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(See the editorial commentary by Tenover on pages 675–7)

**Background.** This report compares the clinical characteristics, epidemiologic investigations, infection-control evaluations, and microbiologic findings of all 7 of the cases of vancomycin-resistant *Staphylococcus aureus* (VRSA) infection in the United States during the period 2002–2006.

**Methods.** Epidemiologic, clinical, and infection-control information was collected. VRSA isolates underwent confirmatory identification, antimicrobial susceptibility testing, pulsed-field gel electrophoresis, and typing of the resistance genes. To assess VRSA transmission, case patients and their contacts were screened for VRSA carriage.

**Results.** Seven cases were identified from 2002 through 2006; 5 were reported from Michigan, 1 was reported from Pennsylvania, and 1 was reported from New York. All VRSA isolates were vanA positive and had a median vancomycin minimum inhibitory concentration of 512 mg/mL. All case patients had a history of prior methicillin-resistant *S. aureus* and enterococcal infection or colonization; all had several underlying conditions, including chronic skin ulcers; and most had received vancomycin therapy prior to their VRSA infection. Person-to-person transmission of VRSA was not identified beyond any of the case patients. Infection-control precautions were evaluated and were consistent with established guidelines.

**Conclusions.** Seven patients with vanA-positive VRSA have been identified in the United States. Prompt detection by microbiology laboratories and adherence to recommended infection control measures for multidrug-resistant organisms appear to have prevented transmission to other patients.

*Staphylococcus aureus* and *Enterococcus* species are gram-positive, human commensal bacteria. *S. aureus* is commonly found on the skin and in the nares of healthy people. Enterococci are normally present in the human intestines. Both of these bacteria are opportunistic pathogens and have been among the most common causes of nosocomial infections [1, 2]. During the past 2 decades, these bacteria have developed resistance to commonly prescribed antimicrobial agents. Methicillin-resistant *S. aureus* (MRSA) infection first emerged in the United States in the 1970s, and by the 1990s, MRSA was considered to be endemic in most large urban medical centers [3, 4]. Vancomycin-resistant enterococci (VRE) were first reported in a US hospital in 1989 and rapidly became a common cause of health care–associated infections [5–7]. Although vancomycin could no longer be used to treat the growing number of VRE infections, it remained the only uniformly effective antimicrobial agent to treat the numerous MRSA infections [8–10]. In 1992, Noble et al. [11] demonstrated that conjugal transfer of the vanA gene, which mediates vancomycin resistance, from VRE to MRSA on the skin surface of hairless mice could be achieved, creating vancomycin-resistant *S. aureus* (VRSA). In an era of increasing rates of VRE and MRSA infection, the prospect of this transfer occurring spontaneously in vivo was of serious concern. In 1997, the first case of vancomycin-intermediate *S. aureus* infection was reported from Japan [12]. However, the mechanism of resistance was not mediated by vanA but rather by a change in cell physiology caused by genetic mutations and altered expression of certain genes, resulting in a
characteristic thickened cell wall that prevented vancomycin from reaching its target [13, 14].

In June 2002, the Michigan Department of Community Health reported the first clinical case of vanA-mediated VRSA infection in the world [15, 16]. Since then, 6 additional cases have been confirmed by the Centers for Disease Control and Prevention (1 case each from Pennsylvania and New York and 5 cases from Michigan) [17–21]. Information regarding only the first 3 cases has been published. This report will compare the clinical characteristics, epidemiologic investigations, infection-control evaluations, and microbiologic findings of all 7 documented cases of VRSA infection in the world.

METHODS

Patients and medical history. A patient with VRSA infection was defined as an individual from whom an S. aureus isolate was recovered for which the vancomycin MIC was \( \geq 32 \mu g/mL \) before 2006 and \( \geq 16 \mu g/mL \) after the vancomycin breakpoint was changed in 2006 [22–24]. Information regarding medical history, clinical course, treatment modalities (including antimicrobial and surgical therapy), and outcome was obtained through medical record review and interviews with patients, close family and friends, and medical personnel.

