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Efficacy of topical benzoyl peroxide on the reduction of *Propionibacterium acnes* during shoulder surgery

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Background: *Propionibacterium acnes* infection is a significant problem after shoulder surgery. Residual *P. acnes* is found on the skin up to 29% of the time immediately after surgical skin preparation and in 70% of dermal biopsy specimens. These residual bacteria may be a source for infection. Identifying more ideal skin preparation may help reduce the risk of infection. The purpose of this study was to evaluate the effect that topical benzoyl peroxide (BPO), with chlorhexidine skin preparation, would have on the presence of *P. acnes* cultured at the time of shoulder surgery. We hypothesized that adding topical BPO to our skin preparation would reduce the number of positive *P. acnes* cultures identified during surgery.

Methods: Fifty patients undergoing first-time shoulder surgery were treated with topical 5% BPO cream 48 hours before surgery. After skin preparation, 13 samples per subject were obtained. Cultures were held for 14 days.

Results: Fifty patients underwent arthroscopic shoulder surgery; 650 culture specimens were obtained. The skin was positive at the initiation of surgery in 6% of cases. Tissue samples were positive in 6%. The skin was positive in 10% at the end of surgery. None of these rates of positive culture were different from the 4% rate observed with a control swab.

Conclusion: Application of BPO is an effective way to reduce *P. acnes* on skin at the beginning and, importantly, at the end of a surgical procedure. This may result in a lower risk for postoperative infection.

Level of evidence: Level IV, Case Series, Treatment Study.

Keywords: Shoulder; infection; *P. acnes*; culture; arthroscopy; aspiration

Propionibacterium acnes is a significant pathogen in patients undergoing shoulder surgery.[3-5] Infection after shoulder surgery has a serious impact on patient outcome, costs, and value associated with care. Numerous methods for reducing surgical site infection (SSI) have been studied, with a particular interest in chlorhexidine as the most ideal skin preparation.[2,9,12,16,20,21]

The Greenwich Hospital Institutional Review Board approved this study: No. 2014001.

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Chlorhexidine gluconate combined with isopropyl alcohol (ChloraPrep; Care Fusion Corp., San Diego, CA, USA) has been suggested to be the most effective surgical skin preparation for shoulder surgery, but this effect is not specific for *P. acnes*.[12,20,21] *P. acnes* may persist on the skin from 7% to 29% of the time immediately after skin preparation.[10,17,21] The chance of finding these bacteria at the end of the surgical procedure may increase to 41% to 63%.[22] Furthermore, *P. acnes* was identified in 70% of subjects undergoing a dermal biopsy after skin preparation with ChloraPrep.[12] These residual bacteria may be present because current skin preparations do not sufficiently penetrate the dermal layer of skin, whereas *P. acnes* resides in the sebaceous glands.[16] Alternatively, *P. acnes* may reside in the joint of the normal shoulder and may even be a precursor pathologic organism to development of arthritis.[13]

The high rate of residual bacteria left on the epidermis and dermis after surgical skin preparation may be the source of infection in susceptible patients, particularly those having procedures with a surgical implant.[12,16,20,21] These studies suggest a need for a more ideal surgical skin preparation to address the residual bacteria and potentially to reduce the risk for SSI.

Benzoyl peroxide (BPO) has been an important component of topical therapy for acne vulgaris for more than 5 decades because of its ability to markedly reduce *P. acnes*.[1,6,7,14,15] This study used dermatologic principles of reducing *P. acnes* as part of the surgical skin preparation.

The purpose of this study was to evaluate the effect that topical BPO, when used in addition to chlorhexidine skin preparation, would have on the presence of *P. acnes* cultured at the time of shoulder surgery. Our hypothesis was that treatment with BPO would reduce the proportion of subjects with positive *P. acnes* cultures.

Material and methods

A consecutive 54 patients indicated for first-time arthroscopic shoulder surgery were identified. Our inclusion criterion for participation was patients indicated for primary arthroscopic shoulder surgery. Subjects were excluded if they had previous shoulder surgery or if they had taken any antibiotics 2 months before surgery. Two subjects did not want to participate.

All patients were consented to participate in this study. Patients were asked to apply the provided 5% BPO gel starting 2 mornings before their surgery. After a wash, rinse, and dry of the area, patients were asked to apply a half-dollar-size dollop of BPO to the entire shoulder and armpit area. This application was repeated at night, the following morning and night, and the morning of surgery, for a total of 5 applications. Patients were asked to record the times and dates of application on a provided data sheet.

A total of 12 samples were obtained from each subject; 8 sterile skin swabs, an aspirated joint fluid sample, and 3 tissue samples were collected from 50 patients undergoing shoulder arthroscopy without any previous shoulder surgery. A thirteenth control swab was exposed to the air and sent for culture for each subject. Demographic data, visual analog scale score for pain, medical comorbidities, history of cortisone injection, antibiotics used during surgery, and duration of the surgery were also collected.

