12-1-2021

Vancomycin-Resistant Enterococci: Epidemiology, Infection Prevention, and Control

Seema Joshi
Henry Ford Health, sjoshi5@hfhs.org

Anita B. Shallal
Henry Ford Health, ashalla2@hfhs.org

Marcus J. Zervos
Henry Ford Health, mzervos1@hfhs.org

Recommended Citation
Joshi S, Shallal A, and Zervos M. Vancomycin-Resistant Enterococci: Epidemiology, Infection Prevention, and Control. Infect Dis Clin North Am 2021; 35(4):953-968.

Vancomycin-Resistant Enterococci

Epidemiology, Infection Prevention, and Control

Seema Joshi, MD[a,*], Anita Shallal, MD[a], Marcus Zervos, MD[b]

KEYWORDS

• VRE • Infection control • Enterococci • Health-care–associated infections
• Antimicrobial stewardship

KEY POINTS

- Due to expanding resistance patterns, VRE infections are becoming more difficult to treat.
- Infection control practices are crucial in management of VRE infections and should be based on patient characteristics, hospital needs, and available resources.
- The use of active surveillance screening and contact precautions has not shown to reduce VRE transmission in endemic settings.
- Measures to interrupt indirect contact transmission, including hand hygiene, chlorhexidine bathing, environmental cleaning, and antimicrobial stewardship, are the main components for prevention and control of VRE.

SIGNIFICANCE OF VANCOMYCIN-RESISTANT ENTEROCOCCI COLONIZATION AND INFECTION

In the United States, enterococci have been ranked as the third most frequently reported pathogen across all types of adult health-care–associated infections in 2015 to 2017.[1] The rising concern for vancomycin-resistant enterococci (VRE) within hospital systems has placed a larger emphasis on revisiting infection control practices, as VRE infection has been known to be associated with excess mortality, prolonged hospitalization, and increased treatment costs.[2] Obtaining source control, and ensuring prompt susceptibility testing and appropriate choice of antimicrobial therapy are key in management of VRE infections.

VRE is defined as having a minimum inhibitory concentration to vancomycin of greater than or equal to 32 mg/mL based on the Clinical and Laboratory Standard Institute guidelines.[3] Enterococci intrinsically have developed a variety of resistance

[a] Division of Infectious Diseases, Henry Ford Hospital, CFP-3, 2799 W Grand Boulevard, Detroit, MI, USA; [b] Wayne State University, CFP-3, 2799 W Grand Boulevard, Detroit, MI, USA
* Corresponding author.
E-mail address: Sjoshi5@hfhs.org

Infect Dis Clin N Am 35 (2021) 953–968
https://doi.org/10.1016/j.idc.2021.07.002
id.theclinics.com

mechanisms. These include penicillin-binding proteins with low affinity to beta-lactams, production of beta-lactamases, and decreased cellular permeability to antibiotics. VRE infections in particular contain plasmid-based genotypes (most common *van*A), which encode resistance to glycoproteins.[4] Individuals who are at increased risk for developing infections due to VRE are those with multiple medical comorbidities, those who have received multiple courses of antibiotics in the past, and those who are critically ill. Common VRE infections include urinary tract infections associated with urethral catheters, bacteremia, catheter-related infections, endocarditis, wound infections, and intra-abdominal infections.[5] Enterococci are remarkable in their ability to develop rapid antimicrobial resistance. High-dose daptomycin and linezolid are agents for the treatment of VRE infections; however, emerging antibiotic resistance to these agents limits potential available therapies.[6,7]

EPIDEMIOLOGY

Most enterococci cause infection that originates from the intestinal flora, which can then spread and cause a variety of infections. Colonization with VRE generally precedes infection. There is a 10-fold increased risk of developing a VRE asymptomatic colonization compared with clinically recognized infection. The following individuals are at risk of VRE colonization: health care providers (HCPs), critically ill patients who have received long courses of antibiotics (in particular vancomycin, ceftriaxone, fluoroquinolones, and meropenem), individuals from long-term care facilities, solid-organ transplant patients, and patients with hematological malignancies.[8,9] Colonization can persist for months to years.

Vancomycin-resistant strains of enterococci have been endemic in large hospital settings with epidemics also reported. There is also growing resistance of enterococcus to daptomycin, which is concerning, as this may limit appropriate antibiotic therapy. In 2017, there were an estimated 54,500 patients hospitalized for VRE infections and an estimated 5400 VRE-associated deaths.[10] *Enterococcus faecalis* remains the most common pathogen; however, rising numbers of *Enterococcus faecium* have been noted. Not only is there a local concern for rise of VRE, but in 2017 the World Health Organization identified VRE as an important resistant bacteria in their "Global Priority List of Antibiotic-Resistant Bacteria."[11]

TRANSMISSION OF VANCOMYCIN-RESISTANT ENTEROCOCCI

VRE colonization, contact with HCPs, and environmental contamination are all associated with transmission of VRE.[12] Little is known about the dynamics of VRE transfer in hospitals.[13] Recent studies have shown there may be a causal relationship between patient VRE colonization and time-dependent environmental contamination within the hospital.[14] VRE colonization, when compared with vancomycin-susceptible strains, has been shown to be a precursor for developing VRE bloodstream infections (BSIs). The risk of VRE BSIs among colonized patients varies dependent on patient risk factors.[15] VRE is known to survive exposure to heat and certain disinfectants and has been found on numerous inanimate objects within hospitals. HCPs in adjunct with the environment are at the center of enterococcal transmission from patient to patient.

