European Journal of Clinical Pharmacy

Print ISSN: 2385-409X **Online ISSN**: 3105-0409

Website: https://farmclin.com/

Original Research Article

VanA, VanB and Beyond: Molecular Insights into Vancomycin Resistant Enterococcus Isolated from Clinical Specimens

Article History:

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Received: 29-12-2025
Revised: 20-01-2026
Accepted: 20-02-2026
Published: 28-02-2026

Abstract:

Vancomycin-resistant enterococci (VRE) which mainly include Enterococcus faecium and Enterococcus faecalis now present a major medical challenge throughout the current post-antibiotic period. The research presents current molecular evidence about VRE from clinical specimens while revealing the complete genetic system that allows glycopeptideresistance. The vanA and vanB operons enable hospitals to develop high-level inducible resistance which constitutes the primary threat for healthcare facilities yet the emergence of uncommon genotypes such as vanM and vanN proves that enterococci possess extraordinary genetic adaptability. The review studies how bacteria change their biochemical processes by replacing normal D-Ala–D-Ala ends of peptidoglycan synthesis with D-Ala–D-Lac or D-Ala–D-Ser ends which greatly reduce vancomycin binding. The discussion shows how mobile genetic elements particularly transposon Tn1546 create conditions which enable resistance genes to spread worldwide. The diagnostic difficulties which arise from phenotypic susceptibility testing and rapid genotypic detection methods undergo complete examination. A comprehensive approach which combines genomic surveillance with strict antibiotic stewardship and correct usage of lipoglycopeptide treatments should be adopted to reduce the growing clinical challenges posed by VRE.

Keywords: Vancomycin-resistant enterococci, Enterococcus faecalis, Enterococcus faecium, Tn1546, Lipoglycopeptide treatments etc.

Introduction

The Historical Emergence of a Clinical Adversary
Vancomycin-resistant enterococci (VRE) demonstrate how bacteria can adapt when scientists impose selective pressures on them. Vancomycin established itself as the primary treatment method for multidrug-resistant Gram-positive infections which included penicillin-resistant staphylococci and enterococci. The clinical field entered a permanent new state after European and United States health organizations confirmed the first cases of acquired vancomycin resistance between 1986 and 1988 (American Psychological Association, 2024). The emergence of this disease spread worldwide because of its ability to turn the Enterococcus genus from a low-virulence bacteria into a major source of hospital-acquired infections. The use of broad-spectrum cephalosporins by medical professionals acceleratedthe transition of enterococci from their natural role as commensal bacteria in the human gastrointestinal tract to their current status as opportunistic pathogens. The use of broad-spectrum cephalosporins eliminated competing gut flora which allowed enterococci to expand their population until they gained access to complex van gene clusters.

The Clinical Burden and Pathogenic Impact

The current problem with VRE in modern healthcare facilities stems from two factors which include its ability to survive in the environment and its high transmission rates within both intensive care units and long-term care facilities. VRE shows greater survival capabilities than most viruses because it can withstand drying processes and common disinfectant methods, which allows it to spread on medical devices and through healthcare workers. The process of a person moving from being a colonized patient to developing an infection leads to dangerous health problems for that individual. The development of bloodstream infections and endocarditis together with complex urinary tract infections occurs most frequently in VRE cases among immunocompromised patients who include organ transplant recipients and chemotherapy patients. Medical professionals need to use dangerous "last-resort" drugs because vancomycin resistance restricts their treatment options to a small range of alternatives. The restriction creates two problems for patient management because it makes treatment harder to execute while it increases the time patients spend in hospitals and raises costs for the medical system.

The Threat of the Post-Antibiotic Era

The development of VRE represents the first indication of an upcoming "post-antibiotic era," which describes a future period when ordinary illnesses will again lead to death. Enterococcus faecium and Enterococcus faecalis display dangerous molecular flexibility because they function as genetic reservoirs. The vanA gene cluster which usually exists on highly mobile transposons like Tn1546, enables its transfer from enterococci to more dangerous bacterial species which include Staphylococcus aureus (Arias & Murray, 2024). In infectious disease medicine Vancomycin-Resistant Staphylococcus aureus (VRSA) emergence poses a serious problem because it could make our most powerful antibiotics useless against extremely dangerous bacteria. The process of horizontal gene transfer shows that VRE presents a danger that extends beyond its own genus because it drives a complete breakdown of antibiotic effectiveness in medical systems.