Epidemiologic investigations. A comprehensive epidemiologic contact investigation was conducted for each case patient with VRSA infection and their contacts. Specimens were collected from the nares, axilla, groin, wounds, and rectum of each case patient to determine both VRSA and VRE colonization status. To assess the extent of transmission beyond the case patients, nare, skin wound, and catheter exit site swab specimens were collected from all available patient contacts during the period of transmissibility. This period was defined as the time from the last date of a culture negative for VRSA through the date that appropriate infection-control precautions were implemented following the isolation of VRSA. Places where the case patients resided or visited within the period of transmissibility were identified as facilities where transmission could have occurred. These facilities included patient homes, hospitals, rehabilitation and long-term care facilities, physician offices, dialysis centers, an infusion center, a wound care clinic, and a nail salon. Patient contacts considered to be at risk for transmission included people who had direct physical contact with patients, shared the same living space, or had the same health care providers during the period of transmissibility. Persons who worked in laboratories where VRSA organisms were initially identified were also considered to be at risk. Overall, at-risk individuals included physicians, nurses, therapists, other patients, family members, friends, laboratory technologists, and a manicurist. On-going surveillance cultures were performed for the case patients and all individuals who remained at risk because of direct patient contact throughout the investigations.

Infection-control policies and procedures. Infection-control policies and procedures were assessed in all health care facilities where the patients with VRSA infection had received care during their periods of transmissibility. These assessments were conducted through interviews with infection control supervisors, review of written procedures, and direct observation of health care worker practices.

Laboratory procedures. Isolate identification and antimicrobial susceptibility testing were conducted at local clinical laboratories and then confirmed at state health department laboratories. VRSA isolates were then sent to the Centers for Disease Control and Prevention (Atlanta, GA) for further characterization. Species identification was determined using standard biochemical and molecular methods [25]. Antimicrobial susceptibility testing was performed using the reference broth microdilution method according to the Clinical and Laboratory Standards Institute [22–24]. Genomic DNA from VRSA isolates was isolated by the silica-gel membrane method (Qiagen DNeasy) and was used as a template for PCR to detect the presence of mecA, vanA, vanB, vanC, and vanD [26–28]. PFGE was performed using SmaI-digested DNA from VRSA isolates, and banding patterns were analyzed and classified as described elsewhere [29]. All isolates underwent typing of the staphylococcal cassette chromosome mec (SCCmec) genetic element using PCR [30].

RESULTS

Case descriptions. Five (71%) of the 7 cases of VRSA infection were reported from Michigan (table 1). Four (57%) of the 7 case patients with VRSA infection were female, 5 (71%) were white, and the median age was 58 years (range, 40–78 years). All 7 case patients had a history of previous MRSA and enterococcal (4 with VRE) infections or colonization. Most case patients had several underlying conditions, including 5 patients (71%) with chronic skin ulcers, 4 (57%) with diabetes, and 3 (43%) with chronic renal failure; 2 (29%) were considered to be obese. One of the case patients (patient 2) had not received vancomycin therapy during the 5 years prior to VRSA infection, 1 had not received vancomycin therapy during the previous 4 months (patient 3), 4 had received vancomycin therapy for 5–9 weeks in the previous 3 months, and 1 had intermittently received vancomycin therapy for \( \sim 10 \) years. VRSA was isolated from specimens of either ulcers or wounds for 6 (86%) of the case patients and from urine specimens from a nephrostomy tube for the other case patient. In all but 1 case patient (patient 3), specimen collection was prompted by a wound or ulcer that appeared infected or was healing (in patient 5). Enterococcal species were recovered from the sites from which specimens...

