

## 1.15. PREVENTION: ANTISEPTIC IRRIGATION SOLUTION

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### QUESTION 1: What antiseptics can be used to prevent biofilm formation?

**RECOMMENDATION:** Although several studies have demonstrated the ability of certain antiseptic agents to prevent biofilm formation in vitro, the ability of antiseptics to provide prevention of biofilm formation in vivo is uncertain. They may have utility in the context of revision surgery due to existing infection, but this issue has not been adequately studied.

**LEVEL OF EVIDENCE:** Limited

**DELEGATE VOTE:** Agree: 93%, Disagree: 2%, Abstain: 5% (Super Majority, Strong Consensus)

### RATIONALE

It has not been established whether a specific antiseptic or a combination of agents is better to eradicate biofilms from an implant surface in vivo [1]. So far, almost all of the studies focused on the abilities of antiseptics to inhibit biofilm formation have been demonstrated in in vitro studies [2–5].

Santos et al. performed a crossover, randomized double-blind clinical trial to evaluate the effects of two chlorhexidine solutions (alcohol-containing 0.12% chlorhexidine solution and alcohol-free 0.12% chlorhexidine solution) against supra- and sub-gingival biofilm formation. The group found that both solutions had similar inhibitory effects on the formation of biofilms [6]. In addition, Quintas et al. performed an observer-masked, crossover, randomized clinical trial to evaluate the in situ antiplaque effect after four days of using two commercial antimicrobial agents (essential oils and 0.2% chlorhexidine) in the short-term on undisturbed plaque-like biofilm [7]. Although the 0.2% chlorhexidine showed better results with regard to reducing the thickness and covering grade by the biofilm, both antiseptics had high and similar antiplaque effects.

The ability of acetic acid and polyhexanide to prevent biofilm formation has also been mentioned in the literature. Halstead et al. demonstrated that acetic acid at low concentrations of 0.16 to 0.31% was able to inhibit biofilm formation in vitro [8]. Lenselink et al. performed a cohort study to evaluate the clinical efficacy of the polyhexanide-containing bio cellulose dressing for the eradication of biofilms in non-healing wounds [9]. They suggested that continuous application of polyhexanide, using a bio cellulose wound dressing, reduced biofilm in the stagnating wounds treated, thus promoting healing.

Regarding the clinical use of povidone-iodine to prevent the formation of biofilms, there are limited studies in vitro. Hill et al. utilized a sophisticated in vitro biofilm model that was designed to closely mimic chronic wound biofilms and demonstrated the complete destruction of an established seven-day mixed *Pseudomonas* and *Staphylococcus* biofilm by iodine-based dressings [10]. Kanno et al. suggested that irrigation of wounds with 1% povidone-iodine was an effective way to reduce bacterial counts on the wound surface and prevent new biofilm formation by using a rat model of wound chronic biofilm infection [11]. However, Presterl et al. found that povidone-iodine was inferior to hydrogen peroxide and alcohol for the eradication of *Staphylococcus epidermidis* biofilms [12].

It is worth noting that many biofilm infections occur much later in the postoperative period, often due to the hematogenous dissemination of bacteria to the site of an implanted device from a breach in surface structures [13]. Indeed, this can occur months or even years after implantation and it is unlikely to prevent this mode of infection development with the use of antiseptic agents at the time of perioperative period. The role of antiseptics in various debridement protocols for the treatment of established periprosthetic joint infections (PJIs) remains controversial. Each clinical scenario is unique in terms of causative pathogen, host factors, local tissue viability, as well as the duration and virulence of the infection. If the surgeon is attempting to salvage the existing prosthesis through a debridement, antibiotics and implant retention (DAIR) protocol, it is imperative that all biofilm should be removed through mechanical and chemical disruption [14–16]. If a one-stage revision including component explantation, debridement and reimplantation of a new prosthesis is to be undertaken in a single surgical setting, the importance of debriding all infected tissue is vital. The role of antiseptics, in this case, is not to treat existing biofilm, as all prosthetic components will have been removed. Instead, the purpose is to aggressively treat the remaining bone and its soft tissue envelope to prevent recolonization. Antiseptics used for this purpose include acetic acid, Dakins solution (NaOCl), povidine-iodine and hydrogen peroxide [17]. In this situation, the volume of antiseptic solution may be more important than the combination and sequence of agents [17,18].

The use of antiseptic agents during the perioperative period has the potential to reduce the rate of surgical infection early in the postoperative period. Additionally, the use of certain antiseptic solutions for lavage, during primary and revision total joint arthroplasty operations, has the potential to reduce infection rates [19]. However, validated protocols do not exist for the use of such solutions in terms of concentration, volume and duration of exposure. More in vivo studies are needed to evaluate the use of various antiseptic agents for this purpose, such that direct comparisons between agents can be made.

Ultimately, although several studies have demonstrated the ability of certain antiseptic agents to prevent biofilm formation in vitro, the ability of antiseptics to provide protection against biofilm formation in vivo is uncertain. They may have utility in the context of revision surgery due to existing infection, but this issue has not been adequately studied.

### REFERENCES

- [1] Lora-Tamayo J, Murillo O, Iribarren JA, Soriano A, Sánchez-Somolinos M, Baraia-Etxaburu JM, et al. A large multicenter study of methicillin-susceptible and methicillin-resistant staphylococcus aureus prosthetic joint infections managed with implant retention. *Clin Infect Dis*. 2013;56:182–194. doi:10.1093/cid/cis746.
- [2] Percival SL, Finnegan S, Donelli G, Vuotto C, Rimmer S, Lipsky BA. Antiseptics for treating infected wounds: efficacy on biofilms and effect of pH. *Crit Rev Microbiol*. 2016;42:293–309. doi:10.3109/1040841X.2014.940495.
- [3] Ortega-Peña S, Hidalgo-González C, Robson MC, Krötzsch E. In vitro microbicidal, anti-biofilm and cytotoxic effects of different commercial antiseptics. *Int Wound J*. 2017;14:470–479. doi:10.1111/iwj.12625.

[4] Théraud M, Bédouin Y, Guiguen C, Gangneux JP. Efficacy of antiseptics and disinfectants on clinical and environmental yeast isolates in planktonic and biofilm conditions. *J Med Microbiol.* 2004;53:1013–1018. doi:10.1099/jmm.0.05474-0.