Redefining Global Health Priorities

The World Health Organization has accurately designated vancomycin-resistant E. faecium as a "priority pathogen," which demonstrates the urgent need for both new drug development and better control initiatives. The dangerous time period requires society to shift from treating diseases after they occur to using molecular monitoring methods and environmental protection procedures. The molecular examination of vanA and vanB together with the new genetic variants shows that the battle against VRE requires scientists to race against the pace of evolutionary development (World Health Organization, 2024). The clinical specimens collected today serve as complex genetic maps which show how bacteria successfully navigate through the chemical defenses that scientists have developed during the last hundred years. The current surgical techniques and advanced medical procedures need this understanding because they rely on preventing all forms of untreatable sepsis for their success.

1. Enterococcal Biology: The Architecture of an Ideal Opportunist

The Ecological Resilience of Enterococci
The study of vancomycin-resistant enterococci treatment outcomes requires an understanding of Enterococcus bacteria's fundamental biological resistance capabilities. The organisms which were first identified as Group D Streptococci exhibit outstanding survival skills which enable them to withstand extreme environmental conditions (Hota et al., 2025). The bacteria live as intestinal bacteria in mammal guts where they developed the ability to survive high bile salt concentrations and varying pH levels and all temperature ranges. Enterococci demonstrate their capacity to survive outside the host because they can maintain their existence for several weeks on non-living objects found in medical facilities which include

hospital bed rails and stethoscopes and doorknobs. The bacteria possess the ability to survive both dry conditions and oxidative damage which enables them to withstand standard cleaning procedures without suffering permanent damage. The base level of "hardiness" functions as a stable foundation which permits antibiotic resistance to build up until a resistant strain enters a hospital environment where it will continuously endanger patient health.

The Foundation of Intrinsic Resistance

Enterococci display their unique biological characteristics through their multiple natural defense mechanisms which protect them from various antibiotic classes which exist before any medical selection process begins. The bacterium enterococci show natural resistance against multiple beta-lactams because their critical penicillin-binding proteins (PBPs) display decreased binding strength to beta-lactam antibiotics. The bacterium shows natural resistance against all aminoglycosides because the drug fails to enter bacterial cells at standard treatment levels. Bacteria show natural resistance to drugs because they use exogenous folates as a solution to replace sulfonamides. The bacteria show this resistance pattern which gives them a biological advantage that drives their development towards acquiring multiple drug resistance. Enterococci show high resistance against standard medical treatments which allows them to survive through empirical illness treatment while they remain as the only remaining species in their environment which has no other competing organisms (MDPI One Health Continuum, 2026).

Mechanisms of Acquired Resistance and Genetic Plasticity

The basic resistance shown by enterococci creates a foundation that proves their actual clinical danger arises from their ability to acquire new resistance genes through horizontal gene transfer. The genetic makeup of enterococci functions as a "genetic sponge" which accepts foreign DNA material into its genome. They utilize various mobile genetic elements which include plasmids together with transposons and integrative conjugative elements to conduct genetic exchanges between different species and within their own species. The mobile genetic elements which enable this process led to the acquisition of vancomycin resistance through the vanA and vanB operons. The vanA gene cluster usually exists on the Tn1546 transposon which easily binds to pheromone-responsive plasmids. The advanced system for communication and conjugation provides a single resistant cell the ability to turn an entire local community into a resistant population which transforms a manageable outbreak into a multidrug-resistant epidemic within days (Miller & Munita, 2024).

Why Enterococci are "Ideal" Pathogens

The combination of environmental resilience and natural defense systems together with genetic adaptability makes enterococci the ideal pathogens for modern medical practices. They achieve disease transmission without needing strong toxins or standard disease-causing agents because their strength lies in their ability to exploit the medical system's unintentional effects. When broad-spectrum antibiotics are given to patients, they kill off the vulnerable gut bacteria which create a protective barrier, thus enabling enterococci bacteria which have developed resistance to take over the empty space in the host system, a process known as "overgrowth."

