Regional Dissemination of Vancomycin-Resistant Enterococci Resulting from Interfacility Transfer of Colonized Patients


During early 1997, the Siouxland District Health Department (SDHD; Sioux City, IA) reported an increased incidence of vancomycin-resistant enterococcal (VRE) isolates at area health care facilities. To determine the prevalence and risk factors for colonization with VRE strains at 32 health care facilities in the SDHD region, a prevalence survey and case-control study were performed. Of 2266 patients and residents, 1934 (85%) participated, and 40 (2.1%) were positive for (gastrointestinal) VRE colonization. The prevalence of VRE isolates was significantly higher in acute care facilities (ACFs) than in long-term care facilities (LTCFs) (10/152 [6.6%] vs. 30/1782 [1.7%]; odds ratio [OR], 4.1; 95% confidence interval [CI], 1.8–9.0). LTCF case patients were significantly more likely than controls to have been inpatients at any ACF (19/30 vs. 12/66; OR, 8.0; 95% CI, 2.7–23.8). Of 40 VRE isolates, 34 (85%) were a related strain. The predominant strain was present in all 12 LTCFs that had at least 1 case patient in each facility. Soon after the introduction of VRE isolates into this region, dissemination to multiple LTCFs resulted from resident transfer from ACFs to LTCFs.

Enterococci are a common and increasing cause of nosocomial infection. During 1989–1996, the proportion of enterococci reported to be vancomycin resistant in the National Nosocomial Infections Surveillance system increased from 0.3% to 14.2%. Once patients become colonized with vancomycin-resistant enterococci (VRE), they may remain colonized for long periods of time, creating a reservoir of VRE and thereby increasing the likelihood of nosocomial VRE transmission and subsequent patient infection. Although risk factors for colonization or infection of patients with VRE in acute care facilities (ACFs) have been established [1–3], few studies describe the epidemiology of VRE transmission within long-term care facilities (LTCFs) and between health care facilities [4].

Implementation of Centers for Disease Control and Prevention (CDC) recommendations in some ACFs has helped to control VRE transmission [5–7]. However, despite aggressive intrafacility infection-control efforts, unrecognized transfer of VRE-colonized patients between facilities can occur [8]. The transfer of VRE-colonized patients may promote regional transmission of VRE. A complete regional health care facility VRE point prevalence survey previously had not been conducted in the United States, and the contribution of interfacility transfer of VRE-colonized patients in establishing VRE endemicity in a community of health care facilities had not been determined. To assess such transmission, we conducted a point prevalence survey of all health care facilities in the Siouxland District Health Department (SDHD; Sioux City, IA) region and evaluated the role of interfacility VRE transmission.

Before December 1996, the SDHD had received no reports of VRE isolates at area health care facilities. From December 1996 through April 1997, the SDHD received reports of 58 VRE isolates from area health care facilities. Two ACFs sent 30 isolates to a reference laboratory for DNA typing by pulsed-field gel electrophoresis (PFGE). All isolates had a related genome pattern. The abrupt recent increase in the number of patients with VRE infection or colonization and the genetic similarity of the isolates suggested recent introduction of VRE to this region. A task force was created to address the increased number of VRE isolates. CDC was contacted to assist the task force in designing an infection-control strategy for the region, including Sioux City and 16 predominantly rural communities. Facilities in three states and two facilities under the jurisdiction of the Indian Health Service were included. A prevalence survey, in both ACFs and LTCFs, was designed to assess the
prevalence of VRE, to determine risk factors for patient acqui-
sition of VRE, and to assist in the implementation of a reg-
aional VRE prevention and control program.

Methods

Facility recruitment and prevalence survey instruction. All 32 health care facilities (4 ACFs and 28 LTCFs) in the region were contacted and invited to participate in the project. The Iowa, Nebraska, and South Dakota state health departments and the Indian Health Service assisted with the investigation. All health care fa-
cilities were located within 50 miles of Sioux City. Of the 32 health care facilities, 13 (46%) of 28 LTCFs and 2 of 4 ACFs were located in the Sioux City metropolitan area.