[5] Schmidt K, Estes C, McLaren A, Spangehl MJ. Chlorhexidine antiseptic irrigation eradicates staphylococcus epidermidis from biofilm: an in vitro study. *Clin Orthop Relat Res.* 2018;476:648–653. doi:10.1007/s11999-0000000000000052.

[6] Santos GOD, Milanesi FC, Greggiani BF, Fernandes MI, Oppermann RV, Weidlich P. Chlorhexidine with or without alcohol against biofilm formation: efficacy, adverse events and taste preference. *Braz Oral Res.* 2017;31:e32. doi:10.1590/1807-3107BOR-2017.vol31.0032.

[7] Quintas V, Prada-López I, Donos N, Suárez-Quintanilla D, Tomás I. Antiplaque effect of essential oils and 0.2% chlorhexidine on an in situ model of oral biofilm growth: a randomised clinical trial. *PLoS One.* 2015;10:e0117177. doi:10.1371/journal.pone.0117177.

[8] Halstead FD, Rauf M, Moiemens NS, Bamford A, Wearn CM, Fraise AP, et al. The antibacterial activity of acetic acid against biofilm-producing pathogens of relevance to burns patients. *PLoS One.* 2015;10:e0136190. doi:10.1371/journal.pone.0136190.

[9] Lenseleink E, Andriessen A. A cohort study on the efficacy of a polyhexanide-containing biocellulose dressing in the treatment of biofilms in wounds. *J Wound Care.* 2011;20:534, 536–539. doi:10.12968/jowc.2011.20.11.534.

[10] Hill KE, Malic S, McKee R, Rennison T, Harding KG, Williams DW, et al. An in vitro model of chronic wound biofilms to test wound dressings and assess antimicrobial susceptibilities. *J Antimicrob Chemother.* 2010;65:1195–1206. doi:10.1093/jac/dkq105.

[11] Kanno E, Tanno H, Suzuki A, Kamimatsuno R, Tachi M. Reconsideration of iodine in wound irrigation: the effects on pseudomonas aeruginosa biofilm formation. *J Wound Care.* 2016;25:335–339. doi:10.12968/jowc.2016.25.6.335.

[12] Presterl E, Suhomel M, Eder M, Reichmann S, Lassnigg A, Graninger W, et al. Effects of alcohols, povidone-iodine and hydrogen peroxide on biofilms of staphylococcus epidermidis. *J Antimicrob Chemother.* 2007;60:417–420. doi:10.1093/jac/dkm221.

[13] Zimmerli W. Clinical presentation and treatment of orthopaedic implant-associated infection. *J Intern Med.* 2014;276:111–119. doi:10.1111/joim.12233.

[14] Qasim SN, Swann A, Ashford R. The DAIR (debridement, antibiotics and implant retention) procedure for infected total knee replacement – a literature review. *SICOT J.* 2017;3:2. doi:10.1051/sicotj/2016038.

[15] Schwechter EM, Folk D, Varshney AK, Fries BC, Kim SJ, Hirsh DM. Optimal irrigation and debridement of infected joint implants: an in vitro methicillin-resistant staphylococcus aureus biofilm model. *J Arthroplasty.* 2011;26:109–113. doi:10.1016/j.arth.2011.03.042.

[16] Jiranek WA, Waligora AC, Hess SR, Golladay GL. Surgical treatment of prosthetic joint infections of the hip and knee: changing paradigms? *J Arthroplasty.* 2015;30:912–918. doi:10.1016/j.arth.2015.03.014.

[17] Williams RL, Ayre WN, Khan WS, Mehta A, Morgan-Jones R. Acetic acid as part of a debridement protocol during revision total knee arthroplasty. *J Arthroplasty.* 2017;32:953–957. doi:10.1016/j.arth.2016.09.010.

[18] Haddad FS, Sukeik M, Alazzawi S. Is single-stage revision according to a strict protocol effective in treatment of chronic knee arthroplasty infections? *Clin Orthop Relat Res.* 2015;473:8–14. doi:10.1007/s11999-014-3721-8.

[19] Ruder JA, Springer BD. Treatment of periprosthetic joint infection using antimicrobials: dilute povidone-iodine lavage. *J Bone Jt Infect.* 2017;2:10–14. doi:10.7150/jbji.16448.



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## QUESTION 2: What is the optimal irrigation solution (i.e., type, volume, frequency) to be used during clean elective orthopaedic procedures?

RECOMMENDATION: There is ample evidence to support the World Health Organization’s (WHO) and Centers for Disease Control and Prevention’s (CDC) recommendations that advocate the use of dilute betadine for the irrigation of wounds during surgical procedures. The optimal volume of irrigation solution is not known.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 75%, Disagree: 16%, Abstain: 9% (Super Majority, Strong Consensus)

### RATIONALE

Intraoperative irrigation during clean elective orthopaedic procedures is one aspect of the operative protocol to reduce surgical site infections (SSIs), and there is general consensus that this technique in some form should be performed. Recently released guidelines by the CDC and WHO recommend intraoperative irrigation with dilute betadine prior to closure [1,2]. Betadine contains aqueous iodophor in the form of povidone-iodine which becomes chemically toxic to microorganisms when released as free iodine [3,4].

Povidone-iodine irrigation initially garnered support from studies in other fields, such as general, urologic, cardiovascular and spine surgeries [5–14]. A meta-analysis of seven randomized control trials demonstrated a statistically significant benefit for incisional wound irrigation with aqueous betadine, compared to normal saline solution (odds ratio (OR): 0.31,  $p = 0.007$ ) [2]. In a larger meta-analysis of 15 level I or II studies in various surgical fields, 10 studies demonstrated that povidone-iodine irrigation was more effective than the control method that included irrigation with saline, water or no irrigation [15].

Although well-studied in other specialties, only one retrospective cohort study addresses intraoperative betadine irrigation in primary joint arthroplasty [16]. Brown et al. demonstrated a statistically significant reduction in SSI from 0.97 to 0.15% with the use of 0.35% povidone-iodine. Kokavec et al. studied betadine irrigation in a pediatric population undergoing surgery on the proximal femur, hip and pelvis [7]. In this study, two superficial wound infections were identified in the non-betadine group (2/73, 2.7%) and no infections were identified in the betadine group (0/89, 0%). (Table 1).

