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Antibiotic Prophylaxis in Total Joint Arthroplasty

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Abstract

Periprosthetic joint infection (PJI) following total hip or knee arthroplasty is a serious complication that contributes to early revision surgery, increased morbidity, and elevated healthcare costs. This review evaluates current evidence on antibiotic strategies for PJI preven-tion, focusing on perioperative prophylaxis. Intravenous cefazolin, administered within one hour before incision, remains the gold standard due to its broad-spectrum activity and safety profile, including in many patients with reported penicillin allergies. Alternatives such as ce-furoxime and vancomycin are considered in specific cases, though vancomycin monotherapy is less effective and carries higher risks. Dual antibiotic prophylaxis, particularly adding vancomy-cin in MRSA-colonized or high-risk patients, has not consistently shown benefit in broader pop-ulations. Local delivery methods such as intraosseous regional antibiotics (IORA) and vancomy-cin powder have shown promise in increasing tissue concentrations but lack definitive clinical benefit, with concerns about complications. Similarly, extended oral antibiotic prophylaxis postoperatively may reduce PJI risk in high-risk populations, though evidence remains mixed. The article concludes by recommending weight-based cefazolin as standard prophylaxis, dual therapy for high-risk individuals, and further research to clarify the role of adjunctive and local delivery methods in PJI prevention.

Keywords

Periprosthetic Joint Infection (PJI), Total Knee Arthroplasty (TKA), Total Hip Arthro-plasty (THA), Surgical Prophylaxis, Orthopaedic Implants; Postoperative Complications, Antibi-otic Stewardship, Infection Prevention; Revision Surgery, Bone and Joint Infections

1. Interdiction

Periprosthetic joint infection (PJI) following total knee (TKA) or total hip arthroplasty (THA) is a serious condition that adversely affects patient outcomes, often leading to low satisfaction rates even after successful treatment [1]. PJI significantly increases patient morbidity and mortality and is the leading cause of early revision surgery after total joint arthroplasty [2]. This condition not only impacts individual patients but also places a substantial financial burden on the healthcare system [3]. In the United States, the inci-dence of PJI varies by joint, with estimates of 1-2% for primary THA and TKA [4]. The most common pathogens are Gram-positive bacteria, followed by Gram-negative bacteria and fungi [5]. Typical Gram-positive pathogens include coagulase-negative staphylococci, Staphylococcus aureus, enterococci, streptococci and micrococci. Infections can arise from local spread from the skin or air, or through hematogenous seeding of the affected joint. It is estimated that a minimum of 10^5 bacteria per gram of tissue can cause PJI, while as few as 50 colony-forming units per milliliter in an intraoperative tissue sample are sufficient to diagnose the infection [6,7]. Therefore, reducing the bacterial burden at the surgical site is crucial for preventing postoperative infections. This can be accomplished both through efforts to maintain perioperative sterility and through the use of antibiotics. Effective anti-biotic administration plays

a vital role in minimizing infection risk during total joint arthroplasty. Antibiotic prophylaxis has been proven to reduce the number of PJIs and is considered the gold standard in PJI prevention. There is variability and debate on what is the ideal route of antibiotic administration to prevent prosthetic joint infection in THA and TKA. We present here a brief review of the current literature and evidence on antibiotic use during primary total hip and knee replacements.

2. Intravenous Perioperative Antibiotic Administration

Use of intravenous (IV) perioperative antibiotics has been one of the most noteworthy interventions in the prevention of PJI. Evidence in support of perioperative antibiotic prophylaxis dates back to the late 1960s and the practice became the standard of care decades before the Center for Disease Control and Prevention (CDC) established in 1999 perioperative antibiotic prophylaxis as a major guideline [8,9]. There are several important parameters to consider in optimizing the efficacy of antibiotic prophylaxis. These include choice of antibiotic, route of administration, dosage, timing of dose, duration, side effects, and potential bacterial resistance. Antimicrobial stewardship, which is a systematic effort to support evidence-based antibiotic use, is one of the main considerations in the judicious utilization of perioperative antibiotics [10]. Inappropriate antibiotic use may lead to in-creased adverse effects, secondary infections, drug interactions, additional costs, pro-longed lengths of stay, and hospital readmissions. Furthermore, bacterial resistance may develop, which can then lead to treatment failure in confirmed cases of PJI [11,12].

While antibiotic choices vary in the literature, the American Academy of Orthopaedic Surgeons (AAOS) 2019 clinical guidelines for diagnosis and prevention of periprosthetic joint infection recommend the use of the first (cefazolin) or second (cefuroxime) generation cephalosporin, or a glycopeptide (vancomycin) [13]. First and second generation cephalo-sporins are preferred for their adequate Gram positive and negative coverage as well as their favorable side effect profile. The current AAOS guidelines recommend a weight-based dose of 1 to 3 grams of cefazolin to be administered within 1 hour of surgical inci-sion. The rationale for giving antibiotics within one hour of incision emerges from prior pharmacokinetic and clinical studies demonstrating that the infectious and immunologic status of a patient in the 1 hour prior to surgical incision has the greatest influence on the risk of PJI [14].

