Community-Onset Methicillin-Resistant *Staphylococcus aureus* Associated with Antibiotic Use and the Cytotoxin Panton-Valentine Leukocidin during a Furunculosis Outbreak in Rural Alaska

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**Background.** Community-onset methicillin-resistant *Staphylococcus aureus* (CO-MRSA) reports are increasing, and infections often involve soft tissue. During a CO-MRSA skin infection outbreak in Alaska, we assessed risk factors for disease and whether a virulence factor, Panton-Valentine leukocidin (PVL), could account for the high rates of MRSA skin infection in this region.

**Methods.** We conducted *S. aureus* surveillance in the outbreak region and a case-control study in 1 community, comparing 34 case patients with MRSA skin infection with 94 control subjects. An assessment of traditional saunas was performed. *S. aureus* isolates from regional surveillance were screened for PVL genes by use of polymerase chain reaction, and isolate relatedness was determined by use of pulsed-field gel electrophoresis (PFGE).

**Results.** Case patients received more antibiotic courses during the 12 months before the outbreak than did control subjects (median, 4 vs. 2 courses; *P = .01*) and were more likely to use MRSA-colonized saunas than were control subjects (44% vs. 13%; age-adjusted odds ratio, 4.6; 95% confidence interval, 1.7–12). The PVL genes were present in 110 (97%) of 113 MRSA isolates, compared with 0 of 81 methicillin-susceptible *S. aureus* isolates (*P < .001*). The majority of MRSA isolates were closely related by PFGE.

**Conclusion.** Selective antibiotic pressure for drug-resistant strains carrying PVL may have led to the emergence and spread of CO-MRSA in rural Alaska.

Once considered to be nearly an exclusive nosocomial pathogen, methicillin-resistant *Staphylococcus aureus* (MRSA) has recently become an established cause of community infections [1–15]. In parts of the United States, MRSA accounts for the majority of community-onset (CO) *S. aureus* infections [11, 14, 15]. CO-MRSA is most often associated with skin and soft tissue infections rather than with invasive disease [1, 2, 8, 14, 16, 17]. CO-MRSA is commonly resistant only to β-lactam antibiotics and typically demonstrates susceptibility to trimethoprim-sulfamethoxazole, fluoroquinolones, and aminoglycosides [1, 4, 7, 11–17]. Previously published studies indicate that isolates causing CO-MRSA infections are of a different genetic background, compared with hospital-acquired isolates from the same region [17–19].

Risk factors for nosocomial MRSA are well established and include prolonged antibiotic exposure, dialysis, and admission to an intensive care unit [20, 21],...
but factors associated with CO-MRSA are poorly characterized. Although several studies have described CO-MRSA infections in patients without previous risk factors [1, 2, 7, 9, 11], most studies of CO-MRSA have been subject to ascertainment bias by including a majority of subjects with significant health-care exposure [22]. Community-based assessments are needed to improve our understanding of CO-MRSA epidemiology and to develop effective prevention measures and treatment strategies.

We recently reported a large outbreak of *S. aureus* skin infections in southwestern Alaska beginning in May 1999, in which 86% of infections were MRSA, and most affected persons had no history of hospital exposure [14]. We now report an epidemiological and environmental microbiological assessment during this outbreak, to identify risk factors for CO-MRSA infections and to determine whether a virulence factor previously associated with skin and soft tissue infections, Panton-Valentine leukocidin (PVL) [23–25], could account for the high rates of MRSA skin infection.

**PATIENTS, MATERIALS, AND METHODS**

**Setting.** The outbreak occurred in a region of southwestern Alaska with a population of ~25,000 persons. The population is 85% Alaska Native (Yup’ik Eskimo), who live in 52 villages (population, 150–1000 persons/village) and the regional commercial center (population, 5700 persons). Travel between villages is limited to airplane, boat, and snow machine; no roads connect the region to the rest of Alaska. The current case-control study was conducted in 1 village (Village A; population, ~700 persons) selected for its high number of cases. Alaska Natives are eligible for free medical care through a tribally operated system of village clinics [26] and a single regional hospital in the commercial center. This system provides the only health-care service available in Village A.

