

# COST-EFFECTIVENESS OF PERIRECTAL SURVEILLANCE CULTURES FOR CONTROLLING VANCOMYCIN-RESISTANT *ENTEROCOCCUS*

Carlene A. Muto, MD, MS; Eve T. Giannetta, BSN, CIC; Lisa J. Durbin, BS, MT (ASAP); Barbara M. Simonton, CLT (HEW); Barry M. Farr, MD, MSc

## ABSTRACT

**BACKGROUND:** Several hospitals opting not to use active surveillance cultures to identify carriers of vancomycin-resistant *Enterococcus* (VRE) have reported that adoption of other parts of the Centers for Disease Control and Prevention guideline for controlling VRE has had little to no impact. Because use of surveillance cultures and contact isolation controlled a large outbreak at this hospital, their costs were estimated for comparison with the excess costs of VRE bacteremias occurring at a higher rate at a hospital not employing these measures.

**SETTING:** Two university hospitals.

**METHODS:** Inpatients deemed high risk for VRE acquisition at this hospital underwent weekly perirectal surveillance cultures. Estimated costs of cultures and resulting isolation during a 2-year period were compared with the estimated excess costs of more frequent VRE bacteremias at another hospital of similar size

and complexity not using surveillance cultures to control spread throughout the hospital.

**RESULTS:** Of 54,052 patients admitted, 10,400 had perirectal swabs taken. Cultures and isolation cost an estimated \$253,099. VRE culture positivity was limited to 193 (0.38%) and VRE bacteremia to 1 (0.002%) as compared with 29 bacteremias at the comparison hospital. The estimated attributable cost of VRE bacteremia at the comparison hospital of \$761,320 exceeded the cost of the control program at this hospital by threefold.

**CONCLUSIONS:** The excess costs of VRE bacteremia may justify the costs of preventive measures. The costs of VRE infections at other body sites, of deaths from untreatable infections, and of dissemination of genes for vancomycin resistance also help to justify the costs of implementing an effective control program (*Infect Control Hosp Epidemiol* 2002;23:429-435).

The Centers for Disease Control and Prevention (CDC) guideline for isolation recommends contact isolation for "patients known or suspected to be colonized or infected with epidemiologically important microorganisms."<sup>1</sup> The CDC made clear that vancomycin-resistant *Enterococcus* (VRE) was considered "epidemiologically important" by issuing a separate guideline just for control of VRE.<sup>2</sup> The guideline indicated that data were limited and that research would be required to elucidate more fully the epidemiology of VRE and to determine cost-effective strategies for control. The guideline made several recommendations, the first of which was to educate healthcare workers as to why VRE was epidemiologically important and needed to be isolated. Active surveillance cultures to identify and isolate VRE-colonized patients were recommended "for more efficient containment."<sup>2</sup>

The data from three hospitals opting not to use active surveillance cultures to identify and isolate patients colonized with VRE as a control measure throughout the hospital have been used to suggest that other parts of the CDC guideline for control of VRE, such as vancomycin restriction and enhanced disinfection of clinical areas, have had

little to no impact on the increasing rates of VRE infection.<sup>3-5</sup>

In 1994, VRE was introduced into our facility and resulted in an outbreak that included three primary bacteremias and two secondary bacteremias. Active surveillance for VRE was initiated for all high-risk patients. During the first month of culturing, eight hospital wards were found to be involved with an overall VRE prevalence of 30%, including one intensive care unit (ICU), which had a 100% prevalence. Because active surveillance cultures and contact isolation for patients identified as being colonized helped to rapidly control this large outbreak<sup>6</sup> and low levels of VRE colonization were maintained during the ensuing 2 years, the costs of these measures during this 2-year period were estimated. Had no intervention been implemented, we suspect our rates of VRE colonization and infection would have increased as they did throughout the United States.<sup>7</sup> The cost-effectiveness of this approach was also estimated by comparing these costs with the estimated attributable costs due to the higher rate of VRE bacteremia at a comparison hospital of similar size and complexity that chose not to use this approach throughout the hospital.<sup>5</sup>

*The authors are from the University of Virginia Health System, Charlottesville, Virginia.*

*Address reprint requests to Barry M. Farr, MD, MSc, Box 473, University of Virginia Health System, Charlottesville, VA 22908.*

*Presented at the Ninth Annual Meeting of the Society for Healthcare Epidemiology of America; April 18-20, 1999; San Francisco, CA.*

**TABLE 1**  
CRITERIA USED TO IDENTIFY PATIENTS AT INCREASED RISK FOR ACQUISITION OF VANCOMYCIN-RESISTANT *ENTEROCOCCUS*

Unit Type	Length of Stay	Other Requirement
ICU	≥ 4 days	None
Selected high-risk wards	≥ 5 days	Plus antibiotics
All other wards	≥ 6 days	Plus antibiotics
Any	≥ 3 weeks	None
Any	Any	Co-colonization with other resistant flora (ie, MRSA)
Any	Any	Roommate of newly identified VRE-colonized patient

ICU = intensive care unit; MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = vancomycin-resistant *Enterococcus*.