Cefazolin produces its antibacterial effect by inhibiting penicillin-binding proteins (PBPs), which are essential for the crosslinking of peptidoglycan in the bacterial cell wall which is necessary for the structural integrity of the bacterial cell wall [15]. Additionally, cefazolin may inhibit the activity of gamma chain receptor-dependent cytokines, includ-ing IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21, resulting in an anti-inflammatory effect [16]. Its antimicrobial spectrum includes Gram-positive bacteria such as Streptococcus, Staphylo-coccus, and Enterococcus, as well as Gram-negative bacteria like Haemophilus, Klebsiella, Escherichia, Proteus, Pseudomonas, Serratia, and Enterobacter [17]. Cefazolin's pharmacological properties and broad-spectrum coverage include the most common pathogens associated with periprosthetic joint infections, making it an ex-cellent choice as the primary prophylactic agent. Wyles and colleagues investigated the ef-ficacy of cefazolin compared to alternative agents used in cases of cefazolin allergy. Their study revealed that cefazolin use reduced the risk of PJI by 32% compared to alternatives. Furthermore, they found cefazolin to be safe for patients with a reported penicillin allergy [18]. Chaudry and colleagues investigated the cross-reactivity between penicillin and cephalosporins, highlighting the critical role of the R1 side chain in allergic reactions. Their analysis demonstrated that cefazolin has a unique R1 side chain distinct from that found in most penicillins, significantly reducing the risk of cross-reactivity [19]. Addition-ally, cefazolin exhibits an acceptable safety profile, boasting a low risk of hypersensitivity and allergic reactions, with infrequent adverse effects. While rare, cases of Clostridium dif-ficile infection and oral candidiasis, nephrotoxicity, and neurological hyperactivity with risk of seizures have been reported following cefazolin administration [20].

Cefuroxime is another single-agent antibiotic approved for prophylaxis prior to total joint arthroplasty. As a second-generation cephalosporin, cefuroxime has less activity against Gram-positive cocci compared to first-generation cephalosporins like cefazolin but offers enhanced activity against Gram-negative bacilli. The recommended dosage is a standard 1500 mg administered within one hour before surgery, which is weight inde-pendent. A meta-analysis conducted by Ahmed and colleagues compared the efficacy of cefazolin and cefuroxime in preventing surgical site infections and found no significant differences between the two agents. The authors concluded that both antibiotics are equal-ly effective in preventing surgical site infections; however, due to its cost-effectiveness, cefazolin was recommended as the first-choice prophylactic agent [21]. Vancomycin is a glycopeptide antibiotic which functions by binding to the terminal D-alanyl-D-alanine residues of NAM/NAG-peptides, thereby preventing their incorpora-tion into the peptidoglycan matrix and inhibiting bacterial cell wall synthesis. Additional-ly, vancomycin disrupts bacterial cell membrane permeability and interferes with RNA synthesis [22].

Its antimicrobial activity is limited to Gram-positive bacteria, with no effect on Gram-negative organisms, mycobacteria, or fungi. The recommended dosage of van-comycin for perioperative prophylaxis is weight-based, at 15 mg/kg, and should be ad-ministered as a slow infusion within two hours before surgery. Kheir and colleagues eval-uated the efficacy and safety of vancomycin as a single agent for perioperative prophylax-is in total joint arthroplasty. Their analysis found vancomycin to be less effective than cefazolin in preventing surgical site infections (2% vs 1% of PJI respectively). They con-cluded that vancomycin not only has a less favorable bacterial coverage profile but is often underdosed (in 64% of cases) or administered at

an inappropriate time (in 72% of cases). These factors frequently result in failure to achieve adequate therapeutic concentrations thus compromising its effectiveness [23]. Additionally, vancomycin has a narrow thera-peutic index, increasing the risk of systemic complications such as nephrotoxicity, red man syndrome, phlebitis, neutropenia, thrombocytopenia, and other allergic reactions. The authors recommend restricting the use of vancomycin as a single prophylactic agent. For these reasons, the use of intravenous vancomycin is primarily reserved for cases of verified anaphylaxis to cefazolin.

3. Dual Antibiotic Prophylaxis

The combination of two perioperative antibiotics has been studied to determine whether they provide greater efficacy in reducing the incidence of periprosthetic joint in-fections compared to single-agent prophylaxis. Multi-drug protocols typically include combinations of cephalosporins, aminoglycosides, and glycopeptides. Peel and col-leagues conducted a multicenter, randomized, placebo-controlled trial to evaluate the effi-cacy of double antibiotic prophylaxis with cefazolin and vancomycin in patients without MRSA colonization. They concluded that adding vancomycin to antibiotic prophylaxis with cefazolin was not superior to placebo in preventing surgical site infections [24]. However, adding vancomycin to the prophylactic regimen may be beneficial for patients colonized with MRSA, or at high risk for MRSA infection, such as healthcare workers, in-stitutionalized patients, and those treated in centers with a high prevalence of MRSA in-fections [25-27]. Another commonly used antibiotic in dual prophylaxis are aminoglycosides.

Ashke-nazi and colleagues conducted a retrospective cohort study of patients undergoing prima-ry total knee arthroplasty (TKA) to analyze the effect of gentamicin in combination with cefazolin. The study showed a slight, yet statistically insignificant, reduction in surgical site infections in the gentamicin group (0.86% vs. 1.3% in the control group, $p = 0.43$), without significant increase in gentamycin associated complications. The authors' final recommendation was against the routine use of a single dose of gentamicin in combina-tion with routine cefazolin for dual antibiotic prophylaxis [28]. Aminoglycosides may still be useful in specific situations, such as patients at high risk of gram-negative infections, especially those in institutions with a high prevalence of such infections. Additionally, they may be considered for patients with anaphylactic reac-tion to cefazolin who receive vancomycin. Adding gentamicin or tobramycin in such sce-narios can broaden and extend bacterial coverage. There are concerns about the cumula-tive side effects with the concurrent administration of glycopeptides and aminoglycosides, particularly nephrotoxicity and ototoxicity [29,30]. Further research is required before aminoglycosides can be recommended for use in dual prophylaxis.