<table>
<thead>
<tr>
<th>Patient</th>
<th>Date</th>
<th>State</th>
<th>Age,  years</th>
<th>Sex</th>
<th>Culture source</th>
<th>Diagnosis</th>
<th>Underlying conditions</th>
<th>Duration of VAN exposure in previous 3 months</th>
<th>Therapy</th>
<th>Outcome</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>June 2002</td>
<td>Michigan</td>
<td>40</td>
<td>Female</td>
<td>Central venous catheter exit site, catheter tip, and plantar ulcers</td>
<td>Suspected exit site infection and plantar soft-tissue infection</td>
<td>Diabetes, chronic renal failure requiring hemodialysis</td>
<td>6.5 weeks</td>
<td>Catheter removed, TMP-SMX (2 weeks after surgical procedure), surgical debridement of ulcers and twice per week evaluation with debridement, application of gentian violet and contact casts</td>
<td>Infection cleared at both culture sites (first culture positive for VRSA in August); follow-up continued through November (for 20 weeks); foot ulcers healed in December 2002</td>
<td>[15, 16]</td>
</tr>
<tr>
<td>2</td>
<td>September 2002</td>
<td>Pennsylvania</td>
<td>70</td>
<td>Male</td>
<td>Plantar ulcer</td>
<td>Cellulitis along plantar fascia and polymicrobial osteomyelitis of the right calcaneus</td>
<td>Obesity with multiple lower extremity ulcers, osteomyelitis, and status after amputation</td>
<td>0 weeks (exposure in September 1997)</td>
<td>LNZ (stopped after 4 weeks because of thrombocytopenia), PTZ and TMP-SMX (6 weeks), daily chlorhexidine washes for 2 weeks, wound care</td>
<td>VRSA not recovered again after initiation of antimicrobial therapy; ulcer was healing when patient died 11 weeks after isolation of VRSA; death was attributable to underlying diseases</td>
<td>[17, 18]</td>
</tr>
<tr>
<td>3</td>
<td>March 2004</td>
<td>New York</td>
<td>63</td>
<td>Female</td>
<td>Urine from nephrostomy tube and nephrostomy exit site</td>
<td>Cloudy urine, no systemic symptoms</td>
<td>Advanced stage of multiple sclerosis, diabetes, recurrent UTIs, kidney stones, nephrostomy tube, gastrostomy tube</td>
<td>0 weeks (exposure in November 2003)</td>
<td>LEV (10 days)</td>
<td>Persistently culture positive for VRSA; admitted for SOB, ruled out pneumonia; blood specimen positive for <em>Morganella</em> species; died during hospitalization April 2005</td>
<td>[19–21]</td>
</tr>
<tr>
<td>4</td>
<td>February 2005</td>
<td>Michigan</td>
<td>78</td>
<td>Male</td>
<td>Toe wound</td>
<td>Gangrene of the second toe</td>
<td>Non-insulin-dependent diabetes, coronary artery disease, peripheral vascular disease, chronic renal failure, obstructive uropathy, aortic valve replacement (October 2004)</td>
<td>9 weeks</td>
<td>Gangrenous toe amputation (February 2005), LNZ and RIF (3.5 weeks), wound care</td>
<td>Toe wound specimen cultured weekly for 7 weeks; no VRSA detected; follow-up discontinued mid-April 2005</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>October 2005</td>
<td>Michigan</td>
<td>58</td>
<td>Female</td>
<td>Surgical site wound</td>
<td>Surgical site infection after pancreatectomy and ventral hernia repair</td>
<td>Morbid obesity, hypertension, asthma, chronic bronchitis, arthritis</td>
<td>8 weeks</td>
<td>No antimicrobial therapy; debridement; wound vacuum therapy</td>
<td>Groin colonization, chlorhexidine showers for 5 days; no subsequent wound or surveillance cultures yielded VRSA (for 5 weeks); wound healed (February 2006)</td>
<td>NA</td>
</tr>
<tr>
<td>6</td>
<td>December 2005</td>
<td>Michigan</td>
<td>48</td>
<td>Male</td>
<td>Two nonhealing plantar ulcers</td>
<td>Plantar soft-tissue infection and osteomyelitis of the right lower limb</td>
<td>MVA (1981), open fracture of tibia and fibula, compartment syndrome and osteomyelitis following leg-lengthening surgical procedure (1990), nonhealing foot ulcers</td>
<td>~10 years (to control acute occurrences of infection)</td>
<td>DAP (4 weeks), debridement and wound care, BKA (May 2006)</td>
<td>Nasal colonization, mucopurulent decolonization (2 times daily for 5 days); subsequent cultures negative for VRSA (for 10 weeks)</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>October 2006</td>
<td>Michigan</td>
<td>43</td>
<td>Female</td>
<td>Triceps wound</td>
<td>Necrotizing fasciitis of the right upper limb</td>
<td>Diabetes, chronic renal failure requiring hemodialysis, multiple extremity ulcers, chronic diabetes</td>
<td>5 weeks</td>
<td>LNZ and ETP (2 weeks), wound care</td>
<td>VRSA not recovered again after wound debridement and initiation of antimicrobial therapy; follow-up discontinued after 8 weeks; wound healing</td>
<td>NA</td>
</tr>
</tbody>
</table>

