OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Review Article **Medicine and Pharmacy**

Enterococcus Species: Pathogen or Innocent Bystander?

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DOI: https://doi.org/10.36348/sjmps.2026.v12i11.001 | **Received:** 04.09.2026 | **Accepted:** 28.10.2026 | **Published:** 02.11.2026

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Abstract

Enterococcus species inhabit the human gastrointestinal tract and may be recovered from urine, wounds, abdominal specimens, and blood. Their isolation raises a recurring clinical question: does the organism represent harmless colonization, contamination, or a causative pathogen requiring treatment? This narrative review synthesizes contemporary clinical guidelines and selected studies, emphasizing practical interpretation across specimen types, species-level identification, and antimicrobial stewardship. *Enterococcus faecalis* and *Enterococcus faecium* differ substantially in epidemiology, antimicrobial susceptibility, and association with healthcare exposure. Asymptomatic bacteriuria generally should not be treated, except during pregnancy or before selected endourological procedures associated with mucosal trauma. Conversely, enterococcal bloodstream infection requires prompt clinical assessment, source investigation, and consideration of endocarditis, especially for E. faecalis. Deep or normally sterile-site specimens provide stronger evidence of pathogenicity than superficial swabs or surveillance cultures, although specimen quality and the possibility of contamination remain critical. Intra-abdominal isolation must be interpreted in relation to source control, severity, healthcare association, and polymicrobial growth. Species identification, susceptibility testing, and targeted therapy are essential because intrinsic cephalosporin resistance and acquired vancomycin resistance limit treatment options. A stepwise clinical–microbiological framework can reduce both missed invasive infections and unnecessary antibiotic exposure. Enterococci should neither be dismissed reflexively nor treated solely because a culture is positive; management must be driven by syndrome, specimen validity, host factors, and the strength of microbiological evidence.

Keywords: *Enterococcus faecalis; Enterococcus faecium*; colonization; bacteremia; infective endocarditis; asymptomatic bacteriuria; antimicrobial stewardship; vancomycin resistance.

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INTRODUCTION

Enterococci are facultatively anaerobic, Gram-positive cocci that commonly colonize the gastrointestinal tract and, to a lesser extent, the genitourinary tract. Among human pathogens, Enterococcus faecalis and Enterococcus faecium predominate. Their frequent recovery from clinical material creates an interpretive dilemma: the same genus can be a normal colonizer, a participant in polymicrobial microbiota, or a cause of invasive disease. The distinction matters because unnecessary treatment selects resistant strains, whereas under-recognition of genuine bloodstream infection or endocarditis can have serious consequences [1–4].

A culture result alone does not establish causality. Interpretation requires an integrated assessment of the anatomical site, collection technique, clinical syndrome, host vulnerability, microbiological reproducibility, and presence of alternative pathogens or diagnoses. This review provides a clinically oriented synthesis rather than a systematic review or a quantitative meta-analysis. Emphasis is placed on guideline-concordant practice and on developments relevant to E. faecalis bacteremia and drug-resistant E. faecium through October 2026 [1–6].

REVIEW

Scope and evidence approach

The manuscript is a narrative synthesis of published professional-society guidance and selected peer-reviewed investigations, with particular emphasis on the Infectious Diseases Society of America (IDSA) guidance on asymptomatic bacteriuria and complicated intra-abdominal infection, the European Society of

Cardiology (ESC) guidelines on endocarditis, European Association of Urology guidance, and recent evidence concerning endocarditis risk stratification in E. faecalis bacteremia [1–7]. The sources were purposively selected for clinical relevance rather than through a predefined systematic search, formal risk-of-bias scoring, or meta-analysis; consequently, this review does not claim systematic completeness.