4. Local Perioperative Antibiotic Delivery Systems

4.1. Intraosseous Regional Antibiotics

Local antibiotic delivery systems offer the advantage of delivering high concentra-tions of antibiotics directly to the surgical field, maximizing antimicrobial efficacy while minimizing systemic side effects. One emerging technique in this regard involves the in-tramedullary injection of antibiotics at the surgical site, known as intraosseous regional antibiotics (IORA) [31,32]. This technique achieves significantly higher tissue concentra-tions of antibiotics compared to systemic intravenous routes, despite requiring smaller dosages. This not only reduces the potential for antibiotic-related side effects but also shows promise in lowering postoperative infection rates [33-42]. IORA offers additional benefits, including shorter infusion times and reduced sus-ceptibility to variations in patient body weight [31-41]. It is particularly advanta-geous for patients requiring vancomycin, as it eliminates the need for prolonged infusion times and minimizes systemic effects such as nephrotoxicity and red man syndrome. Ad-ditionally, IORA has demonstrated improved tissue concentrations when used with cefazolin [38-41]. The efficacy of IORA remains significant even when performed without a tourniquet for total hip arthroplasty (THA) or with limited tourniquet use for total knee arthroplasty (TKA) [34,35]. A recent meta-analysis of data from four randomized controlled trials per-formed by Miltenberg et al, revealed that tissue concentrations of antibiotics with IORA in TKA are, on average, ten times higher than those achieved with IV infusion, along with significantly lower postoperative rates of periprosthetic joint infection (PJI) [43].

5. Topical Vancomycin Powder

Another widely used antibiotic delivery system is the direct application of antibiotic powder into the surgical field, with vancomycin powder (VP) being the most commonly used agent. Local application of VP achieves concentrations up to ten times the therapeu-tic levels, lasting for at least 24 hours post-wound closure, with minimal systemic absorp-tion [44]. VP has shown potential to reduce rates of postoperative deep joint infections [45–53]. Some studies, however, have raised concerns about increased rates of wound compli-cations associated with VP use [52–54]. A 2023 randomized controlled trial (RCT) involv-ing 165 patients (80 receiving VP and 85 controls) was stopped early after one-year prelim-inary data demonstrated a higher incidence of periprosthetic joint infections (PJI) in the VP group ($n = 3$) compared to the control group ($n = 0$). Additionally, eight patients in the VP group experienced postoperative complications such as myocardial infarction, pulmo-nary embolism, or anemia requiring transfusion, compared to only two patients in the control group [55]. A randomized controlled trial by Mulpur et al., involving 1,022 pa-tients, found no significant difference in periprosthetic joint infection (PJI) rates at 12 months ($p = 0.264$). However, the study did report a significantly higher rate of postopera-tive wound complications in the vancomycin powder (VP) group (13.2% vs. 7.56%), with an odds ratio of 1.64 for minor wound complications [56]. Given the methodological limi-tations and heterogeneity of many retrospective studies—along with the lack of compel-ling results from more rigorous RCTs—a 2023 editorial in

The Bone & Joint Journal con-cluded that "the evidence is not strong enough to recommend the use of vancomycin powder." [57].

6. Antibiotic-Laden Materials

Antibiotic-laden bone cement (ALBC) is another vehicle for local antibiotic delivery that is often used in the setting of existing periprosthetic joint infection and has been eval-uated for use in primary total knee arthroplasty [58]. Numerous large systematic reviews and RCTs alike suggest that ALBC is not associated with decreased rates of post-operative infection [58-60]. The technique has been associated with significantly higher procedure costs without statistically significant reduction in infection rates [61]. Calcium phosphate antibiotic beads are an alternative local antibiotic delivery system that has shown success in reducing both planktonic and biofilm forms of bacteria in-vitro [62]. Vancomycin and tobramycin are the most commonly used antibiotics with this delivery vehicle. Lachica and coauthors conducted a randomized controlled trial evaluating the effectiveness of vancomycin-loaded calcium sulfate in reducing the risk of periprosthetic joint infection (PJI) in patients with non-modifiable risk factors. Their study demonstrated a significant reduction in three-month postoperative PJI rates compared to patients receiving intrave-nous antibiotics alone [63]. However, the use of calcium sulfate beads has been associated with specific complications, including wound drainage, hypercalcemia, and potential abrasion of the implants' bearing surface [64,65]. Due to these concerns, their use during primary total joint arthroplasty has not gained widespread acceptance and is primarily reserved for the management and treatment of PJI [65].

7. Antibiotic Irrigation Solutions

Antibiotic irrigation solutions were evaluated in the context of primary total joint ar-throplasty. Goswami and coauthors reported the inferiority of polymyxin-bacitracin, van-comycin, and gentamicin solutions compared to povidone-iodine or chlorhexidine solu-tions in eradicating Staphylococcus and Escherichia coli in vitro. Chlorhexidine demon-strated a favorable antibacterial effect, but was also cytotoxic to fibroblasts. Povidone-iodine showed antibacterial efficacy without significant cytotoxicity [66]. Similarly, An-glen and colleagues observed a lack of superiority of antibiotic irrigation solutions in-traoperatively. In their randomized trial comparing bacitracin solution to castile soap so-lution for irrigation in open fracture cases, they found no significant differences in the rate of SSI and fracture healing complications between the two agents [67]. In a meta-analysis of randomized controlled trials evaluating the efficacy of different irrigation solutions for preventing surgical site infections in general surgery, de Jonge and colleagues reported the superiority of povidone-iodine solution over antibiotic solutions [68].

8. Dilute Betadine Lavage

Unlike other antibiotic solutions, there has been growing evidence that dilute beta-dine lavage (DBL) is associated with decreased rates of postoperative infection in primary total joint arthroplasty [69–72]. A 2018 analysis found DBL to be highly cost effective as a infection prophylactic measure in primary total joint arthroplasty [73]. However, other studies have raised skepticism. A large retrospective cohort study by Hernandez et al. ana-lyzed the use of dilute betadine lavage (DBL) during primary total hip and knee arthro-plasty (THA and TKA) compared to procedures without DBL. The study found no signifi-can't reduction in infection-related reoperations associated with betadine use [74].

