# G81: What is the optimal antimicrobial treatment for patients with orthopedic infections caused by *Kingella kingae*?

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## Response/Recommendation

Beta-lactam antibiotics are the most effective first-line treatment for *Kingella kingae* infections. For cases involving biofilm-associated infections, adjunctive rifampin may be included. The recommended duration of therapy spans 4–6 weeks for intravenous treatment and 6–12 weeks for oral therapy, with adjustments based on infection severity, chronicity, and patient response.

Level of Evidence: Limited

**Delegate Vote:** Agree: [% vote], Disagree: [%], Abstain: [%]

### Rationale

*Kingella kingae* is a leading cause of musculoskeletal infections in children under 5 years and is increasingly recognized in adults with invasive orthopedic infections. Its intrinsic resistance to certain antibiotics (such as clindamycin and vancomycin vancomycin) necessitates careful antibiotic selection. Traditional culture methods often fail to detect *K. kingae* due to its slow growth. Advanced molecular diagnostics, such as 16S rRNA gene sequencing and the BIOFIRE Joint Infection (BJI) Panel, improve accuracy and speed by identifying *K. kingae* DNA even when cultures are negative.

Beta-lactams are generally highly effective against *K. kingae*, and intravenous cephalosporins (ceftriaxone or cefotaxime) are the preferred initial therapy. Step-down oral therapy with amoxicillin-clavulanate demonstrates robust efficacy with good bone penetration. The typical response to these agents is rapid, with clinical improvement often seen within 48 hours of starting treatment (Yagupsky et al., 2022; Ceroni et al., 2010).

For patients with beta-lactam allergies, ciprofloxacin or levofloxacin can be considered. However, their efficacy is not as well-documented in pediatric populations. Macrolides (such as erythromycin) and fluoroquinolones (such as ciprofloxacin) have been tested, but evidence supports the efficacy of beta-lactams due to better bone penetration and higher inherent susceptibility (Ilharreborde et al., 2014; Williams et al., 2018). Clindamycin, oxacillin, and vancomycin are not recommended due to resistance. (Yagupsky et al., 2011).

Biofilm formation complicates treatment, especially in prosthetic joint infections. Adjunctive rifampin is recommended during IV therapy for its biofilm-disruptive properties. For chronic infections, prolonged suppressive therapy may be required, particularly in cases involving retained hardware.

# **Diagnostic and Therapeutic Approaches**

Use molecular diagnostic tools such as the BIOFIRE JI Panel or 16S rRNA gene sequencing for rapid identification. Combine joint or synovial fluid samples with blood culture broths to enhance sensitivity.

Initial IV Therapy typically starts with Ceftriaxone (2g once daily) or cefotaxime (1–2g every 6–8 hours), for a period of 4–6 weeks. Consider adjunctive rifampin (600mg once or twice daily) should be considered for cases involving biofilm-associated infections. A conversion to step-down oral therapy is recommended thereafter, including amoxicillin-clavulanate (1g every 8 hours) or cefixime (400mg daily). Levofloxacin (500-750mg qd) or ciprofloxacin (500mg BD) are the preferred alternatives in cases of beta-lactam allergy or intolerance. The duration of antibiotic coverage should span a period of 6–12 weeks total.

Early surgical intervention, including debridement and hardware removal, may be necessary in chronic infections. Monitor inflammatory markers and clinical response to guide therapy duration.

## **Evidence Summary**

Intravenous beta-lactam therapy followed by oral amoxicillin-clavulanate has consistently demonstrated good clinical and functional outcomes. Studies report rapid symptom resolution within 48 hours of initiating treatment.

Lower complication rates were noted with conversion to oral step-down therapy compared to prolonged IV therapy. Biofilm-associated infections require longer antibiotic durations and adjunctive therapies.

Most *K. kingae* infections occur in children under 60 months. Tailored pediatric dosing of ceftriaxone and amoxicillin-clavulanate ensures efficacy and safety. Molecular diagnostics are particularly beneficial in pediatric cases, where traditional methods may yield false negatives.

## Conclusion

Beta-lactam antibiotics remain the cornerstone for treating *Kingella kingae* infections. Their efficacy, coupled with advanced diagnostic tools, ensures rapid pathogen identification and effective treatment. Adjunctive therapies and prolonged suppressive regimens may be necessary in complex or chronic cases. Further research is warranted to optimize therapy duration and evaluate emerging antibiotic alternatives.