At the time of surgery, patients were given preoperative antibiotics. Preoperatively, 2 g of cefazolin was routinely administered, or 900 mg of clindamycin was given if cephalosporin allergy was present. At this time, 4 skin swabs were taken: the anterior deltoid of the surgical arm, the axilla of the surgical arm, the anterior deltoid of the nonsurgical arm, and the axilla of the nonsurgical arm. After this, patients were draped and prepared by scrubbing the arm, shoulder, and axilla with a scrub brush and 3.3% chloroxylenol cleansing solution. The skin was then patted dry with a sterile towel. The surgical site was prepared with 3 applications of 2% chlorhexidine gluconate (ChloraPrep). This is the routine for all patients undergoing shoulder surgery at our institution. After preparations and draping, the skin of the anterior deltoid and the axilla were each swabbed with a skin swab. A cotton swab of the air was taken at this time as a control. Each swab was placed into an individual charcoal medium.

After incision for trocar placement, the glenohumeral joint was aspirated. If no fluid was available, the glenohumeral joint was flushed with 5 mL of saline, which was then collected in a sterile specimen container. Three samples of débrided tissue were collected through a cannula. The first tissue sample was collected from the middle glenohumeral ligament. If the patient was having a rotator cuff repair, the second tissue sample came from the rotator interval and the third from the bursa. For a patient undergoing a labral repair, the second tissue sample was collected from the high rotator interval and the third from the low rotator interval. Each sample was placed into an individual specimen container.

Before skin closure, 2 final skin swabs of the anterior deltoid and axilla were taken and placed into a charcoal medium. The skin swabs were placed into individual charcoal mediums.

All samples for each patient were placed into individual transport bags and delivered to the Greenwich Hospital microbiology laboratory within 1 hour, where they were placed in a fume hood that had been sterilized with 1.4% hydrogen peroxide spray for 1 minute. Medical technicians, following sterile procedure, processed all samples. Each sample was plated on a blood agar plate (BAP) to facilitate the growth of any organism, a MacConkey agar plate to select for gram-negative rods, a colistin and nalidixic acid plate to identify gram-positive organisms, and a CDC blood agar plate kept in anaerobic conditions with a gentamicin disk (ANA CDC) to select for anaerobic organisms.

Each control and skin swabs were removed from their transport bag and streaked across a microscope slide to check immediately for contaminating organisms with a Gram stain. The swabs were next streaked across the first quadrant of each agar plate. The swabs were then placed in a test tube of thioglycollate broth to encourage the growth of any organisms present. Individual, disposable sterile loops were used to streak the remaining quadrants of each plate.

One drop of the joint fluid aspirate was transferred to each agar plate as well as a microscope slide for immediate analysis. Four or 5 drops of joint fluid were transferred to thioglycollate broth test tubes. Each drop of joint fluid was streaked across the agar plates with individual, disposable sterile loops.

Each tissue sample was combined with 1 mL of thioglycollate broth in a sterile tissue grinder (Precision disposable tissue grinder; Covidien, Dublin, Ireland) and ground for 1 minute or until homogenized. One drop of the dissolved tissue sample was

transferred to each agar plate and to a microscope slide. Individual, disposable sterile loops were used to streak the agar plates. Four or 5 drops of the tissue sample were then placed into a test tube of thioglycollate broth.

The blood agar, MacConkey, and colistin and nalidixic acid plates were incubated aerobically at 37°C for 48 hours and then checked for growth to rule out contamination. The ANA CDC plates with gentamicin disks were kept in sterile bags with a carbon dioxide pouch system to maintain anaerobic conditions. Each sterile bag included an oxygen indicator to ensure that anaerobic conditions were met. The ANA CDC plates were incubated at 37°C for 7 days and then analyzed for *P. acnes*. Thioglycollate broth test tubes were sealed with parafilm to protect against contamination. These samples were incubated at 37°C for 30 days or until a positive *P. acnes* diagnosis could be made. All cultures were checked daily for bacterial growth.

Bacterial colonies suspected of being *P. acnes* were smeared onto microscope slides and Gram stained. Isolated *P. acnes* were tested for biotype with a MicroScan rapid anaerobe identification system (Siemens, Erlangen, Germany). Isolated *P. acnes* were then streaked on brucella agar/ANA CDC agar to measure hemolysis. Hemolysis was defined as when there was at least 2 mm of hemolysis around bacterial colonies.[8] Each biotype isolated from a patient was also tested for antimicrobial sensitivities with Epsilometer tests (Etest; bioMérieux, Durham, NC, USA).

A positive culture was defined by growth on the anaerobic plate within 7 days or if the thioglycollate broth became turbid and subtyped as *P. acnes* within 14 days.

An a priori power analysis was carried out. To detect a 50% reduction in the risk of positive culture, based on a previous 58% chance of having positive culture for *P. acnes*, with α set at .05, power set at 0.8, 47 subjects were required for this study.

A full-time statistician performed statistical analysis. Bivariate tests of statistical significance were conducted with a statistical significance level set to $P \leq .05$. Related sample comparisons for skin swab cultures were made by the McNemar (binomial and χ^2) test; a χ^2 test, *t* test, binomial test, or Wilcoxon test was used to test all independent bivariate associations. Statistical analysis was performed with SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA).

