

Molecular Epidemiology of Methicillin-Resistant *Staphylococcus aureus*, Rural Southwestern Alaska¹

Michael Z. David, Karen M. Rudolph, Thomas W. Hennessy, Susan Boyle-Vavra, and Robert S. Daum

USA300 is the dominant strain responsible for community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) infections in most of the United States. We examined isolates from outbreaks of MRSA skin infections in rural southwestern Alaska in 1996 and 2000 (retrospective collection) and from the hospital serving this region in 2004–2006 (prospective collection). Among 36 retrospective collection isolates, 92% carried Pantone-Valentine leukocidin (PVL) genes; all carried staphylococcal chromosomal cassette *mec* (SCC*mec*) type IV. None belonged to clonal complex (CC) 8, the CC associated with USA300; 57% were sequence type (ST) 1, and 26% were ST30; 61% were clindamycin resistant. In the prospective collection, 42 isolates were PVL+ and carried SCC*mec* type IV; 83.3% were ST1, 9.5% were ST30, and 7.1% were ST8. Among 120 prospective isolates, 57.5% were clindamycin resistant. CA-MRSA epidemiology in southwestern Alaska differs from that in the lower 48 states; ST8 strains were rarely identified and clindamycin resistance was common.

Staphylococcus aureus is a common cause of skin and soft tissue infections (SSTIs), endovascular infections, pneumonia, septic arthritis, endocarditis, osteomyelitis, foreign-body infections, and sepsis (1). In the United States, epidemic infection with community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) is occurring, with many reports of MRSA infections among persons without traditional healthcare-associated MRSA risk

Author affiliations: University of Chicago, Chicago, Illinois, USA (M.Z. David, S. Boyle-Vavra, R.S. Daum); and Centers for Disease Control and Prevention, Anchorage, Alaska, USA (K.M. Rudolph, T.W. Hennessy)

DOI: 10.3201/eid1411.080381

factors (2–4). As a result, the epidemiology of CA-MRSA has become complex (5).

Novel MRSA isolates that are less likely to be resistant to antimicrobial drugs other than β -lactams have been identified in association with epidemic CA-MRSA infections. These CA-MRSA strains are commonly susceptible to drugs such as clindamycin, gentamicin, tetracyclines, and rifampin. Moreover, the genes encoding the pore-forming, bicomponent cytotoxin, Pantone-Valentine leukocidin (PVL), are nearly universally present in novel CA-MRSA strains. However, evidence from animal studies has been contradictory in assessing the importance of PVL in the virulence of these isolates (6,7).

In addition to the PVL genes, strains that cause CA-MRSA infections typically carry staphylococcal chromosomal cassette *mec* (SCC*mec*) types IV and V, small genetic resistance elements that are presumably mobile. A single CA-MRSA genetic background, USA300 (defined by pulsed-field gel electrophoresis), corresponding to sequence type (ST) 8 by multilocus sequence typing (MLST), has become predominant among CA-MRSA isolates in many centers in the United States (8–10). The reason for the dominance of USA300 is not clear.

Other MRSA strains that are broadly susceptible to non- β -lactams and have PVL genes and SCC*mec* IV or V have predominated among CA-MRSA strains collected in various regions of the world (11). In an area of rural Alaska, SSTIs caused by CA-MRSA isolates have been a public health concern since 1996 (12–14). We explored the molecular diversity of strains causing CA-MRSA in this region and

¹Portions of this study were presented at the 47th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, September 17–20, 2007, Chicago, IL, USA.

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

Michael Z. David, Karen M. Rudolph,
Thomas W. Hennessy, Diana L. Zychowski,
Karthik Asthi, Susan Boyie-Vavra,
and Robert S. Daum

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

Author affiliations: The University of Chicago, Chicago, Illinois, USA (M.Z. David, D.L. Zychowski, K. Asthi, S. Boyie-Vavra, R.S. Daum); and Centers for Disease Control and Prevention, Anchorage, Alaska, USA (K.M. Rudolph, T.W. Hennessy)

DOI: <http://dx.doi.org/10.3201/eid1801.110746>

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* (SCC*mec*) typing was performed (8), and the presence of Pantone-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 χ^2 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