**Case-control study.** We defined a case patient as a Village A resident who had a culture-confirmed *S. aureus* skin infection (furunculosis or cellulitis) diagnosed from 1 April through 10 September 2000. For case patients with MRSA, infection was defined as CO when diagnosed in an outpatient clinic or within 48 h after hospital admission. Control subjects were Village A residents with no history of skin infection during the previous 12 months by medical record review and interview. Potential control subjects were identified by use of an age-stratified random sample of Village A residents generated from the electronic medical records system (age groups: 0–14, 15–34, and ≥35 years). They were selected to have a similar age distribution as case patients, with 3 control subjects for each case patient. Written consent was obtained from adult participants in this study and from a parent of all participants aged <18 years. Verbal assent was obtained from children aged 7–17 years. This study was conducted in accordance with policy for the protection of human research subjects of the US Department of Health and Human Services.

Interviews were conducted in person by use of a standard questionnaire to assess for potential risk factors during the 12 months before infection for case patients and during the 12 months before the interview for control subjects. Antibiotic use was assessed by medical record review. To exclude antibiotics used as a result of this outbreak, antibiotic use was determined for the 12 months (June 1998–May 1999) before the outbreak began [14]. For case patients with MRSA infections, significant health-care exposure in the 12 months before infection was assessed by medical record review and interview; significant health-care exposure was defined as hospitalization, surgery, dialysis, an indwelling line or catheter, or admission to a long-term care facility.

**Nasal carriage survey.** Anterior nares swabs for *S. aureus* culture were obtained from case patients and control subjects and from all their available household members. Swabs were immediately plated onto mannitol salt agar and were incubated aerobically for 48 h at 35°C.

**Environmental assessment.** Because use of traditional saunas has been associated with staphylococcal skin infections in rural Alaska [27], we assessed saunas used by case patients and control subjects. Saunas were designated as “case saunas” if used by any case patient; all others were designated as “control saunas.” Sauna owners were asked about sauna age, cleaning practices, and the number of people using the sauna with each use. Surface cultures for *S. aureus* were collected from seating areas in 4 similar locations in each sauna. For each culture, a 161-cm² area was swabbed with a saline-moistened rayon-tipped Culturette (Becton Dickinson), which was stored overnight, transported at room temperature in Stuart’s bacterial transport medium, and then plated onto mannitol salt agar. Three wood samples were collected from seating areas of 1 sauna that was determined by surface culture to be MRSA positive. These samples were processed to determine whether MRSA was present in biofilms [28]. Two pieces from each sample were processed for scanning electron microscopy (SEM) [28].

**Regional surveillance for *S. aureus* infections.** The majority of clinical isolates from case patients were no longer available at the time of the investigation. To obtain disease-causing *S. aureus* isolates from the outbreak region, we prospectively collected all *S. aureus* isolated from clinical specimens at the regional hospital's laboratory from 15 August to 30 September 2000.