The bacteria start from their expanded gut reservoir position to enter the bloodstream through the intestinal wall or they infect the skin which leads to surgical wound infections. Their success demonstrates their ability to use hospitals' most effective devices which include antibiotics and medical procedures to create new pathways for hospital infection. The study of Enterococcus biology includes not only bacterium research but also research about how living organisms adapt to survive in completely clean and sterile environments which humans have built through their technological achievements.

2. The Molecular Machinery: A Deep Dive into the *van* Operons

Genetic Architecture of Vancomycin Resistance in Enterococci

The evolution of enterococci from vancomycin-susceptible to vancomycin-resistant phenotypes is not caused by a solitary point mutation but through acquisition of complex genetic elements which represent a complete genetic system. The mechanism of resistance operates through dedicated operons which contain multiple genes that work together to produce the necessary enzymes for bacterial cell wall alterations. The core of this mechanism functions through its ability to avoid the standard human body process which creates peptidoglycan (von Wintersdorff et al., 2026).

The antibiotic establishes a strong bond with the terminal D-alanyl-D-alanine (D-Ala-D-Ala) motif in vancomycin-susceptible cells because it targets this specific site on the peptidoglycan pentapeptide precursor which leads to cell wall cross-linking blockage through both transglycosylation and transpeptidation processes. The vancomycin-resistant enterococci (VRE) bypass this blockage by using different dipeptides which replace the D-Ala-D-Ala terminus with D-alanyl-D-lactate (D-Ala-D-Lac) or D-alanyl-D-serine (D-Ala-D-Ser) as substitutes. The changes result in a binding affinity decrease for vancomycin which reaches a binding distance of 1000

times, but they still allow the cells to maintain their complete organic structure and functional abilities.

The vanA Operon: Prototype of High-Level Resistance
The most important study of vancomycin resistance shows that the vanA genotype stands as the primary genetic cause of this antibiotic resistance. The vanA operon which normally resides on the transposon Tn1546 contains seven vital components that include vanR vanS vanH vanA vanX vanY and vanZ. The operon provides a system that enables bacteria to develop high levels of resistance against both vancomycin and teicoplanin.

The vanA operon is regulated by the vanRS two-component system. VanS functions as a membrane-bound sensor kinase which detects glycopeptide antibiotics and transfers a phosphate group to VanR, the response regulator. The activated VanR protein stimulates the transcription of the downstream resistance genes.

The vanA system's enzyme core modifies peptidoglycan production. VanH, a D-lactate dehydrogenase, converts pyruvate into D-lactate through its enzymatic activity. VanA, a ligase, subsequently catalyzes the synthesis of the D-Ala-D-Lac depsipeptide. The system destroys vancomycin-sensitive precursors to create effective resistance through VanX, which acts as a D,D-dipeptidase to break down remaining D-Ala-D-Ala, while VanY functions as a D,D-carboxypeptidase to remove terminal D-alanine from pentapeptides that VanX cannot reach. All enzymes work together to execute a comprehensive "search-and-destroy" procedure that ensures resistant cell wall precursors will prevail.

The final gene vanZ provides additional resistance against teicoplanin but scientists have not yet identified its specific molecular function.

The vanB Operon: Selective Induction and Clinical Implications
The VanS sensor kinase creates this distinction between the two groups. The VanS_B system activates in response to vancomycin yet remains inactive when teicoplanin is present. The presence of vanB in organisms allows them to show teicoplanin susceptibility in laboratory tests yet they develop resistance after exposure to vancomycin which poses a major threat to successful treatment outcomes (Schwartzman et al., 2024).

The core genes vanH_B vanB and vanX_B function in D-Ala-D-Lac terminal synthesis according to the same mechanism that their vanA counterparts use. The vanB operons typically find their way into the bacterial chromosome through large conjugative elements which include Tn1547 and Tn5382 instead of plasmids. The chromosomal placement of these elements provides hospitals with long-lasting stability because they can endure antibiotic use without interruptions.
The vanC Genotype: Intrinsic Low-Level Resistance
The vanC genotype functions as a permanent characteristic of Enterococcus gallinarum and E. casseliflavus and E. flavescens which differs from the way acquired resistance mechanisms function. The genotype offers vancomycin resistance which remains at minimal levels while the organism shows total susceptibility to teicoplanin.