9. Other Techniques

Antibiotic-laden sponges have gained interest with mixed evidence in other surgical fields, however, research on their application to hip and knee arthroplasty is limited with-out significant evidence to support an association with reduced infection rates despite some concerns for technique-related complications [75-76]. Intra-articular injection of antibiotic solution, usually vancomycin with or without tobramycin in normal saline injected after fascial closure, has been shown to have high in-tra-articular antibiotic concentrations up to 48 hours post-operatively without toxic sys-temic levels, but data regarding clinical implications and effectiveness is limited [77-80].

10. Extended Postoperative Antibiotic Prophylaxis

The use of extended postoperative antibiotics remains a topic of debate. While the American Association of Hip and Knee Surgeons (AAHKS) recommends administering parenteral antibiotics during the first 24 hours postoperatively, the latest CDC guidelines do not support their use after wound closure [81 82]. A recent meta-analysis of 14 studies by Siddiqi et al found no difference in PJI rates between patients who received a single preoperative antibiotic dose and those who underwent extended parenteral postoperative prophylaxis. However, the authors noted that many of these studies were underpowered and potentially biased [83]. Several studies have suggested that extended oral postoperative antibiotic prophylax-is may reduce the risk of PJI, particularly in high-risk patients. Those considered high risk include individuals with a high body mass index (BMI 35 kg/m^2 or higher), active smok-ing status, diabetes, autoimmune disease, chronic kidney disease, or colonization with methicillin-sensitive Staphylococcus aureus (MSSA) or methicillin-resistant Staphylococ-cus aureus (MRSA).

In this population, the use of extended oral antibiotic prophylaxis with cefadroxil reduced the risk of SSI at 90 days postoperatively by four times compared to those who did not receive postoperative antibiotics [84]. Additionally, a retrospective study by Khair et al. found a statistically significant reduction in 1-year PJI rates among patients who received extended oral antibiotics for seven days postoperatively [85]. Despite these findings, a recent study by Flynn and colleagues reported no statistical-ly significant difference in 1-year PJI rates between high-risk patients who received ex-tended oral antibiotic prophylaxis and those who received only the standard perioperative antibiotic

prophylaxis with intravenous Ancef and Vancomycin [86]. Further large-scale, prospective, randomized trials are needed to elucidate whether extended oral antibiotic prophylaxis provides a meaningful benefit for high-risk patients.

11. Discussion

Periprosthetic joint infection remains a significant concern in total joint arthroplasty, with multiple established risk factors. These risks can be divided into patient-related and surgery-related factors. Patient-related risk factors include obesity (BMI 35 kg/m^2 or high-er), diabetes, malnutrition, anemia, smoking, Staphylococcus aureus colonization, vita-min D deficiency, active urinary tract infections, poor dental hygiene, and chronic renal, cardiac, autoimmune or inflammatory diseases. Surgery-related factors include perioperative sterility, surgical time, type of anesthesia, surgical site preparation, perioperative antibiotic prophylaxis, surgical technique, blood preservation, wound management, and pain control. Since many surgical risk factors are modifiable, implementing strategies to reduce infection risk is critical. Among these, prophylactic antibiotic use plays a key role in min-imizing the likelihood of PJI. Current CDC guidelines support the administration of a sin-gle preoperative dose of an antibiotic, preferably a first-generation cephalosporin, within one hour of incision as a key recommendation in preventing PJIs. Intraosseous antibiotic prophylaxis has emerged as a promising method in total knee arthroplasty, particularly when a tourniquet is used.

This technique enables timely antibiotic administration before surgery, achieving high tissue concentrations while minimizing systemic exposure. It is especially beneficial when dual antibiotic prophylaxis is utilized with vancomycin, as in-traosseous delivery ensures effective tissue penetration without the need for strict dosing protocols. Additional Level 1 evidence is needed to evaluate the safety and efficacy of in-traosseous prophylaxis in total hip arthroplasty. Extended postoperative antibiotic prophylaxis remains variable and further higher-level studies are warranted to elucidate whether these protocols are effective in reducing the rate of PJIs. Based on current available literature, we recommend the routine use of a single pre-operative dose of cefazolin based on the body weight, dual antibiotic prophylaxis with Vancomycin for patients with MRSA colonization, health care workers or institutional-ized patients. For patients considered to be at high risk for PJI, a 7-day extended postopera-tive course of antibiotics should be considered. Other antibiotic protocols and routes of administration remain controversial and re-quire further research to establish their effectiveness.