Biological and epidemiological context

E. faecalis is typically more susceptible to ampicillin than hospital-adapted E. faecium, while E. faecium more frequently exhibits multidrug resistance and vancomycin resistance. Enterococci tolerate adverse environmental conditions, persist in healthcare environments, form biofilms on foreign material, and exploit antibiotic pressure. Cephalosporins lack clinically reliable activity against enterococci as a group. Microbiology reports should therefore identify isolates to species level whenever clinical significance is plausible and should distinguish the susceptibility phenotype, especially ampicillin and vancomycin susceptibility, with further testing driven by the infection syndrome [3,4,8].

A unified approach: colonizer, contaminant, or pathogen?

Three concepts must remain distinct. Colonization refers to microbial presence without tissue-invasive disease or attributable symptoms. Contamination denotes introduction during collection or processing that does not represent the sampled compartment. Infection is supported by compatible symptoms or systemic manifestations, an anatomically credible source, and valid microbiological evidence. Detection in a normally sterile compartment strengthens the case for invasive infection but does not negate the need to appraise collection quality. In nonsterile sites, high organism burden alone is insufficient to prove causality [1,2,5].

Table 1: Clinical and microbiological criteria for distinguishing true enterococcal infection from colonization or contamination

Domain	Features supporting true infection	Features favoring colonization or contamination
Clinical	Fever or organ-specific symptoms, sepsis, inflammatory focus	No attributable symptoms; another convincing diagnosis
Specimen	Aseptic deep sample or normally sterile site; good collection	Surface swab, poor sampling, or colonization screen
Microbiology	Repeated concordant blood cultures; predominant growth compatible with syndrome	Single low-quality sample; mixed flora without a compatible syndrome
Host and devices	Recent instrumentation, valve/prosthesis, postoperative infection, immunosuppression	Stable colonized patient without inflammatory or systemic findings
Evolution	Source identified; concordant imaging; clinical improvement after appropriate therapy/source control	Stable untreated course or improvement through management of another etiology

Urine: bacteriuria is not synonymous with urinary tract infection

Urine is among the most frequent contexts of enterococcal overdiagnosis. The IDSA defines asymptomatic bacteriuria by quantitative bacterial growth in the absence of attributable urinary symptoms, regardless of pyuria. Routine treatment is not recommended for most adults, including older people, patients with diabetes, and patients with long-term urinary catheters. The main established exceptions are pregnancy and before endoscopic urological procedures anticipated to cause mucosal trauma. These rules apply regardless of whether the isolate is E. faecalis or E. faecium [1,2].

For symptomatic cystitis, suggestive features include dysuria, new frequency or urgency, suprapubic discomfort, and an appropriately collected positive urine culture. Febrile illness, flank pain, bacteremia, or hemodynamic instability may indicate systemic urinary infection. Pyuria may support inflammation but cannot independently distinguish infection from colonization, especially in catheterized patients. In older patients with confusion or falls but without local genitourinary symptoms or systemic signs, other explanations should be actively assessed instead of automatically treating bacteriuria [1,2].

When treatment is indicated, agents must be matched to the syndrome and susceptibility. Ampicillin or amoxicillin may be useful for susceptible E. faecalis; nitrofurantoin and oral fosfomycin are options only for selected lower-tract infections where activity and local standards support use. These urinary agents are inappropriate as sole therapy for pyelonephritis, bacteremia, or endocarditis. Device exchange or removal and correction of obstruction are often more important than repeated antibiotic courses [1,2].

Bloodstream isolation: a result that warrants active evaluation

Enterococcus recovered from a properly obtained blood culture should not be dismissed as a harmless bystander without assessment. Although contamination can occur, particularly with suboptimal collection or complex polymicrobial specimens, the clinical default should be prompt consideration of a genuine bloodstream infection. Determine the likely

source (urinary tract, biliary system, gastrointestinal tract, vascular catheter, surgical site, or endovascular infection), obtain further blood cultures when indicated to document persistence or clearance, and evaluate the need for device removal or drainage. A single positive culture does not, by itself, classify the event as contamination or define its source [3,4].