## METHODS

### Population

The University of Virginia provides primary and tertiary care in a 600-bed hospital, which includes 31 wards including 9 ICUs. This hospital admitted, on average, 2,252 patients per month during 1995 and 1996. The comparison university hospital is a 757-bed facility that admitted 59,196 patients in a 26-month period (from May 1992 through June 1994) or, on average, 2,277 patients per month.<sup>5</sup> For purposes of comparison it was therefore assumed that 54,648 patients would have been admitted during a 24-month period.<sup>5</sup> Both hospitals offer a cancer center, a trauma center, and transplantation services.

### Surveillance for Nosocomial Infections

Hospital-wide surveillance for nosocomial infections was conducted at this hospital using the Kardex method as previously described<sup>8</sup> and definitions published by the CDC.<sup>9</sup> Methods and definitions used at the comparison hospital were also previously published.<sup>5</sup>

### Active Surveillance Cultures

Inpatients at this hospital were evaluated weekly by one of four infection control practitioners (ICPs) to identify those at increased risk for becoming VRE culture positive. Criteria for establishing increased risk consisted of varying combinations of antimicrobial use, hospital location, and duration of stay (Table 1). Patients deemed to be at high risk for VRE acquisition had perirectal surveillance cultures taken for VRE. A total of 10,400 perirectal surveillance cultures for VRE were collected during 1995 and 1996 from patients meeting these criteria. Nurses spent approximately 20 hours per week selecting patients, labeling swabs, and obtaining cultures. Swabs were processed and cultures evaluated in the Hospital Epidemiology Laboratory. Cultures obtained to control nosocomial transmission have been considered necessary for patient safety. The rare high-risk patient not wishing to have a culture

taken (approximately 1 in 5,000) was placed in contact precautions.

### Microbiology

Isolation of VRE was accomplished by standard methods. Perirectal swabs were inoculated onto blood agar (BBL Prepared Media TSA II 5% SB, Becton Dickinson, Cockeysville, MD) and campy CVA media (BBL Prepared Media, Becton Dickinson), which contains cefoperazone (20 mg/L), vancomycin (10 mg/L), and amphotericin B (2 mg/L). Colonies were then Gram stained. Gram-positive organisms were subcultured and tested for catalase and pyrrolidonyl-beta-naphthylamide (Identical-AE, PML Microbiologicals, Inc., Tualatin, OR) production. Isolates were speciated using API Strep strips (bioMérieux, Inc., Hazelwood, MO). Vancomycin resistance was confirmed using Kirby-Bauer disk diffusion (Mueller-Hinton agar, Baxter Healthcare Corp., Columbia, MD). Vancomycin-resistant organisms were defined as those with a zone of inhibition of 14 mm or less from the 30- $\mu$ g vancomycin-impregnated disk. E-tests were used to assess rare isolates with apparent intermediate resistance (AB BIODISK, Piscataway, NJ).

### Cost of Contact Isolation for VRE-Colonized Patients

The cost of entering a room of a patient in contact isolation was estimated by summing the costs of gowns (82 cents apiece) and examination gloves (6.5 cents per pair) and the additional labor cost of 29.4 cents for approximately 1 minute of time needed to don and remove these items.<sup>10</sup> These totaled \$1.18 per visit (Table 2). It was estimated that healthcare personnel entered a patient's room an average of 25 to 50 times per day<sup>10</sup> and that patients with VRE remained hospitalized for a mean of 19 days after being identified as colonized with VRE.<sup>6</sup>

### Cost of VRE Identification

The cost for laboratory supplies for each initial culture was \$1.76 (Table 3). The additional cost for laboratory supplies for processing presumptively positive cultures was \$7.76 per positive culture. Technologist time was estimated to be 10 minutes per negative culture and 15 minutes per positive culture at a rate of \$17 per hour. Therefore, the laboratory cost of each negative culture was \$4.59 and the cost of each positive culture was \$13.77.

In addition to laboratory costs, nurses spent approximately 20 hours per week selecting and swabbing approximately 100 patients and labeling swabs at \$20 per hour. No new personnel were hired to do this work during the first year. A licensed practical nurse swabbed patients during the second year, resulting in lower nursing costs for this work than represented in the calculations (Table 3).

### Excess Costs of VRE Bacteremia

One case-control study found that VRE bacteremia was associated with an 18.1-day prolongation of hospital stay, a \$27,190 increase in hospital costs, and 29% attributable mortality as compared with vancomycin-susceptible *Enterococcus*

**TABLE 2**  
COST OF CONTACT ISOLATION FOR EACH PATIENT COLONIZED WITH VANCOMYCIN-RESISTANT *ENTEROCOCCUS*

Itemization	Item Cost per Patient Visit	Item Costs per Patient Hospitalization
Gown	\$0.820	$37.5^* \times 19^\dagger \times 0.820 = \$584.25$
Gloves	\$0.064	$37.5 \times 19 \times 0.064 = \$45.60$
Labor (don and remove)	\$0.294	$37.5 \times 19 \times 0.294 = \$209.48$
Total	\$1.18	\$839.33

\*Estimated number of visits to isolation rooms per day.