LTCFs had a median of 74 beds and 70 residents. ACFs had a median of 110 beds and 58 patients. Of the 4 ACFs, two were referral centers for regional community hospitals. The two referral ACFs had intensive care units, a burn unit, and postcardiothoracic surgery units. There were no dedicated bone marrow or solid organ transplant units. The majority of LTCFs were skilled care facilities. One LTCF had the capacity to care for residents receiving chronic ventilator therapy.

Eligible participants included all patients \( \geq 18 \) years of age who were registered as inpatients at 7 AM on the survey date for each facility. All samples were collected on swabs during 29–31 July 1997. Inpatients in psychiatric wards were excluded. Each facility assembled a team to collect perianal swab samples. Before specimen collection, a slide presentation with a question and answer session was conducted to instruct personnel on the proper technique for specimen collection. To ensure facility confidentiality, the director of the SDHD designated a code for each institution. At each facility, patients were not identified by name; numbers were assigned to patients in the order in which their specimens were collected. All eligible patients were recorded in a log book by the facility regardless of whether they participated. Specimens were delivered to and processed at SDHD.

Microbiologic investigations. To detect GI colonization, per-
ianal samples were obtained from all participants [9]. The perianal skin was swabbed at the anal verge with a cotton-tipped swab (Becton Dickinson, Cockeysville, MD) without rectal insertion. Patients with a colostomy or ileostomy stoma were swabbed at the junction of the epidermal and mucosal surfaces.

All swabs collected from participants at both ACFs and LTCFs were inoculated into the VRE SELECT Test (VST; IDEXX, West-
brook, ME), a rapid colorimetric test for the detection of VRE [10, 11]. The VST media contains \( \alpha \)-nitrophenyl \( \beta \)-naphthylamide, which can be hydrolyzed by an enterococcal enzyme, \( \beta \)-glucosidase, producing a yellow color change in the media; vancomycin (20 \( \mu g \)/mL); and other selective antimicrobial agents. Positive results by VST were identified by either a yellow color change or turbidity after 24–28 h of incubation at 35°C and a positive \( \alpha \)-pyroglutamatic acid-\( \beta \)-naphthylamide spot test.

Positive VST media were then streaked onto bile esculin azide with 6 \( \mu g/mL \) vancomycin agar media (BEAV; Remel, Lenexa, KS) and incubated at 35°C for 48 h. If there was no growth after the initial 48 h, repeat streaking and another 48-h incubation were done. If there was no growth after the second 48-h incubation, the test was interpreted as negative for VRE. Patients were considered VRE-positive if the VST was positive and there was growth on BEAV agar. If there was growth on the BEAV media, colonies were transferred to blood agar slants and transported to CDC for species identification, vancomycin susceptibility testing, and molecular typing by PFGE.

To confirm the validity of the VST, 2 samples were simulta-
neously obtained from each ACF participant and from a conven-
ience sample of hemodialysis and endoscopy outpatients. One swab sample from each person was inoculated into the VST media and incubated at 35°C for 24–28 h; the second swab sample was streaked onto BEAV media and incubated at 35°C for 48 h. A positive VST result required a positive interpretation of the colori-
metric assay in conjunction with growth on BEAV media. Growth from the second simultaneously collected swab, which was inoculated onto BEAV, was confirmed for vancomycin resistance by agar gradient diffusion [12].

Epidemiologic studies. A case-control study was designed to as-
sess interfacility patient transfer as a risk factor for VRE gas-
trointestinal colonization. A case patient was defined as any patient from the SDHD study facilities with gastrointestinal VRE coloni-
zation detected by our point prevalence survey. Two randomly selected control patients were chosen from each of the 16 facilities at which case patients were identified. Controls did not have gastrointestinal VRE colonization and were matched to participants by facility. Participants initially identified as case patients on the basis of a positive VST result and growth on BEAV were excluded if VRE was not confirmed at CDC. Since control patients had been matched by facility, all control patients were included in the analyses, and therefore the ratio of case patients to control patients varied by facility. Antimicrobial use, underlying diagnoses, and previous VRE colonization or infection were ascertained to evaluate known risk factors for VRE colonization or infection [3, 13, 14]. The admission source to the patient’s current facility was as-
certained and coded for those admitted since 1 January 1997. Transfer of patients between facilities was determined during the month before specimen collection.

