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

Vancomycin goal troughs:
- Vancomycin trough goal 10-15 mcg/dL for pediatric patients with normal renal function (doses ≥60 mg/kg/day)
- Vancomycin trough 15-20 mcg/dL for pediatric patients with significant renal impairment (requiring doses <50 mg/kg/day)
- Consultation with a pediatric pharmacy specialist is recommended for establishing goals in children receiving 50-60 mg/kg/day

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

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### Definitive Therapy (Once Pathogen is Identified)

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<thead>
<tr>
<th>Pathogens</th>
<th>Antibiotic Therapy (renal dose adjustments may be necessary)(^1)</th>
<th>Duration</th>
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| **Viridans group streptococci OR Streptococcus galaloyticus (bovis)** | **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. |
| Penicillin MIC ≤0.12 mg/L | **Preferred (alternative):**
- **Penicillin G** 50,000 units/kg/dose IV q4h\(^{1,2}\) (max: 3 million units/dose)
  - **OR**
- **Gentamicin IV**\(^4\)
  + **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose)
  | 2 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 |  |
| Penicillin MIC ≥0.5 mg/L | **Preferred (alternative):**
- **Penicillin G** 50,000 units/kg/dose IV q4h\(^{1,2}\) (max: 4 million units/dose)
  - **OR**
  + **Gentamicin IV**\(^4\) for first 2 weeks\(^3\)
  | 4 weeks |  |
| Penicillin MIC >0.12-<0.5 mg/L | **Alternative for Severe PCN Allergy:**
- **Vancomycin IV**\(^3\)
  | 4 weeks |  |
| Penicillin MIC ≥0.5 mg/L | **Preferred (if susceptible):**
- **Ceftriaxone** 100 mg/kg/dose IV q24h (max: 2 g/dose)
  + **Gentamicin IV**\(^4\)
  | 4 weeks |  |
| Penicillin MIC >0.12-<0.5 mg/L | **Preferred (alternative):**
- **Penicillin G** 50,000 units/kg/dose IV q4h\(^{1,2}\) (max: 4 million units/dose)
  + **Gentamicin IV**\(^4\)
  | 4-6 weeks | • 4 week duration indicated only if symptoms of infection are <3 months in duration. |
| Penicillin MIC ≥0.5 mg/L | **Alternative for Severe PCN Allergy:**
- **Vancomycin IV**\(^3\)
<p>| 4 weeks |  |</p>
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| Enterococci strains susceptible to penicillin and gentamicin | **Preferred:**  
Ampicillin 75 mg/kg/dose IV q6h¹  
(max: 3 g/dose)  
+ Gentamicin IV¹  
OR  
Penicillin 60,000 units/kg/dose IV q4h¹,²  
(max: 4 million units/dose)  
+ Gentamicin IV¹  
**Preferred (alternative):**  
Ampicillin 75 mg/kg/dose IV q6h¹  
(max: 3 g/dose)  
+ Ceftriaxone 50 mg/kg/dose IV q12h  
(max: 2 g/dose)  
Alternative for Severe PCN Allergy:  
Vancomycin IV³  
+ Gentamicin IV 1 mg/kg/dose q8h¹ | 4-6 weeks  
6 weeks  
6 weeks |  
- Request susceptibility testing for penicillin if used for therapy.  
- 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  
Streptomycin peak goal 20-35 mg/L and trough goal <5 mg/L. |
| Enterococci strains susceptible to penicillin and resistant to gentamicin | **Preferred:**  
Ampicillin 75 mg/kg/dose IV q6h¹  
(max: 3 g/dose)  
+ Ceftriaxone 50 mg/kg/dose IV q12h  
(max: 2 g/dose)  
Alternative for Severe PCN Allergy (for streptomycin susceptible):  
Vancomycin IV³  
+ Streptomycin 10 mg/kg IV q12h¹  
(max: 1 g/dose)  
Alternative for Severe PCN Allergy (for streptomycin resistant):  
Consult Infectious Diseases  
+ Vancomycin IV³  
+ Obtain allergy consult for desensitization to ampicillin and ceftriaxone | 6 weeks |  
Streptomycin peak goal 20-35 mg/L and trough goal <5 mg/L. |
| Enterococci strains resistant to penicillin | Vancomycin IV³  
+ Gentamicin IV⁴ | 6 weeks |  |
| Enterococci strains resistant to vancomycin, aminoglycosides, and penicillin | Daptomycin 10-12 mg/kg IV q24h¹  
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 ceftriaxone may be considered in patients with persistent disease |
| Staphylococci (MSSA) | **Preferred:**  
Nafcillin 33 mg/kg/dose IV q4h²  
(max: 2 g/dose)  
Alternative for PCN Allergy (non-anaphylaxis):  
Cefazolin 33 mg/kg/dose IV q8h¹  
(max: 2 g/dose)  
Alternative for PCN Allergy (Anaphylaxis):  
Vancomycin IV³ | 6 weeks |  
- Cefazolin should not be used if CNS disease present. |
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| Staphylococci (MRSA)      | **Preferred:**  
|                           | Vancomycin IV³                                                | 6 weeks  | • Follow baseline and weekly CK with daptomycin therapy                                            |
|                           | Alternative for Vancomycin Allergy or Failure:  
|                           | Daptomycin 10 mg/kg IV q24h¹                                  |          |                                                                                                    |
| HACEK Group               | **Preferred:**  
|                           | Ceftriaxone 100 mg/kg/dose IV q24h (max: 2 g/dose)           | 4 weeks  |                                                                                                    |
|                           | Alternative:  
|                           | Ampicillin-sulbactam 75 mg/kg/dose IV q6h¹ (max: 3 g of ampicillin/dose) |          |                                                                                                    |
|                           | Alternative for Severe PCN Allergy:  
|                           | Ciprofloxacin 10 mg/kg/dose IV q8h¹ (max: 400 mg/dose)       |          |                                                                                                    |
| Candida spp.              | **Preferred:**  
|                           | Liposomal amphotericin B 3-5 mg/kg/dose IV q24h¹ + Flucytosine 25 mg/kg/dose PO q6h³ | ≥6 weeks | • Following initial therapy with IV antifungal agent, long-term suppression with an oral azole may be considered for sensitive pathogens.  
|                           | Alternative for Intolerance to Liposomal Amphotericin B/Flucytosine:  
|                           | Micafungin 5 mg/kg/dose IV q24h (max: 150 mg/dose)           |          | • 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 IV³ + 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 (max 2 g) IV q8h¹ 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 IV³ + Ampicillin-sulbactam 75 mg/kg/dose IV q6h¹ (max: 3 g of ampicillin/dose) OR Vancomycin IV³ + 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 Gentamicin/Tobramycin in Pediatric Patients