The evolution of antimicrobial resistance in enterococcus is complex. Besides patient characteristics, the spread of vancomycin resistance in *Enterococcus* occurs through clonal transmission as well as plasmid and transposon dissemination of resistance determinants. There are common issues that exist with regard to prevention, infection control, and management of both VRE and methicillin-resistant *Staphylococcus aureus* (MRSA) organisms. An investigation completed from a 900-bed tertiary

care facility in urban Detroit showed a prevalence rate of almost 20% of coinfection or co-colonization of VRE and MRSA.[16] The study concluded that isolation of vancomycin-resistant *E faecalis* (rather than *E faecium*) and the use of linezolid or clindamycin were risk factors for VRE and MRSA coinfection or co-colonization. In vitro transfer of the *van*A gene from *E faecium* to *S aureus* has been noted, thus making the proximity of VRE and MRSA a risk factor for development of vancomycin-resistant *S aureus*.[17] Vancomycin-resistant *E faecalis* isolates containing Inc18 plasmids and the vancomycin resistance transposon Tn1549 have been identified as precursors for vancomycin resistance in *S aureus*.[16]

ISSUES AND STRATEGIES IN PREVENTION AND CONTROL OF VANCOMYCIN-RESISTANT ENTEROCOCCI INFECTIONS

After understanding the pathogenesis of VRE development, we know that acknowledging risk factors and understanding transmission are keys to prevention. Patient risk factors include prior antimicrobial use, working in health care, admission to the intensive care unit (ICU) with prolonged hospital stay, and being a resident from a long-term care facility. Colonization pressure within hospitals can also lead to contaminated surfaces and increase exposure to other patients. Community-acquired VRE infections are uncommon; however, risk factors for community-acquired VRE include presence of indwelling device, Foley catheter placement, and recent invasive procedures.[18,19]

There is a wide variation in infection control practices for multidrug-resistant organisms (MDROs) by hospitals within the United States and worldwide. Infection prevention and control strategies include hand hygiene, screening for resistance among isolates, surveillance cultures, contact isolation, environmental cleaning, and antimicrobial stewardship. Although infection control guidelines for MDROs from gram-negative organisms are well established, there continues to be varying ideology for infection control practices for gram-positive organisms including VRE and MRSA. The relative impact of the effectiveness of preventive measures for *E faecalis* and *E faecium* is not well established. **Table 1** provides a summary of strategies used in prevention and control of VRE infections.

HAND HYGIENE

Hands are a known major vector of patient-to-patient transmission of VRE. There is a large burden on HCPs to prevent transmission of MDROs; however, recent studies show patient hands while in hospital are just as important a reservoir for transmission within the hospital. This study published in 2019 shows that hand contamination with MDROs, including VRE, is common and has a direct correlation with contamination on high-touch room surfaces in a time-dependent manner.[20] The implementation of hand hygiene (both with soap and water and alcoholic chlorhexidine gel) has been shown to cause a 47% decrease in the acquisition of VRE.[21] Compliance with proper hand hygiene remains an opportunity for improvement, including when to wash hands, what to use to wash hands, and the duration of hand washing. A 30-second wash with soap and water has been shown to eliminate all VRE from hands, whereas a 5-second wash with water had no impact.[22]

COLONIZATION WITH VANCOMYCIN-RESISTANT ENTEROCOCCI

Colonization pressure, which is defined as the proportion of patients colonized with a particular organism during a specified period in a defined geographic area within

Table 1
Summary of strategies in infection prevention and control of VRE infections

Prevention and Control Strategy	What	When	Why
In vitro susceptibility testing	VRE definition are enterococci with MIC to vancomycin ≥32 μg/mL	Always	Early detection of vancomycin resistance is needed to determine appropriate antimicrobial therapy
Hand hygiene	Hand washing before and after contact with the patient and the patient's environment Hand washing with alcohol hand sanitizer Hand washing with soap and water when hands are soiled	Always	VRE has high predisposition to be transmitted through the hands of health care workers
Colonization and decolonization	Colonization occurs in patients with previous antimicrobial therapy	No recommendation	Colonization generally precedes infection Certain patients are high risk for infections and complications
Active surveillance	Use of rectal swabs, perirectal swabs, or stool samples	Not routine May consider if the incidence or prevalence of VRE in the facility is high Always in outbreak situations	To monitor prevalence of colonization and infection May consider in areas of skin breakdown and wounds
Chlorhexidine bathing	Daily bathing with chlorhexidine-impregnated washcloth	Always in patients in intensive care unit Not routine in general medical wards	Daily bathing with chlorhexidine-impregnated washcloths has been shown to decrease the risk of acquisition of MDROs
Environmental cleaning	Adherence to cleaning protocols Monitor effectiveness of routine cleaning	Always May consider novel technologies May consider environmental cultures in outbreak settings	VRE may survive in the environment for up to 1 y

(*continued on next page*)

Table 1
(*continued*)

Prevention and Control Strategy	What	When	Why
Antimicrobial stewardship	Appropriate use of antibiotics to prevent development and spread of resistance	Always	VRE is associated with use of vancomycin, cephalosporin, and antibiotics with anaerobic activity

Abbreviations: MDROs, multidrug-resistant organisms; MIC, minimum inhibitory concentration; VRE, vancomycin-resistant enterococci.

Adapted from Reyes, K., A.C. Bardossy, and M. Zervos, *Vancomycin-Resistant Enterococci: Epidemiology, Infection Prevention, and Control.* Infect Dis Clin North Am, 2016. **30**(4): p. 953-965; with permission.

the hospital, is a crucial factor in VRE acquisition.[23] ICUs, a common reservoir for VRE, showed rates of colonization via rectal swab ranging from 9.7% to 51.9%.[24] Colonization pressure of greater than 50% may outweigh other risk factors. A recent study evaluated 244 hospital rooms that were either hosted by VRE-colonized patients or non–VRE-colonized patients. Of the rooms, 89 were hosting a VRE-colonized patient and 62% (55 rooms) became contaminated with VRE compared with 155 rooms hosting non–VRE colonized patients in which only 28% (43 rooms) became contaminated with VRE.[14] VRE colonization has not only a local, but regional effect, and the presence of VRE in one hospital can have up to a 62% increase in prevalence to another hospital by means of patient transfers or staff working at multiple hospitals.[25]