TABLE 1. Summary of orthopaedic literature comparing the efficacy of irrigation solutions with respect to prevention of SSI

Author	Category	N	Intervention	Comparison	Study Design	Analysis	Outcome	Incidence of SSI	P Value
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Brown	TJA	2,550 (1,862 pre/ 688 post)	Betadine	Saline	Retrospective, pre-post	Univariate	D	0.15% vs. 0.97%	0.04
Cheng	Spine	414 (206 Ccrl/208 intervention)	Betadine	Saline	RCT	Multivariate	S & D	0% vs. 3.4%	0.01
Chang	Spine	244 (124 ctrl/120 intervention)	Betadine	Saline	RCT	Univariate	S & D	0% vs. 4.8%	0.03
Kokavec	Ortho	162 (73 ctrl/89 intervention)	Betadine	Saline	RCT	NA	S	0% vs. 2.7%	NA
Frisch	THA	391 (253 pre/ 138 post)	Chlorhexidine	Betadine	Retrospective, pre-post	Multivariate	S & D	(S) 0% vs. 1.2%	0.56
								(D) 0.8% vs. 1.6%	0.30
Frisch	TKA	659 (411 pre/ 138 post)	Chlorhexidine	Saline	Retrospective; pre-post	Multivariate	S & D	(S) 0.8% vs. 0.7%	0.91
								(D) 1.2% vs. 0.7%	0.53

S, superficial infections; D, deep infections

In addition to isotonic saline and ringers lactate, several solutions such as antiseptics and antibiotic solutions have also been proposed as potential irrigation fluids in orthopaedic surgery. However, there is no consensus on a gold standard because of lack of clinical studies on the topic. Chlorhexidine is an antiseptic that alters the osmotic equilibrium of bacterial cells by binding to negatively charged molecules on the cell wall [17,18]. Chlorhexidine has a broad spectrum of activity [19] and can be bacteriostatic or bactericidal depending on its concentration [20]. Frisch et al. compared 0.05% chlorhexidine to normal saline irrigation in total knee arthroplasty (TKA) and 0.05% chlorhexidine to < 2% dilute betadine in total hip arthroplasty (THA) [21]. There was no significant difference in the rate of superficial or deep SSI between groups, which suggest that chlorhexidine may be comparable to normal saline in reducing infection rates.

While there is some evidence for the optimal irrigation solution, few studies have demonstrated an optimal volume or method for performing irrigation [22,23]. Additionally, there is little support for the benefits of adding antibiotics to irrigation solution, which was shown to be ineffective on metal surfaces in vitro, and thus this practice is not currently recommended by the WHO [22,24]. However, a single surgeon has reported beneficial results when vancomycin and polymyxin was added to irrigation solution in 2,293 TJAs [25].

Overwhelming evidence from published randomized control trials (RCTs) on the use of irrigation solutions for clean, elective orthopaedic procedures or surgeries suggest that both normal isotonic saline and ringers lactate solutions are safe and effective irrigation fluids. However, the majority of these studies were based on shoulder arthroscopic surgery [26–32], with limited studies on TKAs [31,33,34]. Whether ringers lactate is better than normal saline or vice versa is not known. However, in a laboratory-based study on surgically resected menisci from patients who underwent arthroscopic knee surgery, investigators aimed to determine whether there was a difference in the effect on cell morphology and function between isotonic saline and ringers lactate solutions. The findings showed that ringers lactate maintained better meniscal cell integrity compared with isotonic saline [35].

Emerging and consistent evidence suggests that warming of irrigation fluids (whether normal isotonic saline or ringers lactate) to temperatures of 32 to 40°C compared with room temperature irrigation fluids, decrease the risk of perioperative hypothermia and reduces inflammatory response in patients undergoing shoulder, hip or knee arthroscopy [28,31,36–38]. Only two RCTs have, to our knowledge, reported that warmed irrigation fluids were not superior to room temperature fluids in reducing the occurrence of perioperative hypothermia [30,39].

Results from three RCTs provided evidence that the addition of epinephrine to irrigation fluids improved the clarity of the visual field of surgery, reduced intraoperative bleeding and reduced total operating time compared with plain irrigation fluids [27,29,32]. The benefits of using chilled irrigation solutions in orthopaedic procedures was uncertain until recently. Li and colleagues performed an RCT and compared the effects of continuous irrigation

of 4,000 mL cold saline plus 0.5% epinephrine vs. 4,000 mL normal saline at room temperature in patients undergoing TKAs [33]. Irrigation with cold saline was demonstrated to be associated with decreased postoperative pain, reduced intraoperative blood loss and improved quality of life.

Though commonly-used isotonic solutions such as normal saline or ringers lactate have been reported to be safe for joint irrigation in orthopaedic procedures, rare adverse events from excessive fluid irrigation have been documented. It has been reported that hyperosmolar solutions may have the potential to minimize these problems. However, their benefits have only so far been demonstrated in animal models. In a recent RCT, hyperosmolar irrigation was shown to decrease periarticular fluid retention in shoulder arthroscopy compared with standard of care irrigation fluid [26].

The role of continuous irrigation or pulse lavage in orthopaedic surgery has progressed from open fractures and contaminated wounds to being used in clean elective procedures. Furthermore, the optimum volume of irrigation solution used during orthopaedic procedures varies from one surgery to another. In studies of patients undergoing shoulder arthroscopy, average volume of fluid used for irrigation ranged from 3.7 to 11.4 L, and this was based on continuous irrigation with a pressure-control pump maintained at pressure settings of 30 to 60 mmHg [26–32].

For hip arthroscopy, evidence was based on an observational prospective study [38]. Median volume of irrigation solution was 27 L using an infusion pump with pressure between 45 and 65 mmHg. In the RCT by Kelly et al. investigating patients undergoing knee arthroscopy, the average volume of irrigation fluid used was 11.7 L [39]. In two studies of TKA (one RCT and one case series), continuous irrigation with 4 L of normal saline solution was used during surgery in each study [33,34]. In an RCT of hip hemiarthroplasty, 2 L of normal saline administered by pulse lavage was associated with a 30-day lower infection rate compared to 2 L normal saline washout by jug or syringe [10]. No data was reported on the pressure settings of the infusion pump in these studies.