**Isolate analysis.** For all cultures, colonies morphologically consistent with *S. aureus* were confirmed by use of the Staphaurex (Abbott Laboratories) latex slide agglutination kit. Oxacillin susceptibility was determined by disk diffusion, ac-
Table 1. Risk factor assessment for case patients with methicillin-resistant Staphylococcus aureus and control subjects in southwestern Alaska, September 2000.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Case patients</th>
<th>Control subjects</th>
<th>AOR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–14</td>
<td>8 (24)</td>
<td>24 (26)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–34</td>
<td>14 (41)</td>
<td>33 (35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;35</td>
<td>12 (35)</td>
<td>37 (39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>14 (41)</td>
<td>54 (57)</td>
<td>0.53 (0.24–1.2)</td>
<td>.1</td>
</tr>
<tr>
<td>Persons in household (HH), median (range), no.</td>
<td>6 (1–12)</td>
<td>6 (1–13)</td>
<td></td>
<td>.4</td>
</tr>
<tr>
<td>HH density (persons/room), median (range), no.</td>
<td>1.9 (0.2–6)</td>
<td>1.8 (0.5–7)</td>
<td></td>
<td>.8</td>
</tr>
<tr>
<td>HH members with skin infections, median (range), no.</td>
<td>2 (0–5)</td>
<td>1 (0–5)</td>
<td></td>
<td>.005</td>
</tr>
<tr>
<td>Sauna history</td>
<td>29 (85)</td>
<td>84 (89)</td>
<td>0.6 (0.18–2.1)</td>
<td>.4</td>
</tr>
<tr>
<td>Used saunas &gt;2 h/week</td>
<td>20 (69)</td>
<td>57 (68)</td>
<td>1.0 (0.32–3.3)</td>
<td>1.0</td>
</tr>
<tr>
<td>Median no. of persons/use in sauna</td>
<td>4.0</td>
<td>3.0</td>
<td></td>
<td>.05</td>
</tr>
<tr>
<td>Used abrasive scrubbers</td>
<td>20 (69)</td>
<td>59 (70)</td>
<td>0.88 (0.36–2.1)</td>
<td>.7</td>
</tr>
<tr>
<td>Used bar vs. liquid soap</td>
<td>5 (17)</td>
<td>22 (26)</td>
<td>0.55 (0.18–1.6)</td>
<td>.3</td>
</tr>
<tr>
<td>Shared soap</td>
<td>21 (75)</td>
<td>58 (69)</td>
<td>1.4 (0.55–3.9)</td>
<td>.5</td>
</tr>
<tr>
<td>Sat directly on sauna wood</td>
<td>19 (68)</td>
<td>65 (77)</td>
<td>0.60 (0.23–1.6)</td>
<td>.4</td>
</tr>
<tr>
<td>Antimicrobial courses during 12 months before outbreak</td>
<td>4.0</td>
<td>2.0</td>
<td></td>
<td>.005</td>
</tr>
<tr>
<td>Courses prescribed for skin infections, median (range), no.</td>
<td>0 (0–4)</td>
<td>0 (0–3)</td>
<td></td>
<td>.6</td>
</tr>
<tr>
<td>Courses prescribed for nonskin infections, median, no.</td>
<td>3.5</td>
<td>2.0</td>
<td></td>
<td>.007</td>
</tr>
<tr>
<td>No. of antimicrobial courses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>2 (6)</td>
<td>19 (21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>7 (21)</td>
<td>16 (18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2–3</td>
<td>7 (21)</td>
<td>26 (29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3 (9)</td>
<td>10 (11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5</td>
<td>15 (44)</td>
<td>18 (20)</td>
<td></td>
<td>.007</td>
</tr>
</tbody>
</table>

NOTE. Data are no. (%) of case patients or control subjects, unless otherwise indicated. AOR, age-adjusted odds ratio.

a Mantel-Haenszel OR adjusted for age group (0–14, 15–34, and ≥35 years).
b Case patients and control subjects were matched by age group; therefore, no statistical comparison was done.
c Includes only persons who reported sauna use.
d Two-hour cutoff represents median for study group.
e 1 June 1998 to 31 May 1999.
f χ² for trend, 7.4

cording to the National Committee for Clinical Laboratory Standards guidelines [29].

**Pulsed-field gel electrophoresis (PFGE).** Molecular subtyping was done by use of PFGE, using *SmaI* digests. The gel images were analyzed by use of MultiAnalyst software (version 1.1; Bio-Rad). Isolate relatedness was assigned by use of established criteria [30].

**PVL.** All MRSA and methicillin-susceptible S. aureus (MSSA) surveillance and carriage isolates were screened for the PVL genes by use of polymerase chain reaction (PCR) analysis [25]. MRSA isolates cultured from sauna surfaces also were screened for the PVL genes.

**SCCmec typing.** SCCmec typing was performed for 5 MRSA isolates (2 skin-infection isolates from case patients, 2 carriage isolates from different case patients, and 1 sauna isolate) by use of PCR with SCCmec region-specific primers [31, 32].