VanC enables bacteria to develop resistance because it produces D-Ala-D-Ser terminus molecules which replace D-Ala-D-Lac. The operon lacks a vanH homolog because the vanC locus and its related genes produce D-serine through a racemase enzyme (Zhang & Luan, 2024). The chromosomal encoding of vanC resistance combined with its occurrence in specific species makes it impossible for horizontal gene transfer to occur. The situation creates diagnostic challenges because clinical laboratories may mistake intrinsic resistance for acquired vancomycin resistance.

Rare and Emerging Operons: vanD, vanE, and vanG
The advanced genomic monitoring system has discovered additional rare vancomycin resistance operons which demonstrate that the van gene family contains multiple genetic variations. The vanD genotype which researchers discovered in E. faecium shows no restriction on its gene expression which occurs permanently. The condition develops when either vanS or vanR regulatory genes become mutated or when the D-Ala-D-Ala ligase native protein undergoes mutation because this condition causes permanent need for D-Ala-D-Lac pathway operation (Lebreton & Courvalin, 2025).

The E. faecalis bacterium acquires vanE and vanG operons which use D-Ala-D-Ser pathway instead of being part of its natural genetic makeup. The vanG cluster displays a complex structure which includes multiple genes that make up the vanG, vanW, vanXY_G, vanS_G, vanR_G, and vanL_G gene component. The operons demonstrate how enterococci developed their ability to adapt when exposed to glycopeptide antibacterial treatment.

New Frontiers: vanL, vanM, and vanN
The emergence of new resistance genotypes vanL vanM and vanN has occurred during the past thirty years. The rising incidence of VanM in clinical isolates from China and other East Asian countries makes it a major threat. The vanM gene provides extensive protection against both vancomycin and teicoplanin which results in a phenotype that resembles vanA. The system operates through its particular genetic code

which functions as a vanA/vanB PCR method that drives identification through standard techniques. The pandemic potential of vanM continues to grow because of its repeated association with powerful conjugative plasmids. The vanL genotype discovered in E. faecalis and vanN located in E. faecium represent two additional variations of D-Ala-D-Ser and D-Ala-D-Lac detection pathways. The current diagnosis and surveillance systems demonstrate major deficiencies through their emerging genotypes which remain uncommon at this time. The research which concentrates on vanA and vanB only will miss detection of emerging resistance patterns that currently occur at low intensity. The genetic framework that causes vancomycin resistance in enterococci continues to develop its molecular foundation throughout time. The increasing variety of van operons demonstrates the exceptional adaptability of enterococci under prolonged glycopeptide pressure. The study of this variability enables better diagnostic accuracy and more effective antimicrobial treatment and assistance in predicting future resistance trends.

Genotype	Ligase Type	Peptidoglycan Precursor Produced	Resistance Level (Vancomycin / Teicoplanin)	Genetic Location	Origin / Clinical Significance
VanA	VanA	D-Ala-D-Lac	High / High	Transposon (Tn1546)	Most prevalent genotype worldwide; highly mobile and clinically significant
VanB	VanB	D-Ala-D-Lac	Variable / Low	Chromosomal or plasmid-associated	Induced by vancomycin only; may appear teicoplanin-susceptible
VanC	VanC	D-Ala-D-Ser	Low / Susceptible	Chromosomal	Intrinsic resistance in *E. gallinarum* and *E. casseliflavus*
VanD	VanD	D-Ala-D-Lac	Moderate / Moderate	Chromosomal	Constitutively expressed; rare but stable
VanE	VanE	D-Ala-D-Ser	Low / Susceptible	Chromosomal	Acquired resistance in *E. faecalis*
VanG	VanG	D-Ala-D-Ser	Moderate / Susceptible	Chromosomal	Complex seven-gene operon; recombinant origin
VanM	VanM	D-Ala-D-Lac	High / High	Plasmid	Emerging genotype in Asia; genetically distinct from *vanA*
VanN	VanN	D-Ala-D-Lac	Moderate / Moderate	Chromosomal	Identified in *E. faecium* (first reported in 2010)