## REFERENCES

- [1] Berriós-Torres SJ, Yi SH, Bratzler DW, Ma A, Mu Y, Zhu L, et al. Activity of commonly used antimicrobial prophylaxis regimens against pathogens causing coronary artery bypass graft and arthroplasty surgical site infections in the United States, 2006–2009. *Infect Control Hosp Epidemiol*. 2014;35:231–239. doi:10.1086/675289.
- [2] World Health Organization. Global guidelines for the prevention of surgical site infection. 2016. <http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=1>.
- [3] Oduwale KO, Glynn AA, Molony DC, Murray D, Rowe S, Holland LM, et al. Anti-biofilm activity of sub-inhibitory povidone-iodine concentrations against *Staphylococcus epidermidis* and *Staphylococcus aureus*. *J Orthop Res*. 2010;28:1252–1256. doi:10.1002/jor.21110.
- [4] Zamora JL. Chemical and microbiologic characteristics and toxicity of povidone-iodine solutions. *Am J Surg*. 1986;151:400–406.
- [5] Cheng Q, Zhang XF, Di DH, Zhao GY, Cui XW. Efficacy of different irrigation solutions on the early debridement of open fracture in rats. *Exp Ther Med*. 2015;9:1589–1592. doi:10.3892/etm.2015.2325.
- [6] Chang FY, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Can povidone-iodine solution be used safely in a spinal surgery? *Eur Spine J*. 2006;15:1005–1014. doi:10.1007/s00586-005-0975-6.
- [7] Kokavec M, Frísková M. [Efficacy of antiseptics in the prevention of post-operative infections of the proximal femur, hip and pelvis regions in orthopedic pediatric patients. Analysis of the first results]. *Acta Chir Orthop Traumatol Cech*. 2008;75:106–109.
- [8] Rogers DM, Blouin GS, O’Leary JP. Povidone-iodine wound irrigation and wound sepsis. *Surg Gynecol Obstet*. 1983;157:426–430.
- [9] Sindelar WF, Brower ST, Merkel AB, Takesue EI. Randomised trial of intraperitoneal irrigation with low molecular weight povidone-iodine solution to reduce intra-abdominal infectious complications. *J Hosp Infect*. 1985;6 Suppl A:103–114.
- [10] Sindelar WF, Mason GR. Irrigation of subcutaneous tissue with povidone-iodine solution for prevention of surgical wound infections. *Surg Gynecol Obstet*. 1979;148:227–231.
- [11] Lau WY, Fan ST, Chu KW, Yip WC, Chong KK, Wong KK. Combined topical povidone-iodine and systemic antibiotics in postappendicectomy wound sepsis. *Br J Surg*. 1986;73:958–960.
- [12] Angelini GD, Lamarra M, Azzu AA, Bryan AJ. Wound infection following early repeat sternotomy for postoperative bleeding. An experience utilizing intraoperative irrigation with povidone iodine. *J Cardiovasc Surg (Torino)*. 1990;31:793–795.
- [13] Ko W, Lazenby WD, Zelano JA, Isom OW, Krieger KH. Effects of shaving methods and intraoperative irrigation on suppurative mediastinitis after bypass operations. *Ann Thorac Surg*. 1992;53:301–305.
- [14] Richter S, Kotliroff O, Nissenkorn I. Single preoperative bladder instillation of povidone-iodine for the prevention of postprostatectomy bacteriuria and wound infection. *Infect Control Hosp Epidemiol*. 1991;12:579–582.
- [15] Chundamala J, Wright JG. The efficacy and risks of using povidone-iodine irrigation to prevent surgical site infection: an evidence-based review. *Can J Surg*. 2007;50:473–481.
- [16] Brown NM, Cipriano CA, Moric M, Sporer SM, Della Valle CJ. Dilute betadine lavage before closure for the prevention of acute postoperative deep periprosthetic joint infection. *J Arthroplasty*. 2012;27:27–30. doi:10.1016/j.arth.2011.03.034.
- [17] Milstone AM, Passaretti CL, Perl TM. Chlorhexidine: expanding the armamentarium for infection control and prevention. *Clin Infect Dis*. 2008;46:274–281. doi:10.1086/524736.
- [18] Lim K-S, Kam PCA. Chlorhexidine—pharmacology and clinical applications. *Anaesth Intensive Care*. 2008;36:502–512.
- [19] McDonnell G, Russell AD. Antiseptics and disinfectants: activity, action, and resistance. *Clin Microbiol Rev*. 1999;12:147–179.
- [20] Oosterwaal PJ, Mikx FH, van den Brink ME, Renggli HH. Bactericidal concentrations of chlorhexidine-digluconate, amine fluoride gel and stannous fluoride gel for subgingival bacteria tested in serum at short contact times. *J Periodont Res*. 1989;24:155–160.
- [21] Frisch NB, Kadri OM, Tenbrunsel T, Abdul-Hak A, Qatu M, Davis JJ. Intraoperative chlorhexidine irrigation to prevent infection in total hip and knee arthroplasty. *Arthroplast Today*. 2017;3:294–297. doi:10.1016/j.artd.2017.03.005.
- [22] Barnes S, Spencer M, Graham D, Johnson HB. Surgical wound irrigation: a call for evidence-based standardization of practice. *Am J Infect Control*. 2014;42:525–529. doi:10.1016/j.ajic.2014.01.012.
- [23] Hassinger SM, Harding G, Wongworawat MD. High-pressure pulsatile lavage propagates bacteria into soft tissue. *Clin Orthop Relat Res*. 2005;439:27–31.
- [24] Anglen JO, Apostoles S, Christensen G, Gainor B. The efficacy of various irrigation solutions in removing slime-producing *Staphylococcus*. *J Orthop Trauma*. 1994;8:390–396.
- [25] Whiteside LA. Prophylactic peri-operative local antibiotic irrigation. *Bone Joint J*. 2016;98-B:23–26. doi:10.1302/0301-620X.98B1.36357.
- [26] Capito NM, Cook JL, Yahuaa B, Capito MD, Sherman SL, Smith MJ. Safety and efficacy of hyperosmolar irrigation solution in shoulder arthroscopy. *J Shoulder Elbow Surg*. 2017;26:745–751. doi:10.1016/j.jse.2017.02.021.
- [27] Jensen KH, Werther K, Stryger V, Schultz K, Falkenberg B. Arthroscopic shoulder surgery with epinephrine saline irrigation. *Arthroscopy*. 2001;17:578–581. doi:10.1053/jars.2001.23590.
- [28] Kim YS, Lee JY, Yang SC, Song JH, Koh HS, Park WK. Comparative study of the influence of room-temperature and warmed fluid irrigation on body temperature in arthroscopic shoulder surgery. *Arthroscopy*. 2009;25:24–29. doi:10.1016/j.arthro.2008.08.005.
- [29] van Montfoort DO, van Kampen PM, Huijsmans PE. Epinephrine diluted saline-irrigation fluid in arthroscopic shoulder surgery: a significant improvement of clarity of visual field and shortening of total operation time. a randomized controlled trial. *Arthroscopy*. 2016;32:436–444. doi:10.1016/j.arthro.2015.08.027.
- [30] Oh JH, Kim JY, Chung SW, Park JS, Kim DH, Kim SH, et al. Warmed irrigation fluid does not decrease perioperative hypothermia during arthroscopic shoulder surgery. *Arthroscopy*. 2014;30:159–164. doi:10.1016/j.arthro.2013.11.017.
- [31] Pan X, Ye L, Liu Z, Wen H, Hu Y, Xu X. Effect of irrigation fluid temperature on core body temperature and inflammatory response during arthroscopic shoulder surgery. *Arch Orthop Trauma Surg*. 2015;135:1131–1139. doi:10.1007/s00402-015-2246-2.
- [32] Avery DM, Gibson BW, Carolan GF. Surgeon-rated visualization in shoulder arthroscopy: a randomized blinded controlled trial comparing irrigation fluid with and without epinephrine. *Arthroscopy*. 2015;31:12–18. doi:10.1016/j.arthro.2014.08.010.