Fecal burden of enterococci in hospitalized patients are a concern, as VRE often dominates the gut microbiome and is at risk to displace commensal anaerobes.[24] Asymptomatic carriage of VRE in the gastrointestinal tract may be one reason for the persistence of VRE in health care settings. Colonization with VRE, along with bacterial burden, can cause more environmental contamination, particularly in patients with diarrhea, and result in spread to other patients. High bacterial burden is more likely to result in spread.[26]

DECOLONIZATION

Natural clearance of VRE is variable, as colonization has been known to persist from anywhere between 204 and 1371 days.[27] Prolonged asymptomatic colonization of VRE in the gastrointestinal tract can perpetuate endemicity and spread. The modality of VRE decolonization was previously through the use of antibiotics. Newer studies are now evaluating the effectiveness of mechanical decolonization. Ultimately, the method of decolonization to decrease VRE burden is not recommended, as recolonization often occurs within a short time.

Decolonization may, however, be considered in an epidemic or a focused high-risk patient group in which populations are at high risk to develop VRE infections with significant morbidity and mortality. A prospective cohort study conducting active surveillance in a transplant ICU found that liver transplant candidates and recipients colonized with VRE had an increased risk of developing both VRE infection and death compared with noncolonized patients.[28] Among liver transplant patients, active

surveillance showed similar VRE isolates suggesting linked transmission during hospital admissions.[29] Among patients about to receive hematopoietic stem cell transplantation, VRE colonization increased the incidence of VRE BSI; however, it was not associated with increased mortality.[30] This occurred despite infection control measures being implemented effectively.

Decolonization protocols consist of antimicrobials, as well as mechanical modalities which are becoming of more common practice. Antibiotics used for decolonization include oral bacitracin, oral absorbable linezolid, and nonabsorbable daptomycin.[31] One decolonization protocol used the administration of polyethylene glycol bowel preparation to wash-out fecal bacterial microbiome and *Lactobacillus rhamnosus* probiotic to maintain colonization resistance after antimicrobial decolonization.[31] A more recent study used a multisystem, mechanical decolonization protocol without antimicrobials and was shown to have high success rates.[32] This included a combination of environmental cleansing, mechanical evacuation with glycerin enemas, replacement of normal gut flora, and nutrition support and skin hygiene cleansing.[32] VRE decolonization is not generally recommended and should be considered only in certain high-risk populations, or in an outbreak situation.[30,32]

ACTIVE SURVEILLANCE FOR VANCOMYCIN-RESISTANT ENTEROCOCCI

Active surveillance has been used to identify VRE-colonized patients in epidemic and outbreak situations. This may benefit patients for targeted antimicrobial prophylaxis in situations such as transplant or nursing home patients, and also enhance infection prevention measures to prevent VRE infection and spread.[33] Obtaining stool cultures, and rectal and perirectal swabs are screening methods to detect VRE. The use of real-time polymerase chain reaction (to detect *van*A and *van*B genes), VRE screening broth, and automated DNA extraction are some methods used to expedite VRE detection.[34] Identifying positive VRE status can result in earlier antibiotic administration in an infected patient, as a delay of more than 2 days in effective antimicrobial therapy for VRE infection can be associated with a threefold increase in 30-day mortality.[35] The sensitivity of first rectal VRE screening can be less than 50%, an important factor to remember when obtaining surveillance cultures.[36]

High-risk patient groups may need screening for VRE, such as those admitted to the ICU, oncology and transplant wards, patients on chronic dialysis, and patients admitted to acute hospitals from long-term facilities. This is because active surveillance within this population may decrease the risk of developing VRE infection and screening may decrease transmission.[33]

The exact frequency of active screening to identify VRE is not well established. Different screening approaches that have been studied include culturing on admission and periodically, assuming a positive culture pending VRE screen and cohorting colonized patients.[37] There are varying data on clinical care and cost-effectiveness of active screening for VRE within the general public. More recent studies have revealed that discontinuation of active surveillance culturing leads to facility cost saving, with no increased harm, including mortality, was observed.[38]

As VRE surveillance culturing is a sensitive detection method, it is important to note that active surveillance cultures may be of benefit during a rare VRE outbreak. In outbreak situations, microbiologic surveillance and prompt contact precautions (CPs) with strict hand hygiene are vital to control VRE spread. Hospitals with high rates of VRE infections may also benefit from surveillance cultures to identify a genetic or clonal link within the reservoir of VRE-colonized patients to prevent an epidemic.

CONTACT PRECAUTIONS

There are a variety of modes of transmission with VRE; however, most infections are felt to be related to indirect contact transmission being spread between a patient and HCPs, or contamination between the patient and the surrounding hospital environment. The Healthcare Infection Control Practices Advisory Committee (HICPAC) and the Centers for Disease Control and Prevention (CDC) recommend CPs for "all patients infected with target MDROs and for patients that have been previously identified as being colonized with target MDROs (eg, patients transferred from other units of facilities who are known to be colonized)" who are admitted to acute care hospitals.[39] Previously, the use of CPs for VRE was a common practice, with up to 90% of acute care hospitals complying with recommendations made by the CDC; with heterogeneity in its practices.[40] As more knowledge has been acquired in approaches to infection prevention, newer studies around the globe have found lacking utility in the use of CPs for VRE and MRSA.[41]

The use of CPs includes the practice of isolated patient rooms, dedicated equipment, and use of gloves and gowns. Dedicated time for training staff and the monetary cost of extra gowns and gloves are needed to achieve high compliance. Considerations for maintaining CP in patients with VRE include known colonization, pending negative stool or rectal swabs to guide discontinuation, and high-risk patients (including those who are immunosuppressed, those receiving broad-spectrum antibiotic therapy without VRE activity, those in high-risk hospital units or hospitals with high rates of VRE infection).[42] The duration of CP for VRE varies widely in hospitals: on a case-by-case basis, indefinitely after a positive culture for VRE, or until repeat cultures have cleared.[43] Within each hospital, discontinuation of CPs for patients with VRE colonization or infection should address laboratory testing and surveillance strategies, VRE CP policy implementation and oversight, and which patients should be included.[42]