Statistical methods. Data were collected on a standardized form, entered into the database, and analyzed by use of Epi Info software (version 6.03) [15] and PC SAS [16]. Categorical variables were compared by matched analysis by use of Fisher’s exact or \( \chi^2 \) test. Mantel-Haenszel summary odds ratios (ORs) and 95% confi-

Results

Prevalence survey. All 32 facilities that were contacted par-
ticipated in the VRE prevalence survey. Swab samples were obtained for 1934 (85%) of 2266 eligible patients, including 152 (53%) of 286 ACF patients and 1782 (90%) of 1980 LTCF patients. ACFs reported that patients on obstetric and surgical wards frequently refused to have samples obtained. Of 1934 swab samples that were collected, 44 were positive for VRE as determined by a positive VST result and growth on BEAV. Because 4 isolates were not identified as VRE during confirm-
Iatory testing, these 4 case patients were not included in the analysis. There were 40 (2.1%) positive samples, of 1934 samples tested. All 40 VRE isolates were Enterococcus faecium (vancomycin MIC $\geq 256$ mg/L). The VRE prevalence was significantly higher in ACFs than in LTCFs (10/152 [6.6%] vs. 30/1782 [1.7%]; OR, 4.1; 95% CI, 1.8-9.0).

At least 1 VRE-colonized participant was identified in 3 of 4 ACFs and in 12 (43%) of 28 LTCFs. Facility-specific VRE prevalence rates ranged from 0% to 24% (median, 4.8%; mean, 8.2%) at ACFs and from 0% to 14% (median, 0%; mean, 1.8%) in LTCFs.

### Case-control study

Of the 40 case patients who were identified, 39 (98%) were white, 1 (2%) was Native American, and 25 (62%) were women. Case patients ranged in age from 43 to 101 years (median, 84). Case patients had a variety of underlying diagnoses, including congestive heart failure (15 [38%]), cancer (9 [22%]), diabetes (10 [25%]), chronic obstructive pulmonary disease (7 [18%]), gastrointestinal bleeding (5 [12%]), stroke (5 [12%]), and renal failure necessitating hemodialysis (3 [8%]). Of the 128 patients in the case-control study, 8 were known to have had gastrointestinal VRE colonization before the study, and all 8 were detected in the prevalence survey.

ACF case and control patients were similar in age, sex, and underlying diagnosis. In contrast, case patients were significantly more likely than control patients to have been hospitalized at any ACF since 1 January 1997, particularly ACF A, and to have had a shorter duration of stay (table 2).

For the 11 case patients who had not been transferred to an ACF during the month before the survey date, we ascertained transfer data from 1 January 1997 to the survey date. An additional 4 case patients had been hospitalized between 1 January 1997 and the survey date; therefore, 23 of 30 case patients had been hospitalized (table 3).

### VST validity

VST and BEAV results after species identification and confirmation of vancomycin resistance showed 97% correlation (204/210 specimens). By our study design, the VST, compared with BEAV, had a sensitivity of 68% (13/19), a specificity of 100% (191/191), a positive predictive value of 100% (13/13), and a negative predictive value of 97% (191/197).

### Molecular epidemiology

Genome typing of the 30 VRE isolates from case patients at LTCFs revealed 2 genotypes: 28 type a, and 2 type b. Genome typing of the 10 VRE isolates from case patients at ACFs revealed 4 genotypes: 6 type a, 2 type b, and 1 each of types c and d. All 16 case patients who had inpatient exposure to ACF A were colonized by strain type a.

All of the 12 LTCFs with case patients had at least 1 type a isolate. One LTCF had 2 strain types, a and b. Of the three ACFs with at least 1 case patient, 2 had only strain type a, and 1 (ACF B) had all of the isolates that were strain types b, c, or d. In addition, all of the non–strain type a isolates in the region (i.e., 4 type b isolates and the type c and d strains) were from case patients at either ACF B or the LTCF that was in close proximity to that facility. These two facilities were geographically remote from other health care facilities in the SDHD region, and both had case patients who had been transferred from tertiary-care facilities outside of the SDHD region.

