

ated 557 patients who used preoperative chlorhexidine cloths and 1901 patients who did not. There was a statistically significant lower infection rate among the patients who used the cloths (0.5%) when compared to patients who did not (1.7%) [6].

Murray et al. explored the use of 2% chlorhexidine no rinse clothes used twice before any type of shoulder surgery in a prospective randomized trial of 100 patients with a control group that used only soap. Cutaneous cultures were taken before surgery and patients were monitored for postoperative infections. There were no infections in either group. The positive culture rate was 66% in the treatment group and 94% ( $p = .0008$ ) in the control group, and the positive culture rate for coagulase-negative *Staphylococcus* was 30% and 70% respectively ( $p = .0001$ ) [7].

In general, most studies have focused on hip and knee replacement surgery rather than shoulder surgery. However, the studies referenced above demonstrate the efficacy of CHG-containing products when applied at a minimum of two applications. Despite weak recommendations by the CDC, clinical evidence supports a minimum of two preadmission 4% CHG showers or no-rinse 2% CHG cloth applications as a critical component of a broader interventional strategy for reducing the risk of SSIs in shoulder surgery [3,8].

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## QUESTION 2: What is the optimal perioperative surgical skin prep for primary or revision shoulder arthroplasty?

**RECOMMENDATION:** The best available evidence supports 2% chlorhexidine gluconate and 70% isopropyl alcohol for surgical skin prep for shoulder arthroplasty.

**LEVEL OF EVIDENCE:** Moderate

**DELEGATE VOTE:** Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

## RATIONALE

A comprehensive search of several databases from 1988 to January 15<sup>th</sup>, 2018 (any language) was conducted. The databases included Ovid Medline Epub Ahead of Print, Ovid Medline In-Process & Other Non-Indexed Citations, Ovid Medline, Ovid Embase, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews and Scopus. The search strategy was designed and conducted by an experienced librarian with input from the study's principle investigator. Controlled vocabulary supplemented with keywords was used to search for surgical site preparation for prosthetic shoulder joint infections. The complete search strategies are listed below.

The rationale for the use of chlorhexidine surgical prep prior to shoulder arthroplasty is based on one level-I randomized controlled trial by Saltzman et al. [1]. In this trial, patients were randomized to compare ChlorPrep™ (Becton Dickinson) (2% w/v chlorhexidine gluconate (CHG) in 70% v/v isopropyl alcohol (IPA)), DuraPrep™ (3M™) (Iodine Povacrylex (0.7% available iodine) and isopropyl alcohol, 74%), and povidone-iodine ((0.75% iodine scrub and 1.0% iodine paint; Tyco Healthcare Group, Mansfield, Massachusetts) for patients undergoing shoulder surgery. The rate of positive skin cultures was reduced but not eliminated with ChlorPrep™ (7%) when compared with DuraPrep™ (18%) or povidone-iodine (31%). Furthermore, there were no infections in any of the

patients at a mean of 10 months follow-up. In this trial, while a chlorhexidine solution was most active against the bacteria on the shoulder in general, there was no significant difference detected among the agents in their ability to eliminate *Cutibacterium acnes* from the shoulder region [1]. As *Cutibacterium acnes* is increasingly recognized as a key player in shoulder periprosthetic joint infection (PJI), there is concern that the current prep solutions are inadequate to treat this pathogen. Despite this, there were no postoperative infections in any of the groups at a minimum of 10 months of follow-up.

Chlorhexidine waterless wipes have also been advocated to decrease bacterial burden preoperatively. Murray et al. in another level-I study randomly assigned patients to one of two groups. Group 1 wiped the shoulder with 2% chlorhexidine gluconate impregnated cloths and group 2 showered with soap and water before surgery [2]. Again, none of the patients developed a postoperative infection and the cultured sites on the skin showed a reduction in positive cultures for coagulase-negative *Staphylococcus* and *Cutibacterium acnes*. Nevertheless, others have found the persistence of *Cutibacterium* within the skin dermis despite standard skin prep with chlorhexidine [3–7]. There is significant literature establishing a high rate of *Cutibacterium acnes* positive surgical sites despite standard skin preparation in both the primary and revision settings, likely due to the fact that