**Statistical methods.** Statistical analysis was performed by use of Epi Info 6.0 (Centers for Disease Control and Prevention [CDC]), SAS software (SAS Institute), and Stat Xact 4.0 (Cytel Software). Continuous variables were compared by use of the *t* test, Mann-Whitney 2-sample test, or χ² test for trend. Dichotomous variables were compared by use of the χ² or Fisher’s exact test. Analysis was stratified by age group, and 95% confidence intervals (CIs) around age-adjusted odds ratios (AORs) were calculated by use of the method described by Robbins et al. [33].

**RESULTS**

**Case-control study.** Thirty-four case patients with *S. aureus* skin infections in Village A were enrolled. All 34 case patients had been infected with MRSA, and all had CO-MRSA infections. Twenty-four (71%) case patients had no significant health-care
exposure during the 12 months before illness, and the remaining 10 had been hospitalized or had undergone surgery. Three hundred potential control subjects were identified; 99 (33%) were excluded for a history of skin infection, 6 (2%) declined to participate, 55 (22%) were unavailable or had moved from Village A, and 94 (31%) were enrolled. No attempt was made to contact the remaining 46 control subjects.

Case patients and control subjects were similar in age and sex and had similar household characteristics (table 1). Case patients had more household members with skin infections during the previous year than did control subjects. Sauna use was reported by 88% of study participants. Case patients were as likely as control subjects to use saunas and used saunas a similar number of hours per week. Saunas were used a median of 3 times/week and usually by >1 person at a time. Case patients used saunas that were used by more people with each use, compared with control subjects (median, 4 vs. 3 persons, respectively; \( P = .05 \)). Other sauna use practices were similar for case patients and control subjects. Case patients were as likely as control subjects to take showers or baths, have dogs, or play contact sports (data not shown). A history of eczema was reported by 15% of case patients and 5% of control subjects (AOR, 4.2; 95% CI, 1.0–17).

We assessed antibiotic use during the 12 months before the outbreak for all 34 case patients and for the 89 control subjects born before 1 January 1999. During those 12 months, case patients received a median of 4 antibiotic courses, compared with 2 courses for control subjects (\( P = .01 \)), and the odds of a skin infection during the outbreak increased with the number of preoutbreak antibiotic courses (table 1; \( P = .007 \)). Antibiotics prescribed for skin infections before the outbreak did not differ between case patients and control subjects. Of 102 persons receiving antibiotics, 93 (91%) had received ≥1 course of a \( \beta \)-lactam agent. Antibiotic use among case patients with significant health-care exposure did not differ from those without such exposure (median no. of antibiotic courses, 4.5 vs. 3.0, respectively; \( P = .4 \)).

Nasal carriage survey. Nasal swabs were obtained from 32 (94%) case patients and 90 (96%) control subjects. Cultures also were obtained from 194 (52%) of 373 household members of study participants. These 316 persons represented 44% of the 2000 Village A population. One hundred twenty-six (40%) of 316 were colonized with \textit{S. aureus}, and 41 (33%) of the 126 \textit{S. aureus} carriers were colonized with MRSA. Case patients were far more likely to be colonized with MRSA than were control subjects (31% vs. 3%; AOR, 13; 95% CI, 3.2–51). Case patients and control subjects were similar in age and sex and had similar household characteristics (table 1). Case patients had more household members with skin infections during the previous year than did control subjects. Sauna use was reported by 88% of study participants. Case patients were as likely as control subjects to use saunas and used saunas a similar number of hours per week. Saunas were used a median of 3 times/week and usually by >1 person at a time. Case patients used saunas that were used by more people with each use, compared with control subjects (median, 4 vs. 3 persons, respectively; \( P = .05 \)). Other sauna use practices were similar for case patients and control subjects. Case patients were as likely as control subjects to take showers or baths, have dogs, or play contact sports (data not shown). A history of eczema was reported by 15% of case patients and 5% of control subjects (AOR, 4.2; 95% CI, 1.0–17).