Results

Fifty-two consecutive subjects were enrolled in this study. Two patients each missed 1 application of BPO and were excluded from the study, leaving 50 subjects.

There were 23 men (46%) and 27 women (54%). The mean age of patients was 52.3 years (range, 17-87 years). Regarding medical comorbidities, 5 patients had osteoarthritis of joints other than the shoulder, 1 had a history of smoking, 3 had type 2 diabetes mellitus, and 14 were obese. Sixty percent of subjects did not have a cortisone injection in the surgical shoulder before surgery, and 40% had either 1 or more cortisone injections in the operative shoulder. Patients underwent arthroscopic shoulder surgery for either subacromial decompression or débridement (6.0%), subacromial decompression and biceps tenodesis (16.0%), rotator cuff repair (68.0%), or labrum or instability repair (10.0%). The average duration of surgery was 56 minutes (range, 28-115 minutes). Thirty-two percent of patients had surgery on the left shoulder, and 68% of patients had surgery on the right shoulder. The average visual analog scale score for pain recorded by a patient was 4.38, and the minimum recorded was 0.

A total of 650 culture specimens were obtained and studied. Fifty control culture specimens (1 per patient) with cotton swabs exposed to the air were collected; 4% (2 of 50) of the controls were positive for *P. acnes*.

Before skin preparation, 200 culture specimens were obtained; 16% (8 of 50) of cultures 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 ($P = .001$). Samples of the nonsurgical (untreated) side of the anterior deltoid before skin preparation also demonstrated a significant difference between men (47.8%) and women (18.5%) ($P = .036$). Similarly, the axilla was positive in 8% (4 of 50) of the BPO-treated arms and in 28% (14 of 50) of the untreated arms ($P = .013$).

After comprehensive skin preparation as described in the Methods section, 400 samples were obtained; 6.25% (25 of 100) grew *P. acnes*. This was not significantly different compared with the 4% rate for control ($P = 1.0$). The rate of positive culture increased to 10% at the end of the procedure, before removal of the drapes. This was not different compared with the control rate ($P = .375$) or the rate observed at the initiation of surgery ($P = .625$). There were no significant differences in the rate of positive cultures between any of the specimens obtained after skin preparation and the control swab (Table I). In contrast to the skin before preparation, there were no significant difference rates of male subjects with positive cultures (4.0%) and female subjects (2.25%) ($P = 0.6$).

There was no association with positive culture for age and history of cortisone injection. Duration of surgery, type of surgery, and medical comorbidity (osteoarthritis, diabetes mellitus, smoking) also had no significant bearing on culture results among patients with a single positive culture. Age, when evaluated above and below 55 years, and duration of surgery, when evaluated as longer or shorter than 60 minutes, were both not significant (Table II).

There was a statistically significant difference in the mean body mass index for samples taken in the anterior deltoid surgical side, treated with BPO ($P = .045$) and the anterior deltoid nonsurgical side, not treated with BPO ($P = .043$) before skin preparation and in the axilla surgical side at the end of surgery ($P = .022$) but not for the remaining samples (Table III).

All patients in this study had serial examinations at 2-month intervals. None of the patients in this study have had unusual pain, delayed wound healing, erythema, or fever that would suggest clinical infection. None of the patients in this study have had poor clinical outcome or required additional surgery. The mean follow-up for patients in this study was 9 months.

Table I Rate of positive *P. acnes* culture by individual specimen location

Specimen		Rate of positive culture (%)	*P* values	Sethi et al (%)
Sample 0	Control air swab	4.0		5.13
Before surgical skin preparation with ChloraPrep				
Sample 1	Skin anterior deltoid surgical side, BPO treated	16.0	.109	
Sample 2	Skin axilla surgical side, BPO treated	8.0	.625	
Sample 3	Skin anterior deltoid nonsurgical side, no BPO	32.0	**.001***	
Sample 4	Skin axilla nonsurgical side, no BPO	28.0	**.004***	
After surgical skin preparation with ChloraPrep and BPO				
Sample 5†	Anterior deltoid surgical side	6.0	1.000	15.8
Sample 6†	Axilla surgical side	6.0	1.000	
Sample 7	Joint fluid	4.0	1.000	17.5
Sample 8	Tissue 1 (MGHL)	6.0	1.000	31.6
Sample 9	Tissue 2 (rotator interval)	2.0	1.000	22.8
Sample 10	Tissue 3 (bursa/high interval)	6.0	1.000	22.8
Sample 11‡	Skin anterior deltoid surgical side (end of procedure)	10.0	.453	22.8
Sample 12‡	Skin axilla surgical side (end of procedure)	10.0	.375	40.4

MGHL, middle glenohumeral ligament; *BPO,* benzoyl peroxide.