TABLE 1. Search strategy

#	Searches	Results
1	Arthroplasty, Replacement/	6266
2	exp joint prosthesis/	96013
3	exp shoulder/	44325
4	exp Shoulder Joint/	50050
5	(1 or 2) and (3 or 4)	3220
6	exp shoulder arthroplasty/	2921
7	exp shoulder prosthesis/	997
8	exp Arthroplasty, Replacement, Shoulder/	1056
9	exp shoulder/su	3240
10	exp Shoulder Joint/su	7682
11	((“glenohumeral joint” or “glenoid labrum” or “humeroscapular joint” or “scapulo humeral joint” or “scapulohumeral joint” or shoulder) adj4 (prosthesis* or implant* or reconstruct* or replacement* or arthroplast* or “artificial joint*” or surg* or operation* or reconstruct* or procedure*)).ti,ab,hw,kw.	21875
12	5 or 6 or 7 or 8 or 9 or 10 or 11	27190
13	exp Preoperative Care/	99126
14	exp SKIN/	487534
15	13 and 14	692
16	((((“Anti-infective*” or Antiinfective* or antiseptic* or “anti-septic*” or antimicrobial* or “anti-microbial*” or antiseptics or “anti-sepsis” or disinfect* or steriliz*) adj3 (agent* or prep* or product* or solution* or topical* or skin or cutaneous*)) or ((preop* or “pre-op*” or protocol*) adj5 (skin or cutaneous*)) or ((surgical or operative or skin or cutaneous* or steriliz* or disinfect*) adj3 prep*) or ((wound* or skin or cutaneous*) adj5 (contaminat* or infect* or steriliz* or disinfect*)) or (local* adj3 Infect*) or alcohol or “benzoyl peroxide” or Chlorhexidine or DuraPrep or “hydrogen peroxide” or iodophor* or iodopovidone or “microbial skin burden*” or “povidone-iodine” or “PVP-I” or “site prep*” or “Surgical drape*” or “Surgical-Site Infection*”).ti,ab,hw,kw.	1406854
17	15 or 16	1407106
18	12 and 17	581
19	(case adj3 report).mp.pt.	2235257
20	18 not 19	544
21	limit 20 to (letter or conference abstract or editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,CCTR,CDSR,Ovid Medline(R),Ovid Medline(R) Daily Update,Ovid Medline (R) In-Process,Ovid Medline (R) Publisher; records were retained]	38
22	from 21 keep 36	1
23	(20 not 21) or 22	507
24	limit 23 to yr=“1980 -Current”	496
25	remove duplicates from 24	348

the preparation solutions do not adequately penetrate the deep dermal sebaceous glands where *C. acnes* resides [5,8].

Benzoyl peroxide (BPO), which has known bactericidal properties against *C. acnes*, has been investigated for use in shoulder surgery [9–11]. BPO is a lipophilic compound directly toxic to both surface and ductal bacteria via penetration of pilosebaceous ducts. Once applied to the skin, the decomposition of BPO creates free oxygen radicals, which have potent bactericidal activity directly within the sebaceous follicles. In a study by Sabetta et al., patients were randomly assigned to wipe the surgical site with 5% topical benzoyl peroxide 48 hours before arthroscopic surgery [10]. These authors found five applications of BPO were effective in reducing *C. acnes* on the skin at the beginning and end of surgical procedures. A more recent randomized controlled single-blinded trial by Scheer et al. was performed utilizing BPO applications versus chlorhexidine wipes and subsequent chlorhexidine surgical scrub on the ability to reduce bacteria cultured from skin over a deltopectoral approach in healthy volunteers [11]. BPO applications were also performed 48 hours prior to culture in this study and samples taken before and after standard surgical prep with chlorhexidine. These authors found cultures remained negative for up to two hours after application in the BPO group. As these were healthy volunteers without a surgical intervention, no clinical effect could be measured.

A topical preparation of BPO combined with clindamycin applied in the evenings prior to surgery may be an alternative method to decrease bacterial load, particularly of *Cutibacterium acnes*, in the setting of shoulder surgery. In a level II prospective cohort study of patients undergoing shoulder arthroscopy, Dizay et al. found a statistically significant decrease in *Cutibacterium acnes* colonization of the skin at the time of surgery, particularly when more than one application was used leading up to surgery [9].

Despite the positive findings of the above studies of BPO in reducing *C. acnes* on the skin, none have shown a clinical reduction in infections in arthroplasty patients. Therefore, a clinical trial in this specific patient population is needed.