Figure 1. Scanning electron micrograph of wood sample taken from the seating area of a sauna with a known methicillin-resistant \textit{Staphylococcus aureus} (MRSA)–positive surface culture. Surface and crevices contain a biofilm matrix with coccoid organisms consistent in size and shape with staphylococci. Bacterial cultures from this wood sample grew MRSA.
Table 2. Pulsed-field gel electrophoresis (PFGE) patterns of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) isolates tested in outbreak investigation, southwestern Alaska, 2000.

<table>
<thead>
<tr>
<th>Isolate type, source, regional surveillance</th>
<th>No. tested</th>
<th>MRSA PFGE pattern</th>
<th>MSSA PFGE pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease causing</td>
<td></td>
<td>A₀ A₁ A₂ A₃ B  Other</td>
<td>A₀ A₁ C D E F  Other</td>
</tr>
<tr>
<td>Non–Village A</td>
<td>74</td>
<td>47 4 3 1 14 5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>34 1 0 10 5 3 3 12&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Village A</td>
<td>5</td>
<td>3 2</td>
<td>49 3 1 6 10 6 3 20&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Nasal carriage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Village A</td>
<td>41</td>
<td>33 3 0 3 0 2&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Environmental</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sauna surface culture, village A</td>
<td>15</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Sauna biofilm culture, village A</td>
<td>22</td>
<td>22</td>
<td>0</td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. of isolates with each PFGE pattern. A₀, predominant MRSA outbreak pattern; A₁, closely related to outbreak pattern (<3-band difference); A₂, closely related to outbreak pattern; A₃, closely related to outbreak pattern; A₄, possibly related to outbreak pattern (4-band difference); B, MRSA pattern from 1996 outbreak [27]; C–F, most common MSSA patterns.

<sup>a</sup> Five isolates in 3 different PFGE patterns.

<sup>b</sup> Twelve isolates in 11 different PFGE patterns.

<sup>c</sup> Two isolates in 2 different PFGE patterns.

<sup>d</sup> Twenty isolates in 11 different PFGE patterns.

patients also were more likely than control subjects to have an MRSA-colonized household member (44% vs. 18%; AOR, 3.3; 95% CI, 1.3–8.3).

**Environmental assessment.** Of the 70 saunas in Village A, 49 were used by at least 1 case-control study participant. We assessed 47 (96%) of these saunas; 20 had been used by ≥1 case patient (case saunas) and 27 were determined to be control saunas. Case saunas did not differ from control saunas in age or how they were cleaned (data not shown). *S. aureus* was recovered from at least 1 site in 12 (60%) of 20 case saunas and 11 (41%) of 27 control saunas (*P* = .2). Six (30%) case saunas had MRSA isolated from ≥1 site, compared with 2 (7%) control saunas (OR, 5.4; 95% CI 0.8–45; *P* = .056). We also compared the use of MRSA-positive saunas by case patients and control subjects; 12 (44%) of 27 case patients used an MRSA-positive sauna, compared with 10 (13%) of 78 control subjects (AOR, 4.6; 95% CI, 1.7–12). MRSA colonies were isolated from all 3 sauna wood samples after biofilm processing. SEM showed biofilm containing coccoid bacteria (figure 1).

**Regional surveillance for *S. aureus* infections.** From 15 August to 30 September, *S. aureus* was isolated from 113 clinical specimens at the regional medical center; 79 (70%) isolates were MRSA. Of the 75 MRSA isolates from a known site of infection, 70 (93%) were from skin infections, compared with 15 (54%) of 28 MSSA isolates from a known site of infection (*P* < .001). Surveillance isolates were cultured from patients residing in 29 villages in the outbreak region; 5 of the isolates (all MRSA) were from Village A residents.

**PFGE.** Of the 79 disease-causing MRSA isolates from regional surveillance, 74 were from non–Village A residents; 47 (64%) were indistinguishable by PFGE (outbreak pattern, A₀), and 8 (11%) were closely related (patterns A₁₋₃) (table 2; figure 2). A second unique pattern (B) was seen among 14 MRSA surveillance isolates; the remaining 5 MRSA isolates showed 3 patterns unrelated to A₀ or B. All 5 disease-causing MRSA isolates from Village A showed pattern A₀ or were closely related. Of the 41 MRSA carriage isolates from Village A, 39 (95%) were pattern A₀ or were closely related. All environmental MRSA isolates showed pattern A₀. MSSA surveillance and carriage isolates were diverse; 1 surveillance and 3 carriage isolates were closely related to pattern A₀ (pattern A₄), and 1 carriage isolate was possibly related (A₄, 4-band difference). The remaining 33 MSSA surveillance and 45 MSSA carriage isolates had 26 unique PFGE patterns.