### Discussion

Our data demonstrate that $\sim$7 months after the first VRE isolates were reported to the SDHD, VRE had spread to many of the health care facilities in the region. In residents of LTCFs

### Table 1: Comparison of characteristics of case and control patients at long-term care facilities, Siouxland District Health Department (SDHD; Sioux City, IA), July 1997.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case patients ($n = 30$)</th>
<th>Control patients ($n = 66$)</th>
<th>Matched OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Categorical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>5 (16.7)</td>
<td>2 (3.0)</td>
<td>5.0 (0.9–27)</td>
<td>.08</td>
</tr>
<tr>
<td>Recent transfer to or admission from any acute care facility</td>
<td>19 (63.3)</td>
<td>12 (18.2)</td>
<td>8.0 (2.7–23.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Recent transfer to or admission from acute care facility A</td>
<td>11 (36.7)</td>
<td>3 (4.5)</td>
<td>21 (4.2–101)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antimicrobial use during week before specimen collection</td>
<td>10 (33.3)</td>
<td>10 (15.2)</td>
<td>3.0 (1.0–8.9)</td>
<td>.05</td>
</tr>
<tr>
<td>Admission source from outside SDHD region</td>
<td>3 (10.0)</td>
<td>1 (1.5)</td>
<td>7.2 (0.6–81.4)</td>
<td>2</td>
</tr>
<tr>
<td><strong>Continuous</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time as resident (days)</td>
<td>110 (50–218)</td>
<td>202 (123–295)</td>
<td></td>
<td>.01</td>
</tr>
</tbody>
</table>

Note: Data are no. (%) or median (interquartile range), except as otherwise indicated. OR, odds ratio; CI, confidence interval.

* Recent admission was defined as patients admitted between 1 January 1997 and survey date. Recent transfer was defined as transfer within 1 month before specimen collection date.
there was a lower VRE prevalence than in inpatients at ACFs, and ~77% of VRE-colonized LTCF residents had been admitted to an ACF in the 7 months before our prevalence survey.

Transfer of residents between LTCFs was not a common occurrence, and this was unlikely to have contributed to the dissemination of VRE to multiple facilities in the region. In addition, a single strain type was implicated in the spread of VRE to a majority of the facilities with colonized residents. The only other strain types isolated were from two health care facilities that were geographically remote from other health care facilities in the SDHD region. These two facilities had case patients who had been transferred between the two facilities and from ACFs outside the SDHD region.

Now that VRE is established in multiple facilities in this community, the epidemiology of transmission may change. In LTCFs, persistent environmental contamination and health care worker hand colonization may exceed that of ACFs [4]. This may result in intrafacility VRE transmission in LTCFs, with a subsequent increase in the prevalence of VRE colonization. Eventually, LTCFs may become a reservoir of VRE-colonized persons, contributing to reintroduction of VRE to ACFs during each admission.

Several studies have documented the efficacy of CDC recommendations in limiting VRE transmission within ACFs [6, 7, 17, 18]. These include cohorting or isolation precautions with appropriate gown and glove use and restriction of antimicrobial use, particularly vancomycin [19]. Whether these measures are practical, feasible, and effective in LTCFs has not been established. Regardless, the identification of VRE-colonized patients before admission to a facility enables early implementation and emphasis on infection-control measures (e.g., judicious roommate selection, improved hand hygiene by health care workers, and attempts to minimize environmental contamination). These infection-control measures should minimize VRE transmission to other residents.

Large-scale prevalence surveys are easier to accomplish with a rapid and simple diagnostic test. The VST performed well in this capacity. The VST has not been approved by the Food and Drug Administration, reportedly because it did not perform well in detecting enterococcal species with low or moderate levels of vancomycin resistance. In this study, although not all VRE isolates were detected, the VST accurately identified the VRE species of epidemiologic importance in this community (i.e., *E. faecium* with high-level vancomycin resistance). Although the sensitivity of VST was not optimal, the test correlated well with conventional screening methods and performed well on other measures of validity (i.e., specificity, positive predictive value, and negative predictive value). Such a screening method is essential if large population surveys are to be performed with limited personnel and financial resources.