†Estimated number of days of hospitalization after turning culture positive for vancomycin-resistant *Enterococcus*.

**TABLE 3**  
TOTAL COST OF ACTIVE SURVEILLANCE CULTURES FOR VANCOMYCIN-RESISTANT *ENTEROCOCCUS*

Itemization	Cost	No. of Cultures	Total Cost
Initial laboratory supply cost per culture	\$1.76	10,400	\$18,304
Extra laboratory supply cost per positive culture	\$7.76	193	\$1,498
Technologists' time			
10 minutes per negative culture	\$2.83	10,207*	\$28,886
15 minutes per positive culture	\$4.25	193 <sup>†</sup>	\$820
Nurses' time <sup>‡</sup>			
20 hours per week	\$400 per week	104 weeks	\$41,600
Total cost of identification			\$91,108

\*Estimated number of negative cultures.

†Number of positive cultures.

‡Estimated time for identifying and swabbing patients.

(VSE) bacteremia.<sup>11</sup> A more recent case-control study using cases with VRE bacteremia and controls matched by age, gender, date, length of hospital stay before onset of bacteremia in the case, principal diagnosis, and complexity level reported that VRE bacteremia was associated with a 28-day increase in length of hospital stay, mean excess hospital costs of \$79,589, and attributable mortality of 17.7%.<sup>12</sup>

### **Cumulative Excess Costs Due to VRE Bacteremia at the Comparison Hospital**

One primary VRE bacteremia occurred at the University of Virginia hospital during 1995 and 1996. Thirty-one primary VRE bacteremias occurred at the comparison hospital during a 26-month period.<sup>5</sup> It was therefore assumed that 29 bacteremias would have occurred during a 24-month period. The comparison hospital thus had 28 more VRE bacteremias than this hospital during a 2-year period. The estimated attributable cost of these 28 extra VRE bacteremias was obtained by multiplying the number of bacteremias by the estimate of the attributable cost of VRE bacteremia (compared with that of VSE bacteremia) cited above.<sup>11</sup>

### **Cost-Benefit Analysis**

The estimated excess cost of the 28 extra VRE bacteremias at the comparison hospital was compared with the

estimated cost of active surveillance cultures and resulting isolation of VRE-colonized patients during a 2-year period to assess the relative cost-effectiveness of these control measures.

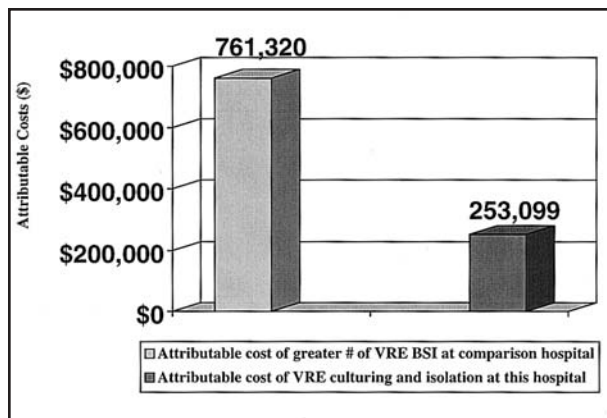
### **Statistical Methods**

Colonization and bloodstream infection rates were compared using a chi-square test or a Fisher's exact test when any chi-square cell expected value was less than 5. *P* values of less than .05 were considered significant. Confidence intervals were calculated using standard methods.<sup>13</sup>

## **RESULTS**

### **Rates of Colonization**

Of 54,052 patients admitted to this hospital during the 2-year period, 10,400 were deemed high risk and had perirectal swabs taken. Of these, 193 had a positive culture for VRE resulting in colonization prevalence rates of 0.37% for 1995 and 0.39% for 1996. The overall colonization prevalence rate at the University of Virginia was 0.38% as compared with 20% from several point-prevalence studies at the comparison hospital<sup>5</sup> (relative risk [RR] = 0.02; 95% confidence interval [CI<sub>95</sub>], 0.01 to 0.03;  $P < 1 \times 10^{-7}$ ).



**FIGURE.** An estimate of the attributable cost of 28 additional vancomycin-resistant *Enterococcus* (VRE) bacteremias at the comparison hospital not using active surveillance cultures to control the spread of VRE throughout the hospital (ie, 29 at that hospital as compared with 1 at this hospital during the 2-year study period), and an estimate of the attributable cost of surveillance cultures and resulting contact isolation at this hospital. BSI = bloodstream infection.