NOTE. BKA, below knee amputation; BID, twice daily; DAP, daptomycin; ETP, ertapenem; LEV, levofloxacin; LNZ, linezolid; MVA, motor vehicle accident; NA, not applicable; PTZ, piperacillin-tazobactam; RIF, rifampin; SOB, shortness of breath; TMP-SMX, trimethoprim-sulfamethoxazole; VAN, vancomycin; UTI, urinary tract infection.
were culture positive for VRSA for 5 of the 7 case patients; 3 of the isolates were VRE. All culture specimens were polymicrobial and included a variety of gram-negative organisms. At the time of specimen collection, 4 case patients (57%) were inpatients, 2 (29%) were outpatients, and 1 (14%) was a long-term care resident. Case patients were observed for a median of 10 weeks (range, 5–56 weeks) after initial VRSA isolation. Follow-up was concluded after culture results remained negative for VRSA for at least 3 consecutive weeks without antimicrobial therapy, when the culture site healed, or at the time of death. One case patient persistently tested positive for VRSA, and 6 case patients became culture negative for VRSA following multimodal therapy, including wound care (n = 6), surgical intervention (n = 5), and antimicrobial therapy (n = 5).

Epidemiologic investigation results. Two case patients were colonized with VRSA at body sites other than the initial culture sites; 1 case patient (patient 5) had VRSA isolated from a specimen from the groin, adjacent to the VRSA-infected wound site, and 1 case patient (patient 6) had VRSA isolated from a specimen from the nares. After showering with chlorhexidine for 5 days (patient 5) and using nasal mupirocin twice daily for 5 days (patient 6), VRSA was not recovered again from either site. VRE isolates (5 *Enterococcus faecalis* and 1 *Enterococcus faecium*; 1 patient was colonized with both) were recovered from specimens from either a wound, nephrostomy tube, or gastrointestinal tract for 5 (71%) of the case patients.

The median number of case patient contacts for whom surveillance cultures for VRSA were performed was 42 (range, 23–371 case patient contacts) (table 2). Fourteen percent to 30% of case patient contacts were colonized with methicillin-susceptible *S. aureus*, 3%–8% were colonized with MRSA, and none were colonized with VRSA.

Infection-control findings. Standard infection-control precautions were in place at all of the involved health care facilities prior to identification of the cases of VRSA infection, and the policies and practices were appropriate for the respective settings. Prior to recovery of VRSA, most case patients had known MRSA infection or colonization; therefore, contact precautions were being used. Once VRSA was identified, contact precautions were reinforced, and some enhanced measures were instituted at all facilities and for all staff having continued contact with the infected patients. For inpatients, the enhanced precautions included placing patients in private rooms. For outpatients, treatment was administered in dedicated rooms or areas separate from other patients and during the last appointment of the day. For all patients, enhanced measures included dedicated staff and equipment, new gloves and gowns for each patient interaction, masks with eye protection when the potential for splashing and/or spraying of infectious material existed (e.g., during wound care in the podiatry clinic for patient 1), and thorough cleaning and disinfecting of all patient rooms and equipment after each use and after discharge from the hospital. Enhanced contact precautions remained in place throughout the follow-up period for both inpatients and outpatients. Follow-up was discontinued if culture results remained negative for VRSA for at least 3 consecutive weeks without antimicrobial therapy or if the primary culture site healed. However, contact precautions remained in place if outpatient care continued.