One limitation to our study was the poor participation rate by ACF inpatients. The poor participation may have limited an accurate assessment of the VRE prevalence in ACFs. However, in the only ACF that had closed a unit because of a high rate of VRE colonization, patient participation in the intensive care units and on the previously closed unit was excellent (91%), suggesting that, in this facility, high-risk patient populations were not excluded. In addition, assuming 100% participation at all four ACFs, and assuming that all ACF residents that did not participate were VRE-negative, the VRE prevalence in ACFs would have remained greater than twice the prevalence detected in LTCFs (3.5% vs. 1.7%). Because the case-control study was stratified by facility type, the strong association between VRE colonization among LTCF residents and recent

### Table 2. Comparison of characteristics of case and control patients from acute care facilities, Siouxland District Health Department, July 1997.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case patients</th>
<th>Control patients</th>
<th>Matched OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Categorical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimicrobial receipt in week before specimen collection</td>
<td>9 (90.0)</td>
<td>10 (45.5)</td>
<td>11.5 (1.1–119)</td>
<td>.02</td>
</tr>
<tr>
<td>Intravenous antimicrobial receipt in week before specimen collection</td>
<td>8 (80.0)</td>
<td>7 (31.8)</td>
<td>8.9 (1.4–55.4)</td>
<td>.02</td>
</tr>
<tr>
<td>Admitted from a long-term care facility</td>
<td>3 (30.0)</td>
<td>0 (0.0)</td>
<td>≥(1.5–∞)</td>
<td>.05</td>
</tr>
<tr>
<td>Continuous</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>7.5 (5–17)</td>
<td>3.0 (1–6)</td>
<td>.02</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. (%) or median (interquartile range), except as otherwise specified. OR, odds ratio; CI, confidence interval.

### Table 3. Summary of the 12 long-term care facilities with vancomycin-resistant enterococci (VRE)–colonized residents, Siouxland District Health Department.

<table>
<thead>
<tr>
<th>Facility</th>
<th>No. of VRE-colonized residents</th>
<th>No. with strain type a</th>
<th>No. recently hospitalizedb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facility</td>
<td>(n = 30)</td>
<td>(n = 28)</td>
<td>(n = 23)</td>
</tr>
<tr>
<td>A</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>D</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>E</td>
<td>7</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>F</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>G</td>
<td>2</td>
<td>2</td>
<td>2</td>
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<tr>
<td>H</td>
<td>5</td>
<td>5</td>
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<td>I</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>J</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>K</td>
<td>4</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>L</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*Includes admission or transfer to acute care facility between 1 January 1997 and survey date.
hospitalization would not have been diminished by increased ACF patient participation.

We were unable to determine in which facility or type of facility VRE initially was introduced. However, regardless of the type of facility in which VRE entered the community, our data suggest that, after the introduction of VRE into the community, intrafacility VRE transmission occurred in ACFs with subsequent transfer of VRE-colonized patients to LTCFs. This is not surprising since known risk factors for VRE acquisition (e.g., use of antimicrobials and increased severity of illness) [2, 14, 20] are more common to patients at ACFs.

In a health care community in which VRE-colonized or -infected patients have recently been identified, screening of high-risk ACF patients (e.g., those with prolonged lengths of stay, increased severity of illness, or antimicrobial use) at the time of interfacility transfer may prevent the unknown dissemination of VRE-colonized patients to multiple LTCFs. This should prevent the development of an unrecognized reservoir of VRE-colonized patients and minimize unknown VRE transmission within and between health care facilities. Once introduced, VRE becomes an infection-control challenge for all health care facilities within a community. A recent study in 35 San Francisco Bay Area hospitals demonstrated the rapid dissemination of VRE, from 3% of the hospitals in 1993 to 95% in 1996 [21]. Another study suggests that a high prevalence of VRE is the strongest determinant of VRE transmission within an intensive care unit [13].

These data suggest that VRE emerged at ACFs among patients with long hospital stays and a history of antimicrobial use and that discharge of these patients resulted in dissemination of VRE to multiple LTCFs. If other regions are to avoid such community-wide VRE transmission among health care facilities, the coordination of VRE detection and control measures will be necessary. Communication between receiving and discharging facilities should occur before patient transfer, to identify VRE-colonized patients before admission and allow implementation of infection-control practices at the time of admission. Last, further studies are needed to evaluate risk factors for intrafacility VRE transmission between LTCFs and to determine feasible and effective infection-control measures in these facilities where the risk of VRE transmission may be high.

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