This table depicts the rate of positive cultures by location of specimen obtained. The top half of the chart depicts rate of positive culture before ChloraPrep skin preparation. Samples 3 and 4, the nonsurgical arm that did not have topical BPO, were significantly greater than the control swab. Sample 3, the untreated anterior deltoid skin, was also significantly greater than sample 1, the BPO-treated anterior deltoid skin ($P = .001$). Similarly, sample 4, the untreated axilla skin, was significantly greater than sample 2, the BPO-treated axilla skin.

None of the samples obtained after skin preparation with ChloraPrep and BPO were significantly different from control.

* Statistically significant ($P \leq .05$).

† Preincision skin sample taken after patient was surgically prepared and draped and before incision.

‡ Skin sample at closure taken at the completion of the procedure with surgical draping still in place.

Discussion

This study demonstrated that when topical BPO cream is used starting 48 hours before shoulder surgery, there was no significant detectable difference in the rate of positive cultures between a control air swab and surgically obtained samples. This is a pertinent negative finding in an appropriately powered study; 6.1% of tissue and skin culture specimens obtained after skin preparation were positive for *P. acnes*, compared with 4.0% for the control swab ($P = .40$). Our findings are important as recent studies have demonstrated a 36% to 70% increased risk above controls for having a positive *P. acnes* culture.[10,12,16] This study demonstrates that adding 5% BPO cream to current skin preparation can reduce the rate at which residual *P. acnes* is identified. We hope that this may extrapolate to a lower risk of clinical infection with *P. acnes.*

Current skin preparations do not eliminate *P. acnes* from cleansed skin up to 29% of the time at the onset of surgery.[10,16,22] This rate may be as high as 63% when the skin of male subjects is measured at the end of the surgical procedure.[22] Dermal biopsy of surgically cleansed skin was positive in 70% of patients in whom ChloraPrep was used.[12] We believe that this is a consequence of imperfect skin preparation that does not reach the dermis. Furthermore, there is subsequent bacterial leakage from sebaceous glands released into the wounds after skin incision.[16] This residual bacterial exposure may be the source of infection in those patients who develop infection. It is for these reasons we sought to improve current skin cleansing methods. Although it is possible that *P. acnes* resides in the normal joint and that it may be a pathologic precursor to shoulder arthritis, we believe that it is more likely contamination from the dermis.[13,16] This current study supports the dermis as the primary source of *P. acnes* rather than its being part of the normal joint flora and a cause for aseptic arthritis. Use of BPO to improve skin preparation substantially reduced the bacteria that were identified in the joint and on the skin, suggesting that the dermis may contaminate the deep tissue.

The ability of 5% BPO to suppress *P. acnes* is well established in the dermatologic literature. Leyden described a 90% reduction in *P. acnes* after 48 hours of topical treatment and a 99% reduction after 72 hours of treatment.[14,15] We used Leyden's described 48-hour skin treatment protocol for this study, 5 skin applications during 2½ days. In contrast to antibiotics, which alter bacterial structure, BPO is a powerful antimicrobial agent that is directly toxic to both surface and ductal bacteria. Its lipophilic properties permit penetration of the pilosebaceous duct. Once it is applied to the skin, BPO decomposes to release free oxygen radicals, which have potent bactericidal activity in the sebaceous follicles.[6,8] Given its efficacy, relatively low cost, and low risk of adverse events, we chose to study this in surgical skin preparation, which has not yet been done.

Table II Discrete factors associated with having a risk of a single culture positive for *P. acnes*

