

## QUESTION 4: Does the addition of topical antibiotics (polymyxin and/or bacitracin) to irrigation solution offer additional antibacterial properties?

**RECOMMENDATION:** Guidelines from the World Health Organization (WHO) and National Institute for Health and Clinical Excellence (NICE) advise against the addition of topical antibiotics to irrigation solutions. Recent Centers for Disease Control and Prevention (CDC) recommendations suggest an uncertain trade-off between the benefits and risks of intraoperative antimicrobial irrigation for the prevention of surgical site infections (SSIs). While data regarding the antimicrobial efficacy of irrigation solutions containing antibiotics, such as polymyxin-bacitracin is conflicting and largely based on non-orthopaedic studies, we advocate against its intraoperative usage in the face of growing antimicrobial resistance concerns, costs and hypersensitivity implications.

**LEVEL OF EVIDENCE:** Moderate

**DELEGATE VOTE:** Agree: 92%, Disagree: 4%, Abstain: 4% (Super Majority, Strong Consensus)

### RATIONALE

While the intraoperative use of irrigation solutions is an important strategy for mitigation of SSIs and periprosthetic joint infections (PJIs) in patients undergoing orthopaedic procedures [1–3], the optimal irrigation solution remains unknown. Surgeons worldwide continue to add topical antibiotics to irrigation fluid [4], assuming that this solution has local activity that can help eliminate bacteria. However, published literature suggests that the addition of antibiotics to irrigation confers no added benefits [5–7], and may even be deleterious [7–9].

Two clinical practice guidelines issued by the WHO and NICE advise that antibiotic incisional wound irrigation before closure should not be used for the purposes of preventing SSIs, although these were based on generally low-quality evidence [10–12,5]. Furthermore, using available data from five randomized controlled trials [13–17], the CDC concluded that antibiotic irrigation of the incisional wound conferred neither benefits nor harms in reducing SSIs when compared to no irrigation or saline irrigation [12]. Additionally, the WHO guideline development group highlighted the risks of emergence of antimicrobial resistance (AMR) with the use of antibiotics for wound irrigation.

Moreover, *in vitro* studies have raised concerns about the bactericidal efficacy of adding antimicrobials to irrigation fluids [18,19]. Anglen et al. found that the addition of antibiotic drugs (including bacitracin and polymyxin/neomycin) to irrigation solutions had no significant effects on bacterial removal. None of the antibiotic solutions tested were statistically different from saline alone in the amount of bacteria removed from a *Staphylococcus*-coated stainless steel screw model [18]. In a series of breakpoint experiments, Goswami et al. showed polymyxin-bacitracin solution was significantly less efficacious ( $p < 0.001$ ) in eradicating *S. aureus* versus other tested irrigation solutions, including 0.3% povidone-iodine, 0.05% chlorhexidine and 0.125% sodium hypochlorite [19]. Similarly, using a rat model of a contaminated paravertebral wound containing a wire implant, Conroy et al. found no significant benefit with respect to the rates of positive wound cultures following bacitracin-antibiotic irrigation over normal saline [20].

In addition to the questionable efficacy and perpetuating AMR, concerns have been raised about the harmful effects on wound healing of bacitracin-containing irrigation solutions, as have been reported in a prospective randomized clinical trial [7]. The study recruited 400 patients with a lower extremity open fracture who received irrigation with either a bacitracin antibiotic solution or a nonsterile castile soap solution. No differences in infection rates were seen between the two study arms ( $p = 0.2$ ), but wound healing problems were found to be significantly higher in the bacitracin group (9.5% vs. 4%,  $p = 0.03$ ).

An increased risk of hypersensitivity and the potential for anaphylactic reactions have also been cited [7–9]. Bacitracin is a polypeptide antibiotic effective against a variety of gram-positive bacteria and its pharmacological activity is exerted by the inhibition of prokaryotic cell-wall synthesis. Polymyxins are a group of cyclic non-ribosomal polypeptide antibiotics that have gram-negative activity. Studies have reported that these antibiotics may produce serious systemic effects. Damm et al. reported three cases with a severe anaphylactic reaction after prophylactic bacitracin irrigation in the setting of pacemaker insertion [21]. Similarly, Antevil et al. attributed the use of bacitracin irrigation to anaphylactic shock during a case of revision total knee arthroplasty (TKA) [8]. Furthermore, in a multi-institutional study by the North American Contact Dermatitis Group involving patients with suspected allergic contact dermatitis, bacitracin was noted as the sixth most common allergen with 9.2% positive on patch testing [22].

Efficacy data from largely historical studies suggests some utility for polymyxin-bacitracin irrigation. Savitz et al. investigated the addition of polymyxin-bacitracin to saline lavage in 50 spinal procedures [23]. They reported that the incidence of bacterial growth reduced from 64 to 4% with the addition of antibiotics to irrigation and no wound infections were reported in postoperative phase. Similarly, in 1972, Scherr et al. showed a significant *in vitro* decrease in local bacterial concentrations after topical administration of bacitracin and other antimicrobials [24]. Rosenstein et al. also showed that irrigation with 50 mL of bacitracin solution into the intramedullary canal of canine femora inoculated with staphylococci decreased the number of positive cultures one week later [25]. A single surgeon series also reported beneficial results when vancomycin and polymyxin were added to irrigation solution in 2,293 total joint arthroplasties (TJA) [26]. Despite these reports, data within the orthopaedic literature remains unconvincing due to poor study design or limitations with defining appropriate endpoints for efficacy in musculoskeletal wounds [9].

More recent data from five non-orthopaedic randomized control trials compared irrigation of the incisional wound with an antibiotic solution to irrigation with normal saline or no irrigation showed limited efficacy [13–17]. A meta-analysis of these trials demonstrated no significant differences between antibiotic irrigation and no irrigation or irrigation with only saline solution (odds ratio (OR): 1.16, 95% confidence interval (CI) 0.64 to 2.12,  $p = 0.63$ ). The overall quality of evidence in this meta-analysis was cited as low, however, due to the risk of bias and imprecision [6].

While the cost-effectiveness of polymyxin-bacitracin has not been formally evaluated, 1 operative orthopaedic procedure typically uses 150,000 units of bacitracin (50,000 units per liter of saline), which adds a cost of \$150.00 according to estimates by Anglen et al. [9].

In conclusion, two clinical practice guidelines based on a review of the evidence, recommend against antimicrobial wound irrigation to reduce the risk of SSIs [5,10,11]. The efficacy of irrigation solutions with supplemental topical antibiotics in orthopaedic procedures remains controversial due to the paucity of available evidence. Future well-designed randomized controlled trials using current standard of care protocols for SSI prevention are needed to evaluate commonly used irrigation practices with a special emphasis on the agents used and a focus on orthopaedic procedures [26,27].

Trials should also address cost-effectiveness and adverse events associated with the agents used for irrigation. In the interim, given the lack of proven efficacy and the potential for harm, we advise against the addition of topical antibiotics to irrigation solution.

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