### Rates of Infection and Projected Benefit of Surveillance Cultures

The cumulative incidence of all types of VRE infections at this hospital was 0.02% (12 of 54,052) during the 2-year period. Surveillance cultures help identify VRE-colonized patients so that isolation precautions can be implemented. Isolation limits cross-transmission,<sup>6</sup> resulting in a lower prevalence of VRE colonizations and ultimately VRE bacteremias. The benefit of isolating VRE patients identified by active surveillance cultures at our hospital was to ultimately limit VRE bacteremia to 1 patient (0.002%) during the 2-year period as compared with 29 (0.05%) of an estimated 54,648 patients admitted to the comparison hospital during a 2-year period (RR = 0.03; CI<sub>95</sub>, 0.00 to 0.26;  $P = 1 \times 10^{-6}$ ).

### Estimated Costs of VRE Identification and Isolation

There were 10,207 negative cultures (\$4.59 per culture) during the 2-year period at an estimated laboratory cost of \$46,850 and 193 positive cultures (\$13.77 per culture) at an additional cost of \$2,658. The cost of nurses' time amounted to an estimated \$41,600. The total cost of identification was thus \$91,108 (Table 3). The cost of isolation was estimated at \$1.18 per patient visit. Patients with VRE were assumed to have remained hospitalized for a mean of 19 days based on the study of Byers et al.,<sup>6</sup> resulting in an isolation cost of \$839.33 per hospitalization per patient (Table 2). When this cost per isolation patient was multiplied by the 193 isolation patients, a total estimated isolation cost of \$161,991 was the result. The total estimated cost for surveillance cultures and isolation was thus \$253,099 during the 2-year period.

### Comparison of Costs at the Two Hospitals

The estimated attributable cost of the additional 28 VRE bacteremias at the comparison hospital was \$761,320.

This excess cost from a higher rate of VRE bacteremia exceeded the cost of the VRE prevention program at this hospital by threefold (Figure).

### DISCUSSION

VRE infections are important because of rapid spread, prolongation of hospital stay, greater difficulty achieving satisfactory therapy, and higher attributable mortality. From 1988 to 2000, the prevalence of vancomycin resistance among enterococcal infections in National Nosocomial Infections Surveillance System hospitals rose from 0% to 26%.<sup>7</sup>

VRE bacteremia has been associated with significantly higher attributable mortality than has bacteremia due to antibiotic-susceptible strains of enterococci in multiple studies.<sup>11,14-23</sup> Although some studies adjusting for severity of illness and other prognostic variables have concluded that patients with VRE suffer higher mortality merely because of greater comorbidity and higher underlying severity of illness,<sup>15,19,20</sup> others have concluded that the antibiotic resistance per se contributes to the higher mortality.<sup>11,18,23</sup> One study adjusted for severity of illness and found that VRE bacteremia was still associated with a doubling of the risk of death, which approached statistical significance.<sup>22</sup> Another reported that 46% of neutropenic patients receiving a bone marrow transplant died of VRE bacteremia as compared with none with VSE bacteremia.<sup>14</sup>

Cost has become an increasingly important determinant of healthcare practice patterns during the past decade.<sup>24-29</sup> The excess costs of VRE bacteremias during a 2-year period at a hospital of comparable size and complexity not using active surveillance cultures as a control measure throughout the hospital appeared to greatly exceed the cost of the prevention program at this hospital as estimated in the current study. For this purpose, the attributable cost of VRE bacteremia at the comparison hospital was the excess cost for VRE bacteremia as compared with VSE bacteremia. This means that even if the rates of enterococcal bacteremia had been equal at the two institutions, the hospital with the higher rates of resistant organisms would bear a higher cost. It thus appears that the attributable costs of VRE bacteremias could be used to justify the costs of a program for preventing these infections.

Published estimates of the attributable cost of VRE bacteremia have ranged from \$18,000<sup>30</sup> to \$79,589.<sup>12</sup> The lower estimate was published on the CDC web site without a methods statement and without providing the source of the data. The estimate used in the current study (\$27,190) was based on comparison with the costs of VSE bacteremia in a case-control study.<sup>11</sup> For comparison, other estimates of the total excess cost related to nosocomial bloodstream infection have ranged from \$3,517<sup>31</sup> to \$33,268.<sup>32</sup> The lower end of the range was derived from an uncontrolled case series conducted in 1975 that included only eight cases of bloodstream infection.<sup>33</sup> That estimate was published in 1981<sup>33</sup> and again in 1992<sup>31</sup> after adjustment for inflation. If used for comparison with the data in this study, it would require adjustment for subsequent inflation and the greater

increase in the cost of health care during this interval. The reliability of that estimate is questionable due to the small sample size of the 1975 study, its lack of uninfected control patients, and the possibility of change during the intervening 27 years. Of note, the authors of the original study stated that they had probably underestimated the cost.<sup>33</sup> It was \$29,751 lower than the attributable cost of nosocomial bloodstream infection calculated in a more recent case-control study.<sup>32</sup> The latter estimate was derived using control patients without bacteremia matched for ward location and age. The attributable cost of bloodstream infections in surviving patients in that study was found to be \$40,890 per infection.