	Before surgical skin preparation with ChloraPrep					After surgical skin preparation with ChloraPrep and BPO							
	Control air swab	1: Skin anterior deltoid surgical side, BPO treated	2: Skin axilla surgical side, BPO treated	3: Skin anterior deltoid nonsurgical side, no BPO	4: Axilla nonsurgical side, no BPO	5: Skin anterior deltoid surgical side†	6: Skin axilla surgical side†	7: Joint fluid	8: Tissue 1 (MGHL)	9: Tissue 2 (rotator interval)	10: Tissue 3 (bursa/ high interval)	11: Skin anterior deltoid surgical side (end of procedure)‡	12: Skin axilla surgical side (end of procedure)‡
Total (650)	50	50	50	50	50	50	50	50	50	50	50	50	50
Positive (69)	2 (4.0%)	8 (16.0%) *	4 (8.0%)	16 (32.0%) *	14 (28.0%)	3 (6.0%)	3 (6.0%)	2 (4.0%)	3 (6.0%)	1 (2.0%)	3 (6.0%)	5 (10.0%)	5 (10.0%)
Gender													
Male (23)	1 (4.3%)	**7 (30.4%)**	2 (8.7%)	**11 (47.8%)**	9 (39.1%)	2 (8.7%)	2 (8.7%)	1 (4.3%)	1 (4.3%)	0 (0%)	2 (8.7%)	4 (17.4%)	4 (17.4%)
Female (27)	1 (3.7%)	**1 (3.7%)**	2 (7.4%)	**5 (18.5%)**	5 (18.5%)	1 (3.7%)	1 (3.7%)	1 (3.7%)	2 (7.4%)	1 (3.7%)	1 (3.7%)	1 (3.7%)	1 (3.7%)
P value	1.000	**.017**	1.000	**.036**	.126	.588	.588	1.000	1.000	1.000	.588	.167	.167
Age												*	
<55 years (35)	0 (0%)	3 (12.5%)	2 (8.3%)	7 (29.2%)	8 (33.3%)	1 (4.2%)	3 (12.5%)	1 (4.2%)	1 (8.3%)	0 (0%)	0 (0%)	5 (20.8%)	4 (16.7%)
55+ years (34)	2 (7.7%)	5 (19.2%)	2 (7.7%)	9 (34.6%)	6 (23.1%)	2 (7.7%)	0 (0%)	1 (3.8%)	2 (3.8%)	1 (3.8%)	3 (11.5%)	0 (0%)	1 (3.8%)
P value	.491	.704	1.000	.767	.533	1.000	.103	1.000	.602	1.000	.236	.020	.182
Cortisone					*								
No (56)	2 (6.7%)	6 (20.0%)	2 (6.7%)	13 (43.3%)	12 (40.0%)	3 (10.0%)	3 (10.0%)	2 (6.7%)	2 (6.7%)	1 (3.3%)	3 (10.0%)	4 (13.3%)	3 (10.0%)
Yes (13)	0 (0%)	2 (10.0%)	2 (10.0%)	3 (15.0%)	2 (10.0%)	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	0 (0%)	0 (0%)	1 (5.0%)	2 (10.0%)
P value	.510	.450	1.000	.062	.026	.265	.265	.510	1.000	1.000	.265	.636	1.000
Osteoarthritis													
No (67)	2 (4.4%)	7 (15.6%)	4 (8.9%)	16 (35.6%)	13 (28.9%)	3 (6.7%)	3 (6.7%)	2 (4.4%)	3 (6.7%)	1 (2.2%)	3 (6.7%)	5 (11.1%)	5 (11.1%)
Yes (2)	0 (0%)	1 (20.0%)	0 (0%)	0 (0%)	1 (20.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
P value	1.000	1.000	1.000	.163	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
Diabetes													
No (66)	2 (4.3%)	7 (14.9%)	4 (8.5%)	15 (31.9%)	14 (29.8%)	3 (6.4%)	3 (6.4%)	2 (4.3%)	3 (6.4%)	1 (2.1%)	2 (4.3%)	5 (10.6%)	5 (10.6%)
Yes (3)	0 (0%)	1 (33.3%)	0 (0%)	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (33.3%)	0 (0%)	0 (0%)
P value	1.000	.414	1.000	1.000	.550	1.000	1.000	1.000	1.000	1.000	.173	1.000	1.000
Smoker													
No (64)	2 (4.1%)	7 (14.3%)	4 (8.2%)	15 (30.6%)	14 (28.0%)	3 (6.1%)	3 (6.1%)	2 (4.1%)	3 (6.1%)	1 (2.0%)	3 (6.1%)	5 (10.2%)	5 (10.2%)
Yes (2)	0 (0%)	1 (100%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
P value	1.000	.160	1.000	.320	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
Diagnosis													
Rotator cuff tear (56)	2 (5.7%)	8 (22.9%)	2 (5.7%)	12 (34.3%)	12 (34.3%)	3 (8.6%)	2 (5.7%)	1 (2.9%)	3 (8.6%)	1 (2.9%)	3 (6.0%)	4 (11.4%)	3 (8.6%)
Impingement (4)	0 (0%)	0 (0%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (16.7%)
Degenerative (0)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Labral tear (11)	0 (0%)	0 (0%)	1 (16.7%)	3 (50.0%)	3 (50.0%)	0 (0%)	1 (16.7%)	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	1 (16.7%)	1 (16.7%)
Glenoid fracture (0)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

(*continued on next page*)

Table II (*continued*)