- [33] Li Z, Liu D, Dong J, Gong L, Wang Y, Tang P, et al. Effects of cold irrigation on early results after total knee arthroplasty: a randomized, double-blind, controlled study. *Medicine* (Baltimore). 2016;95:e3563. doi:10.1097/MD.0000000000003563.
- [34] Niki Y, Matsumoto H, Otani T, Tomatsu T, Toyama Y. How much sterile saline should be used for efficient lavage during total knee arthroplasty? Effects of pulse lavage irrigation on removal of bone and cement debris. *J Arthroplasty*. 2007;22:95–99. doi:10.1016/j.arth.2006.02.078.
- [35] Shinjo H, Nakata K, Shino K, Hamada M, Nakamura N, Mae T, et al. Effect of irrigation solutions for arthroscopic surgery on intraarticular tissue: comparison in human meniscus-derived primary cell culture between lactate Ringer's solution and saline solution. *J Orthop Res*. 2002;20:1305–1310. doi:10.1016/S0736-0266(02)00062-1.
- [36] Board TN, Srinivasan MS. The effect of irrigation fluid temperature on core body temperature in arthroscopic shoulder surgery. *Arch Orthop Trauma Surg*. 2008;128:531–533. doi:10.1007/s00402-007-0368-x.
- [37] Steelman VM, Chae S, Duff J, Anderson MJ, Zaidi A. Warming of irrigation fluids for prevention of perioperative hypothermia during arthroscopy: a systematic review and meta-analysis. *Arthroscopy*. 2018;34:930–942.e2. doi:10.1016/j.arthro.2017.09.024.
- [38] Parodi D, Valderrama J, Tobar C, Besomi J, López J, Lara J, et al. Effect of warmed irrigation solution on core body temperature during hip arthroscopy for femoroacetabular impingement. *Arthroscopy*. 2014;30:36–41. doi:10.1016/j.arthro.2013.08.035.
- [39] Kelly JA, Doughty JK, Hasselbeck AN, Vacchiano CA. The effect of arthroscopic irrigation fluid warming on body temperature. *J Perianesth Nurs*. 2000;15:245–252. doi:10.1053/jpan.2000.9463.



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### QUESTION 3: Does the pressure of the pulsatile delivery mechanism for irrigation fluid influence the efficacy of the irrigation solution to eradicate infecting organisms in the wound?

RECOMMENDATION: A series of clinical studies have been unable to observe differences in clinical outcomes or reoperation rates between high-pressure vs. low-pressure wound irrigation. Tangential hydrosurgery is an emerging irrigation method that, though promising, still requires further investigation.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 90%, Disagree: 4%, Abstain: 6% (Super Majority, Strong Consensus)

#### RATIONALE

There has been a combination of in vitro models, animal models and clinical studies that have investigated the efficacy of irrigation pressure in wounds. The majority of the in vitro and in vivo studies have been completed in regards to traumatic wound debridement. These studies have looked at the ability of irrigation methods to remove bacteria, inorganic contaminate, tissue damage induced from irrigation and possible differences in distribution of contaminate in the wound after irrigation. A series of clinical studies have been completed that do not demonstrate any difference in clinical efficacy between high-pressure and low-pressure irrigation.

High and low-pressure lavage has mixed results in removing contaminants from the wound. In vitro studies have shown an increased ability of pulsatile lavage to remove inorganic debris [1,2] and bacteria [3]. Animal models have had indeterminate results. In a rabbit animal model, high-pressure irrigation and bulb syringe irrigation were equally as effective at removing debris. In an animal model using bioluminescent bacteria, high-pressure lavage demonstrated an increased ability to remove bacteria [4].

Concerns have been raised that high-pressure irrigation may distribute contaminants deeper into soft tissues. Paradoxical results that high-pressure irrigations have fewer contaminants removed support these results [5,6]. This data is supported by luminescent bacteria in wound animal models where high-pressure irrigation has improved or has an equivalent ability to initially remove bacteria, but that there is a higher rebound of bacteria several hours after completion of the procedure [7]. In an in vitro model of a contaminated human tibial fracture, high-pressure pulsatile lavage followed by cultures of serial sections at increasing distance from the fracture site revealed a reproducible pattern of bacterial propagation into the intramedullary canal [8]. In addition, bone destruction was found to vary proportionally with the depth into the canal.

There have been a large number of in vitro studies demonstrating possible increased levels of microscopic and macroscopic bone and tissue destruction after high-pressure pulse lavage as compared to low-pressure irrigation. On bone specimens, high-pressure pulse lavage was associated with more fissures and defects in cancellous bone [3], bone structure and fracture healing [3,9]. Similar results have been seen with high-pressure irrigation having increased gross damage to soft tissue as compared to low-pressure irrigation [1,5,10]. These results show that high-pressure pulsatile lavage penetrates and disrupts soft tissue to a deeper level than low-pressure lavage, causing considerable gross and microscopic tissue disruption [5].