A recent study at a university hospital that was performed in collaboration with the CDC found that control measures including antibiotic control, active surveillance cultures, and contact precautions for VRE resulted in savings for that hospital of \$189,318 per year,<sup>34</sup> lending support to the view that prevention of VRE infection might be cost-effective. Another recent study reported that use of active surveillance cultures for VRE and for multidrug-resistant Enterobacteriaceae can enhance infection control efforts by early detection and containment of patients harboring these resistant organisms. The added direct cost of that comprehensive surveillance program (\$200,000) was minimal when compared with overall healthcare dollars saved (\$2,184,050) from prevention of healthcare-associated infections.<sup>35</sup>

Identification and isolation of colonized patients has resulted in control of multiple VRE outbreaks<sup>6,36-45</sup> even in the absence of control of antibiotics except vancomycin, which has not been associated with control of VRE when used alone.<sup>3,5</sup> Some may wonder whether such outbreaks happened to end by chance alone right after implementing these control measures. This is unlikely given that the experience at U.S. hospitals not implementing these measures has almost universally been the establishment of endemicity. One hospital reported that stopping such control measures in two wards was associated with a statistically significant increase in the VRE incidence rate.<sup>46</sup> Resuming these control measures was associated with a significant decrease in the VRE incidence rate.

Although some studies have found higher sensitivity of perirectal cultures using broth enhancement, a recent study found no difference using standard plated media methodology<sup>47</sup> and directly plated cultures have been associated with successful control of both epidemic and endemic VRE.<sup>6,37,38,45,48</sup> The results of perirectal cultures were found to be 100% concordant with those of cultures of stool and rectal swabs in one study.<sup>49</sup> Some may be concerned that this approach was associated with a low yield from active surveillance cultures in the current study as we found only 1.9% (193 of 10,400) of all patients who had cultures to be VRE positive. It should be remembered that when VRE was first recognized at this hospital, active surveillance cultures found 30% of all patients screened on the outbreak wards to be culture positive. When spread was controlled, VRE infections were prevented, resulting in a

much lower positivity rate for subsequent surveillance cultures.<sup>6</sup> The active surveillance cultures were never stopped because complete eradication of the pathogen was never achieved. This may have been because a few colonized patients might not have been identified and isolated as the sensitivity of the culture has never been 100%<sup>47</sup> and because some high-risk patients may not have had cultures. Additionally, new reservoirs in surrounding health-care facilities began to emerge.

A higher prevalence for VRE positivity has been reported when VRE cultures were done on stool submitted for *Clostridium difficile* testing. Reported yields with that approach have been 16.5% and 19.8%.<sup>50,51</sup> However, a recent study compared cultures of stools submitted for *C. difficile* screening with active rectal surveillance cultures for VRE. The authors found that VRE prevalence was 10.4% in stools submitted for *C. difficile* testing, but 52% of patients with positive results on VRE culture would have been missed if this had been the only approach used.<sup>52</sup> The authors concluded that VRE cultures of stool submitted for *C. difficile* testing would not effectively identify the full reservoir for spread.

Some may wonder whether antibiotic control would be a more cost-effective approach to the problem because eliminating excessive and inappropriate antibiotic prescriptions saves money and decreases the selection pressure for antibiotic resistance. Two studies found threefold reductions in VRE prevalence by greatly reducing or stopping the use of one or more third-generation cephalosporins and increasing the use of beta-lactam-beta-lactamase inhibitor combinations coupled with implementation of measures for preventing spread.<sup>53,54</sup> In one, the prevalence almost doubled again with a switch back to the third-generation cephalosporin while trying to hold the measures for preventing spread constant. These are useful findings that suggest that antibiotic control will indeed be helpful in controlling antibiotic-resistant pathogens such as VRE. However, the reduced prevalence rates cited in these two studies were still 30-fold or more higher than the prevalence maintained during a 2-year period at this hospital without use of an antibiotic control program, as described in the current study. Also, most hospitals recently surveyed throughout Virginia and North Carolina related that they already had antibiotic control programs, but that their VRE rates still kept rising.<sup>55</sup> More studies are needed of the utility of various approaches by antibiotic control programs. The interrelationship between optimal therapy for individual patients (eg, who might have serious, penicillin-resistant *Streptococcus pneumoniae* infection usually treated with a third-generation cephalosporin) and optimal therapy for populations of patients requires further study with the goal of providing optimal therapy to individuals while preventing further development of antimicrobial resistance. Another recent study reported that anti-anaerobic activity was most predictive of potentiation of VRE growth in patients' colonic contents,<sup>56</sup> suggesting that beta-lactam-beta-lactamase inhibitor combinations may inhibit VRE in one way, but potentiate it in another.