**PVL.** Among surveillance isolates, 73 (92%) of 79 MRSA isolates had the PVL genes, compared with 0 of 34 MSSA isolates (*P* < .001; table 3). Of the 73 PVL-positive MRSA isolates, 60 were closely related to the predominant outbreak PFGE pattern, A₀; the remaining 13 isolates showed pattern B, which was seen in a 1996 furunculosis outbreak in a different region of Alaska [27]. Three of the 6 PVL-negative MRSA surveillance isolates were from nonskin infections. Of the 41 MRSA carriage isolates, 40 (98%) carried the PVL genes, compared to 0 of 49 MSSA carriage isolates (*P* < .001). Thus, all the carriage or disease-causing MSSA isolates were PVL negative, including 5 isolates with a PFGE pattern closely related to the outbreak MRSA strain. All 15 MRSA isolates cultured from sauna surfaces were PVL positive. One of the 7 PVL-negative MRSA isolates was PFGE pattern A₁, whereas the remaining 6 were unrelated to pattern A₀ (≥6-band difference).
SCCmec typing. All 5 MRSA isolates tested contained features of SCCmec type IV: the class B mec gene complex (ϕIS1272-ΔmecR1-mecA-ϕIS431) and the type 2 ccr genes. All 5 isolates tested were PVL positive and PFGE pattern A0 or were closely related.

DISCUSSION

During an MRSA furunculosis outbreak in southwestern Alaska, we found that the majority of disease-causing and carriage MRSA isolates were closely related and that the genes for PVL were present exclusively in MRSA. We also found that persons who developed furunculosis or cellulitis were more likely than uninfected persons to have been prescribed antibiotics during the year before the outbreak. This suggests that antimicrobial drug use facilitated the selection of drug-resistant strains carrying PVL. These findings are consistent with the observation that the number of staphylococcal skin infections and MRSA isolates increased concurrently in the region during the start of the outbreak in 1999 [14].

One unique aspect of this investigation was that most case patients (71%) had no significant health-care exposure during the year before their illness, although our case definition included all patients with CO-MRSA, regardless of previous health-care exposure. In contrast, a recent meta-analysis found that 85% of reported patients with community-acquired MRSA had ≧1 health-care-associated risk factor for MRSA [22]. Although 10 (29%) of our case patients had been hospitalized or had undergone surgery during the year before illness, several lines of evidence suggest that some or all of these case patients acquired infection in the community. MRSA carriage isolates from case patients were determined to be similar by use of PFGE, regardless of health-care history, and our epidemiologic findings did not change when analysis was restricted to case patients without health-care exposure (data not shown). Furthermore, there were no nosocomial MRSA infections at the regional hospital during the 3 years before our investigation (Linda Russell, Yukon-Kuskokwim Delta Regional Hospital, personal communication), which suggests that most, if not all, MRSA transmission in the region occurs outside of health-care settings.

In MRSA isolates tested from this outbreak, the methicillin-resistance determinant was carried on a SCCmec type IV element [31, 32]. SCCmec type IV is the smallest of the 4 known SCCmec types (21–24 kb) and contains no resistance determinants, except for the mecA gene. Whether the predominant MRSA strain came to rural Alaska by importation or by acquisition of SCCmec type IV by an endemic MSSA strain is unknown. We also have found SCCmec type IV in 2 MRSA isolates genetically unrelated to the current outbreak strain (CDC, unpublished data), which suggests that SCCmec type IV may have inserted into >1 genetic background in Alaska.