References

1. Helwig, P., Morlock, J., Oberst, M., Hauschild, O., Hübner, J., Borde, J., ... & Konstantinidis, L. (2014). Periprosthetic joint infection—effect on quality of life. International orthopaedics, 38(5), 1077-1081.
2. Wildeman, P., Rolfson, O., Söderquist, B., Wretenberg, P., & Lindgren, V. (2021). What are the long-term outcomes of mortality, quality of life, and hip function after prosthetic joint infection of the hip? A 10-year follow-up from Sweden. Clinical Orthopaedics and Related Research®, 479(10), 2203-2213.
3. Premkumar, A., Kolin, D. A., Farley, K. X., Wilson, J. M., McLawhorn, A. S., Cross, M. B., & Sculco, P. K. (2021). Projected economic burden of periprosthetic joint infection of the hip and knee in the United States. The Journal of arthroplasty, 36(5), 1484-1489.
4. Ayoade, F., Li, D. D., Mabrouk, A., & Todd, J. R. (2021). Prosthetic joint infection. StatPearls; StatPearls Publishing: Treasure Island, FL, USA.
5. Fröschen, F. S., Randau, T. M., Franz, A., Molitor, E., & Hischebeth, G. T. R. (2022). Microbiological profiles of patients with periprosthetic joint infection of the hip or knee. Diagnostics, 12(7), 1654.
6. Krizek, T. J., & Robson, M. C. (1975). Evolution of quantitative bacteriology in wound management. The American Journal of Surgery, 130(5), 579-584.
7. Li, C., Renz, N., & Trampuz, A. (2018). Management of periprosthetic joint infection. Hip & pelvis, 30(3), 138-146.
8. Bernard, H. R., & Cole, W. R. (1964). The prophylaxis of surgical infection: the effect of prophylactic antimicrobial drugs on the incidence of infection following potentially contaminated operations. Surgery, 56, 151-157.
9. AlBuhairan, B., Hind, D., & Hutchinson, A. (2008). Antibiotic prophylaxis for wound infections in total joint arthroplasty: a systematic review. The Journal of Bone & Joint Surgery British Volume, 90(7), 915-919.
10. Shrestha, J., Zahra, F., & Cannady Jr, P. (2024). Antimicrobial Stewardship. [Updated 2023 Jun 20]. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2020-01.
11. Craxford, S., Bayley, E., & Needoff, M. (2014). Antibiotic-associated complications following lower limb arthroplasty: a comparison of two prophylactic regimes. European Journal of Orthopaedic Surgery & Traumatology, 24(4), 539-543.
12. Llor, C., & Bjerrum, L. (2014). Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. Therapeutic advances in drug safety, 5(6), 229-241.
13. American Academy of Orthopaedic Surgeons Diagnosis and Prevention of Periprosthetic Joint Infections Evi-dence-Based Clinical Practice Guideline. https://www.aaos.org/pjicpg Published March 11, 2019.
14. Parvizi, J., Gehrke, T., & Chen, A. F. (2013). Proceedings of the international consensus on periprosthetic joint infection. The bone & joint journal, 95(11), 1450-1452.
15. Karunarathna, Indunil & Gunasena, P & Hapuarachchi, T & Ekanayake, U & Gunawardana, K & Aluthge, P & Bandara, Sau & Jayawardana, Asoka & Alvis, Kapila & Gunathilake, S. (2024). Mechanism of Action and Clas-sification of Cephalosporins. 10.13140/RG.2.2.15854.22081.
16. Żyżyńska-Granica, B., Trzaskowski, B., Dutkiewicz, M., Zegrocka-Stendel, O., Machcińska, M., Bocian, K., ... & Koziak, K. (2020). The anti-inflammatory potential of

cefazolin as common gamma chain cytokine inhibitor. Scientific Reports, 10(1), 2886.
17. Bergeron, M. G., Brusch, J. L., Barza, M., & Weinstein, L. (1973). Bactericidal activity and pharmacology of cefazolin. Antimicrobial agents and chemotherapy, 4(4), 396-401.
18. Wyles, C. C., Hevesi, M., Osmon, D. R., Park, M. A., Habermann, E. B., Lewallen, D. G., ... & Sierra, R. J. (2019). 2019 John Charnley Award: increased risk of prosthetic joint infection following primary total knee and hip arthroplasty with the use of alternative antibiotics to cefazolin: the value of allergy testing for antibiotic prophylaxis. The bone & joint journal, 101(6_Supple_B), 9-15.
19. Chaudhry, S. B., Veve, M. P., & Wagner, J. L. (2019). Cephalosporins: a focus on side chains and β-lactam cross-reactivity. Pharmacy, 7(3), 103.
20. Kusaba, T. (2009). Safety and efficacy of cefazolin sodium in the management of bacterial infection and in surgical prophylaxis. Clinical Medicine. Therapeutics, 1, CMT-S2096.
21. Ahmed, N. J., Haseeb, A., Alamer, A., Almalki, Z. S., Alahmari, A. K., & Khan, A. H. (2022). Meta-analysis of clinical trials comparing cefazolin to cefuroxime, ceftriaxone, and cefamandole for surgical site infection prevention. Antibiotics, 11(11), 1543.