E. faecalis bacteremia merits particular attention for infective endocarditis. The ESC guidance emphasizes echocardiography and the interpretation of microbiological findings within a structured diagnostic framework. Transesophageal echocardiography is especially relevant with prosthetic valves, intracardiac devices, poor transthoracic windows, persistent bacteremia, or sustained clinical suspicion. Prediction tools such as DENOVA may aid risk stratification but must not replace clinical judgment or be applied outside the populations in which they were studied. An international prospective external-validation study published in 2026 underscores the ongoing effort to refine echocardiography selection in monomicrobial E. faecalis bacteremia [3,6].

Endocarditis: enterococci as unequivocal invasive pathogens

When enterococcal infective endocarditis is diagnosed, prolonged bactericidal therapy and multidisciplinary management are required. For ampicillin-susceptible *E. faecalis* endocarditis, ampicillin plus ceftriaxone is a guideline-supported synergistic regimen, particularly valuable when high-level aminoglycoside resistance or aminoglycoside toxicity makes gentamicin undesirable. Selected patients may receive a beta-lactam with gentamicin where susceptibility and renal safety permit. Therapy commonly extends for up to six weeks, tailored to valve type, illness duration, susceptibility, and surgical findings [3].

Multidrug-resistant or vancomycin-resistant enterococcal endocarditis demands expert-directed treatment. ESC guidance discusses high-dose daptomycin-based combination strategies in relevant resistant infections, while linezolid may be considered in particular contexts. These approaches cannot be extrapolated uncritically to uncomplicated bacteremia; dosing, toxicity, emergent resistance, and source control require individualized assessment [3].

Intra-abdominal and biliary specimens: clinical significance is contextual

Enterococci may appear among polymicrobial isolates from abdominal infection. Their detection in an old drain or superficial sample is less persuasive than recovery from an intraoperative specimen, newly aspirated collection, or other appropriately obtained deep sample in a patient with compatible disease. The 2024 IDSA update recommends obtaining intra-abdominal cultures in patients undergoing source-control procedures for complicated infection, supporting subsequent targeted therapy [5].

Guidance on empirical anti-enterococcal coverage is context-dependent. The earlier joint SIS/IDSA therapeutic guideline does not support routine enterococcal coverage for mild-to-moderate community-acquired intra-abdominal infection, but recommends consideration for healthcare-associated or postoperative infection and other high-risk situations. The 2024 IDSA update specifically addresses diagnostic evaluation, not a comprehensive replacement of all antimicrobial treatment recommendations. Clinicians should avoid interpreting either guideline as a mandate to treat every abdominal enterococcal isolate [5,7].

Wounds, pressure ulcers, respiratory cultures, and prosthetic infections

Enterococci isolated from superficial wound swabs, chronic ulcers, ostomy-adjacent sites, or respiratory secretions frequently coexist with other flora. Without clinical evidence of invasive infection, such results should not trigger directed therapy. Deep operative tissue specimens, multiple concordant samples, purulent collections, or implant-associated infection present a different level of evidence. Isolation from cerebrospinal fluid, joint aspirate, deep tissue, or other normally sterile samples is important when sampling and symptoms are credible. In suspected device infection, repeated deep sampling and surgical source control are essential components of evaluation. Enterococcal pneumonia is unusual; an isolated positive respiratory specimen should prompt particularly careful assessment for colonization or an alternative pathogen.

Antimicrobial resistance and microbiological pitfalls

Intrinsic resistance to cephalosporins explains why ceftriaxone monotherapy is not an effective anti-enterococcal regimen despite its synergistic role with ampicillin for susceptible E. faecalis endocarditis. E. faecium often shows reduced beta-lactam susceptibility; vancomycin-resistant E. faecium (VRE) is a major stewardship and infection-prevention concern. Species identification, isolate-specific susceptibility data, testing for high-level aminoglycoside resistance when synergy is contemplated, and consultation on complex isolates are therefore important. Daptomycin should not be selected for pneumonia, and nitrofurantoin or fosfomycin for cystitis should not be assumed to treat invasive infection [3,4].