	Before surgical skin preparation with ChloraPrep					After surgical skin preparation with ChloraPrep and BPO							
	Control air swab	1: Skin anterior deltoid surgical side, BPO treated	2: Skin axilla surgical side, BPO treated	3: Skin anterior deltoid nonsurgical side, no BPO	4: Axilla nonsurgical side, no BPO	5: Skin anterior deltoid surgical side†	6: Skin axilla surgical side†	7: Joint fluid	8: Tissue 1 (MGHL)	9: Tissue 2 (rotator interval)	10: Tissue 3 (bursa/ high interval)	11: Skin anterior deltoid surgical side (end of procedure)‡	12: Skin axilla surgical side (end of procedure)‡
P value	1.000	.541	.432	.692	.307	1.000	.666	.514	1.000	1.000	1.000	.847	.550
Procedure													
No RCR (9)	0 (0%)	0 (0%)	1 (9.1%)	2 (18.2%)	1 (2.0%)	1 (9.1%)	0 (0%)	2 (18.2%)	0 (0%)	1 (9.1%)	0 (0%)	0 (0%)	1 (9.1%)
RCR/cuff repair (52)	2 (5.9%)	8 (23.5%)	2 (5.9%)	12 (35.3%)	11 (22.0%)	2 (5.9%)	2 (5.9%)	0 (0%)	3 (8.8%)	0 (0%)	3 (8.8%)	4 (11.8%)	3 (8.8%)
Labral tear (8)	0 (0%)	0 (0%)	1 (25.0%)	2 (50.0%)	2 (4.0%)	0 (0%)	1 (25.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (25.0%)	1 (25.0%)
Glenoid reduction (0)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
P value	1.000	.311	.379	.611	.295	1.000	.380	.126	.685	.320	.685	.348	.473
Surgery duration													
<60 minutes (48)	1 (2.8%)	4 (11.1%)	3 (8.3%)	10 (27.8%)	11 (30.6%)	2 (5.6%)	3 (8.3%)	2 (5.6%)	2 (5.6%)	1 (2.8%)	1 (2.8%)	5 (13.9%)	3 (8.3%)
60+ minutes (21)	1 (7.1%)	4 (28.6%)	1 (7.1%)	6 (42.9%)	3 (21.4%)	1 (7.1%)	0 (0%)	0 (0%)	1 (7.1%)	0 (0%)	2 (14.3%)	0 (0%)	2 (14.3%)
P value	.486	.197	1.000	.330	.729	1.000	.550	1.000	1.000	1.000	.186	.304	.611

MGHL, middle glenohumeral ligament; *BPO,* benzoyl peroxide; *RCR,* rotator cuff repair.

This chart depicts bivariate analysis of risk factors associated with subjects with a positive *P. acnes* culture within 14 days. There was no significant difference associated with positive culture for age above and below 55 years and history of cortisone injection. Duration of surgery longer or shorter than 60 minutes, type of surgery, or medical comorbidity (osteoarthritis, diabetes mellitus, smoking) also had no significant bearing on culture results among patients with a single positive culture. There was a significant difference associated with positive culture among men and women in the untreated skin anterior deltoid ($P = .036$) and in the treated skin anterior deltoid before skin preparation ($P = .017$). There was no significant difference between men and women in any of the subsequent samples.

* Statistically significant ($P \leq .05$), independent *t* test.

† Preincision skin sample taken after patient was surgically prepared and draped and before incision.

‡ Skin sample at closure taken at the completion of the procedure with surgical draping still in place.

Table III Continuous factors associated with having a single culture positive for *P. acnes*

	Before surgical skin preparation with ChloraPrep					After surgical skin preparation with ChloraPrep and BPO							
	Control air swab	1: Skin anterior deltoid surgical side, BPO treated	2: Skin axilla surgical side, BPO treated	3: Skin anterior deltoid nonsurgical side, no BPO	4: Axilla nonsurgical side, no BPO	5: Skin anterior deltoid surgical side†	6: Skin axilla surgical side†	7: Joint fluid	8: Tissue 1 (MGHL)	9: Tissue 2 (rotator interval)	10: Tissue 3 (bursa/ high interval)	11: Skin anterior deltoid surgical side (end of procedure)‡	12: Skin axilla surgical side (end of procedure)‡
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Age (yr)													
Negative	51.6 (15.1)	51.6 (15.7)	51.7 (15.2)	51.4 (15.5)	52.6 (16.7)	51.7 (15.2)	52.8 (15.7)	52.4 (15.6)	52.8 (15.5)	52.1 (15.5)	51.5 (15.2)	53.3 (15.9)	52.3 (15.3)
Positive	70.0 (17.0)	55.9 (14.3)	59.8 (14.3)	54.2 (15.5)	51.6 (11.8)	62.3 (19.0)	45.0 (4.6)	50.0 (15.6)	44.0 (12.8)	61.0	65.0 (14.8)	43.4 (4.0)	52.4 (18.2)
P value	.097	.479	.318	.558	.837	.248	.403	.832	.341	.574	.142	.176	.955
Surgery (min)													
Negative	55.8 (20.8)	54.2 (19.7)	56.3 (21.0)	54.6 (21.7)	57.1 (21.6)	56.2 (20.7)	56.0 (21.0)	56.8 (20.3)	54.7 (19.1)	56.3 (20.3)	55.2 (20.6)	56.4 (21.4)	55.1 (19.0)
Positive	58.0 (11.3)	64.4 (23.3)	50.3 (10.9)	58.4 (17.8)	52.8 (17.4)	51.0 (17.3)	53.0 (3.5)	33.5 (2.1)	73.3 (36.2)	32.0	66.3 (15.5)	50.6 (5.0)	62.6 (32.4)
P value	.882	.201	.572	.546	.512	.675	.417	.115	.127	.242	.365	.145	.442
BMI													
Negative	27.0 (4.5)	**26.5 (4.3)**	26.7 (4.5)	**26.1 (4.4)**	26.8 (5.0)	27.0 (4.4)	27.0 (4.5)	27.2 (4.4)	27.2 (4.5)	27.2 (4.4)	26.8 (4.4)	26.9 (4.6)	**26.7 (4.6)**
Positive	26.4 (6.2)	**29.9 (4.9)**	30.4 (3.3)	**28.9 (4.2)**	27.6 (3.1)	27.2 (7.1)	27.2 (5.1)	22.8 (5.3)	24.5 (4.6)	19.0	30.6 (4.8)	28.0 (3.8)	**29.6 (1.8)**
P value	.833	**.045***	.124	**.043***	.494	.943	.933	.174	.330	.072	.154	.627	**.022***

SD, standard deviation; *BMI,* body mass index; *MGHL,* middle glenohumeral ligament; *BPO,* benzoyl peroxide.