The current study suggests that active surveillance cultures for VRE and contact isolation may cost less than the excess costs of VRE bacteremias that occur at a much higher rate in the absence of effective control measures. This is notable because these savings occurred at a hospital that had already endured a large VRE outbreak and controlled it using this approach,<sup>6</sup> showing that the lower prevalence was maintained because these measures had controlled epidemic spread and kept it from recurring. If VRE primary bacteremias had continued at the same rate of occurrence as before implementation of control measures (ie, 3 during 2 months), then 36 primary bacteremias would have been expected during 2 years, a frequency similar to that of the comparison hospital and significantly higher than the 1 bacteremia that did occur. These findings are also notable because this hospital, with one of the highest acuity of illness levels in the state, was surrounded by other hospitals not taking this approach with much higher rates of VRE infection, not unlike that in the comparison hospital.<sup>55</sup> This suggests that although geographic variation has been reported in VRE prevalence,<sup>57</sup> the difference in prevalence between the two hospitals being compared, which are in cities that are 154 miles apart, was probably not due to geographic differences.

The cost of VRE infections at other body sites, the human costs of deaths from completely untreatable infections, and the cost of allowing genes for vancomycin resistance to spread throughout the hospital population also help to justify the costs of identifying colonized patients and implementing effective barrier precautions. Allowing uncontrolled spread may result in still greater public health problems if those genes are transferred to other more virulent species. Such transfer had been documented to occur in experimental conditions both *in vitro* and *in vivo*,<sup>58</sup> and may have been documented recently in a clinical isolate.<sup>59</sup> Twenty-five centuries ago, Hippocrates advised that physicians should "first, do no harm." Doing no harm in this new millennium would presumably include preventing the spread of antibiotic-resistant infections that are more costly and more lethal.

## REFERENCES

- Garner JS. Guideline for isolation precautions in hospitals: the Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1996;17:53-80.
- Anonymous. Recommendations for preventing the spread of vancomycin resistance: recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC). *MMWR* 1995;44(RR-12):1-13.
- Slaughter S, Hayden MK, Nathan C, et al. A comparison of the effect of universal use of gloves and gowns with that of glove use alone on acquisition of vancomycin-resistant enterococci in a medical intensive care unit. *Ann Intern Med* 1996;125:448-456.
- Quale J, Landman D, Atwood E, et al. Experience with a hospital outbreak of vancomycin-resistant enterococci. *Am J Infect Control* 1996;24:372-379.
- Morris JG, Shay DK, Hebden JN, et al. Enterococci resistant to multiple antimicrobial agents, including vancomycin: establishment of endemicity in a university medical center. *Ann Intern Med* 1995;123:250-259.
- Byers KE, Anglim AM, Anneski CJ, et al. A hospital epidemic of vancomycin-resistant *Enterococcus*: risk factors and control. *Infect Control Hosp Epidemiol* 2001;22:140-147.
- Centers for Disease Control and Prevention. National Nosocomial Surveillance (NNIS) System report, data summary for January 1990-May 1999, issued 1999. *Am J Infect Control* 2001;29:404-421.
- Wenzel RP, Osterman CA, Hunting KJ, Gwaltney JM Jr. Hospital-acquired infections: I. Surveillance in a university hospital. *Am J Epidemiol* 1976;103:251-260.
- Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control* 1988;16:128-140.
- Jernigan JA, Clemence MA, Stott GA, et al. Control of methicillin-resistant *Staphylococcus aureus* at a university hospital: one decade later. *Infect Control Hosp Epidemiol* 1995;16:686-696.