Animal models support the findings from these in vitro models. High-pressure lavage can inhibit early new bone formation in an intraarticular fracture rabbit model. There was a direct relationship between irrigation pressures and the amount of cellular materials removed from the trabeculae at the irrigation site [11]. Animal models have shown that high-pressure pulsatile lavage of musculoskeletal wounds can cause injury to tissue, resulting in myonecrosis and dystrophic calcification [12]. High-pressure pulsatile lavage has also been shown to significantly decrease the mechanical strength of fracture callus (peak bending force and stiffness) during the early phases of healing (three weeks), as compared to bulb syringe techniques in a non-contaminated diaphyseal femoral fracture model in rats [13].

Multiple clinical studies have demonstrated that high or low-irrigation pressure results in similar clinical outcomes. The largest of these was the Fluid Lavage of Open Wounds (FLOW) study [14]. This was a large, well-designed, prospective, randomized, two-by-three factorial design clinical study comparing three irrigation pressures and two irrigation solutions (normal saline and castile soap). A total of 2,551 patients were enrolled and the primary end-points were reoperation within 12 months from the index procedure or treatment of a wound infection. The FLOW study demonstrated that the rates of reoperation were similar regardless of irrigation pressure (ClinicalTrials.gov NCT00788398) [14].

These findings are supported by several smaller studies. The FLOW study design was based on pilot data that suggested that low pressure irrigation of open wounds may decrease reoperation rates for infection, although the pilot study did not observe any statistically significant differences between high and low pressure irrigation groups (ClinicalTrials.gov NCT01069315) [15]. In a small prospective randomized clinical study of acute periprosthetic

joint infection, there were no differences seen with the use of high versus low-pressure irrigation with outcomes defined by retention of prosthesis or elevation of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) at one year [16].

Irrigation pressures may have difficulty removing bacteria from the wound because biofilm acts as a viscous fluid. Biofilms are viscoelastic and resist detachment from increased fluid flow and shear by deformation. This allows the biofilm to remain attached to the surface, or roll along a surface in response to a shear stress from fluid [17]. Given this limitation of pulsatile irrigation as well as the concerns for bone destruction discussed above, there has been a recent interest in exploring novel delivery mechanisms of the irrigation fluid. In a prospective randomized control study, tangential hydrosurgery was compared to standard surgical debridement of grade IIIA and IIIB open tibia fractures in 40 patients. It was found that when hydrosurgery was used, significantly fewer debridement procedures were required prior to final wound closure [18]. Hydrosurgery debridement was also evaluated as a method for removing bacteria from fracture implants. Specifically, when comparing the use of hydrosurgery, pressurized pulsatile lavage and bulb syringe to deliver the same volume of saline to debride *Staphylococcus aureus*-contaminated stainless-steel fracture plates, residual bacterial loads were found to be significantly lower in the hydrosurgery group [19].

## REFERENCES

- [1] Draeger RW, Dirschl DR, Dahners LE. Debridement of cancellous bone: a comparison of irrigation methods. *J Orthop Trauma*. 2006;20:692–698. doi:10.1097/BOT.0b013e31802b41e2.
- [2] Kalteis T, Lehn N, Schröder HJ, Schubert T, Zysk S, Handel M, et al. Contaminant seeding in bone by different irrigation methods: an experimental study. *J Orthop Trauma*. 2005;19:591–596.
- [3] Bhandari M, Schemitsch EH, Adili A, Lachowski RJ, Shaughnessy SG. High and low pressure pulsatile lavage of contaminated tibial fractures: an in vitro study of bacterial adherence and bone damage. *J Orthop Trauma*. 1999;13:526–533.
- [4] Svoboda SJ, Bice TG, Gooden HA, Brooks DE, Thomas DB, Wenke JC. Comparison of bulb syringe and pulsed lavage irrigation with use of a bioluminescent musculoskeletal wound model. *J Bone Joint Surg Am*. 2006;88:2167–2174. doi:10.2106/JBJS.E.00248.
- [5] Draeger RW, Dahners LE. Traumatic wound debridement: a comparison of irrigation methods. *J Orthop Trauma*. 2006;20:83–88. doi:10.1097/01.bot.0000197700.19826.db.
- [6] Hassinger SM, Harding G, Wongworawat MD. High-pressure pulsatile lavage propagates bacteria into soft tissue. *Clin Orthop Relat Res*. 2005;439:27–31.
- [7] Owens BD, White DW, Wenke JC. Comparison of irrigation solutions and devices in a contaminated musculoskeletal wound survival model. *J Bone Joint Surg Am*. 2009;91:92–98. doi:10.2106/JBJS.G.01566.
- [8] Bhandari M, Adili A, Lachowski RJ. High pressure pulsatile lavage of contaminated human tibiae: an in vitro study. *J Orthop Trauma*. 1998;12:479–484.
- [9] Dirschl DR, Duff GP, Dahners LE, Edin M, Rahn BA, Miclau T. High pressure pulsatile lavage irrigation of intraarticular fractures: effects on fracture healing. *J Orthop Trauma*. 1998;12:460–463.
- [10] Boyd JJ, Wongworawat MD. High-pressure pulsatile lavage causes soft tissue damage. *Clin Orthop Relat Res*. 2004:13–17.
- [11] Polzin B, Ellis T, Dirschl DR. Effects of varying pulsatile lavage pressure on cancellous bone structure and fracture healing. *J Orthop Trauma*. 2006;20:261–266.
- [12] Chiaramonti AM, Robertson AD, Nguyen TP, Jaffe DE, Hanna EL, Holmes R, et al. Pulsatile lavage of musculoskeletal wounds causes muscle necrosis and dystrophic calcification in a rat model. *J Bone Joint Surg Am*. 2017;99:1851–1858. doi:10.2106/JBJS.17.00330.
- [13] Adili A, Bhandari M, Schemitsch EH. The biomechanical effect of high-pressure irrigation on diaphyseal fracture healing in vivo. *J Orthop Trauma*. 2002;16:413–417.
- [14] FLOW Investigators, Bhandari M, Jeray KJ, Petrisor BA, Devereaux PJ, Heels-Ansdell D, et al. A trial of wound irrigation in the initial management of open fracture wounds. *N Engl J Med*. 2015;373:2629–2641. doi:10.1056/NEJMoa1508502.
- [15] FLOW Investigators, Petrisor B, Sun X, Bhandari M, Guyatt G, Jeray KJ, et al. Fluid lavage of open wounds (FLOW): a multicenter, blinded, factorial pilot trial comparing alternative irrigating solutions and pressures in patients with open fractures. *J Trauma*. 2011;71:596–606. doi:10.1097/TA.0b013e3181f6f2e8.
- [16] Muñoz-Mahamud E, García S, Bori G, Martínez-Pastor JC, Zumbado JA, Riba J, et al. Comparison of a low-pressure and a high-pressure pulsatile lavage during débridement for orthopaedic implant infection. *Arch Orthop Trauma Surg*. 2011;131:1233–1238. doi:10.1007/s00402-011-1291-8.
- [17] Rupp CJ, Fux CA, Stoodley P. Viscoelasticity of staphylococcus aureus biofilms in response to fluid shear allows resistance to detachment and facilitates rolling migration. *Appl Environ Microbiol*. 2005;71:2175–2178. doi:10.1128/AEM.71.4.2175-2178.2005.
- [18] Oosthuizen B, Mole T, Martin R, Myburgh JG. Comparison of standard surgical debridement versus the VERSAJET Plus™ Hydrosurgery system in the treatment of open tibia fractures: a prospective open label randomized controlled trial. *Int J Burns Trauma*. 2014;4:53–58.
- [19] Hughes MS, Moghadamian ES, Yin LY, Della Rocca GJ, Crist BD. Comparison of bulb syringe, pressurized pulsatile, and hydrosurgery debridement methods for removing bacteria from fracture implants. *Orthopedics*. 2012;35:e1046–e1050. doi:10.3928/01477447-20120621-19.