In order to be effective, skin preparations must cover the skin of the surgical site. One level III investigation by Syed et al. examined the type of application of the prep and found that simple gauze pads were more effective at completely covering the skin than the prep sticks alone [12]. In this study, 22 shoulders of volunteer subjects were prepped with either an applicator stick or two sterile 4x4 cm gauze sponges. ultraviolet-A light and advanced image-analysis software were utilized to determine areas of the skin that remained un-prepped. The applicator stick method resulted in a statistically higher percentage of un-prepped skin than the gauze sponge method and the axilla was the most likely to have un-prepped areas. Nevertheless, this study did not explore the infection implication in the difference between the applicator stick and the gauze sponges, and thus a clinical study is needed prior to making any definitive recommendations.

Other ancillary methods surrounding the skin prep such as axillary hair clipping have not been shown to decrease the bacterial burden or clinical infection rate. In fact, Marecek et al. found that there was a significantly greater bacterial burden in the clipped shoulder compared with the unclipped shoulder before preparation, but this effect was not found after surgical preparation. Importantly, all shoulders showed a significant reduction in total bacterial load, including *Cutibacterium acnes*, for both axillae after surgical preparation with 2% CHG and 70% IPA [13].

There is limited evidence specifically dealing with revision shoulder arthroplasty and skin prep. In an attempt to “seal off” pores and isolate remaining bacteria on and in the skin from the wound during revision arthroplasty, Lorenzetti et al. in a level III study

examined the use of cyanoacrylate prior to barrier drapes. The skin edges were painted with the glue over the area of the planned incision and allowed to dry prior to the placement of barrier drapes. This study showed that the prevalence of cases with positive intraoperative cultures decreased from 18% in the standard prep and iodoform barrier drape to 7% in the group with a cyanoacrylate barrier, but this difference did not reach statistical significance [8]. While noteworthy, this was a single level III study and authors were careful to point out that it was underpowered to make generalizable conclusions. Thus this technique, while the only one specifically addressing skin prep techniques during revision shoulder arthroplasty, requires further study before recommending its use.

## Web of Science

1. TOPIC: (((“glenohumeral joint” or “glenoid labrum” or “humeroscapular joint” or “scapulo humeral joint” or “scapulohumeral joint” or shoulder) NEAR/4 (prosthesis\* or implant\* or reconstruct\* or replacement\* or arthroplasty\* or “artificial joint” or surg\* or operation\* or reconstruct\* or procedure\*)) AND TOPIC: (((“Anti-infective” or Antiinfective\* or antiseptic\* or “anti-septic” or antimicrobial\* or “anti-microbial” or antisepsis or “anti-sepsis” or disinfect\* or steriliz\*) NEAR/3 (agent\* or prep\* or product\* or solution\* or topical\* or skin or cutaneous\*)) or ((preop\* or “pre-op” or protocol\*) NEAR/5 (skin or cutaneous\*)) or ((surgical or operative or skin or cutaneous\* or steriliz\* or disinfect\*) NEAR/3 prep\*) or ((wound\* or skin or cutaneous\*) NEAR/5 (contaminat\* or infect\* or steriliz\* or disinfect\*)) or (local\* NEAR/3 Infect\*) or alcohol or “benzoyl peroxide” or Chlorhexidine or DuraPrep or “hydrogen peroxide” or iodophor\* or iodopovidone or “microbial skin burden” or “povidone-iodine” or “PVP-I” or “site prep” or “Surgical drape” or “Surgical-Site Infection”)) AND DOCUMENT TYPES: (Article OR Abstract of Published Item OR Proceedings Paper OR Review) Indexes=SCI-EXPANDED, ESCI Timespan=1980-2018
2. TS=(case NEAR/3 report)
3. 1 NOT 2
4. PMID=(0\* or 1\* or 2\* or 3\* or 4\* or 5\* or 6\* or 7\* or 8\* or 9\*)
5. 3 NOT 4

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### QUESTION 3: Is there a role for topical skin treatments prior to primary or revision shoulder arthroplasty?

**RECOMMENDATION:** At this time, there is no evidence for or against the use of topical skin treatments to reduce the rate of shoulder periprosthetic joint infection (PJI).