From a patient perspective, the impact of isolation due to CPs may have psychological effects, which include increased rates of anxiety, fear, depression, and uncertainty.[44] Direct patient care may be negatively affected by CPs due to decreased health care contact and increased adverse events (such as falls, pressure ulcers, medication administration errors, and deep vein thrombosis).[44–46] Discontinuing CP from a hospital perspective is also associated with increased bed availability and revenue recovery, as well as a reduction in personal protective equipment expenditures with an annual savings of approximately $650,000.[47–49]

CPs have variable effectiveness in different hospital settings. There are some studies that do show a decreased acquisition of VRE that has been associated with CPs.[50–52] Multiple other studies, however, have shown the use of CPs for VRE was not associated with decreased rates of transmission and can have an overall negative impact.[41,46,49,53] A cluster-randomized trial in 20 ICUs across the United States evaluated the use of mandatory gown and gloves for all patient contacts when entering patient rooms to study VRE and MRSA acquisition over a 10-month period.[54] This study concluded there was no statistical significance in the primary outcome of acquisition of VRE and MRSA with the use of CPs.[54]

The use of CPs for VRE has been in place by the CDC since 1970, when compliance was low with hand hygiene, lack of chlorhexidine bathing, and minimal surveillance for health-care–associated infections.[55] Resources at different institutions have now been focusing on horizontal infection control strategies to prevent spread of multiple MDROs rather than a vertical strategy focusing solely on VRE. This includes increased focus on hand hygiene, bare-below-the-elbows, chlorhexidine bathing, environmental

cleaning, and care bundles.[4,41,56] These factors should be considered before implementing CP for VRE.

CHLORHEXIDINE BATHING

Chlorhexidine gluconate solution is a safe, effective, and low-cost agent for reducing the risk of health-care–associated infections like VRE.[57] The topical antiseptic solution ranges in concentrations from 0.5% to 4.0%, and daily bathing has been shown to reduce body surface bioburden, thus decreasing the risk of acquisition of MDROs.[58]

Earlier studies revealed universal decolonization reduces health-care–related BSI in ICU patients, particularly device-associated infections, reducing the rate by 28%.[59,60] It has since become standardized practice to bathe ICU patients older than 2 months in chlorhexidine to reduce the rates of central-line–associated BSI.[61] A randomized trial showed decolonization with chlorhexidine bathing did not significantly reduce all-cause BSI in non-ICU medical and surgical ward patients, although post hoc analysis noted significant benefit in those with medical devices such as central lines and lumbar drains, decreasing all-cause bacteremia with MRSA or VRE by 32%.[62] Further study is needed on whether the practice reduces outcomes such as mortality or length of hospital stay.[63]

The implications of chlorhexidine bathing on resistance also remains unclear. A study by Alotaibi and colleagues[64] noted that in hospital environments with increased chlorhexidine use, there was less susceptibility of VRE to chlorhexidine compared with vancomycin-sensitive *E faecium*. Another study noted the gene for *van*A-type vancomycin resistance was upregulated after 15 minutes of exposure to chlorhexidine, although the clinical relevance is unclear.[65]

ENVIRONMENTAL CLEANING

Contact with a contaminated environment can transfer VRE to uncontaminated surfaces. In one study,[20] an estimated 29% of rooms were contaminated with an MDRO within 24 hours of admission, and 10% of patients' hands were colonized with an MDRO at enrollment. Although hands of HCPs are recognized as an important vector for MDRO contamination,[66] equipment (including stethoscopes) can also act as a vector.[67] The estimated proportion for transfer frequency was 33% for HCP hands, 30% for gloves, and 10% for gowns. High-touch surfaces, including bed controls, call buttons, and bedside tray tables are also important locations where MDROs can colonize.[20]

Cleaning of patient care areas is often suboptimal, as one study revealed up to 94% of rooms of patients with VRE colonization or infection had 1 or more positive environmental cultures before cleaning, and 71% were still positive after housekeeping cleaning.[68] Use of bleach on bathroom surfaces, sodium hypochlorite, and alcohol for equipment are typical cleaning protocols.[69] Furthermore, the use of vaporized hydrogen peroxide in room disinfection showed patients were 80% less likely to acquire VRE.[70] Newer technologies, including ultraviolet light, have been shown to result in significant decrease in VRE contamination of frequently handled surfaces,[71] particularly when added to standard protocol.[72] These nontouch cleaning machines have the advantage of not requiring changes to the room's ventilation, not leaving residue after treatment, and having rapid exposure times.[73] However, these machines come with issues including cost, installation, hospital layout, and training.

Based on the results of microbiological screening studies, environmental colonization has been shown to correlate with patient VRE colonization.[74] New acquisition of VRE and new contamination of rooms with VRE were independently associated

with increased length of stay in a facility and a higher likelihood of requiring hospitalization.[14] Prior environmental contamination increases the risk of VRE acquisition.[75]

OUTBREAKS OF VANCOMYCIN-RESISTANT ENTEROCOCCI

Outbreaks of VRE are frequently associated with lack of implementation or compliance of infection prevention and control measures.[76] More recently, outbreaks have occurred in solid-organ transplant units,[77] neonatal ICUs,[78,79] and general medical and critical care units.[80,81] Contaminated medical equipment, including rectal thermometers[82] and nonsterile preparation of injectable contrast,[83] have also been implicated as sources for outbreaks.

A multifaceted approach involving infection control specialists, infectious disease physicians, laboratory personnel, and pharmacists is essential in outbreak investigations for VRE.[84] Laboratory testing, including molecular and nucleotide whole genome sequence–based typing, can facilitate the process. Molecular methods should be used only in conjunction with epidemiologic case information. In outbreak settings, a bundle of prevention and control measures are implemented usually simultaneously and are composed of cohorting of patients, active surveillance cultures, environmental culture, extensive environmental cleaning, education, and antimicrobial stewardship.

