Bacteremia – Enterococcus

BACKGROUND

- Facultatively anaerobic gram positive cocci in pairs and chains
- Majority of human infections caused by 2 species: *Enterococcus faecalis* and *Enterococcus faecium*, the latter of which is of low virulence and associated predominantly with disease in compromised hosts
- Enterococcal bacteremia with positive urine cultures should not be assumed to be a urinary source. Other sources should be explored. Enterococcal pyelonephritis is very uncommon.
- *Enterococcus faecalis* can be associated with catheter-associated UTIs.
- *Enterococcus faecium* is a frequent non-pathogenic colonizer of the urinary tract, **not** a cause of UTIs outside of immunosuppressed patients **with** hardware.
- Enterococcal bacteremia associated with IE in up to 25% of patients.
- Ampicillin=**drug of choice** for susceptible isolates; better activity compared to other penicillin derivatives and better activity than vancomycin
- Enterococcal species are **intrinsically resistant to cephalosporins, meropenem, and ertapenem.**

Species of Enterococcus and Associated Disease

***Enterococcus* Species**	**Disease**	**General Susceptibilities**
Enterococcus faecalis	• Native and prosthetic valve endocarditis • Nosocomial and post-surgical intra-abdominal infections* • Line and device infections • Osteomyelitis (less common) • **UTI RARE** unless immunosuppressed, GU hardware, or recent instrumentation	Ampicillin (99-100%)
Enterococcus faecium	• Native and prosthetic valve endocarditis • Nosocomial and post-surgical intra-abdominal infections* • **UTI RARE** unless immunosuppressed, GU hardware, or recent instrumentation	Vancomycin (30%) Linezolid Daptomycin
Enterococcus casseliflavus ***Enterococcus gallinarum***	• Biliary infections • Nosocomial intra-abdominal infections • Rare cause of endocarditis	Ampicillin (99%) Intrinsically resistant to vanco
Other *Enterococcus*	Rare causes of human infection	Ampicillin Vancomycin

*these infections are often polymicrobial and the role of *Enterococcus* as a pathogen is unclear

INITIAL MANAGEMENT

Empiric Therapy

Infectious Source	***E. faecalis* or other non-*E. faecium* Bacteremia**	***E. faecium* Bacteremia**
Monomicrobial	Ampicillin 2 g IV q4h	Linezolid 600 mg PO/IV q12h *If endocarditis suspected:* Daptomycin 10-12 mg/kg IV q24h
Polymicrobial	1. Ampicillin 2 g IV q4h added to usual therapy for source infection 2. Piperacillin-tazobactam	Linezolid 600 mg PO/IV q12h added to usual therapy for source infection

- ✓ Repeat blood cultures x 2 sets immediately when blood cultures return positive, then q48h until clear
- ✓ Identify the source of infection and control the source where applicable
- ✓ TTE recommended for all patients with community-onset Enterococcal bacteremia
- ✓ TEE recommended for majority of patients with community-onset Enterococcal bacteremia, patients with sustained bacteremia, and patients with indwelling cardiac devices or prosthetic valves

- ✓ If source is a central venous catheter, catheter should be removed
- ✓ ID consult highly suggested, in particular if any indwelling hardware, prosthetic cardiac valves, or unclear source

Likelihood of Endocarditis

- DENOVA score can help predict risk of endocarditis and guide use of echocardiography
- DENOVA of less than 3 is unlikely to have IE. However, consider echo for community-onset cases
- DENOVA of 3 or more has a higher likelihood of IE, and should generally have an echo
- DENOVA score validated only for *E. faecalis* monomicrobial bacteremia.

DENOVA SCORE (1 point each)
D – Duration of symptoms 7 days or more
E – Embolization
N – Number of positive blood cultures 2 or more
O – Origin of infection unknown
V – Valvular disease (prior IE, native valve disease, prosthetic valve)
A – Auscultation of murmur

DIRECTED THERAPY

Infection	**Targeted Therapy**		**Duration of Therapy**
	Ampicillin-susceptible	**Ampicillin non-susceptible**	
Known source, Non-endocarditis or osteomyelitis *Monomicrobial source*	1. Ampicillin 2 g IV q4h 2. Vancomycin IV Oral step-down: Amoxicillin 1 g PO TID	1. Vancomycin IV 2. Linezolid 600 mg PO/IV BID 3. Daptomycin 10-12 mg/kg IV q24h	**1-2 weeks** including oral stepdown **or** as per source infection if longer
Known source, Non-endocarditis or osteomyelitis *Polymicrobial source*	1. Ampicillin 2 g IV q4h + therapy targeted to source infection 2. Pip-tazo 3.375 g IV q6h Oral step-down: amox-clav 875 mg PO BID-TID	1. Vancomycin IV + therapy targeted to source infection 2. Linezolid 600 mg PO/IV BID + therapy targeted to source infection 3. Daptomycin 10-12 mg/kg IV q24h + therapy targeted to source infection	**1-2 weeks** including oral stepdown **or** as per source infection if longer
Endocarditis or Osteomyelitis	1. Ampicillin 2 g IV q4h +/- ceftriaxone 2 g IV q12h* 2. Vancomycin IV 3. Linezolid 600 mg PO/IV BID** 4. Daptomycin 10-12 mg/kg IV q24h	1. Vancomycin IV 2. Linezolid 600 mg PO/IV BID** 3. Daptomycin 10-12 mg/kg IV q24h	**6 weeks**

Doses may require adjustment for renal insufficiency
For vancomycin dosing, refer to "Vancomycin Dosing and Therapeutic Monitoring" in ASP Handbook
*Ceftriaxone synergy generally recommended for endocarditis but limited evidence in osteomyelitis.
**Some patients will not tolerate linezolid for prolonged treatment durations, but reasonable option with close monitoring of complete blood counts.