This chart depicts bivariate analysis of risk factors associated with subjects with a positive *P. acnes* culture within 14 days. There was no difference in mean age and duration of surgery for subjects with a positive vs. negative culture. There was a statistically significant difference in the mean BMI for samples taken in the skin anterior deltoid surgical side treated with BPO ($P = .045$) and the skin anterior deltoid nonsurgical side, not treated with BPO ($P = .043$) before skin preparation as well as in the skin axilla surgical side ($P = .022$) at the end of surgery but not for the remaining surgery.

* Statistically significant ($P \leq .05$), independent *t* test.

† Preincision skin sample taken after patient was surgically prepared and draped and before incision.

‡ Skin sample at closure taken at the completion of the procedure with surgical draping still in place.

We previously performed a similar study obtaining skin and tissue specimens in patients undergoing shoulder surgery with skin preparation using ChloraPrep alone.[22] We found that 56% of the 50 subjects had at least 1 culture positive for *P. acnes*. In contrast, after use of topical BPO, only 6.5% of all subjects in this study had at least 1 specimen obtained after skin preparation test positive for *P. acnes*. In this study, the overall rate of 6.5% positive culture was not different from the control rate of 4.0% ($P = .40$), suggesting that the combined skin preparation reduced the risk of having a positive culture equal to that of the control air swab. Whereas it is not appropriate to perform statistical analysis between the 2 distinct studies, the reduction rate of *P. acnes* after use of BPO from 56% to 6.5% is substantial and may be clinically relevant (Table I).

There is some concern that skin swabs may underestimate the presence of *P. acnes* because the organism resides in the sebaceous glands.[16] Although our previous study demonstrated a high rate of *P. acnes* on the postoperative skin,[22] we still chose to include joint fluid aspirate and tissue culture to address this aforementioned concern. The joint fluid aspirate had a 4.0% rate of positive culture, and the tissue samples ranged from 2% to 6% positive, not statistically different from the 4% rate of positive control specimens ($P = 1.00$ for all these values). This is different from our previous study with BPO, in which the aspirate was positive 17.5% and the tissue cultures 22% to 33% of the time.[22]

Furthermore, in this study and our previous study, we obtained culture specimens at the beginning and at the end of the surgical procedure. We believe that this is a particularly important aspect of this study as it assesses how well the skin preparation functions while the epidermis and dermis are manipulated, begin to sweat, and react to surgery. In our previous study, this went from a 15.8% chance of positive culture at the beginning of the procedure to 41% at the end of the procedure. The rate of positive culture went up to 63% when men were examined at the end of the surgical procedure. In the previous study, all these values were statistically different from one another[22] (Table I). This current study had a 6.0% risk of positive culture at the beginning of surgery and a 10% rate of positive culture at the end of the procedure and was no different from control ($P = 1.0$, $P = .375$). The addition of BPO eliminated any statistical differences between the control swab, skin swabs after skin preparation, tissue culture, and skin at the end of the surgical procedure (Table I). There was also no difference in gender and rate of positive culture at the end of this procedure. We believe this is one of our most substantial findings as it suggests that we may have a lower bacterial burden to contaminate and potentially to infect the wound at the end of surgery.

Cultures were examined at the end of 14 days in this study. This cutoff was based on previous findings of no significant difference in the rate of positive cultures that were held for 14, 21, or 28 days.[22]

BPO alone, before ChloraPrep, had a significant effect in reducing *P. acnes*. The untreated arm had a significantly higher rate of *P. acnes* compared with the BPO-treated arm before skin preparation ($P = .039$). The anterior deltoid and axilla of the untreated arm were positive 32% and 28% of the time, respectively. This is a lower incidence of *P. acnes* than we would have expected compared with the general population. The lower overall rate of culture observed in our study may have a few explanations. These patients were all treated with topical BPO on the contralateral arm and may have had some systemic absorption. These patients also had all bathed the morning of surgery, had not been active, and received intravenous antibiotics. The samples were taken before surgical preparation and draping without opportunity to sweat, and certainly no disruption of the dermis occurred. Our pilot studies had a 70% incidence in active men, suggesting our microbiologic methodology is not flawed. Our findings also are consistent with the results of Hudek et al, suggesting that the axilla is not the richest source of *P. acnes*.[10]

Men have a higher chance of having *P. acnes* present on their skin before preparation, after preparation, and at the end of the procedure.[11,12,16,18,19] Our findings are consistent with previous publications, as male subjects had a higher rate of *P. acnes* found on their skin. This effect was significant only in the untreated treatment arm ($P = .036$) and in the treated arm before skin preparation ($P = .017$). Once the skin had been surgically cleansed, however, there was no significant difference between men and women in any of the subsequent specimens (Table II). This suggests that the combination of BPO and ChloraPrep is equally effective in men and women and actually may equalize the risk of residual bacteria in men and women.