- Stosor V, Peterson LR, Postelnick M, Noskin GA. *Enterococcus faecium* bacteremia: does vancomycin resistance make a difference? *Arch Intern Med* 1998;158:522-527.
- Song X, Perl TM. Vancomycin-resistant enterococcal (VRE) nosocomial bloodstream infections (BSI): the attributable mortality, length of stay, and excess cost. Presented at the 37th Annual Meeting of the Infectious Diseases Society of America; November 18-21, 1999; Philadelphia, PA. Abstract.
- Rosner B. *Fundamentals of Biostatistics*. Boston: Duxbury Thomsom Learning; 1990:171-177.
- Jernigan JA, Hadziyannis SC. Vancomycin-resistant *Enterococcus faecium* (VRE) bacteremia (B) in severely neutropenic patients. Presented at the 36th General Meeting of ICAAC; September 15-18, 1996; New Orleans, LA. Abstract J8:219.
- Shay DK, Maloney SA, Montecalvo M, et al. Epidemiology and mortality risk of vancomycin-resistant enterococcal bloodstream infections. *J Infect Dis* 1995;172:993-1000.
- Centers for Disease Control and Prevention. Nosocomial enterococci resistant to vancomycin: United States, 1989-1993. *MMWR* 1993;42:597-599.
- Edmond MB, Jones RN, Pfaller MA, Wallace SE, Wenzel RP. Multicenter surveillance for nosocomial enterococcal bacteremia: a comparison of vancomycin-sensitive vs vancomycin-resistant cases. *Infect Control Hosp Epidemiol* 1996;17(suppl):18.
- Linden PK, Pasculle AW, Manez R, et al. Differences in outcomes for patients with bacteremia due to vancomycin-resistant *Enterococcus faecium* or vancomycin-susceptible *E. faecium*. *Clin Infect Dis* 1996;22:663-670.
- Lautenbach E, Bilker WB, Brennan PJ. Enterococcal bacteremia: risk factors for vancomycin resistance and predictors of mortality. *Infect Control Hosp Epidemiol* 1999;20:318-323.
- Stroud L, Edwards J, Danzing L, Culver D, Gaynes R. Risk factors for mortality associated with enterococcal bloodstream infections. *Infect Control Hosp Epidemiol* 1996;17:576-580.
- Newell KA, Millis JM, Arnow PM, et al. Incidence and outcome of infection by vancomycin-resistant enterococcus following orthotopic liver transplantation. *Transplantation* 1998;65:439-442.
- Lucas GM, Lechtzin N, Puryear DW, Yau LL, Flexner CW, Moore RD. Vancomycin-resistant and vancomycin-susceptible enterococcal bacteremia: comparison of clinical features and outcomes. *Clin Infect Dis* 1998;26:1127-1133.
- Bhavnani SM, Drake JA, Forrest A, et al. A nationwide, multicenter, case-control study comparing risk factors, treatment and outcome for vancomycin-resistant and -susceptible enterococcal bacteremia. *Diagn Microbiol Infect Dis* 2000;36:145-158.
- Grumbach K, Osmond D, Vranizan K, Jaffe D, Bindman AB. Primary care physicians' experience of financial incentives in managed-care systems. *N Engl J Med* 1998;339:1516-1521.
- Simon SR, Pan RJ, Sullivan AM, et al. Views of managed care: a survey of students, residents, faculty, and deans at schools of medical schools in the United States. *N Engl J Med* 1999;340:928-936.
- Bodenheimer T. The Oregon Health Plan: lessons for the nation. *N Engl J Med* 1997;337:651-655.
- Cunningham PJ, Grossman JM, St. Peter RF, Lesser CS. Managed care and physicians' provision of charity care. *JAMA* 1999;281:1087-1092.
- Baker LC. Association of managed care market share and health expenditures for fee-for-service Medicare patients. *JAMA* 1999;281:432-437.
- Bindman AB, Grumbach K, Vranizan K, Jaffe D, Osmond D. Selection and exclusion of primary care physicians by managed care organizations. *JAMA* 1998;279:675-679.
- Centers for Disease Control and Prevention. Vancomycin-resistant enterococci (VRE) facts: 1999. Available at [www.cdc.gov/phtn/old/vrefacts.htm](http://www.cdc.gov/phtn/old/vrefacts.htm).
- Anonymous. Public health focus: surveillance, prevention, and control of nosocomial infections. *MMWR* 1992;41:783-787.
- Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients: excess length of stay, extra costs, and attributable mortality. *JAMA* 1994;271:1598-1601.
- Haley RW, Schaberg DR, Crossley KB, Von Allmen SD, McGowan JE Jr. Extra charges and prolongation of stay attributable to nosocomial infections: a prospective inter-hospital comparison. *Am J Med* 1981;70:51-58.