Laboratory results. The 7 VRSA isolates had a median vancomycin MIC of 512 μg/mL (range, 32–1024 μg/mL) (table 3). All isolates were susceptible to ≥5 antimicrobial agents approved by the Food and Drug Administration for treating *S. aureus* infection, including linezolid, quinupristin-dalfopristin, and trimethoprim-sulfamethoxazole; 6 isolates were susceptible to daptomycin. All of the isolates acquired a *vraA*-containing Tn1546-like element by independent genetic events [15, 21, 31]. In each isolate, the *vraA* gene was localized to a plasmid, which ranged in size from 40 to 120 kb. Five isolates belonged to MRSA lineage USA100 and contained SCCmec type II, and 1 belonged to MRSA lineage USA800 and contained SCCmec type IV. The VRSA isolate from patient 6 did not belong to

| Table 2. Contact investigation results for patients with vancomycin-resistant *Staphylococcus aureus* in the United States, 2002–2006. |

<table>
<thead>
<tr>
<th>Patient</th>
<th>Date</th>
<th>State</th>
<th>Total no. of contacts who had culture performed</th>
<th>No. (%) of patients colonized with MSSA</th>
<th>No. (%) of patients colonized with MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>June 2002</td>
<td>Michigan</td>
<td>371</td>
<td>82 (22)</td>
<td>28 (8)</td>
</tr>
<tr>
<td>2</td>
<td>September 2002</td>
<td>Pennsylvania</td>
<td>262</td>
<td>74 (28)</td>
<td>21 (8)</td>
</tr>
<tr>
<td>3</td>
<td>March 2004</td>
<td>New York</td>
<td>101</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>February 2005</td>
<td>Michigan</td>
<td>35</td>
<td>5 (14)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>5</td>
<td>October 2005</td>
<td>Michigan</td>
<td>23</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>6</td>
<td>December 2005</td>
<td>Michigan</td>
<td>42</td>
<td>10 (24)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>7</td>
<td>October 2006</td>
<td>Michigan</td>
<td>38</td>
<td>6 (16)</td>
<td>2 (5)</td>
</tr>
</tbody>
</table>

**NOTE.** MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*.

* Seven patients (30%) were colonized with *S. aureus*. At the request of the facility, methicillin and oxacillin susceptibility testing was not conducted for the 7 *S. aureus* isolates.
any current PFGE type in the database, and the SCCmec type could not be determined using standard primers.

DISCUSSION

This report describes the clinical and laboratory characteristics of 7 patients from whom vanA-containing VRSA isolates were recovered. Most of these patients had several characteristics in common, including chronic underlying conditions, history of MRSA and VRE infection or colonization, and previous exposure to vancomycin. All but 2 patients had VRE recovered at the time of VRSA isolation, either from a culture site or rectal specimen. One of the 2 patients who did not present with VRE infection or colonization at the time when VRSA was identified had a history of cultures positive for VRE; the other patient had a history of cultures positive for Enterococcus species, but unfortunately, susceptibility testing was never conducted. It is thought that, in all instances, VRE strains likely contributed should be assessed. Guidance has been developed to assist in developing a plan for this contact investigation [35].

To date, no transmission of VRSA beyond any of the case patients reported here has been identified.