There is no universally applicable antibiotic choice or fixed treatment duration for all enterococcal isolates. Local breakpoints (e.g., current EUCAST or CLSI standards), local resistance epidemiology, patient characteristics, pharmacokinetics, source control, and clinical syndrome should drive definitive management. Prolonged therapy without confirmed infection is not an acceptable substitute for diagnostic clarification.

Practical decision framework

Table 2: Clinical interpretation and recommended management of enterococcus spp. isolation in different clinical settings

Clinical situation	Interpretation	Recommended clinical response
Asymptomatic Enterococcus bacteriuria	Usually colonization	No antibiotics except guideline-defined exceptions; review catheter necessity
Symptomatic urinary syndrome + reliable positive culture	Probable pathogen	Targeted therapy based on species, susceptibility and infection site
Positive blood culture	Potentially invasive infection	Immediate assessment; source evaluation; repeat cultures when indicated
E. faecalis bacteremia with endocarditis risk	Potential endovascular source	Appropriate echocardiography; specialist assessment
Postoperative intra-abdominal abscess, deep specimen	Possible co-pathogen	Prioritize drainage/source control; individualize anti-enterococcal treatment
Superficial wound or chronic ulcer swab	Often colonization	Do not treat culture alone; sample deep tissue if true infection suspected
VRE screening rectal swab	Colonization by definition	Infection prevention measures; no eradication antibiotics

Antimicrobial stewardship and unresolved questions

Overtreatment contributes to antimicrobial selective pressure, adverse events, and misallocation of diagnostic resources. Undertreatment carries a different risk: missed endocarditis, persistent bacteremia, or uncontrolled deep infection. Stewardship should therefore emphasize diagnostic stewardship as much as antibiotic choice. Clinician–microbiologist dialogue can clarify the rationale for ordering a culture, the specimen source and quality, whether the isolate is expected commensal flora, and whether the result should prompt imaging, additional cultures, or device management. Recent consensus work in E. faecium bloodstream infection also highlights the limited randomized evidence for many therapeutic choices, cautioning against presenting expert practice as definitive trial-proven standards [4].

Important uncertainties remain, including optimal blood-culture follow-up schedules for distinct enterococcal syndromes, the comparative value of risk scores in selecting echocardiography, oral step-down strategies in carefully selected uncomplicated bacteremia, and comparative treatments for VRE bacteremia. These questions warrant prospective evaluations. No scoring rule or laboratory threshold should be used in isolation to override high clinical suspicion.

CONCLUSIONS

Enterococcus species occupy a spectrum from normal intestinal colonizers to causes of severe invasive infection. Their clinical significance is not determined by culture positivity alone but by the interaction between a valid specimen, an attributable syndrome, host and device-related risk factors, and reproducible microbiological findings. An asymptomatic urinary or superficial-site isolate often calls for restraint, while bloodstream and sterile-site isolation warrant active investigation.

A structured approach centered on species identification, infection-source assessment, judicious echocardiography, source control, and susceptibility-guided antimicrobial therapy offers the best practical balance between overtreatment and missed disease. Multidisciplinary clinical–microbiological interpretation should remain central to decisions involving enterococci, especially in patients with persistent bacteremia, prosthetic material, complicated postoperative infection, or antimicrobial resistance.

Author Contributions

E.B. conceived the review topic, conducted the literature appraisal, and drafted the initial manuscript. Y.B. and N.H. provided scientific supervision, contributed to the interpretation of the literature, and critically reviewed the content. M.C. contributed to manuscript preparation and critically revised the manuscript for important intellectual content. All authors are requested to review and approve the final version before submission. (Confirm the contribution statements and final approval with every author.)

DISCLOSURES

Human Subjects: This review used only previously published data and did not involve new human subject data.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Funding: No specific funding was received for this work.

Data Availability: All data discussed in this review are available in the published articles cited in the reference list.

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