Table 1: Characteristics of Vancomycin Resistance (van) Genotypes in Enterococci, Source: Author Geberated

Gene	Functional Category	Specific Biochemical Activity
vanR	Regulatory	Response regulator that activates transcription of resistance genes following phosphorylation
vanS	Regulatory	Sensor histidine kinase that detects glycopeptide antibiotics and phosphorylates *vanR*
vanH	Precursor synthesis	D-lactate dehydrogenase; converts pyruvate to D-lactate

vanA	Ligase	Catalyzes formation of the D-Ala–D-Lac depsipeptide
vanX	Elimination	D,D-dipeptidase that hydrolyzes native D-Ala–D-Ala dipeptides
vanY	Elimination	D,D-carboxypeptidase that removes terminal D-Ala residues from pentapeptide precursors
vanZ	Accessory	Confers resistance to teicoplanin; precise biochemical mechanism remains undefined

Table 2: Functional Roles of Genes in the vanA Operon, Source: Author Generated

3. The Biochemical Basis of Glycopeptide Resistance

The D-Ala–D-Lac Pathway: A Paradigm of Molecular Evasion

The primary mechanism of elevated vancomycin resistance in enterococci is the production of modified peptidoglycan precursors that exhibit significantly less affinity for the antibiotic. The principal mechanism of increased resistant to vancomycin in enterococci is the synthesis of altered peptidoglycan precursors that demonstrate markedly reduced affinity for the antibiotic. The peptidoglycan precursor in standard physiological conditions reaches its final form through the completion of D-alanyl-D-alanine which acts as its ultimate dipeptide. Vancomycin reaches its bactericidal effect through its strong binding to the terminal which occurs by five hydrogen bonds that prevent both transglycosylation and transpeptidation processes needed for cell wall cross-link construction (Mokhtar & Attallah, 2025).

Two factors prevent drug-target interaction because the ester oxygen lone pairs create an electrostatic force that repels from the carbonyl group of vancomycin. The structural changes result in vancomycin binding affinity loss which reaches a 1,000-fold reduction that enables ongoing cell wall synthesis during periods when antibiotics are used at elevated doses.

Enzymatic Coordination: Dehydrogenases and Ligases

The D-Ala–D-Lac pathway requires precise control through various enzymes that function as specialized components. The D-lactate substrate production begins when VanH, the D-specific 2-hydroxy acid dehydrogenase, performs his initial work. This enzyme reduction process converts pyruvate, which serves as a key intermediate in glycolysis, into D-lactate.

The VanA (or VanB) ligase uses D-lactate to create the D-Ala–D-Lac depsipeptide. The native D-Ala–D-Ala ligase binds only to D-alanine but van-type ligases have an altered active site that supports binding both D-alanine and D-lactate. The enzymatic flexibility of this system ensures that researchers can produce strong peptidoglycan precursors through uninterrupted processes (Davis et al., 2025).

Enterococci demonstrate their ability to switch between different metabolic modes through their system operate with high accuracy. The cell redirects essential metabolites from its main metabolic routes to build an altered cell wall structure which allows the cell to maintain its normal growth and viability.

The D-Ala–D-Ser Pathway: Low-Level and Intrinsic Resistance

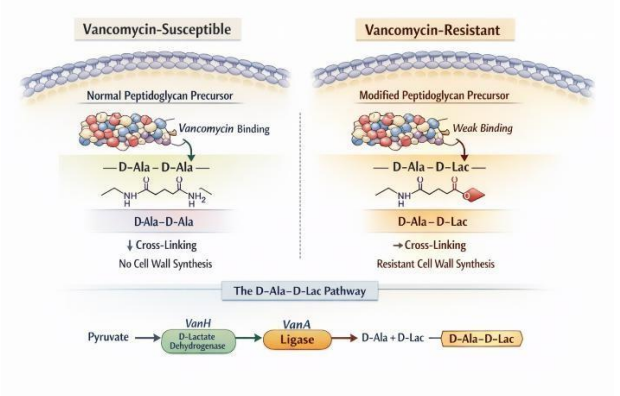

Figure 1:vancomycin-susceptible to vancomycin-resistant phenotypes, Source: Author Researched & Generated