One of the most prominent, outstanding questions is why 5 of the 7 cases of VRSA infection occurred in Michigan. This regional emergence likely occurred because of the convergence of several factors, including population characteristics, antimicrobial pressure, and the presence of VRE strains that are more likely to donate vanA operon. Michigan has a large population of individuals with chronic underlying conditions, such as diabetes and end-stage renal disease, both of which are conditions that appear to be associated with these infections. It is estimated that 590,000 adults (7.8% of the adult population) in Michigan have received diagnoses of diabetes [36]. Often, patients with diabetes develop other chronic health conditions, including impaired sensation in the feet, leading to unrecognized injuries (such as foot ulcers) from which VRSA has been isolated. In addition, diabetes is the leading cause of end-stage renal disease. Compared with the other states, Michigan has the ninth greatest incidence of end-stage renal disease, and the ninth greatest

### Table 3. Laboratory aspects of vancomycin-resistant *Staphylococcus aureus* infections in patients in the United States, 2002–2006.

<table>
<thead>
<tr>
<th>Patient</th>
<th>PFT</th>
<th>SCCmec</th>
<th>CC</th>
<th>DAP</th>
<th>ERY</th>
<th>GM</th>
<th>OXA</th>
<th>LEV</th>
<th>LNZ</th>
<th>PEN</th>
<th>O-D</th>
<th>RIF</th>
<th>TMP-SMX</th>
<th>TEC</th>
<th>TET</th>
<th>VAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>USA100</td>
<td>II</td>
<td>&gt;8 (R)</td>
<td>0.5 (S)</td>
<td>&gt;8 (R)</td>
<td>64 (R)</td>
<td>&gt;16 (R)</td>
<td>16 (R)</td>
<td>2 (S)</td>
<td>&gt;2 (R)</td>
<td>&lt;1 (S)</td>
<td>&gt;8 (R)</td>
<td>0.25 (S)</td>
<td>32 (R)</td>
<td>1 (S)</td>
<td>1024 (R)</td>
</tr>
<tr>
<td>2</td>
<td>USA100</td>
<td>II</td>
<td>&gt;8 (R)</td>
<td>0.5 (S)</td>
<td>&gt;8 (R)</td>
<td>64 (R)</td>
<td>&gt;16 (R)</td>
<td>16 (R)</td>
<td>2 (S)</td>
<td>&gt;2 (R)</td>
<td>&lt;1 (S)</td>
<td>&lt;0.25 (S)</td>
<td>0.25 (S)</td>
<td>8 (S)</td>
<td>&gt;16 (R)</td>
<td>32 (R)</td>
</tr>
<tr>
<td>3</td>
<td>USA800</td>
<td>IV</td>
<td>&gt;8 (R)</td>
<td>0.5 (S)</td>
<td>&gt;8 (R)</td>
<td>32 (R)</td>
<td>&gt;16 (R)</td>
<td>16 (R)</td>
<td>2 (S)</td>
<td>&gt;2 (R)</td>
<td>&lt;1 (S)</td>
<td>&lt;0.25 (S)</td>
<td>0.25 (S)</td>
<td>16 (S)</td>
<td>&gt;16 (R)</td>
<td>64 (R)</td>
</tr>
<tr>
<td>4</td>
<td>USA100</td>
<td>II</td>
<td>&gt;16 (R)</td>
<td>&gt;0.5 (S)</td>
<td>&gt;8 (R)</td>
<td>&lt;2 (S)</td>
<td>&gt;16 (R)</td>
<td>&gt;16 (R)</td>
<td>2 (S)</td>
<td>&gt;2 (R)</td>
<td>2 (S)</td>
<td>0.5 (S)</td>
<td>0.25 (S)</td>
<td>16 (I)</td>
<td>&lt;1 (S)</td>
<td>256 (R)</td>
</tr>
<tr>
<td>5</td>
<td>USA100</td>
<td>II</td>
<td>&gt;16 (R)</td>
<td>&gt;0.5 (S)</td>
<td>&gt;8 (R)</td>
<td>&gt;2 (S)</td>
<td>&gt;16 (R)</td>
<td>&gt;16 (R)</td>
<td>4 (S)</td>
<td>&gt;2 (R)</td>
<td>2 (S)</td>
<td>0.5 (S)</td>
<td>0.25 (S)</td>
<td>8 (S)</td>
<td>&lt;1 (S)</td>
<td>512 (R)</td>
</tr>
<tr>
<td>6</td>
<td>Not defined</td>
<td>Nontypable</td>
<td>&gt;16 (R)</td>
<td>1 (S)</td>
<td>&gt;8 (R)</td>
<td>&gt;2 (S)</td>
<td>&gt;16 (R)</td>
<td>&gt;16 (R)</td>
<td>2 (S)</td>
<td>&gt;2 (R)</td>
<td>1 (S)</td>
<td>&lt;0.5 (S)</td>
<td>0.25 (S)</td>
<td>16 (I)</td>
<td>&lt;1 (S)</td>
<td>1024 (R)</td>
</tr>
<tr>
<td>7</td>
<td>USA100</td>
<td>II</td>
<td>&gt;16 (R)</td>
<td>2 (NS)</td>
<td>&gt;8 (R)</td>
<td>&gt;2 (S)</td>
<td>&gt;16 (R)</td>
<td>8 (R)</td>
<td>&gt;2 (S)</td>
<td>&gt;2 (R)</td>
<td>&lt;1 (S)</td>
<td>&lt;0.25 (S)</td>
<td>0.25 (S)</td>
<td>16 (I)</td>
<td>&lt;1 (S)</td>
<td>512 (R)</td>
</tr>
</tbody>
</table>