22. Wang, F., Zhou, H., Olademehin, O. P., Kim, S. J., & Tao, P. (2018). Insights into key interactions between vancomycin and bacterial cell wall structures. ACS omega, 3(1), 37-45.
23. Kheir, M. M., Tan, T. L., Azboy, I., Tan, D. D., & Parvizi, J. (2017). Vancomycin prophylaxis for total joint arthroplasty: incorrectly dosed and has a higher rate of periprosthetic infection than cefazolin. Clinical Orthopaedics and Related Research®, 475(7), 1767-1774.
24. Peel, T. N., Astbury, S., Cheng, A. C., Paterson, D. L., Buising, K. L., Spelman, T., ... & De Steiger, R. (2023). Trial of vancomycin and cefazolin as surgical prophylaxis in arthroplasty. New England Journal of Medicine, 389(16), 1488-1498.
25. Nguyen, C. T., Baccile, R., Brown, A. M., Lew, A. K., Pisano, J., & Pettit, N. N. (2024). When is vancomycin prophylaxis necessary? Risk factors for MRSA surgical site infection. Antimicrobial Stewardship & Healthcare Epidemiology, 4(1), e10.
26. Smith, E. B., Wynne, R., Joshi, A., Liu, H., & Good, R. P. (2012). Is it time to include vancomycin for routine perioperative antibiotic prophylaxis in total joint arthroplasty patients?. The Journal of arthroplasty, 27(8), 55-60.
27. Bosco, J. A., Bookman, J., Slover, J., Edusei, E., & Levine, B. (2015). Principles of antibiotic prophylaxis in total joint arthroplasty: current concepts. JAAOS-Journal of the American Academy of Orthopaedic Surgeons, 23(8), e27-e35.
28. Ashkenazi, I., Amzallag, N., Snir, N., Morgan, S., Garceau, S., Kotz, L., ... & Warschawski, Y. (2023). Does addition of gentamicin for antibiotic prophylaxis in total knee arthroplasty reduce the rate of periprosthetic joint infection?. Archives of Orthopaedic and Trauma Surgery, 143(8), 5255-5260.
29. Clifford, K. M., Selby, A. R., Reveles, K. R., Teng, C., Hall 2nd, R. G., McCarrell, J., & Alvarez, C. A. (2022). The risk and clinical implications of antibiotic-associated acute kidney injury: a review of the clinical data for agents with signals from the Food and Drug Administration's Adverse Event Reporting System (FAERS) database. Antibiotics, 11(10), 1367.
30. Rivetti, S., Romano, A., Mastrangelo, S., Attinà, G., Maurizi, P., & Ruggiero, A. (2023). Aminoglycosides-related ototoxicity: mechanisms, risk factors, and prevention in pediatric patients. Pharmaceuticals, 16(10), 1353.
31. Arthur, J. R., Bingham, J. S., Clarke, H. D., Spangehl, M. J., & Young, S. W. (2020). Intraosseous regional administration of antibiotic prophylaxis in total knee arthroplasty. JBJS Essential Surgical Techniques, 10(4), e20.
32. Harper, K. D., & Incavo, S. J. (2024). Intraosseous administration of medications in total knee arthroplasty: an opportunity for improved outcomes and superior compliance. JBJS Essential Surgical Techniques, 14(2), e22.
33. Chin, S. J., Moore, G. A., Zhang, M., Clarke, H. D., Spangehl, M. J., & Young, S. W. (2018). The AAHKS clinical research award: intraosseous regional prophylaxis provides higher tissue concentrations in high BMI patients in total knee arthroplasty: a randomized trial. The Journal of arthroplasty, 33(7), S13-S18.
34. Harper, K. D., Park, K. J., Brozovich, A. A., Sullivan, T. C., Serpelloni, S., Taraballi, F., ... & Clyburn, T. A. (2023). Otto Aufranc award: intraosseous vancomycin in total hip arthroplasty—superior tissue concentrations and improved efficiency. The Journal of Arthroplasty, 38(7), S11-S15.
35. Spangehl, M. J., Clarke, H. D., Moore, G. A., Zhang, M., Probst, N. E., & Young, S. W. (2022). Higher tissue concentrations of vancomycin achieved with low-dose intraosseous injection versus intravenous despite limited tourniquet duration in primary total knee arthroplasty: a randomized trial. The Journal of arthroplasty, 37(5), 857-863.
36. Young, S. W., Roberts, T., Johnson, S., Dalton, J. P., Coleman, B., & Wiles, S. (2015). Regional intraosseous administration of prophylactic antibiotics is more effective than systemic administration in a mouse model of TKA. Clinical Orthopaedics and Related Research®, 473(11), 3573-3584.
37. Pavlou, P. (2014). The Mark Coventry Award: Higher Tissue Concentrations of Vancomycin With Low-dose Intraosseous Regional Versus Systemic Prophylaxis in TKA. Clinical Orthopaedics and Related Research, 472(1), 57.
38. Young, S. W., Zhang, M., Freeman, J. T., Vince, K. G., & Coleman, B. (2013). Higher cefazolin concentrations with intraosseous regional prophylaxis in TKA. Clinical Orthopaedics and Related Research®, 471(1), 244-249.
39. Young, S. W., Zhang, M., Moore, G. A., Pitto, R. P., Clarke, H. D., & Spangehl, M. J. (2018). The John N. Insall