ANTIMICROBIAL STEWARDSHIP

Inappropriate antibiotic use is associated with the development of antimicrobial resistance. Prior vancomycin or anti-anaerobic antibiotic exposure is a risk factor for VRE infection, and an independent risk factor for mortality in patients with enterococcal bacteremia. The HICPAC guidelines recommend prudent use of vancomycin, third-generation cephalosporins, and anti-anaerobic antimicrobials including metronidazole to prevent VRE infections.[85] More recent studies[9,86] have revealed exposure to fluoroquinolones and carbapenems is also associated with VRE bacteremia. Equally important is the length of antimicrobial therapy, as the risk for VRE increases with longer durations of antibiotic exposure.[9]

Antimicrobial stewardship is particularly challenging in the era of the Coronavirus Disease 2019 (COVID-19) pandemic, when unnecessary antibiotic use is high,[87] with approximately three-quarters of patients with COVID-19 receiving antibiotics.[88] The long-term consequences of increased prescription antibiotic use in both hospitalized and outpatients with COVID-19 is yet to be determined.

The One Health approach focuses on simultaneous protection of humans, animals, and the environment from climate change.[89] Indeed, one key feature that could reduce the burden of disease from antimicrobial resistance is by adopting its public health strategies,[90] including those aimed at reducing antimicrobial use in animals and animal feed.[91]

It is critical for facilities around the globe to implement infectious disease physician–led antimicrobial stewardship programs.[92,93] This multidisciplinary approach optimizes antibiotic choices and discourages antibiotic use when clinically unnecessary.[94] Antimicrobial exposure is an important risk factor for VRE, and stewardship is crucial for infection control.[95] The emergence of resistance of enterococci to newer antimicrobials, including daptomycin, supports the use of antimicrobial stewardship to reduce VRE colonization and infection.[96]

CLINICS CARE POINTS

- VRE is defined as having a minimum inhibitory concentration to vancomycin of greater than or equal to 32 mg/mL based on the Clinical and Laboratory Standard Institute guidelines.
- Risk factors for transmission of VRE include known colonization, contact with HCPs, and environmental contamination.
- Hand hygiene is a key element in decreasing the risk of VRE acquisition.
- Active surveillance and decolonization of VRE carriers is not recommended due to high risk of relapse; however, can be considered in high-risk populations and outbreak situations.
- The use of contact precautions has not been shown to have decreased rates of VRE transmission.
- Chlorhexidine bathing reduces health-care–associated BSIs in ICU patients.
- Environmental cleaning with bleach, sodium hypochlorite, alcohol, vaporized hydrogen peroxide, and ultraviolet light can reduce VRE contamination of surfaces.
- Prudent use and duration of vancomycin, third-generation cephalosporins, and anaerobic antimicrobials can prevent VRE infections.

DISCLOSURE

No disclosures related to present study. Disclosures of Marcus Zervos include grants to institution, Moderna, Johnson & Johnson, Merck, Pfizer, and consultant to Contrafect.

REFERENCES

1. Weiner-Lastinger LM, Abner S, Edwards JR, et al. Antimicrobial-resistant pathogens associated with adult healthcare-associated infections: summary of data reported to the National Healthcare Safety Network, 2015-2017. Infect Control Hosp Epidemiol 2020;41:1–18.
2. Chiang HY, Perencevich EN, Nair R, et al. Incidence and outcomes associated with infections caused by vancomycin-resistant enterococci in the United States: systematic literature review and meta-analysis. Infect Control Hosp Epidemiol 2017;38:203–15.
3. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing (Supplement M100). 30th edition. Wayne, PA: Clinical and Laboratory Standards Institue; 2020.
4. Vehreschild M, Haverkamp M, Biehl LM, et al. Vancomycin-resistant enterococci (VRE): a reason to isolate? Infection 2019;47:7–11.
5. Olivier CN, Blake RK, Steed LL, et al. Risk of vancomycin-resistant enterococcus (VRE) bloodstream infection among patients colonized with VRE. Infect Control Hosp Epidemiol 2008;29:404–9.
6. Kohinke RM, Pakyz AL. Treatment of vancomycin-resistant enterococci: focus on daptomycin. Curr Infect Dis Rep 2017;19:33.
7. Miller WR, Murray BE, Rice LB, et al. Resistance in vancomycin-resistant enterococci. Infect Dis Clin North Am 2020;34:751–71.
8. Kaya A, Kaya SY, Balkan II, et al. Risk factors for development of vancomycin-resistant enterococcal bacteremia among VRE colonizers: a retrospective case control study. Wien Klin Wochenschr 2020;133(9-10):478–83.