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## 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.

## REFERENCES

- [1] Whiteside OJ, Tytherleigh MG, Thrush S, Farouk R, Galland RB. Intra-operative peritoneal lavage—who does it and why? *Ann R Coll Surg Engl.* 2005;87:255–258. doi:10.1308/1478708051847.
- [2] Brown NM, Cipriano CA, Moric M, Sporer SM, Della Valle CJ. Dilute betadine lavage before closure for the prevention of acute postoperative deep periprosthetic joint infection. *J Arthroplasty.* 2012;27:27–30. doi:10.1016/j.arth.2011.03.034.
- [3] Diana M, Hübner M, Eisenring M-C, Zanetti G, Troillet N, Demartines N. Measures to prevent surgical site infections: what surgeons (should) do. *World J Surg.* 2011;35:280–288. doi:10.1007/s00268-010-0862-0.
- [4] Tejwani NC, Immerman I. Myths and legends in orthopaedic practice: are we all guilty? *Clin Orthop Relat Res.* 2008;466:2861–2872. doi:10.1007/s11999-008-0458-2.
- [5] Surgical site infections: prevention and treatment. Guidance and guidelines. NICE <https://www.nice.org.uk/guidance/cg74> (accessed May 17, 2018).
- [6] de Jonge SW, Boldingh QJJ, Solomkin JS, Allegranzi B, Egger M, Dellinger EP, et al. Systematic review and meta-analysis of randomized controlled trials evaluating prophylactic intra-operative wound irrigation for the prevention of surgical site infections. *Surg Infect (Larchmt).* 2017;18:508–519. doi:10.1089/sur.2016.272.
- [7] Anglen JO. Comparison of soap and antibiotic solutions for irrigation of lower-limb open fracture wounds. A prospective, randomized study. *J Bone Joint Surg Am.* 2005;87:1415–1422. doi:10.2106/JBJS.D.02615.
- [8] Antevil JL, Muldoon MP, Battaglia M, Green R. Intraoperative anaphylactic shock associated with bacitracin irrigation during revision total knee arthroplasty. A case report. *J Bone Joint Surg Am.* 2003;85-A:339–342.
- [9] Anglen JO. Wound irrigation in musculoskeletal injury. *J Am Acad Orthop Surg.* 2001;9:219–226.
- [10] World Health Organization. Global guidelines for the prevention of surgical site infection. 2016. <http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=1>.
- [11] Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, Jonge S de, Vries F de, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Diseases.* 2016;16:e288–e303. doi:10.1016/S1473-3099(16)30402-9.

- [12] Berriós-Torres SJ, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg.* 2017;152:784–791. doi:10.1001/jamasurg.2017.0904.
- [13] Pitt HA, Postier RG, MacGowan AW, Frank LW, Surmak AJ, Sitzman JV, et al. Prophylactic antibiotics in vascular surgery. Topical, systemic, or both? *Ann Surg.* 1980;192:356–364.
- [14] Freischlag J, McGrattan M, Busuttill RW. Topical versus systemic cephalosporin administration in elective biliary operations. *Surgery.* 1984;96:686–693.
- [15] Juul P, Merrild U, Kronborg O. Topical ampicillin in addition to a systemic antibiotic prophylaxis in elective colorectal surgery. A prospective randomized study. *Dis Colon Rectum.* 1985;28:804–806.
- [16] Moesgaard F, Nielsen ML, Hjortrup A, Kjersgaard P, Sørensen C, Larsen PN, et al. Intra-incisional antibiotic in addition to systemic antibiotic treatment fails to reduce wound infection rates in contaminated abdominal surgery. *Dis Colon Rectum.* 1989;32:36–38. doi:10.1007/BF02554723.
- [17] Ruiz-Tovar J, Cansado P, Perez-Soler M, Gomez MA, Llaveró C, Calero P, et al. Effect of gentamicin lavage of the axillary surgical bed after lymph node dissection on drainage discharge volume. *Breast.* 2013;22:874–878. doi:10.1016/j.breast.2013.03.008.
- [18] Anglen JO, Apostoles S, Christensen G, Gainor B. The efficacy of various irrigation solutions in removing slime-producing staphylococcus. *J Orthop Trauma.* 1994;8:390–396.
- [19] Goswami K, Cho J, Manrique J, Higuera CA, Della Valle CJ, Parvizi J. Polymyxin and bacitracin in the irrigation solution: there is no role for this practice. *Musculoskeletal Infection Society Annual Open Scientific Meeting (Philadelphia).* 2018.
- [20] Conroy BP, Anglen JO, Simpson WA, Christensen G, Phaup G, Yeager R, et al. Comparison of castile soap, benzalkonium chloride, and bacitracin as irrigation solutions for complex contaminated orthopaedic wounds. *J Orthop Trauma.* 1999;13:332–337.
- [21] Damm S. Intraoperative anaphylaxis associated with bacitracin irrigation. *Am J Health Syst Pharm.* 2011;68:323–327. doi:10.2146/ajhp090238.
- [22] Zug KA, Warshaw EM, Fowler JF, Maibach HI, Belsito DL, Pratt MD, et al. Patch-test results of the North American Contact Dermatitis Group 2005–2006. *Dermatitis.* 2009;20:149–160.
- [23] Savitz SI, Savitz MH, Goldstein HB, Mouracade CT, Malangone S. Topical irrigation with polymyxin and bacitracin for spinal surgery. *Surg Neurol.* 1998;50:208–212.
- [24] Scherr DD, Dodd TA, Buckingham WW. Prophylactic use of topical antibiotic irrigation in uninfected surgical wounds. A microbiological evaluation. *J Bone Joint Surg Am.* 1972;54:634–640.
- [25] Rosenstein BD, Wilson FC, Funderburk CH. The use of bacitracin irrigation to prevent infection in postoperative skeletal wounds. An experimental study. *J Bone Joint Surg Am.* 1989;71:427–430.
- [26] Whiteside LA. Prophylactic peri-operative local antibiotic irrigation. *Bone Joint J.* 2016;98-B:23–26. doi:10.1302/0301-620X.98B1.36357.
- [27] McHugh SM, Collins CJ, Corrigan MA, Hill ADK, Humphreys H. The role of topical antibiotics used as prophylaxis in surgical site infection prevention. *J Antimicrob Chemother.* 2011;66:693–701. doi:10.1093/jac/dkr009.



