Enterococcus faecium (LTR79856)

Edit Approved By: Van der Walt, Peet (08/30/2023) **Revision: 5.00**

Organism	**Enterococcus faecium**
Clinical	*E. faecium* is part of the human gastrointestinal tract and is widely distributed in the environment (soil, water, plants, animals). It is an important pathogen in nosocomial infections, especially urinary tract infections, intra-abdominal infections, and bacteremia. The role of *E. faecium* in polymicrobial wound infections and respiratory tract infections is controversial and requires clinical evaluation, as well as review of Gram stain. *E. faecium* tends to be associated with more serious infections, usually in debilitated/ immunocompromised patients who have received prior antibiotic therapy.
Usual susceptibility pattern	*E. faecium* is usually susceptible to vancomycin, quinupristin/dalfopristin and linezolid but is almost always resistant to ampicillin. Vancomycin resistance is increasing. Vancomycin tolerance has been reported. Vancomycin dependent (unable to grow in the absence of Vancomycin) *E. faecium* have also been described. *E. faecium* is usually resistant to ampicillin although rare strains remain susceptible to ampicillin but may be resistant to penicillin. This organism is resistant to cephalosporins, clindamycin, macrolides, fusidic acid and TMP-SMX. Ciprofloxacin resistance is very common in urinary isolates. Gentamicin synergy resistance is variable. Gentamicin is recommended in serious infections as a synergistic agent if the gentamicin synergy is susceptible. Tobramycin is ineffective as a synergistic agent for this organism. Acquired vancomycin resistance via mobile genetic elements (commonly *vanA*, *vanB*), most often seen in *E. faecium* and less frequently in *E. faecalis*, are of epidemiological significance, as this type of resistance is transferable from one strain to another, and has been associated with outbreaks. Transfer of van genes, especially *vanA*, to other Enterococcus species (e.g. *E. gallinarum, E. casseliflavus, E. raffinosus*) has led to hospital outbreaks in the past and is reported in literature. In the laboratory, *vanA* isolates test resistant to vancomycin with an MIC range of 64 – 1,000 μg/mL (typically > 128 μg/mL). *VanB* isolates typically produce MICs of 16 – 64 μg/mL, but MIC can range from 4 to 1,000 μg/mL. Additional types of vancomycin resistance, encoded by the *vanD*, *vanE*, *vanG*, *vanL*, *vanM*, and *vanN* genes occur rarely. Vancomycin-dependent and vancomycin-heteroresistant enterococcal isolates have been sporadically reported.

Enterococcus faecium, Continued

Susceptibility method VITEK2. Additional tests include disc diffusion and Etest method.

Etest	Vancomycin	Mueller-Hinton agar incubated in ambient air at 35°C for 24 hours. Use 0.5 McFarland suspension in saline. After 24 hours incubation if MIC is 3 or 4 ug/mL extend incubation to 48 hours.
	Other	Mueller-Hinton agar incubated in ambient air at 35°C for 16-20 hours. Use 0.5 McFarland suspension in saline.

Susceptibility reporting

	CSF/ Brain	Blood/ Endo vascular Catheter	Sterile Body Site	Deep Wound	Urine	Other	Comments
Ampicillin	✓	✓	✓	✓	✓	✓	If amp S see **Special Considerations**
Amoxicillin/ clavulanate (oral)				*	*	*	* Report same as amp if *S. aureus* (MSSA) or anaerobes co-isolated
Ciprofloxacin					✓		Do not report if patient <18 y - see **Special Considerations**
Daptomycin		2	2		*		Etest method 2nd line if amp and vanco I/R *Physician request only after microbiologist approval **See Special Considerations**
Gentamicin Synergy		✓					**See Special Considerations**
Imipenem		*	*	*			*Physician request only Consult microbiologist **See Special Considerations**
Linezolid	2	2	2	2	2	2	2nd line if amp and vanco I/R If linezolid I/R see **Special Considerations**
Nitrofurantoin					✓		
Penicillin		*					Etest method *If amp S report upon physician request only after microbiologist approval.
Tetracycline					✓		Do not report if patient <8 y
Tigecycline			*	*			*Physician request only Consult microbiologist **See Special Considerations**
Vancomycin	2	2	2	2	2	2	2nd line if amp I/R Always report if vanco I/R

Enterococcus faecium, Continued

Note

All isolates	If reporting susceptibility results Enterococcus species are uniformly resistant to all cephalosporins, clindamycin and trimethoprim-sulfamethoxazole. &2336