9. Gouliouris T, Warne B, Cartwright EJP, et al. Duration of exposure to multiple antibiotics is associated with increased risk of VRE bacteraemia: a nested case-control study. J Antimicrob Chemother 2018;73:1692–9.
10. Centers for Disease Control and Prevention. Biggest threats and data 2019. Available at: https://www.cdc.gov/DrugResistance/Biggest-Threats.html. Accessed March 25, 2021.
11. World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. 2017. Available at: https://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/. Accessed March 25, 2021.
12. McDermott H, Skally M, O'Rourke J, et al. Vancomycin-resistant enterococci (VRE) in the intensive care unit in a nonoutbreak setting: identification of potential reservoirs and epidemiological associations between patient and environmental VRE. Infect Control Hosp Epidemiol 2018;39:40–5.
13. Zhou MJ, Li J, Salmasian H, et al. The local hospital milieu and healthcare-associated vancomycin-resistant enterococcus acquisition. J Hosp Infect 2019; 101:69–75.
14. Cassone M, Zhu Z, Mantey J, et al. Interplay between patient colonization and environmental contamination with vancomycin-resistant Enterococci and their association with patient health outcomes in postacute care. Open Forum Infect Dis 2020;7:ofz519.
15. Salgado CD. The risk of developing a vancomycin-resistant *Enterococcus* bloodstream infection for colonized patients. Am J Infect Control 2008;36:S175.e5–8.
16. Reyes K, Malik R, Moore C, et al. Evaluation of risk factors for coinfection or cocolonization with vancomycin-resistant enterococcus and methicillin-resistant *Staphylococcus aureus*. J Clin Microbiol 2010;48:628–30.
17. Yoon YK, Lee MJ, Ju Y, et al. Determining the clinical significance of cocolonization of vancomycin-resistant enterococci and methicillin-resistant *Staphylococcus aureus* in the intestinal tracts of patients in intensive care units: a case-control study. Ann Clin Microbiol Antimicrob 2019;18:28.
18. Omotola AM, Li Y, Martin ET, et al. Risk factors for and epidemiology of community-onset vancomycin-resistant *Enterococcus faecalis* in southeast Michigan. Am J Infect Control 2013;41:1244–8.
19. Raja NS, Karunakaran R, Ngeow YF, et al. Community-acquired vancomycin-resistant *Enterococcus faecium*: a case report from Malaysia. J Med Microbiol 2005;54:901–3.
20. Mody L, Washer LL, Kaye KS, et al. Multidrug-resistant organisms in hospitals: what is on patient hands and in their rooms? Clin Infect Dis 2019;69:1837–44.
21. De Angelis G, Cataldo MA, De Waure C, et al. Infection control and prevention measures to reduce the spread of vancomycin-resistant enterococci in hospitalized patients: a systematic review and meta-analysis. J Antimicrob Chemother 2014;69:1185–92.
22. Noskin GA, Stosor V, Cooper I, et al. Recovery of vancomycin-resistant enterococci on fingertips and environmental surfaces. Infect Control Hosp Epidemiol 1995;16:577–81.
23. Ajao AO, Harris AD, Roghmann MC, et al. Systematic review of measurement and adjustment for colonization pressure in studies of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, and *Clostridium difficile* acquisition. Infect Control Hosp Epidemiol 2011;32:481–9.

24. Axelrad JE, Lebwohl B, Cuaresma E, et al. Gut colonization with vancomycin-resistant *Enterococcus* and risk for subsequent enteric infection. Gut Pathog 2018;10:28.
25. Lee BY, Yilmaz SL, Wong KF, et al. Modeling the regional spread and control of vancomycin-resistant enterococci. Am J Infect Control 2013;41:668–73.
26. Jackson SS, Harris AD, Magder LS, et al. Bacterial burden is associated with increased transmission to health care workers from patients colonized with vancomycin-resistant *Enterococcus*. Am J Infect Control 2019;47:13–7.
27. Yoon YK, Lee SE, Lee J, et al. Risk factors for prolonged carriage of vancomycin-resistant *Enterococcus faecium* among patients in intensive care units: a case-control study. J Antimicrob Chemother 2011;66:1831–8.
28. Russell DL, Flood A, Zaroda TE, et al. Outcomes of colonization with MRSA and VRE among liver transplant candidates and recipients. Am J Transpl 2008;8:1737–43.
29. Banach DB, Peaper DR, Fortune BE, et al. The clinical and molecular epidemiology of pre-transplant vancomycin-resistant enterococci colonization among liver transplant recipients. Clin Transpl 2016;30:306–11.
30. Ford CD, Gazdik MA, Lopansri BK, et al. Vancomycin-resistant *Enterococcus* colonization and bacteremia and hematopoietic stem cell transplantation outcomes. Biol Blood Marrow Transpl 2017;23:340–6.
31. Cheng VC, Chen JH, Tai JW, et al. Decolonization of gastrointestinal carriage of vancomycin-resistant *Enterococcus faecium*: case series and review of literature. BMC Infect Dis 2014;14:514.
32. Choi E, Lee SJ, Lee S, et al. Comprehensive, multisystem, mechanical decolonization of vancomycin-resistant *Enterococcus* and carbapenem-resistant Enterobacteriacease without the use of antibiotics. Medicine (Baltimore) 2021;100:e23686.
33. Humphreys H. Controlling the spread of vancomycin-resistant enterococci. Is active screening worthwhile? J Hosp Infect 2014;88:191–8.
34. Drews SJ, Johnson G, Gharabaghi F, et al. A 24-hour screening protocol for identification of vancomycin-resistant *Enterococcus faecium*. J Clin Microbiol 2006;44:1578–80.
35. Zasowski EJ, Claeys KC, Lagnf AM, et al. Time is of the essence: the impact of delayed antibiotic therapy on patient outcomes in hospital-onset enterococcal bloodstream infections. Clin Infect Dis 2016;62:1242–50.
36. Kaki R, Yu Y, O'Neill C, et al, Hamilton Health Sciences Infection Prevention and Control Team. Vancomycin-resistant enterococcus (VRE) transmission and risk factors in contacts of VRE carriers. Infect Control Hosp Epidemiol 2014;35:876–9.
37. Pogorzelska M, Stone PW, Larson EL. Wide variation in adoption of screening and infection control interventions for multidrug-resistant organisms: a national study. Am J Infect Control 2012;40:696–700.
38. Payne VC, Clark CC, Turner N. Clinical and financial implications for discontinuing active surveillance culturing (ASC) for methicillin-resistant *Staphylococcus aureus* & vancomycin-resistant *Enterococcus* in community hospitals [abstract]. Am J Infect Control 2020;48:S52–3.
39. Healthcare Infection Control Practices Advisory Committee, Centers for Disease Control and Prevention. Multidrug-resistant organisms (MRO) management 2015. Available at: https://www.cdc.gov/infectioncontrol/guidelines/mdro/index.html. Accessed March 25, 2021.