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## QUESTION 5: Is there a role for non-antibiotic natural antiseptic agents (e.g., honey, vinegar) as an irrigation solution during surgical debridement for periprosthetic joint infections (PJIs)?

RECOMMENDATION: There may be a role for non-antibiotic antiseptic agents (e.g., honey, vinegar, etc.) as an irrigation solution during surgical debridement.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 39%, Disagree: 43%, Abstain: 18% (NO Consensus)

### RATIONALE

As multi-antibiotic resistant organisms become more prevalent, the need for non-antibiotic anti-microbial therapy becomes important again (as it was in the pre-antibiotic era). Several options are readily-available for use as a local chemical debriding agent for local irrigation of PJI wounds after surgical and mechanical debridement has been completed [1]. Among these options are vinegar (acetic acid), honey, hydrogen peroxide, local anesthetic, iodine and chlorhexidine. There are no randomized control trials of deep wound irrigation using any of these substances in PJIs. The evidence is limited and often inferred from chronic wound management [2,3].

#### Vinegar

Vinegar has been in use for millennia as an antibacterial agent [4]. The only case series reporting its use as a deep wound irrigant in orthopaedics was by Williams et al. in 2015 [5]. This study showed that the use of 3% acetic acid (AA) soak, as part of a debridement protocol, was safe in patients. While the exact mechanism of action is yet to be determined, AA concentrations as low as 0.19% vol/vol in vitro are sufficient to completely inhibit bacterial growth. It is postulated that pH change is a potential mechanism of action.

#### Honey

Honey has a long history of use in topical wound management [6]. There is only a small case series of its use as a topical agent for deep PJI wounds at the time of reimplantation [7]. In this series, sterile, industrially-manufactured SurgiHoney (SurgiHoney RO, Southmoor, Abingdon, United Kingdom) was used in salvage cases. No adverse effects were reported, but no conclusions regarding efficacy can be drawn.

#### Hydrogen Peroxide

Dental publications are a resource that orthopaedic surgeons should review for parallel implant experience. One such paper is by Gustumhaugen et al. [8], who found that hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) was an effective biofilm debriding agent, especially in combination with mechanical debridement.

#### Local Anesthetic

Indirect evidence comes from an experimental study of peritonitis in a rat model. Lavage with normal saline and bupivacaine prolonged survival [9]. Studies on ropivacaine have also proved encouraging [10].

## REFERENCES

- [1] Khan W, Morgan–Jones R. Debridement: Defining something we all do. *J Trauma Orthop*. 2016;04:48.
- [2] Daeschlein G. Antimicrobial and antiseptic strategies in wound management. *Int Wound J*. 2013;10 Suppl 1:9–14. doi:10.1111/iwj.12175.
- [3] Schwartz JA, Goss SG, Facchin F, Avdagic E, Lantis JC. Surgical debridement alone does not adequately reduce planktonic bioburden in chronic lower extremity wounds. *J Wound Care*. 2014;23:S4, S6, S8 passim. doi:10.12968/jowc.2014.23.Sup9.S4.
- [4] Mikoh P, Murray J, Williams R. Novel antibiotic delivery and novel antimicrobials in prosthetic joint infection. *J Trauma Orthop*. 2016;4:52.
- [5] Williams RL, Ayre WN, Khan WS, Mehta A, Morgan–Jones R. Acetic acid as part of a debridement protocol during revision total knee arthroplasty. *J Arthroplasty*. 2017;32:953–957. doi:10.1016/j.arth.2016.09.010.
- [6] Surgery and honey | The Bulletin of the Royal College of Surgeons of England n.d. <https://publishing.rcseng.ac.uk/doi/full/10.1308/rcsbull.2017.52> (accessed August 10, 2018).
- [7] Saeed K, Dryden M, Bassetti M, Bonnet E, Bouza E, Chan M, et al. Prosthetic joints: shining lights on challenging blind spots. *Int J Antimicrob Agents*. 2017;49:153–161. doi:10.1016/j.ijantimicag.2016.10.015.
- [8] Gustumhaugen E, Lönn–Stensrud J, Scheie AA, Lyngstadaas SP, Ekfeldt A, Taxt–Lamolle S. Effect of chemical and mechanical debridement techniques on bacterial re–growth on rough titanium surfaces: an in vitro study. *Clin Oral Implants Res*. 2014;25:707–713. doi:10.1111/clr.12130.
- [9] Camargo MG, Fagundes JJ, Leal RF, Ayrizono M de LS, Rossi DH dos G, Oliveira P de SP, et al. Influence of the peritoneal lavage with bupivacaine on the survival and resistance of colonic anastomoses performed under fecal peritonitis in rats. *Acta Cir Bras*. 2013;28:783–787.
- [10] Brocco MC, Gomez RS, Paulo DNS, Almeida CED de, Baptista JF de A. Histological features of peritoneal lavage with ropivacaine in rats with fecal peritonitis. *Acta Cir Bras*. 2012;27:193–199.