MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

GUIDELINES FOR TREATMENT OF NATIVE VALVE INFECTIVE ENDOCARDITIS IN ADULTS

(Infectious Diseases consultation is STRONGLY recommended)

Empiric Therapy[§]	Pathogens		Subsequent Therapy (Renal Dose Adjustments May Be Necessary)	Duration of Therapy	Comments
Vancomycin IV[4] + Ceftriaxone 2 g IV q24h NOTE: Cefepime 2 g IV q8h[1] should be used instead of ceftriaxone in burn patients and IV drug users	**Viridans group streptococci** **OR** ***Streptococcus gallolyticus (bovis)***	Penicillin MIC ≤0.12 mg/L	Preferred: **Penicillin G** 3 million units IV q4h[1,2] OR **Ceftriaxone** 2 g IV q24h	4 weeks	• Avoid the 2-week regimen with gentamicin in patients with known cardiac or extracardiac abscess, CrCl <20 mL/min, impaired 8th cranial nerve function, or *Abiotrophia*, *Granulicatella*, or *Gemella* spp. infection. • Gentamicin is used for gram positive synergy. For Viridans group streptococci and *Streptococcus gallolyticus* with penicillin MIC <0.5 mg/L, **once daily gentamicin (3 mg/kg IV q24h) is preferred**, with gentamicin trough goal ~1mg/L. • In patients with renal insufficiency, dosing adjustments should be made with PharmD.
			Preferred (alternative): **Penicillin G** 3 million units IV q4h[1,2] + **Gentamicin** IV[3] OR **Ceftriaxone** 2 g IV q24h + **Gentamicin** IV[3]	2 weeks	
			Alternative for Severe PCN Allergy: **Vancomycin** IV[4]	4 weeks	
		Penicillin MIC >0.12-<0.5 mg/L	Preferred (if susceptible): **Ceftriaxone** 2 g IV q24h	4 weeks	
			Preferred (alternative): **Penicillin G** 4 million units IV q4h[1,2] + **Gentamicin** IV[3] for first 2 weeks	4 weeks	
			Alternative for Severe PCN Allergy: **Vancomycin** IV[4]	4 weeks	
		Penicillin MIC ≥0.5 mg/L	Preferred (if susceptible): **Ceftriaxone** 2 g IV q24h + Gentamicin IV[3]	4-6 weeks	• **Traditional gentamicin dosing (1 mg/kg IV q8h) is preferred**, with gentamicin peak goal 3-5 mg/L and trough goal <1 mg/L. • In patients with renal insufficiency, dosing adjustments should be made with PharmD. • 4-week duration indicated only if symptoms of infection <3 month duration.
			Preferred (alternative): **Penicillin G** 4 million units IV q4h[1,2] + **Gentamicin** IV[3]	4-6 weeks	
			Alternative for Severe PCN Allergy: **Vancomycin** IV[4]	4-6 weeks	
	Enterococci strains susceptible to penicillin and gentamicin		Preferred: **Ampicillin** 2 g IV q4h[1,5] + **Gentamicin** IV[3] OR **Penicillin G** 4 million units IV q4h[1,2] + **Gentamicin** IV[3]	4-6 weeks	• Request susceptibility testing for penicillin if used for therapy. • Ampicillin+aminoglycoside regimen: 4-week duration indicated only if symptoms of infection <3 month duration. • **Traditional gentamicin dosing (1 mg/kg IV q8h) is preferred**, with gentamicin peak goal 3-5 mg/L and trough goal <1 mg/L. • In patients with renal insufficiency, dosing adjustments should be made with PharmD. • Ampicillin + ceftriaxone regimen should be considered in patients with renal insufficiency.
			Preferred (alternative): **Ampicillin** 2 g IV q4h[1,5] + **Ceftriaxone** 2 g IV q12h	6 weeks	
			Alternative for Severe PCN Allergy: **Vancomycin** IV[4] + **Gentamicin** IV[3]		
	Enterococci strains susceptible to penicillin and resistant to gentamicin		Preferred: **Ampicillin** 2 g IV q4h[1,5] + **Ceftriaxone** 2 g IV q12h	6 weeks	• **Streptomycin dose 7.5 mg/kg IV q12h is preferred, with peak goal 20-35 mg/L and trough goal <5 mg/L.** • In patients with renal insufficiency, dosing adjustments should be made with PharmD.
			Alternative for Severe PCN Allergy (for streptomycin susceptible): **Vancomycin** IV[4] + **Streptomycin** IV[3]		
			Alternative for Severe PCN Allergy (for streptomycin resistant): **Consult Infectious Diseases** + Start **vancomycin** IV[4] + obtain allergy consult for desensitization to **ampicillin** and **ceftriaxone**		
	Enterococci strains resistant to penicillin		**Vancomycin** IV[4] **+ Gentamicin** IV[3]	6 weeks	• **Traditional gentamicin dosing (1 mg/kg IV q8h) is preferred**, with gentamicin peak goal 3-5 mg/L and trough goal <1 mg/L. • In patients with renal insufficiency, dosing adjustments should be made with PharmD.
	Enterococci strains resistant to vancomycin, aminoglycosides, and penicillin		**Daptomycin** 10-12 mg/kg IV q24h[1] OR **Linezolid** 600 mg IV/PO q12h	>6 weeks	• Follow baseline and weekly CK with daptomycin therapy. • Combination therapy with daptomycin and ampicillin or ceftaroline may be considered in patients with persistent disease