40. Morgan DJ, Murthy R, Munoz-Price LS, et al. Reconsidering contact precautions for endemic methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*. Infect Control Hosp Epidemiol 2015;36:1163–72.
41. Marra AR, Edmond MB, Schweizer ML, et al. Discontinuing contact precautions for multidrug-resistant organisms: a systematic literature review and meta-analysis. Am J Infect Control 2018;46:333–40.
42. Banach DB, Bearman G, Barnden M, et al. Duration of contact precautions for acute-care settings. Infect Control Hosp Epidemiol 2018;39:127–44.
43. Russell D, Beekmann SE, Polgreen PM, et al. Routine use of contact precautions for methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*: which way is the pendulum swinging? Infect Control Hosp Epidemiol 2016;37:36–40.
44. Abad C, Fearday A, Safdar N. Adverse effects of isolation in hospitalised patients: a systematic review. J Hosp Infect 2010;76:97–102.
45. Gandra S, Barysauskas CM, Mack DA, et al. Impact of elimination of contact precautions on noninfectious adverse events among MRSA and VRE patients. Infect Control Hosp Epidemiol 2018;39:1272–3.
46. Martin EM, Bryant B, Grogan TR, et al. Noninfectious hospital adverse events decline after elimination of contact precautions for MRSA and VRE. Infect Control Hosp Epidemiol 2018;39:788–96.
47. Schrank GM, Snyder GM, Davis RB, et al. The discontinuation of contact precautions for methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*: impact upon patient adverse events and hospital operations. BMJ Qual Saf 2020;29:1–2.
48. Edmond MB, Masroor N, Stevens MP, et al. The impact of discontinuing contact precautions for VRE and MRSA on device-associated infections. Infect Control Hosp Epidemiol 2015;36:978–80.
49. Young K, Doernberg SB, Snedecor RF, et al. Things we do for no reason: contact precautions for MRSA and VRE. J Hosp Med 2019;14:178–80.
50. Cheah ALY, Cheng AC, Spelman D, et al. Mathematical modelling of vancomycin-resistant enterococci transmission during passive surveillance and active surveillance with contact isolation highlights the need to identify and address the source of acquisition. BMC Infect Dis 2018;18:511.
51. Mac S, Fitzpatrick T, Johnstone J, et al. Vancomycin-resistant enterococci (VRE) screening and isolation in the general medicine ward: a cost-effectiveness analysis. Antimicrob Resist Infect Control 2019;8:168.
52. Johnstone J, Shing E, Saedi A, et al. Discontinuing contact precautions for vancomycin-resistant enterococcus (VRE) is associated with rising vre bloodstream infection rates in Ontario hospitals, 2009-2018: a quasi-experimental study. Clin Infect Dis 2020;71:1756–9.
53. Hwang JH, Park JS, Lee E, et al. Active surveillance for carbapenem-resistant Enterobacteriaceae, vancomycin-resistant enterococci and toxigenic clostridium difficile among patients transferred from long-term care facilities in Korea. J Hosp Infect 2018;99:487–91.
54. Harris AD, Pineles L, Belton B, et al. Universal glove and gown use and acquisition of antibiotic-resistant bacteria in the ICU: a randomized trial. JAMA 2013;310:1571–80.
55. Wenzel RP, Edmond MB. Infection control: the case for horizontal rather than vertical interventional programs. Int J Infect Dis 2010;14:S3–5.

56. Haessler S, Martin EM, Scales ME, et al. Stopping the routine use of contact precautions for management of MRSA and VRE at three academic medical centers: an interrupted time series analysis. Am J Infect Control 2020;48:1466–73.
57. Edmiston CE Jr, Bruden B, Rucinski MC, et al. Reducing the risk of surgical site infections: does chlorhexidine gluconate provide a risk reduction benefit? Am J Infect Control 2013;41:S49–55.
58. Gall E, Long A, Hall KK. Chlorhexidine bathing strategies for multidrug-resistant organisms: a summary of recent evidence. J Patient Saf 2020;16:S16–22.
59. Climo MW, Yokoe DS, Warren DK, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. N Engl J Med 2013;368:533–42.
60. Denny J, Munro CL. Chlorhexidine bathing effects on health-care-associated infections. Biol Res Nurs 2017;19:123–36.
61. Marschall J, Mermel LA, Fakih M, et al. Strategies to prevent central line-associated bloodstream infections in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol 2014;35:753–71.
62. Huang SS, Septimus E, Kleinman K, et al. Chlorhexidine versus routine bathing to prevent multidrug-resistant organisms and all-cause bloodstream infections in general medical and surgical units (ABATE Infection trial): a cluster-randomised trial. Lancet 2019;393:1205–15.
63. Lewis SR, Schofield-Robinson OJ, Rhodes S, et al. Chlorhexidine bathing of the critically ill for the prevention of hospital-acquired infection. Cochrane Database Syst Rev 2019;8:CD012248.
64. Alotaibi SMI, Ayibiekea A, Pedersen AF, et al. Susceptibility of vancomycin-resistant and -sensitive enterococcus faecium obtained from Danish hospitals to benzalkonium chloride, chlorhexidine and hydrogen peroxide biocides. J Med Microbiol 2017;66:1744–51.
65. Bhardwaj P, Ziegler E, Palmer KL. Chlorhexidine induces VanA-type vancomycin resistance genes in enterococci. Antimicrob Agents Chemother 2016;60:2209–21.
66. Montoya A, Schildhouse R, Goyal A, et al. How often are health care personnel hands colonized with multidrug-resistant organisms? A systematic review and meta-analysis. Am J Infect Control 2019;47:693–703.
67. Wolfensberger A, Clack L, Kuster SP, et al. Transfer of pathogens to and from patients, healthcare providers, and medical devices during care activity-a systematic review and meta-analysis. Infect Control Hosp Epidemiol 2018;39:1093–107.
68. Eckstein BC, Adams DA, Eckstein EC, et al. Reduction of *Clostridium difficile* and vancomycin-resistant *Enterococcus* contamination of environmental surfaces after an intervention to improve cleaning methods. BMC Infect Dis 2007;7:61.
69. Grabsch EA, Mahony AA, Cameron DR, et al. Significant reduction in vancomycin-resistant enterococcus colonization and bacteraemia after introduction of a bleach-based cleaning-disinfection programme. J Hosp Infect 2012;82:234–42.
70. Passaretti CL, Otter JA, Reich NG, et al. An evaluation of environmental decontamination with hydrogen peroxide vapor for reducing the risk of patient acquisition of multidrug-resistant organisms. Clin Infect Dis 2013;56:27–35.
71. Marra AR, Schweizer ML, Edmond MB. No-touch disinfection methods to decrease multidrug-resistant organism infections: a systematic review and meta-analysis. Infect Control Hosp Epidemiol 2018;39:20–31.
72. Anderson DJ, Chen LF, Weber DJ, et al. Enhanced terminal room disinfection and acquisition and infection caused by multidrug-resistant organisms and