#### References

- 1. "in diagnosing periprosthetic hip and knee joint infections in patients with unclear conventional microbiological results" by Sara Hunter et al., Study ID: 39446985.
- 2. "Understanding the management of pediatric spondylodiscitis based on existing literature; a systematic review" by Narges Lashkarbolouk # 1 2 et al., Study ID: 37980513.
- 3. "Global epidemiology of childhood bone and joint infection: a systematic review" by Sarah Hunter 1 et al., Study ID: 35048321.
- 4. "Epidemiology and Management of Acute, Uncomplicated Septic Arthritis and Osteomyelitis: Spanish Multicenter Study" by Cristina Calvo 1 et al., Study ID: 27455444.
- 5. "The Effectiveness of Metagenomic Next-Generation Sequencing in the Diagnosis of Prosthetic Joint Infection: A Systematic Review and Meta-Analysis" by Jun Tan 1 et al., Study ID: 35755833.
- 6. "A Population Pharmacokinetic Analysis of Continuous Infusion of Cloxacillin during Staphylococcus aureus Bone and Joint Infections" by Johan Courjon # 1 2 et al., Study ID: 32988822.
- 7. "Analysis of postoperative and hematogenous prosthetic joint-infection microbiological patterns in a large cohort" by Valérie Zeller 1 et al., Study ID: 29395369.
- 8. "Do Culture Negative Periprosthetic Joint Infections Remain Culture Negative?" by Beverly L Hersh 1 et al., Study ID: 31327645.
- 9. "The Effect of Preoperative Antimicrobial Prophylaxis on Intraoperative Culture Results in Patients with a Suspected or Confirmed Prosthetic Joint Infection: a Systematic Review" by Marjan Wouthuyzen-Bakker 1 et al., Study ID: 28659322.
- 10. "Outpatients with acute osteoarticular infections had favourable outcomes when they received just oral antibiotics without intravenous antibiotics" by Rosa Alcobendas 1 et al., Study ID: 29705992.
- 11. "Spinal infections in children: a multicentre retrospective study" by R Dayer 1 et al., Study ID: 29629576.
- 12. "Epidemiology and Management of Acute, Uncomplicated Septic Arthritis and Osteomyelitis: Spanish Multicenter Study" by Cristina Calvo 1 et al., Study ID: 27455444.
- 13. "[Diffusion in bone tissue of antibiotics]" by E Boselli 1 et al., Study ID: 10636023.
- 14. "Bacterial osteomyelitis in pediatric patients: a comprehensive review" by Ricardo Restrepo 1 et al., Study ID: 38504031.
- 15. "The role of BioFire Joint Infection Panel" by S. Gardete-Hartmann et al., Study ID: DOI: 10.1302/2046-3758.
- 16. "A multicentre evaluation and expert recommendations of use of the newly developed BioFire Joint Infection polymerase chain reaction panel" by Kordo Saeed 1 2 et al., Study ID: 36474096.
- 17. "Antibiotic therapy for osteoarticular infections in 2023: Proposals from the Pediatric Infectious Pathology Group (GPIP)" by Mathie Lorrot 1 et al., Study ID: 37741341.
- 18. "Oral Versus Intravenous Antibiotics for Pediatric Osteoarticular Infection: When and to Whom?" by Rosa M Alcobendas Rueda 1 et al., Study ID: 35763692.

- 19. "Polymerase Chain Reaction Assay Using the Restriction Fragment Length Polymorphism Technique in the Detection of Prosthetic Joint Infections: A Multi-Centered Study" by Ataollah Moshirabadi 1 et al., Study ID: 30471785.
- 20. "Risk factors associated with complications/sequelae of acute and subacute haematogenous osteomyelitis: an Italian multicenter study" by Elena Chiappini 1 et al., Study ID: 29569505.
- 21. "Association between oropharyngeal carriage of Kingella kingae and osteoarticular infection in young children: a case-control study" by Jocelyn Gravel 1 et al., Study ID: 28874431.
- 22. "Kingella kingae and the Empiric Antibiotic Therapy for Skeletal System Infections" by Pablo et al., Study ID: 30137534.
- 23. "Identifying Reservoirs of Infections Caused by Kingella kingae: A Case-Control Study of Oropharyngeal Carriage of K. kingae Among Healthy Adults" by Gabriel Brändle 1 et al., Study ID: 27420804.
- 24. "Beta-lactamase production by Kingella kingae in Israel is clonal and common in carriage organisms but rare among invasive strains" by P Yagupsky 1 et al., Study ID: 23479041.
- 25. "Osteomyelitis pubis caused by Kingella kingae in an adult patient: report of the first case" by Dunja Wilmes 1 et al., Study ID: 23031309.
- 26. "Genotyping of invasive Kingella kingae isolates reveals predominant clones and association with specific clinical syndromes" by Uri Amit 1 et al., Study ID: 22806593.
- 27. "Molecular diagnosis of Kingella kingae pericarditis by amplification and sequencing of the 16S rRNA gene" by Matta Matta 1 et al., Study ID: 17634294.
- 28. "Kingella kingae septic arthritis with endocarditis in an adult" by Bouajina Elyès 1 et al., Study ID: 16807042.
- 29. "An adult case of oral infection with Kingella kingae" by Ph A Van Damme 1 et al., Study ID: 14690666.
- 30. "Septic arthritis due to Kingella kingae in an adult" by V Estève et al., Study ID: 11235790.
- 31. "The Past, Present, and Future of Kingella kingae Detection in Pediatric Osteoarthritis" by Pablo et al., Study ID: https://doi.org/10.3390/diagnostics12122932.
- 32. "Alpha-Defensin Offers Limited Utility in Routine Workup of Periprosthetic Joint Infection" by Lindsay T. Kleeman-Forsthuber MD a et al., Study ID: https://doi.org/10.1016/j.arth.2020.12.018.
- 33. "Antibiotic Therapy for Prosthetic Joint Infections: An Overview" by Benjamin Le Vavasseur 1 et al., Study ID: 35453237.
- 34. "Oral versus Intravenous Antibiotics for Bone and Joint Infection by Ho-Kwong Li et al. DOI: 10.1056" by Oral et al., Study ID: randomized-controlled.
- 35. "Empirical antibiotic therapy in prosthetic joint infections" by Ricardo SOUSA et al., "Acta Orthop. Belg., 2010, 76, 254-259."
- 36. "A Review of the Clinical Utilization of Oral Antibacterial Therapy in the Treatment of Bone Infections in Adults" by Nicholas Haddad et al., https://doi.org/10.3390/