Editorial

Vancomycin-Resistant Enterococci: Pervasive and Persistent Pathogens

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Vancomycin-resistant enterococci (VRE) have emerged rapidly as important nosocomial pathogens in the United States since 1989.[1,2] VRE have been detected in hospitals in 40 states and are likely to be present in all 50 states (Tenover FC, Centers for Disease Control, Atlanta, GA, personal communication, September 1995). Although a majority of isolates initially were recovered from patients in intensive care units, VRE are now becoming increasingly prevalent among patients hospitalized on other wards.[3] Patients with malignancies or chronic renal failure, those undergoing organ transplants, and others who require prolonged hospitalization have been identified as being at increased risk of acquiring VRE.[2,4-13] Other risk factors that have been identified include previous antimicrobial therapy, exposure to contaminated equipment (electronic thermometers), and proximity to previously known VRE cases.[5,6,8,9] Previous vancomycin therapy has been the antimicrobial exposure most frequently implemented as a risk factor, although cephalosporins and antimicrobials with activity against anaerobes also have been identified as risk factors for colonization or infection in some institutions.[5,6,8,12,13]

Vancomycin most likely predisposes patients to colonization and infection with VRE by inhibiting the growth of normal gram-positive gut flora, and by providing a selective advantage for VRE that are colonizing a patient's gut or skin. Because vancomycin resistance of the *vanA* type is mediated by a complex cluster of seven genes (*vanR, vanS, vanH, vanA, vanX, vanY,* and *vanZ*) plus a resolvase and a transposase, simply treating a patient with vancomycin will not cause a vancomycin-susceptible strain to mutate to a vancomycin-resistant strain. The same probably is true for *vanB* type VRE, which possess a similar gene complex. This concept has important implications regarding the potential impact of restricting vancomycin use as a control measure. If no enterococci containing a *vanA* or *vanB* gene complex are present in a hospital, widespread use of vancomycin will not result in the emergence of *vanA* or *vanB* type VRE. Once such strains have been introduced into an institution, curtailing vancomycin use may help to control nosocomial spread of VRE by reducing the likelihood that patients who have acquired the organism will become heavily colonized or infected. However, limiting vancomycin use is unlikely to halt the spread of VRE unless effective surveillance and barrier precautions also are implemented.[13]

Clinical microbiology laboratories play a crucial role in routine surveillance for VRE. Susceptibility tests that have been demonstrated to detect vancomycin resistance accurately must be used, or VRE may not be identified.[14-16] Vancomycin resistance can be confirmed by inoculating enterococcal isolates onto a plate containing brain heart infusion (BHI) agar and 6 μg/mL of vancomycin.[15] Other methods of confirming vancomycin resistance among enterococci include the use of vancomycin E test strips or polymerase chain reaction assays for *vanA* or *vanB* genes.[17-20] Once VRE have been detected in a hospi-

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tal, it is desirable for the laboratory to test enterococcal isolates from all body sites for their susceptibility to vancomycin.[21,22] Laboratories that perform susceptibility tests only on enterococci recovered from normally sterile body fluids will detect only a fraction of clinical VRE isolates. For example, during two outbreaks at Miriam Hospital,[9,23] only 16% of VRE isolates recovered from clinical specimens were from blood cultures, and 25% were from urine cultures. The remaining 59% of VRE isolates detected in specimens submitted for clinical purposes were recovered from wounds (21%), sputum (12%), skin (10%), other body fluids (8%), catheter tips (6%), and other body sites (2%).

Clinical laboratories (or infection control program laboratory personnel, if available) should be prepared to process stool, rectal, or perirectal cultures obtained during periodic point prevalence surveys of patients on high-risk wards of affected facilities.[21] In an accompanying article in this issue of *Infection Control and Hospital Epidemiology,* Montecalvo and colleagues[24] report that prospective surveillance cultures of perirectal specimens obtained from hospitalized oncology patients established that colonization with VRE occurred 10 times more frequently than clinically apparent VRE infections. Their findings confirm earlier reports that prevalence surveys often detect VRE colonization in patients who have not been identified by clinical cultures.[5,6,9,11-13,23] The personnel time required to screen stool or perirectal cultures for VRE can be shortened by using a selective medium. Although BHI/vancomycin screening agar is useful for confirming vancomycin resistance among enterococcal isolates, it is not useful for screening stool specimens for VRE because it will support the growth of many other organisms. Examples of selective media that have been used for performing prevalence surveys include *Campylobacter* agar medium containing vancomycin (10 μg/mL), Columbia CNA agar plus 5% sheep blood with or without vancomycin (25 μg/mL), CNA agar with 5% sheep blood plus vancomycin (10 μg/mL) and amphotericin (1 μg/mL), *Enterococcus* agar with vancomycin (5 μg/mL), and kanamycin-aesculin-azide agar supplemented with vancomycin.[10,11,13,25,26] Further studies are underway to establish an optimal selective medium for VRE prevalence surveys.