The D-Ala–D-Ser pathway serves as a secondary resistance mechanism which operates at reduced efficiency while being connected to the vanC vanE vanG and vanL genotypes. The pathway replaces the D-alanine terminal D-alanine residue with D-serine which replaces D-lactate (PMC Global Health, 2025). The D-Ala–D-Ser terminal of D-serine creates four hydrogen bonds with vancomycin despite D-serine being heavier than D-alanine. The decrease in vancomycin binding affinity is modest—approximately six- to seven-fold compared to the natural D-Ala–D-Ala target. The species using this route show low-level resistance because Enterococcus gallinarum exhibits restricted reduction which results in minimum inhibitory concentrations (MICs) that typically reach established clinical breakpoints.

The enzymatic machinery consists of a D-amino acid racemase which transforms L-serine into D-serine and a specific D-Ala–D-Ser ligase that synthesizes the two components. The D-Ala–D-Ser pathway displays less clinical strength than vanA-mediated resistance but serves as an important evolutionary path which

demonstrates all the various methods enterococci possess to escape glycopeptide suppression.

4. Epidemiology & Transmission: Global Dynamics and Molecular Vectors

Global Trends and Regional Disparities

Vancomycin-resistant enterococci (VRE) first showed up in the late 1980s. Since then, they have changed where they live in big ways. From the first reports of a few isolated cases, it turned into a global health crisis that will last until 2026. According to new information from the Global Antimicrobial Resistance Monitoring System (GLASS) and the World Health Organization (WHO), vancomycin-resistant Enterococcus (VRE) is spread in different ways in different parts of the world (Sood et al., 2025). About one-third of clinical enterococcal isolates in the US and some parts of South Asia are VRE. The phenomenon occurs most frequently within intensive care unit environments.

The Dynamics of Hospital Outbreaks

The primary transmission of VRE occurs in healthcare facilities because these locations maintain constant conditions while they treat numerous patients who have colonized the bacteria. The intestinal tract of patients serves as the primary habitat for the pathogen during hospital outbreaks. The antibiotics cephalosporins and carbapenems create "VRE overgrowth" because they eliminate competing microbiota, which results in high pathogen release into the surrounding environment (Clinical and Laboratory Standards Institute, 2025). Healthcare workers spread the disease through their hands while contaminated fomites transmit the disease through dirty items such as bed rails and medical charts and portable equipment. Whole Genome Sequencing (WGS) molecular epidemiological research demonstrates that what appears to be a single outbreak stems from multiple transmission events. Resistance genes transfer between different enterococcal lineages through horizontal transfer while a dominant strain spreads across the same ward through clonal dissemination.

The Role of Tn1546 and Plasmid-Mediated Dissemination

The transposon Tn1546 increases the speed of vanA gene propagation through its molecular level functions. The element operates as a compact "resistance package" which contains the entire vanA operon because its size reaches 10.8 kb. Tn1546 operates with high adaptability because it can attach to multiple plasmid backbone types which include Inc18-like plasmids and pheromone-responsive plasmids (European Committee on Antimicrobial Susceptibility Testing, 2026). Plasmids function as the main method through which bacteria exchange resistance genes with each other. Tn1546 shows genomic adaptability through its capacity to incorporate additional IS1216V insertion sequences which enables it to function in various host environments. The spread of Tn1546 plasmids between enterococci and Staphylococcus aureus creates a long-term VRE epidemiology threat which leads to worldwide vancomycin-resistant S. aureus (VRSA) emergence and decreases the effectiveness of current antimicrobial therapies.

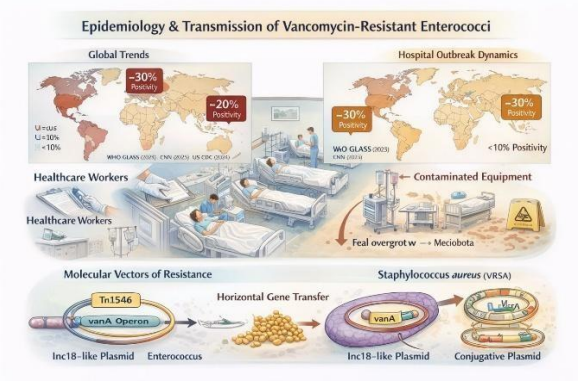

Figure 2: Transmission Dynamic, Source: Author Findings and Generated

6. Clinical Diagnosis: Navigating Phenotypic and Genotypic Landscapes

The Duality of VRE Detection

Healthcare professionals need to know the exact type of vancomycin-resistant enterococci (VRE) because it helps them provide better treatment and implement successful infection control strategies. Clinical microbiology laboratories use two primary diagnostic testing methods which include phenotypic testing that measures bacterial growth under vancomycin conditions and genotypic testing which identifies genetic determinants of resistance (CDC A.R. & Patient Safety Portal, 2024).

