100%), and CC59 (100%) isolates were almost all susceptible to clindamycin. Of all CC1 isolates, 16/25 (64%) were resistant to clindamycin; 14/16 (88%) were not susceptible by virtue of a positive D-zone test result.

Conclusions

We documented the emergence and rapid dominance of USA300 among clinical MRSA isolates from Anchorage-region patients who received treatment at the ANMC in 2002–2006. This complete strain replacement by 2006 suggests that Anchorage-region patients were exposed to a growing reservoir of USA300 during this era. In contrast, in 2006, USA300 still remained a less common cause of MRSA infections among ANMC patients drawn from other regions of Alaska, perhaps because patients from other regions were less likely to have been referred to ANMC for uncomplicated SSTIs.

Of the tested PVL-positive ST8 MRSA isolates bearing SCCmec IV, we confirmed that 100% (30/30) were USA300 by PFGE. This finding has useful implications for comparing MLST and PFGE typing methods.

ST1 isolates frequently had inducible clindamycin resistance, whereas strains with PVL and SCCmec IV of other genetic backgrounds rarely did. This may explain the seemingly anomalous data from the USA400 era in Chicago that 31/33 (94%) of clindamycin-susceptible, erythromycin-resistant strains of MRSA were D-zone test positive (I2).

Documented introduction of USA300 has not resulted in strain replacement in Europe (I3), Asia (I4), or Australia (I5). That USA300 emerged and came to predominate among Anchorage-region residents, mirroring the process that occurred earlier in several cities in North America (4,5), suggests that some characteristic of USA300 provides a survival advantage, enhanced virulence, or both, relative to other MRSA pulsotypes in those regions. The rapid appearance and emergence of USA300 at ANMC in 2002–2006 were remarkable, but its limited global spread remains unexplained.

R.S.D. and S.B.-V. are supported by grants from the Centers for Disease Control and Prevention (R01 CCR523379 and R01 C1000373-01), National Institutes of Health (R01 AI40481-01A1 and 2R56AI040481-08A1), and the Grant Healthcare Foundation. S.B.-V. is supported by the Lawrence Livermore Laboratory. M.Z.D. is supported by grant R01 C1000373-01 (CDC); M.Z.D. and R.S.D. are supported by grant 1 U01 GM087729-01/B270JA.
The Institutional Review Boards of the University of Chicago, Centers for Disease Control and Prevention, and Alaska Area Indian Health Service, and the boards of directors of the Alaska Native Tribal Health Consortium and the Southcentral Foundation approved the study.

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