C.S. MOTT CHILDREN'S HOSPITAL
MICHIGAN MEDICINE

GUIDELINES FOR TREATMENT OF NATIVE VALVE INFECTIVE ENDOCARDITIS in PATIENTS on PEDIATRIC SERVICES

(Infectious Diseases consultation is STRONGLY recommended)

Empiric therapy (prior to confirmation of pathogen):

- **Vancomycin** IV[3] + **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose)
- *NOTE:* **Cefepime** 50 mg/kg/dose IV q8h[1] (max: 2 g/dose) should be used instead of ceftriaxone in burn patients and IV drug users

Gentamicin goals:

- Gentamicin is used for gram positive synergy
- Traditional gentamicin synergy dosing (1 mg/kg/dose IV q8h) is preferred in pediatric patients
- Gentamicin peak goal 3-5 mcg/dL and trough goal <1 mcg/dL

Definitive Therapy (Once Pathogen is Identified)				
Pathogens		**Antibiotic Therapy (renal dose adjustments may be necessary)[1]**	**Duration**	**Comments**
Viridans group streptococci OR ***Streptococcus gallolyticus (bovis)***	Penicillin MIC ≤0.12 mg/L	Preferred: **Penicillin G** 50,000 units/kg/dose IV q4h[1,2] (max: 3 million units/dose) OR **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose)	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.
		Preferred (alternative): **Penicillin G** 50,000 units/kg/dose IV q4h[1,2] (max: 3 million units/dose) + **Gentamicin** IV[4] OR **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose) + **Gentamicin** IV[4]	2 weeks	
		Alternative for Severe PCN Allergy: **Vancomycin** IV[3]	4 weeks	
	Penicillin MIC >0.12-<0.5 mg/L	Preferred (if susceptible): **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose)	4 weeks	
		Preferred (alternative): **Penicillin G** 50,000 units/kg/dose IV q4h[1,2] (max: 4 million units/dose) + **Gentamicin** IV[4] for first 2 weeks[1]		
		Alternative for Severe PCN Allergy: **Vancomycin** IV[3]		
	Penicillin MIC ≥0.5 mg/L	Preferred (if susceptible): **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose) + **Gentamicin** IV[4]	4-6 weeks	• 4 week duration indicated only if symptoms of infection are <3 months in duration.
		Preferred (alternative): **Penicillin G** 50,000 units/kg/dose IV q4h[1,2] (max: 4 million units/dose) + **Gentamicin** IV[4]		
		Alternative for Severe PCN Allergy: **Vancomycin** IV[3]		
Pathogens		**Antibiotic Therapy (renal dose adjustments may be necessary)[1]**	**Duration**	**Comments**
Enterococci strains susceptible to penicillin and gentamicin		Preferred: **Ampicillin** 75 mg/kg/dose IV q6h[1] (max: 3 g/dose)	4-6 weeks	• Request susceptibility testing for penicillin if used for therapy.

	+ Gentamicin IV[4] OR **Penicillin G** 50,000 units/kg/dose IV q4h[1,2] (max: 4 million units/dose) + Gentamicin IV[4]		• Ampicillin + aminoglycoside regimen: 4-week duration indicated only if symptoms of infection are <3 months in duration. Ampicillin + ceftriaxone regimen should be considered in patients with renal insufficiency
	Preferred (alternative): **Ampicillin** 75 mg/kg/dose IV q6h[1] (max: 3 g/dose) + **Ceftriaxone** 50 mg/kg/dose IV q12h (max: 2 g/dose)	6 weeks	
	Alternative for Severe PCN Allergy: Vancomycin IV[3] + Gentamicin IV 1 mg/kg/dose q8h[1]		
Enterococci strains susceptible to penicillin and resistant to gentamicin	Preferred: **Ampicillin** 75 mg/kg/dose IV q6h[1] (max: 3 g/dose) + **Ceftriaxone** 50 mg/kg/dose IV q12h (max: 2 g/dose)	6 weeks	• Streptomycin peak goal 20-35 mg/L and trough goal <5 mg/L.
	Alternative for Severe PCN Allergy (for streptomycin susceptible): Vancomycin IV[3] + **Streptomycin** 10 mg/kg IV q12h[1] (max: 1 g/dose)		
	Alternative for Severe PCN Allergy (for streptomycin resistant): **Consult Infectious Diseases** + Vancomycin IV[3] + Obtain allergy consult for desensitization to ampicillin and ceftriaxone		
Enterococci strains resistant to penicillin	Vancomycin IV[3] + Gentamicin IV[4]	6 weeks	
Enterococci strains resistant to vancomycin, aminoglycosides, and penicillin	**Daptomycin** 10-12 mg/kg IV q24h[1] OR **Linezolid**: *<12 years:* 10 mg/kg/dose IV/PO q8h (max: 600 mg/dose) *≥12 years:* 10 mg/kg/dose IV/PO q12h (max 600 mg/dose)	>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
Staphylococci (MSSA)	Preferred: **Nafcillin** 33 mg/kg/dose IV q4h[2] (max: 2 g/dose)	6 weeks	• Cefazolin should not be used if CNS disease present.
	Alternative for PCN Allergy (non-anaphylaxis): **Cefazolin** 33 mg/kg/dose IV q8h[1] (max: 2 g/dose)		
	Alternative for PCN Allergy (Anaphylaxis): Vancomycin IV[3]		
Pathogens	**Antibiotic Therapy (renal dose adjustments may be necessary)[1]**	**Duration**	**Comments**
Staphylococci (MRSA)	Preferred: Vancomycin IV[3]	6 weeks	• Follow baseline and weekly CK with daptomycin therapy
	Alternative for Vancomycin Allergy or Failure:		

	Daptomycin 10 mg/kg IV q24h[1]		
HACEK Group	Preferred: **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose) Alternative: **Ampicillin-sulbactam** 75 mg/kg/dose IV q6h[1] (max: 3 g of ampicillin/dose) Alternative for Severe PCN Allergy: **Ciprofloxacin** 10 mg/kg/dose IV q8h[1] (max: 400 mg/dose)	4 weeks	
***Candida* spp.**	Preferred: **Liposomal amphotericin B** 3-5 mg/kg/dose IV q24h[1] + **Flucytosine** 25 mg/kg/dose PO q6h[1] Alternative for Intolerance to Liposomal Amphotericin B/Flucytosine: **Micafungin** 5 mg/kg/dose IV q24h (max: 150 mg/dose)	≥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)	Vancomycin IV[3] + **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose)	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. • **Cefepime** 50 mg/kg/dose IV q8h[1] (max: 2 g/dose) 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)	Vancomycin IV[3] + **Ampicillin-sulbactam** 75 mg/kg/dose IV q6h[1] (max: 3 g of ampicillin/dose) OR Vancomycin IV[3] + **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose)	4-6 weeks	

Footnotes:

1. Refer to Antimicrobial Dosing Recommendations for Pediatric Patients
2. If candidate for outpatient therapy, may consider administration via continuous infusion (same daily dose)
3. Refer to Empiric Dosing and Monitoring Recommendations for Vancomycin in Pediatric Patients
4. Refer to Empiric Dosing and Monitoring Recommendations for Aminoglycosides in Pediatric Patients

Antimicrobial Subcommittee Approval: 11/2018	Originated: 03/2016
P&T Approval: 11/2018	Last Revised: 03/2021
Revision History: UMHS P&T Antimicrobial Subcommittee: 02/2016, 11/2018; UMHS P&T Committee: 03/2016, 11/2018 03/21: Updated vancomycin and gentamicin hyperlinks	