34. Montecalvo MA, Jarvis WR, Uman J, et al. Costs and savings associated with infection control measures that reduce transmission of vancomycin-resistant enterococci in an endemic setting. *Infect Control Hosp Epidemiol* 2001;22:437-442.
35. Hacek DM, Suriano T, Noskin GA, Kruszynski J, Reisberg B, Peterson LR. Medical and economic benefit of a comprehensive infection control program that includes routine determination of microbial clonality. *Am J Clin Pathol* 1999;111:647-654.
36. Boyce JM, Mermel LA, Zervos MJ, et al. Controlling vancomycin-resistant enterococci. *Infect Control Hosp Epidemiol* 1995;16:634-637.
37. Muto CA, Karchmer TB, Cage EG, Durbin LJ, Simonton BM, Farr BM. The utility of culturing roommates of patients with vancomycin-resistant enterococcus. Presented at the 8th Annual Meeting of the Society for Healthcare Epidemiology of America; April 5-7, 1998; Orlando, FL. Abstract 76:38.
38. Calfee DP, Giannetta E, Durbin LJ, Farr BM. Control of vancomycin-resistant *Enterococcus* colonization among inpatients at a tertiary care facility. Presented at the CDC Fourth Decennial International Conference in Conjunction with the 10th Annual Meeting of the Society for Healthcare Epidemiology of America; March 5-9, 2000; Atlanta, GA. Abstract 69:217.
39. Dembry L, Uzokwe K, Zervos M. Control of endemic glycopeptide-resistant enterococci. *Infect Control Hosp Epidemiol* 1996;17:286-292.
40. Jochimsen EM, Fish L, Manning K, et al. Control of vancomycin-resistant enterococci at a community hospital: efficacy of patient and staff cohorting. *Infect Control Hosp Epidemiol* 1999;20:106-109.
41. Karanfil LV, Murphy M, Josephson A, et al. A cluster of vancomycin-resistant *Enterococcus faecium* in an intensive care unit. *Infect Control Hosp Epidemiol* 1992;13:195-200.
42. Malik RK, Montecalvo MA, Reale MR, et al. Epidemiology and control of vancomycin-resistant enterococci in a regional neonatal intensive care unit. *Pediatr Infect Dis J* 1999;18:352-356.
43. Rubin LG, Tucci V, Cercenado E, Elipoulos G, Isenberg HD. Vancomycin-resistant *Enterococcus faecium* in hospitalized children. *Infect Control Hosp Epidemiol* 1992;12:700-705.
44. Rupp ME, Marion N, Fey PD, et al. Outbreak of vancomycin-resistant *Enterococcus faecium* in a neonatal intensive care unit. *Infect Control Hosp Epidemiol* 2001;22:301-303.
45. Ostrowsky BE, Trick WE, Sohn AH, et al. Control of vancomycin-resistant enterococcus in healthcare facilities in a region. *N Engl J Med* 2001;344:1427-1433.
46. Siddiqui AH, Harris AD, Hebden J, Wilson PD, Morris JG, Roghmann M. The effect of active surveillance for vancomycin-resistant enterococci in high-risk units on vancomycin-resistant enterococci incidence hospital-wide. *Am J Infect Control* 2002;30:40-43.
47. Reisner BS, Shaw S, Huber ME, et al. Comparison of broth enrichment and direct inoculation of solid media for recovery of vancomycin-resistant enterococci from peri-rectal and environmental surface samples. *Infect Control Hosp Epidemiol* 2000;21:775-779.
48. Muto CA, Posey K, Pokrywka M, et al. The value of identifying the vancomycin-resistant enterococci (VRE) reservoir using weekly VRE surveillance culturing (VRESC): "The iceberg melts." Presented at the 12th Annual Meeting of the Society for Healthcare Epidemiology of America; April 6-9, 2002; Salt Lake City, UT.
49. Weinstein JW, Tallapragada S, Farrel P, Dembry LM. Comparison of rectal and perirectal swabs for detection of colonization with vancomycin-resistant enterococci. *J Clin Microbiol* 1996;34:210-212.
50. Rafferty ME, McCormick MI, Bopp LH, et al. Vancomycin-resistant enterococci in stool specimens submitted for *Clostridium difficile* cytotoxin assay. *Infect Control Hosp Epidemiol* 1997;18:342-344.
51. Leber AL, Hindler JF, Kato EO, Bruckner DA, Pegues DA. Laboratory-based surveillance for vancomycin-resistant enterococci: utility of screening stool specimens submitted for *Clostridium difficile* toxin assay. *Infect Control Hosp Epidemiol* 2001;22:160-164.
52. Hacek DM, Bednarz P, Noskin GA, Zembower T, Peterson LR. Yield of vancomycin-resistant enterococci and multidrug-resistant Enterobacteriaceae from stools submitted for *Clostridium difficile* testing compared to results from a focused surveillance program. *J Clin Microbiol* 2001;39:1152-1154.
53. Bradley SJ, Wilson AL, Allen MC, Sher HA, Goldstone AH, Scott GM. The control of hyperendemic glycopeptide-resistant *Enterococcus* spp. on a haematology unit by changing antibiotic usage. *J Antimicrob Chemother* 1999;43:261-266.
54. Quale J, Landman D, Saurina G, Atwood E, DoTore V, Patel K. Manipulation of a hospital antimicrobial formulary to control an outbreak of vancomycin-resistant enterococci. *Clin Infect Dis* 1996;23:1020-1025.
55. Salgado C, Sherertz R, Karchmer T, et al. Public health initiative to control MRSA and VRE in Virginia and North Carolina. Presented at the 12th Annual Meeting of the Society for Healthcare Epidemiology of America; April 6-9, 2002; Salt Lake City, UT. Abstract 164:75.
56. Donskey CJ, Chowdhry TK, Hecker MT, et al. Effect of antibiotic therapy on the density of vancomycin-resistant enterococci in the stool of colonized patients. *N Engl J Med* 2000;343:1935-1932.
57. Jones RN, Marshall SA, Pfaller MA, et al. Nosocomial enterococcal bloodstream infections in the SCOPE Program: antimicrobial resistance, species occurrence, molecular testing results, and laboratory testing accuracy. SCOPE Hospital Study Group. *Diagn Microbiol Infect Dis* 1997;29:95-102.
58. Noble WC, Virani Z, Cree RG. Co-transfer of vancomycin and other resistance genes from *Enterococcus faecalis* NCTC 12201 to *Staphylococcus aureus*. *FEMS Microbiol Lett* 1992;72:195-198.
59. Anonymous. *Staphylococcus aureus* resistant to vancomycin: United States, 2002. *MMWR* 2002;51:565-567.