award: higher tissue concentrations of vancomycin achieved with intraosseous regional prophylaxis in revision TKA: a randomized controlled trial. Clinical Orthopaedics and Related Research®, 476(1), 66-74.
40. Klasan, A., Patel, C. K., & Young, S. W. (2021). Intraosseous regional administration of vancomycin in primary total knee arthroplasty does not increase the risk of vancomycin-associated complications. The Journal of arthroplasty, 36(5), 1633-1637.
41. Harper, K. D., Lambert, B. S., O'Dowd, J., Sullivan, T., & Incavo, S. J. (2020). Clinical outcome evaluation of intraosseous vancomycin in total knee arthroplasty. Arthroplasty Today, 6(2), 220-223.
42. Parkinson, B., McEwen, P., Wilkinson, M., Hazratwala, K., Hellman, J., Kan, H., ... & Grant, A. (2021). Intraosseous regional prophylactic antibiotics decrease the risk of prosthetic joint infection in primary TKA: a multicenter study. Clinical Orthopaedics and Related Research®, 479(11), 2504-2512.
43. Miltenberg, B., Ludwick, L., Masood, R., Menendez, M. E., Moverman, M. A., Pagani, N. R., ... & Smith, E. L. (2023). Intraosseous regional administration of antibiotic prophylaxis for total knee arthroplasty: a systematic review. The Journal of arthroplasty, 38(4), 769-774.
44. Johnson, J. D., Nessler, J. M., Horazdovsky, R. D., Vang, S., Thomas, A. J., & Marston, S. B. (2017). Serum and wound vancomycin levels after intrawound administration in primary total joint arthroplasty. The Journal of arthroplasty, 32(3), 924-928.
45. Gao, J., Shu, L., Jiang, K., & Muheremu, A. (2024). Prophylactic use of vancomycin powder on postoperative infection after total joint arthroplasty. BMC Musculoskeletal Disorders, 25(1), 68.
46. Heckmann, N. D., Mayfield, C. K., Culvern, C. N., Oakes, D. A., Lieberman, J. R., & Della Valle, C. J. (2019). Systematic review and meta-analysis of intrawound vancomycin in total hip and total knee arthroplasty: a call for a prospective randomized trial. The Journal of arthroplasty, 34(8), 1815-1822.
47. Iorio, R., Yu, S., Anoushiravani, A. A., Riesgo, A. M., Park, B., Vigdorchik, J., ... & Schwarzkopf, R. (2020). Vancomycin powder and dilute povidone-iodine lavage for infection prophylaxis in high-risk total joint arthroplasty. The Journal of arthroplasty, 35(7), 1933-1936.
48. Liao, S., Yang, Z., Li, X., Chen, J., & Liu, J. G. (2022). Effects of different doses of vancomycin powder in total knee and hip arthroplasty on the periprosthetic joint infection rate: a systematic review and meta-analysis. Journal of Orthopaedic Surgery and Research, 17(1), 546.
49. Martin, V. T., Zhang, Y., Wang, Z., Liu, Q. L., & Yu, B. (2024). A systematic review and meta-analysis comparing intrawound vancomycin powder and povidone iodine lavage in the prevention of periprosthetic joint infection of hip and knee arthroplasties. Journal of Orthopaedic Science, 29(1), 165-176.
50. Movassaghi, K., Wang, J. C., Gettleman, B. S., Mayfield, C. K., Oakes, D. A., Lieberman, J. R., & Heckmann, N. D. (2022). Systematic review and meta-analysis of intrawound vancomycin in total hip and total knee arthroplasty: a continued call for a prospective randomized trial. The Journal of Arthroplasty, 37(7), 1405-1415.
51. Patel, N. N., Guild III, G. N., & Kumar, A. R. (2018). Intrawound vancomycin in primary hip and knee arthroplasty: a safe and cost-effective means to decrease early periprosthetic joint infection. Arthroplasty today, 4(4), 479-483.
52. Winkler, C., Dennison, J., Wooldridge, A., Larumbe, E., Caroom, C., Jenkins, M., & Brindley, G. (2018). Do local antibiotics reduce periprosthetic joint infections? A retrospective review of 744 cases. Journal of clinical orthopaedics and trauma, 9, S34-S39.
53. Xu, H., Yang, J., Xie, J., Huang, Z., Huang, Q., Cao, G., & Pei, F. (2020). Efficacy and safety of intrawound vancomycin in primary hip and knee arthroplasty: a systematic review and meta-analysis: implications for the design of a randomized controlled trial. Bone & Joint Research, 9(11), 778-788.
54. Khatri, K., Bansal, D., Singla, R., & Sri, S. (2017). Prophylactic intrawound application of vancomycin in total knee arthroplasty. Journal of Arthroscopy and Joint Surgery, 4(2), 61-64.
55. Abuzaiter, W., Bolton, C. A., Drakos, A., Drakos, P., Hallan, A., Warchuk, D., ... & Woolfrey, M. R. (2023). Is topical vancomycin an option? A randomized controlled trial to determine the safety of the topical use of vancomycin powder in preventing postoperative infections in total knee arthroplasty, as compared with standard postoperative antibiotics. The Journal of Arthroplasty, 38(8), 1597-1601.
56. Mulpur, P., Jayakumar, T., Yakkanti, R. R., Apte, A., Hippalgaonkar, K., Annapareddy, A., ... & Reddy, A. G. (2024). Efficacy of intrawound vancomycin in prevention of periprosthetic joint infection after primary total knee arthroplasty: a prospective double-blinded randomized control trial. The Journal of Arthroplasty, 39(6), 1569-1576.
57. Mancino, F., Gant, V., Meek, D. R., & Haddad, F. S. (2023). Vancomycin powder in total joint replacement: what is the evidence, and is it good enough to support its routine use?. The Bone & Joint Journal, 105(8), 833-836.
58. King, J. D., Hamilton, D. H., Jacobs, C. A., & Duncan, S. T. (2018). The hidden cost of commercial antibiotic-loaded bone cement: a systematic review of clinical results and cost implications following total knee arthroplasty. The Journal of arthroplasty, 33(12), 3789-3792.
59. Li, H. Q., Li, P. C., Wei, X. C., & Shi, J. J. (2022). Effectiveness of antibiotics loaded bone cement in primary total knee arthroplasty: a systematic review and meta-analysis. Orthopaedics & Traumatology: Surgery & Research, 108(5), 103295.
60. Pardo-Pol, A., Fontanellas-Fes, A., Pérez-Prieto, D., Sorli, L., Hinarejos, P., & Monllau, J. C. (2024). The Use of Erythromycin and Colistin Cement in Total Knee Arthroplasty Does Not Reduce the Incidence of Infection: A Randomized Study in 2,893 Knees With a 9-year Average Follow-Up. The Journal of Arthroplasty, 39(9), 2280-2284.