Clostridium difficile (the Benefits of Enhanced Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover study. Lancet 2017;389:805–14.
73. Casini B, Tuvo B, Cristina ML, et al. Evaluation of an ultraviolet C (UVC) light-emitting device for disinfection of high touch surfaces in hospital critical areas. Int J Environ Res Public Health 2019;16:3572.
74. Cassone M, Mantey J, Perri MB, et al. Environmental panels as a proxy for nursing facility patients with methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* colonization. Clin Infect Dis 2018;67:861–8.
75. Drees M, Snydman DR, Schmid CH, et al. Prior environmental contamination increases the risk of acquisition of vancomycin-resistant enterococci. Clin Infect Dis 2008;46:678–85.
76. Fossi Djembi L, Hodille E, Chomat-Jaboulay S, et al. Factors associated with vancomycin-resistant enterococcus acquisition during a large outbreak. J Infect Public Health 2017;10:185–90.
77. Kreidl P, Mayr A, Hinterberger G, et al. Outbreak report: a nosocomial outbreak of vancomycin resistant enterococci in a solid organ transplant unit. Antimicrob Resist Infect Control 2018;7:86.
78. Marom R, Mandel D, Haham A, et al. A silent outbreak of vancomycin-resistant enterococcus faecium in a neonatal intensive care unit. Antimicrob Resist Infect Control 2020;9:87.
79. Andersson P, Beckingham W, Gorrie CL, et al. Vancomycin-resistant *Enterococcus* (VRE) outbreak in a neonatal intensive care unit and special care nursery at a tertiary-care hospital in Australia—a retrospective case-control study. Infect Control Hosp Epidemiol 2019;40:551–8.
80. Garcia Martinez de Artola D, Castro B, Ramos MJ, et al. Outbreak of vancomycin-resistant *Enterococcus* on a haematology ward: management and control. J Infect Prev 2017;18:149–53.
81. Kampmeier S, Tonnies H, Correa-Martinez CL, et al. A nosocomial cluster of vancomycin resistant enterococci among COVID-19 patients in an intensive care unit. Antimicrob Resist Infect Control 2020;9:154.
82. 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;343:1925–32.
83. Sundermann AJ, Babiker A, Marsh JW, et al. Outbreak of vancomycin-resistant *Enterococcus faecium* in interventional radiology: detection through whole-genome sequencing-based surveillance. Clin Infect Dis 2020;70:2336–43.
84. Singh A, Goering RV, Simjee S, et al. Application of molecular techniques to the study of hospital infection. Clin Microbiol Rev 2006;19:512–30.
85. Muto CA, Jernigan JA, Ostrowsky BE, et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and *Enterococcus*. Infect Control Hosp Epidemiol 2003;24:362–86.
86. Cheah AL, Peel T, Howden BP, et al. Case-case-control study on factors associated with vanB vancomycin-resistant and vancomycin-susceptible enterococcal bacteraemia. BMC Infect Dis 2014;14:353.
87. Lucien MAB, Canarie MF, Kilgore PE, et al. Antibiotics and antimicrobial resistance in the COVID-19 era: perspective from resource-limited settings. Int J Infect Dis 2021;104:250–4.
88. Langford BJ, So M, Raybardhan S, et al. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. Clin Microbiol Infect 2021;27(4):520–31.

89. Rabinowitz PM, Natterson-Horowitz BJ, Kahn LH, et al. Incorporating one health into medical education. BMC Med Educ 2017;17:45.
90. Gudipati S, Zervos M, Herc E. Can the one health approach save us from the emergence and reemergence of infectious pathogens in the era of climate change: implications for antimicrobial resistance? Antibiotics (Basel) 2020;9:599.
91. McEwen SA, Collignon PJ. Antimicrobial resistance: a one health perspective. Microbiol Spectr 2018;6.
92. Rupali P, Palanikumar P, Shanthamurthy D, et al. Impact of an antimicrobial stewardship intervention in India: evaluation of post-prescription review and feedback as a method of promoting optimal antimicrobial use in the intensive care units of a tertiary-care hospital. Infect Control Hosp Epidemiol 2019;40:512–9.
93. Nauriyal V, Rai SM, Joshi RD, et al. Evaluation of an antimicrobial stewardship program for wound and burn care in three hospitals in Nepal. Antibiotics (Basel) 2020;9:914.
94. Crnich CJ, Jump R, Trautner B, et al. Optimizing antibiotic stewardship in nursing homes: a narrative review and recommendations for improvement. Drugs Aging 2015;32:699–716.
95. Contreras GA, Munita JM, Arias CA. Novel strategies for the management of vancomycin-resistant enterococcal infections. Curr Infect Dis Rep 2019;21:22.
96. Lee CR, Lee JH, Park KS, et al. Quantitative proteomic view associated with resistance to clinically important antibiotics in gram-positive bacteria: a systematic review. Front Microbiol 2015;6:828.