**LEVEL OF EVIDENCE:** Limited

**DELEGATE VOTE:** Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

#### RATIONALE

The use of chlorhexidine gluconate (CHG) topical skin treatment preoperatively has been recommended by the International Consensus on Periprosthetic Joint Infection. However, specific to shoulder arthroplasty, the use of topical skin treatments has not been shown to significantly reduce the superficial bacterial load of *Cutibacterium acnes* (formerly known as *Propionibacterium acnes*), nor reduce culture positivity of deep samples retrieved from the surgical site during primary shoulder arthroplasty [1-6].

*C. acnes* has been reported as the most common pathogen in shoulder PJI and, as well as being present on the skin, is also present within the sebum-rich pilosebaceous hair follicles of the deep dermis, making it difficult to eradicate with topical antiseptic techniques. Surgical incisions, transecting thousands of these *C. acnes*-filled dermal glands, can lead to contamination of deeper tissues.

*C. acnes* is also implicated in the pathogenesis of acne vulgaris for which the anti-bacterial agent benzoyl peroxide (BPO) has been used as topical therapy. BPO releases free-radical oxygen which oxidizes bacterial proteins in the sebaceous follicles, decreasing the burden of anaerobic bacteria in the deeper tissues and also inflammation due to the reduction of irritating-type free fatty acids. Leyden described a 90% reduction in *P. acnes* after 48 hours of topical treatment and a 99% reduction after 72 hours of treatment [7]. The addition of topical clindamycin phosphate 1.2% has also been demonstrated to further decrease bacterial load [8]. Although BPO with clindamycin may therefore be the optimal treatment for use prior to shoulder surgery to decrease *C. acnes* contamination, further research is needed to correlate superficial decontamination with decreased infection rates and shoulder PJI [9].

Specific to primary shoulder joint replacement, Levy et al. reported 23 of 55 patients had *P. acnes* growth in the joint synovial fluid collected during surgery [10]. Despite their protocol of washing the shoulder, arm and axilla with 4% CHG, they reported high incidence of *P. acnes* [10]. Other recent studies evaluated colonization rates for primary shoulder arthroplasties and found around 70% of cases had positive cultures for *C. acnes* despite using CHG, and patients of male gender and those with body hair had higher rates of superficial *C. acnes* [4,5,11,12]. In study by Koh et al., 30 patients undergoing primary shoulder arthroplasty had superficial swabs and deep

tissue samples sent for culture at various stages of the operation following CHG application. After the chlorhexidine skin scrub in the operating room, 40% (12/30) had positive skin swab cultures and 27% (8/22) after dual application of chlorhexidine to the skin. Forty-three percent had positive deep cultures on entering the glenohumeral joint, and deep cultures after implantation of the prosthesis were positive in 37%. After closure, 43% had positive superficial cultures. In total, 73% of patients had positive cultures and the authors concluded that topical antiseptic measures did not completely eliminate *C. acnes* [12]. Despite its proven antiseptic effects, dermal application of aqueous CHG during shoulder surgery fails to eradicate or reduce *C. acnes* on deep cultures. The current literature is limited by the lack of high quality studies which can provide definitive answers regarding the clinical effectiveness of various CHG preparations preventing prosthetic shoulder joint infections [13].

Sabetta et al. described the preoperative application of topical 5% BPO in addition to the standard use of CHG preoperative skin preparation to reduce *C. acnes* rates in patients undergoing arthroscopic shoulder procedures. BPO was applied twice daily for a total of 5 applications in the 48 hours prior to operation in 50 patients undergoing primary arthroscopic shoulder surgery [14]. Sixteen percent (8 of 50) of skin swab cultures surgical skin prior to preparation with ChloraPrep from the anterior deltoid of the BPO-treated arm were positive, compared with 32% (16 of 50) of the skin on the anterior deltoid of the untreated arm ( $p = .001$ ). The addition of BPO cream to their standard ChloraPrep protocol appeared to provide an improved method of skin cleansing; however, due to the design of the study (non-randomized), differences in deep culture rates could not be determined [14]. Dizay et al. prospectively studied 65 patients undergoing shoulder arthroscopy using topical 5% benzoyl peroxide plus clindamycin phosphate 1.2% (BPO/C) [15]. The preparation was applied for more than two days prior to surgery. Skin surface swab cultures were taken preoperatively and in the operating room before the standard chlorhexadine preparation. A third set of cultures were taken by swabbing the shoulder tissue at the operative site under direct arthroscopic visualization through an arthroscopic cannula upon completion of the procedure. The topical gel was effective in eliminating 74.2% (23 of 31 patients with positive preoperative