The article by Montecalvo et al[24] also emphasizes the fact that patients may remain colonized with VRE for weeks or months and often still are colonized at the time of readmission to the hospital. Their findings support earlier reports of persistent VRE colonization among high-risk patients.[5,7,9] Green et al[7] reported that nearly 60% of liver transplant patients with VRE remained colonized for 12 or more weeks, and Livornese et al[5] found that a majority of patients remained colonized for greater than 3 months. Occasional patients who have remained positive for as long as 1 year have been reported.[9] The study reported in this issue found that some patients were persistently colonized with the same VRE strain, as demonstrated by pulsed-field gel electrophoresis, whereas others were positive for more than one strain during the period of follow up.[24] Because persistently colonized patients may reintroduce VRE into a facility on multiple occasions, hospitals should develop means of promptly identifying such patients at the time of readmission so they can be placed immediately in isolation pending repeat surveillance cultures.[9,21]

Once a patient has been newly identified to be colonized or infected with VRE, infection control personnel should be notified promptly, and appropriate isolation and barrier precautions should be implemented. Control measures designed to interrupt direct contact transmission would appear to be most important. Recovery of enterococci from the hands of healthcare workers suggests that transmission most commonly occurs via the hands of personnel.[11,27-29] Although contact isolation, as it was defined in 1983,[30] and body substance isolation[31] were designed to interrupt direct contact transmission, experience to date suggests that these approaches (as currently practiced) are not very effective in halting nosocomial spread of VRE.[6,9,11,26] Either compliance with contact isolation and body substance isolation is poor in affected facilities or these measures do not interrupt all modes of transmission by which resistant enterococci are spread. Poor compliance with recommended handwashing procedures and other barrier precautions, which has been documented in many studies,[13,32-37] is likely to be the most important cause of the apparent failure of contact isolation and body substance isolation to control VRE.

Another possible explanation for the seemingly poor track record of these barrier precaution systems in halting VRE is that they put little emphasis on the possible role that environmental contamination may play in transmission of enterococci. Contaminated electronic thermometers were implicated as a source of VRE transmission in one outbreak,[5] and enterococci have been recovered from 7% to 30% of environmental surfaces cultured during investigation of several other enterococcal outbreaks.[6,9,12,13,27-29,38-40] Since enterococci may remain viable for periods of several days to weeks on dry surfaces,[9,41] it seems plausible that contaminated surfaces may act as a reservoir from which personnel may contaminate their hands or clothing.

Body substance isolation requires that health-

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care workers wear gloves only when contact with a patient's moist body substances is anticipated and that gowns be worn only if personnel anticipate that they may soil their clothing while caring for a patient.[31] Personnel who intend to touch dry areas of the patient's skin or the patient's gown, bed linen, medical equipment, or other potentially contaminated environmental surfaces in the patient's room are not required to wear gloves. Similarly, contact isolation requires that gloves be worn only when touching known infective material (eg, colonized or infected wound), but not for touching other areas of the patient's skin, gown, bed linen, or medical equipment items.[30] Gowns are required only if soiling of the healthcare worker's clothing is likely to occur. As a result, these barrier precaution systems will not prevent the hands or clothing of personnel from coming in contact with other contaminated surfaces. I suspect that, in many instances, personnel are not aware that patient gowns, bed linen, and medical equipment may become contaminated with enterococci and do not perceive the need to wash their hands after touching such objects.

Recently, the Centers for Disease Control and Prevention's Hospital Infection Control Practices Advisory Committee issued new guidelines for preventing the spread of VRE.[21] The guidelines recommend that hospitals limit the use of both oral and intravenous vancomycin and also point out the important roles that prospective laboratory-based surveillance and prevalence surveys play in detecting colonized and infected patients. Gloves are recommended for all personnel entering the rooms of affected patients, and gowns are recommended if substantial contact with the patient or environmental surfaces in the patient's room is anticipated, or if the patient is incontinent or has diarrhea, an ileostomy, a colostomy, or wound drainage not contained by a dressing.[21] If possible, hospitals should dedicate the use of noncritical medical equipment such as rectal thermometers, stethoscopes, or sphygmomanometers to a single patient. If such items must be used for multiple patients, they should be disinfected between patients. The new guidelines also recommend that personnel remove gloves and gown before leaving the patient's room and either wash their hands with an antiseptic soap or use a waterless antiseptic agent.

At the Miriam Hospital, where two VRE outbreaks have been controlled successfully, we require all personnel entering the rooms of patients with VRE to wear both a gown and gloves regardless of their anticipated activities.[9,23] We favor this approach because we have documented that nurses may contaminate the front of their gowns with VRE while caring for affected patients.[23] Also, we suspect that personnel sometimes enter a room without anticipating any patient contact and then unexpectedly are called on to perform activities that involve contact with the patient or the patient's immediate environment.[35] Whether our more aggressive use of gowns provides better protection against transmission of VRE than routinely wearing gloves alone, or wearing gowns and gloves as recommended by the CDC, is not known.

Further studies are needed to better define the reservoirs and modes of transmission of resistant enterococci and to establish which control measures are most cost effective. Although several investigators in Europe have recovered VRE from farm animals and commercially processed chicken carcasses,[22,42] limited studies in three areas of the United States have not found VRE in chickens or other farm animals sampled to date.[22,43,44] Additional studies with larger sample sizes are needed to determine if food products distributed in the United States are contaminated with VRE, as this would have important implications regarding measures used to control VRE transmission.

More data also are needed regarding how frequently personnel contaminate their hands or clothing following contact with environmental surfaces, the level of contamination that occurs, and whether routine use of gowns leads to more effective control of VRE transmission. Finally, further studies are warranted to establish if some form of oral antimicrobial therapy or microbial interference therapy can reliably decolonize patients with persistent VRE gut colonization. The availability of such an agent would help to reduce the major reservoir of VRE in hospitals.

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