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Vancomycin IV[4] + Ceftriaxone 2 g IV q24h NOTE: Cefepime 2 g IV q8 hours[1] should be used instead of ceftriaxone in burn patients and IV drug users	**Staphylococci (MSSA)**	Preferred: **Oxacillin** 2 g IV q4h[2] Alternative for PCN Allergy (non-anaphylaxis): **Cefazolin** 2 g IV q8h[1] Alternative for PCN Allergy (Anaphylaxis): **Vancomycin** IV[4]	6 weeks	• Cefazolin should not be used if CNS disease present.
	Staphylococci (MRSA)	Preferred: Vancomycin IV[4] Alternative for Vancomycin Allergy or Failure: **Daptomycin** 8-10 mg/kg IV q24h[1]	6 weeks	• Follow baseline and weekly CK with daptomycin therapy
	HACEK Group	Preferred: **Ceftriaxone** 2 g IV q24h Alternative: **Ampicillin-sulbactam** 3 g IV q6h[1,5] Alternative for Severe PCN Allergy: **Ciprofloxacin** 400 mg IV q8h[1]	4 weeks	
	***Candida* spp.**	Preferred: **Liposomal amphotericin B** 3-5 mg/kg IV q24h + **Flucytosine**[1] 25 mg/kg PO q6h Alternative for Intolerance to Liposomal Amphotericin B/Flucytosine: **Micafungin** 150 mg IV q24h	>6 weeks	• Following initial therapy with IV antifungal agent, long-term suppression with an oral azole may be considered for sensitive pathogens. • Flucytosine may cause myelosuppression and therefore a CBC should be routinely obtained. Consider risk versus benefit of use especially in patients with renal insufficiency. • Flucytosine therapeutic drug monitoring is recommended in all patients - peak level should be drawn after 3-5 days. Goal peak 20-80 mg/L. • *Candida parapsilosis* demonstrates innately higher MICs to the echinocandins and thus empiric use of micafungin for this organism is not preferred.
	Culture negative (acute, presents within days of symptom onset; pending definitive diagnosis)	**Vancomycin** IV[4] + **Ceftriaxone** 2 g IV q24h	4-6 weeks	• Receipt of antibiotics prior to obtaining cultures is the most common cause of culture negative IE. There are many infectious and non-infectious causes. An evaluation of epidemiological factors, history of prior cardiovascular infections, exposure to antimicrobials, clinical course, severity, and extracardiac sites of infection should be performed to help guide diagnosis and treatment. • **Gentamicin should be added in patients with a high suspicion for *Enterococcus* infections. Traditional gentamicin dosing (1 mg/kg IV q8h) is preferred**, with gentamicin peak goal 3-5 mg/L and trough goal <1 mg/L. • In patients with renal insufficiency, dosing adjustments should be made with PharmD. • Cefepime 2 g IV q8h[1] should be used instead of ceftriaxone in burn patients and IV drug users for empiric coverage of *Pseudomonas*.
	Culture negative (subacute, presents within weeks of symptom onset; pending definitive diagnosis)	**Vancomycin** IV[4] + **Ampicillin-sulbactam** 3 g IV q6h[1,5] OR **Vancomycin** IV[4] + **Ceftriaxone** 2 g IV q24h	4-6 weeks	

§ Prior to confirmation of pathogen

1. Refer to Antimicrobial Dosing Recommendations for dose adjustments in renal dysfunction
2. If candidate for outpatient therapy, may consider administration via continuous infusion (same daily dose)
3. Please refer to the Aminoglycoside Dosing in Adult Patients for guidance on aminoglycoside dosing.
4. Please refer to the Vancomycin Nomogram for guidance on vancomycin dosing and monitoring.
5. Because of the requirement for frequent dosing and the inability to administer via continuous infusion, these drugs are not recommended for home administration

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