Although sauna use has been implicated in past furunculosis outbreaks in Alaska [27], we did not detect an association between sauna use and skin infections. This was probably due to
the high overall prevalence of sauna use (88%). However, we did find that case patients were more likely to use MRSA-colonized saunas than were control subjects. Although this association does not prove causality, the anatomic distribution of skin infections in this outbreak supports the role of saunas in transmission. More than 60% of MRSA skin infections in this region occurred below the waist, with 20% on the buttocks (CDC, unpublished data). In other skin infection outbreaks, most infections occurred equally on upper and lower extremities and rarely occurred on the buttocks [34–36].

We believe that MRSA survival and transmission was enhanced by biofilm formation in the sauna wood [37]. Most saunas were made of plywood, which provides a semiporous and irregular surface for biofilm attachment. Biofilm formation may allow for MRSA to survive sauna temperatures that can range from −18°C during nonuse periods to 93°C during use. In previous furunculosis outbreaks, transmission has been primarily person-to-person, and fomite transmission has been rarely implicated [34–36]. We found that infected household contacts also may be an important risk factor for disease, but, in this outbreak, we could not quantify the relative contribution of person-to-person transmission within households versus sauna exposure.

All 34 case patients were infected with MRSA; however, only one-third of the S. aureus carriage isolates in Village A were MRSA. A possible explanation for the predominance of MRSA among skin infections is the strong association of MRSA with PVL, a potent cytotoxin previously associated with skin and soft tissue infections [23–25]. PVL was not found among disease-causing MSSA isolates in this region. The combination of β-lactam antimicrobial resistance and the PVL cytotoxin may have provided the outbreak S. aureus strain with characteristics favorable for causing a furunculosis outbreak, despite this strain’s minority role as a carriage isolate. It should be noted that, although we found an association between MRSA and the PVL genes, we did not test for PVL toxin production.

The emergence of MRSA strains that cause skin infections in rural Alaska appears attributable to the selective pressure of antibiotic use for drug-resistant strains expressing PVL. The vast majority of MRSA isolates in this region were closely related by PFGE, in contrast with the much greater diversity observed among MSSA isolates. Clonal spread of PVL-producing strains has been suggested by analysis of isolates from a series of patients with CO-MRSA in France [38]. A unique aspect of our investigation was the availability of genetically diverse disease-causing and colonizing MSSA isolates from the same region for PVL testing. No MSSA isolate carried the PVL genes, including 5 MSSA isolates closely related to the outbreak MRSA strain, which suggests that the clonal spread of PVL-containing MRSA isolates led to the current furunculosis outbreak in southwestern Alaska.

This study has several important limitations. Only 5 of the disease-causing MRSA surveillance isolates were from Village A residents. However, all 34 case patients had MRSA infections, and >95% of the disease-causing, nasal carriage, and environmental MRSA isolates from Village A were closely related to the regional outbreak MRSA strain. Therefore, it seems likely that the MRSA regional surveillance isolates were representative of the clinical isolates from the case patients. Other study limitations relate to the case-control design. We only enrolled case patients with culture-confirmed S. aureus skin infections, who may have had more-severe disease than persons with skin infections that were never cultured. The case-control design also limits our ability to prove causality. We cannot be sure that the association between antibiotic use and CO-MRSA is causal, because case patients may have been more likely to receive antibiotics as a result of their disease. To minimize this limitation, we assessed antibiotic use during the 12 months before the outbreak began and excluded antibiotics prescribed for skin infections. Furthermore, the dose-response relationship between antibiotic use and disease supports causality.

In response to this outbreak, we educated health-care providers about the emergence of MRSA as the predominant skin pathogen and developed skin infection treatment guidelines that emphasize local care and reserving antibiotics for severe infections [14]. A program developed to encourage appropriate antibiotic use in rural Alaska may be a means to reduce antibiotic pressure and to prevent the selection of drug-resistant bacteria [39]. Future efforts may include a program for maintenance and cleaning of saunas. Although rural Alaska villages are unique in many respects, we believe the relationships among MRSA, antibiotic use,
and PVL cytotoxin may explain the emergence of CO-MRSA in other settings.

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