61. Yayac, M., Rondon, A. J., Tan, T. L., Levy, H., Parvizi, J., & Courtney, P. M. (2019). The economics of antibiotic cement in total knee arthroplasty: added cost with no reduction in infection rates. The Journal of arthroplasty, 34(9), 2096-2101.
62. Howlin, R. P., Brayford, M. J., Webb, J. S., Cooper, J. J., Aiken, S. S., & Stoodley, P. (2015). Antibiotic-loaded synthetic calcium sulfate beads for prevention of bacterial colonization and biofilm formation in periprosthetic infections. Antimicrobial agents and chemotherapy, 59(1), 111-120.
63. de Lachica, J. C. V., Reyes, S. S. S., Ureña, J. A. P., & Fragoso, M. A. R. (2022). Decrease in acute periprosthetic joint infections incidence with vancomycin-loaded calcium sulfate beads in patients with non-modifiable risk factors. A randomized clinical trial. Journal of ISAKOS, 7(6), 201-205.
64. Ahuja, R., Mehta, S., Galustian, S., Walewicz, D., & Drees, B. (2023). Hypercalcemia Secondary to Antibiotic-Eluting Calcium Sulfate Beads. Cureus, 15(7).
65. Abosala, A., & Ali, M. (2020). The use of calcium sulphate beads in periprosthetic joint infection, a systematic review. Journal of bone and joint infection, 5(1), 43-49.
66. https://journals.lww.com/jbjsjournal/_layouts/15/oaks.journals/downloadpdf.aspx?an=00004623-201909180-00009&casa_token=QsJyPN26ZowAAAAA:CNJz4zvDhwBFNBGBU9glpPSFGnm4mmHY8XvnTIbThqoDY8_yx4bYZcEp14Wfta62h-T2aGg_Q5EfBWFMGewKZcedbOP8uisXVW4
67. Anglen, J. O. (2005). Comparison of soap and antibiotic solutions for irrigation of lower-limb open fracture wounds: a prospective, randomized study. JBJS, 87(7), 1415-1422.
68. de Jonge, S. W., Boldingh, Q. J., Solomkin, J. S., Allegranzi, B., Egger, M., Dellinger, E. P., & Boermeester, M. A. (2017). Systematic review and meta-analysis of randomized controlled trials evaluating prophylactic intra-operative wound irrigation for the prevention of surgical site infections. Surgical infections, 18(4), 508-519.
69. Brown, N. M., Cipriano, C. A., Moric, M., Sporer, S. M., & Della Valle, C. J. (2012). Dilute betadine lavage before closure for the prevention of acute postoperative deep periprosthetic joint infection. The Journal of arthroplasty, 27(1), 27-30.
70. Calkins, T. E., Culvern, C., Nam, D., Gerlinger, T. L., Levine, B. R., Sporer, S. M., & Della Valle, C. J. (2020). Dilute betadine lavage reduces the risk of acute postoperative periprosthetic joint infection in aseptic revision total knee and hip arthroplasty: a randomized controlled trial. The Journal of Arthroplasty, 35(2), 538-543.
71. Shohat, N., Goh, G. S., Harrer, S. L., & Brown, S. (2022). Dilute povidone-iodine irrigation reduces the rate of periprosthetic joint infection following hip and knee arthroplasty: an analysis of 31,331 cases. The Journal of Arthroplasty, 37(2), 226-231.
72. Slullitel, P. A., Dobransky, J. S., Bali, K., Poitras, S., Bhullar, R. S., Gofton, W. T., ... & Kim, P. R. (2020). Is there a role for preclosure dilute betadine irrigation in the prevention of postoperative infection following total joint arthroplasty?. The Journal of Arthroplasty, 35(5), 1374-1378.
73. Kerbel, Y. E., Kirchner, G. J., Sunkerneni, A. R., Lieber, A. M., & Moretti, V. M. (2019). The cost effectiveness of dilute betadine lavage for infection prophylaxis in total joint arthroplasty. The Journal of arthroplasty, 34(7), S307-S311.
74. Hernandez, N. M., Hart, A., Taunton, M. J., Osmon, D. R., Mabry, T. M., Abdel, M. P., & Perry, K. I. (2019). Use of povidone-iodine irrigation prior to wound closure in primary total hip and knee arthroplasty: an analysis of 11,738 cases. JBJS, 101(13), 1144-1150.
75. Westberg, M., Frihagen, F., Brun, O. C., Figved, W., Grøgaard, B., Valland, H., ... & Snorrason, F. (2015). Effectiveness of gentamicin-containing collagen sponges for prevention of surgical site infection after hip arthroplasty: a multicenter randomized trial. Clinical Infectious Diseases, 60(12), 1752-1759.
76. Swieringa, A. J., & Tulp, N. J. (2005). Toxic serum gentamicin levels after the use of gentamicin-loaded sponges in infected total hip arthroplasty. Acta Orthopaedica, 76(1), 75-77.
77. Burns, A. W., Chao, T., Tsai, N., Lynch, J. T., & Smith, P. N. (2023). The use of intra-articular vancomycin is safe in primary hip and knee arthroplasty. Journal of Orthopaedics, 46, 161-163.
78. Roy, M. E., Peppers, M. P., Whiteside, L. A., & LaZear, R. M. (2014). Vancomycin concentration in synovial fluid: direct injection into the knee vs. intravenous infusion. The Journal of Arthroplasty, 29(3), 564-568.
79. Burns, A. W., Smith, P., & Lynch, J. (2024). Intra-articular vancomycin reduces prosthetic infection in primary hip and knee arthroplasty. Arthroplasty Today, 26, 101333.
80. Lawrie, C. M., Kazarian, G. S., Barrack, T., Nunley, R. M., & Barrack, R. L. (2021). Intra-articular administration of vancomycin and tobramycin during primary cementless total knee arthroplasty: determination of intra-articular and serum elution profiles. The Bone & Joint Journal, 103(11), 1702-1708.
81. Berríos-Torres, S. I., Umscheid, C. A., Bratzler, D. W., Leas, B., Stone, E. C., Kelz, R. R., ... & Schecter, W. P. (2017). Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. JAMA surgery, 152(8), 784-791.
82. Yates Jr, A. J., of Hip, A. A., & Knee Surgeons Evidence-Based Medicine Committee. (2018). Postoperative prophylactic antibiotics in total joint arthroplasty. Arthroplasty Today, 4(1), 130-131.
83. Siddiqi, A., Forte, S. A., Docter, S., Bryant, D., Sheth, N. P., & Chen, A. F. (2019). Perioperative antibiotic prophylaxis in total joint arthroplasty: a systematic review and meta-analysis. JBJS, 101(9), 828-842.
84. Inabathula, A., Dilley, J. E., Ziemba-Davis, M., Warth, L. C., Azzam, K. A., Ireland, P. H., & Meneghini, R. M. (2018). Extended oral antibiotic prophylaxis in high-risk patients substantially reduces primary total hip and knee arthroplasty 90-day infection rate. JBJS,

100(24), 2103-2109.

85. Kheir, M. M., Dilley, J. E., Ziemba-Davis, M., & Meneghini, R. M. (2021). The AAHKS clinical research award: extended oral antibiotics prevent periprosthetic joint infection in high-risk cases: 3855 patients with 1-year follow-up. The Journal of arthroplasty, 36(7), S18-S25.
86. Flynn, J. B., Yokhana, S. S., Wilson, J. M., Schultz, J. D., Hymel, A. M., & Martin, J. R. (2024). Not so fast: extended oral antibiotic prophylaxis does not reduce 90-day infection rate following joint arthroplasty. The Journal of Arthroplasty, 39(9), S122-S128.