Special considerations

Ampicillin:	**CSF / Brain isolates:** • If ampicillin S – confirm ampicillin by Etest • If confirmed as S add comment: "Ampicillin susceptibility result confirmed by two methods." #2108 • Consult Technical Supervisor
	Other body sites: • If ampicillin S - confirm ampicillin by disc diffusion • If confirmed as S add comment: "Ampicillin susceptibility result confirmed by two methods." #2108
Ciprofloxacin:	If patient < 18 years old, ciprofloxacin may be reported on urine specimens at physician request only, add comment: "Susceptibility testing requested by physician." #STRB
Daptomycin:	*Enterococcus sp.* should be susceptible to this antibiotic. Consult microbiologist if not susceptible.
	CLSI breakpoints for E. faecium: MIC: ≤ 4 µg/mL — Interpretation: SDD — Add Comment: 26141 MIC: ≥ 8 µg/mL — Interpretation: R — Add Comment: "The daptomycin interpretation is based on a dosage of 8-12 mg/kg q24h in adults with normal renal function. Consultation with an infectious diseases specialist is recommended. **(26141)**
	Daptomycin is inactivated by surfactant in the lungs. Therefore this antibiotic should not be used for the treatment of respiratory infections. For **blood isolates** where daptomycin is reported, add comment: "Daptomycin is inactivated by lung surfactant and should not be used for respiratory infections" **(21127)**
Gentamicin Synergy:	If gentamicin synergy **Sensitive**, "Combination therapy with a susceptible aminoglycoside for synergy is recommended for treatment of serious infections." #2114
	If gentamicin synergy **Resistant**, "Combination therapy with Gentamicin for synergy is NOT indicated." #2116

Enterococcus faecium, Continued

Special considerations (continued)

<table>
<tr><td>Imipenem:</td><td>If imipenem requested by physician and ampicillin is susceptible:
After microbiologist's approval imipenem testing may be performed by imipenem Etest and interpreted using EUCAST breakpoints. Consult microbiologist prior to reporting.</td></tr>
<tr><td></td><td>If imipenem requested by physician and ampicillin is resistant, consult microbiologist.</td></tr>
<tr><td>Linezolid:</td><td>If linezolid susceptibility reported, confirm all resistant isolates with second method. If confirmed I/R, consult microbiologist.</td></tr>
<tr><td>Tigecycline:</td><td>This agent may be an option in non-urinary infections (hepatic metabolism) where therapeutic choices are limited. It may not achieve adequate serum levels to be effective in bacteremia. Consult microbiologist before testing and reporting. Send to reference lab for testing.</td></tr>
<tr><td></td><td>Note: No CLSI breakpoints available, use EUCAST breakpoints:

EUCAST breakpoints:
<table>
<tr><th>MIC</th><th>Interpretation</th></tr>
<tr><td>≤ 0.25 µg/mL</td><td>S</td></tr>
<tr><td>≥ 0.5 µg/mL</td><td>R</td></tr>
</table>
Add comment:
"Interpretation is based upon EUCAST breakpoints." (21178)</td></tr>
<tr><td></td><td>Enterococcus sp. are usually susceptible to this antibiotic. Consult microbiologist if not susceptible.</td></tr>
</table>

Interpretation

For Etest, report actual MIC result. For interpretation (S, I, or R) report according to the nearest higher doubling dilution **(Appendix 1)**.

Use CLSI interpretive document for ***Enterococcus* spp.**

Note: Strains of *Enterococcus spp.* with ampicillin and penicillin MICs ≥16 µg/mL are categorized as resistant. However, *Enterococcus spp.* with penicillin MICs ≤64 µg/mL or ampicillin ≤32 µg/mL may be susceptible to synergistic killing by these penicillins in combination with gentamicin or streptomycin (in the absence of high-level resistance to gentamicin or streptomycin) if high doses of penicillin or ampicillin are used. Refer to "Test for High-Level Aminoglycoside Resistance in Enterococcus spp." table in CLSI M100 document for additional information.

For **multi-resistant isolates of *E. faecium* (vancomycin and linezolid R) from sterile body sites** where therapeutic options are limited and ampicillin 16-32 µg/mL (confirmed by Etest):

- Consider performing penicillin Etest.
- If penicillin MIC 16-64 µg/mL, this indicates low level resistance.
- If gentamicin synergy S, high dose ampicillin with gentamicin may achieve therapeutic levels despite testing ampicillin R in vitro.
  Therapy with ampicillin should only be given under supervision of a specialist.