Phenotypic testing establishes the clinical standard for definitive testing because it determines whether an isolate exhibits actual resistance. Laboratories use broth microdilution to determine the minimum inhibitory concentration (MIC) which serves as the industry standard and they also use automated systems like Vitek 2 and Phoenix for susceptibility testing. The phenotypic testing method produces reliable results but its accuracy for testing enterococci remains restricted because enterococci require 18 to 24 hours to show complete results.

The identification of the vanB phenotype poses an additional barrier. The isolates appear susceptible during in vitro assessments because they develop resistance through vanB induction.

Genotypic Approaches: Speed with Limitations

The tests use conserved gene segments from vanA and vanB to deliver results within three hours (Hussain & Ullah, 2025). Genotypic testing methods provide high test accuracy but they contain critical testability issues.

The main obstacle requires researchers to find isolates that demonstrate genotype positive results yet show phenotype testing negative results. Some enterococcal strains contain the vanA gene but they lack the ability to show it which results in their in vitro vancomycin susceptibility (Davlieva & Shamoo, 2025). The findings can lead to unnecessary patient isolation, increased medical costs, and false resistance burden assessments. The process of molecular diagnosis faces obstacles because new resistance genes become available. The vanM genotype represents a genetic variation that scientists track with PCR testing, which fails to identify vanM through regular testing. The PCR methods cannot differentiate between active bacterial cells and inactive DNA, and they cannot provide the minimum inhibitory concentration results needed to improve other antibacterial treatments.

Integrating Phenotypic and Genotypic Strategies

Molecular diagnostics perform essential functions for rapid patient assessment and disease tracking and epidemic control although they cannot replace phenotypic susceptibility testing (Carter & Pitcher, 2026). The combination of rapid genotypic testing and complete phenotypic testing provides healthcare professionals with essential tools for making medical decisions and managing antibiotic usage.

1. Current & Future Therapies: Managing the Resistance Frontier

The Forefront of Defense and Emerging Opposition
The clinical treatment for VRE relies on "last-resort" antibiotics which include linezolid and daptomycin after vancomycin loses its effectiveness. Linezolid operates as an oxazolidinone which blocks protein synthesis while it achieves high efficacy against most VRE strains; however, doctors typically limit its use because it causes myelosuppression and patients develop mutations in 23S rRNA. The bactericidal agent daptomycin serves as the primary treatment for life-threatening diseases including endocarditis because it destroys bacterial cell membranes.

Daptomycin-resistant VRE has developed into an international crisis. The cell develops resistance when mutations affect the liaFSR regulatory system which enables the cell to "divert" standard antibiotics away from their intended septum target sites. The medical field has needed to increase daptomycin treatment levels together with additional treatments which include daptomycin and ceftaroline as a combined method. The modern lipoglycopeptides oritavancin and dalbavancin have been employed to address these shortcomings. These drugs possess a "dual mechanism" which allows them to bind to the cell wall while they damage membrane structure thus achieving effectiveness against particular vanB and some vanA bacterial strains.

Conclusion

The battle against vancomycin-resistant enterococci needs advanced molecular tracking systems because current treatment methods face limitations. The genetic plasticity of enterococci through their vanA vanB and emerging vanM genotypes enables them to outwit our chemical treatments. The upcoming projects should implement "metabolic stewardship" through Whole Genome Sequencing (WGS) to track plasmid movement in real-time across hospital patient areas. The combination of rapid molecular testing with cleaning procedures and targeted use of novel lipoglycopeptides will reduce VRE clinical impact while preventing the transmission of its most dangerous genetic elements to severe infections.

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