**NOTE.** CC, clindamycin; DAP, daptomycin; ERY, erythromycin; GM, gentamicin; I, intermediate; LEV, levofloxacin; LNZ, linezolid; NS, nonsusceptible; OXA, oxacillin; PEN, penicillin; PFT, pulsed-field type; O-D, quinupristin-dalfopristin; R, resistant; S, susceptible; SCCmec, staphylococcal cassette chromosome mec; TEC, teicoplanin; TET, tetracycline; TMP-SMX, trimethoprim-sulfamethoxazole; VAN, vancomycin.
number of dialysis and transplant facilities [37]. Patients receiving dialysis are at high risk of infection with invasive MRSA, leading to increased vancomycin exposure and, because of their reduced renal clearance of the drug, prolonged exposure to subtherapeutic levels of vancomycin. A recent report noted that the rate of invasive MRSA infection among patients receiving dialysis is higher than that among any other known patient population and is 100 times higher than that among the general population [38]. In addition to these patient population factors, Michigan was 1 of the first locations in the United States to document MRSA infection occurring outside of health care facilities in the 1980s [39]. Therefore, the early use of vancomycin in Michigan for treatment of these MRSA infections may have provided increased selective pressure for the development of vancomycin-resistant organisms.

The demographic characteristics and risk factors of Michigan’s population may favor the emergence of VRSA, yet other regions have similar populations and have not witnessed this emergence. Therefore, specific characteristics of either the S. aureus or VRE strains circulating in Michigan may lead to a greater propensity for them to donate and/or acquire vanA. Although each VRSA strain has been distinct, the associated VRE strains from the Michigan patients contain a broad host-range Inc-18 conjugative plasmid that may be more likely to donate vanA to other bacterial species, compared with VRE strains from other regions [31, 40]. Studies are currently under-way to examine the prevalence of these plasmids in enterococcal isolates from Michigan and nationally.

In summary, VRSA infection continues to be a rare occurrence. A few specific existing factors seem to have predisposed these case patients to VRSA infection, including prior MRSA and enterococcal infections or colonization, underlying conditions (such as chronic skin ulcers and diabetes), and previous treatment with vancomycin. Further studies are necessary to investigate the specific characteristics of the S. aureus and VRE plasmids isolated from these case patients. Appropriate antimicrobial prescribing by health care providers, adherence to recommended infection-control guidelines, and, ultimately, the control of both MRSA and VRE are necessary to prevent further emergence of VRSA strains.

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