This study does have weaknesses. It is not a randomized trial comparing patients treated with and without BPO by comparing clinical infection as a primary outcome. We did not reduce infection rates; rather, we reduced the risk of having a positive culture for *P. acnes*. We also did not study this in open arthroplasty procedures. We anticipate studying this in a larger multicenter trial in shoulder arthroplasty patients.

Another concern is that whereas we have successfully identified positive cultures in patients, we have not determined if these patients have a subclinical infection. However, no patient has developed signs or symptoms of acute infection, and none has required reoperation. No patients have been lost to follow-up at this point. Although all patients with positive cultures are being observed carefully with repeated serial examinations, it may be years before any clinical manifestation appears. It is possible that with a larger study sample, a longer follow-up, or a susceptible patient, clinical infection may be manifested. Conversely, this degree of bacterial inoculation may not be enough to cause infection with this regimen of skin preparation and antibiotics in a nonarthroplasty population. All patients with positive

P. acnes cultures in our study will be observed periodically for an extended time.

It is possible that our own *P. acnes* plays a role in bacterial homeostasis, and by reducing it, we could create new vulnerability for another bacterium. We did not see a rise in other bacteria cultured in this study, nor did we identify any clinical infections to suggest this was the case.

Finally, these are data from a single center, and our techniques may be flawed.

The BPO is inexpensive ($8.66 [US] per patient). Two patients reported mild rash that resolved without treatment and did not alter the timing of surgery. Two patients, however, were not able to comply with the prescribed 5 treatments; 96% of patients were able to comply. Further research with fewer treatments, perhaps as a single dose on the day of surgery to improve compliance, is merited.

Conclusions

P. acnes is a significant pathogen with a specific predilection for SSI in shoulder surgery. Current skin preparation with chlorhexidine gluconate and alcohol is imperfect; residual bacteria are identified on the skin up to 29% of the time at the beginning of the surgical procedure and 63% of the time at the conclusion of surgery in individuals undergoing first-time shoulder surgery and in 70% of dermal biopsy specimens. The high rate of residual bacteria left on the epidermis and dermis may be the source of infection in susceptible patients, particularly those having procedures with a surgical implant. The addition of 5% topical BPO cream to current skin preparation substantially reduces the rate at which *P. acnes* is identified to 6%, which is no different compared with control samples.

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References

1. Amin K, Riddle CC, Aires DJ, Schweiger ES. Common and alternate oral antibiotic therapies for acne vulgaris: a review. J Drugs Dermatol 2007;6:873-80.
2. Bayston R, Ashraf W, Barker-Davies R, Tucker E, Clement R, Clayton J, et al. Biofilm formation by *Propionibacterium acnes* on biomaterials in vitro and in vivo: impact on diagnosis and treatment. J Biomed Mater Res A 2007;81:705-9. http://dx.doi.org/10.1002/jbm.a.31145
3. Butler-Wu SM, Burns EM, Pottinger PS, Magaret AS, Rakeman JL, Matsen FA 3rd, et al. Optimization of periprosthetic culture for diagnosis of *Propionibacterium acnes* prosthetic joint infection. J Clin Microbiol 2011;49:2490-5. http://dx.doi.org/10.1128/JCM.00450-11
4. Cheung EV, Sperling JW, Cofield RH. Revision shoulder arthroplasty for glenoid component loosening. J Shoulder Elbow Surg 2008;17:371-5. http://dx.doi.org/10.1016/j.jse.2007.09.003
5. Dramis A, Aldlyami E, Grimer RJ, Dunlop DJ, O'Connell N, Elliott T. What is the significance of a positive *Propionibacterium acnes* culture around a joint replacement? Int Orthop 2009;33:829-33. http://dx.doi.org/10.1007/s00264-008-0534-y
6. Fulton JE, Farzad-Batshandeth A. Studies on the mechanism of action of topical benzyl peroxide in acne vulgaris. J Cutan Pathol 1974;1:194-200.
7. Gollnick H, Cunliffe W, Berson D, Dreno B, Finlay A, Leyden JL, et al. Management of acne: a report from a global alliance to improve outcomes in acne. J Am Acad Dermatol 2003;49:S1-37. http://dx.doi.org/10.1067/mjd.2003.618
8. Haider A, Shaw JC. Treatment of acne vulgaris. JAMA 2004;292:726-35. http://dx.doi.org/10.1001/jama.292.6.726
9. Hasan SS, Leith JM, Campbell B, Kapil R, Smith KL, Matsen FA 3rd. Characteristics of unsatisfactory shoulder arthroplasties. J Shoulder Elbow Surg 2002;11:431-41. http://dx.doi.org/10.1067/mse.2002.125806
10. Hudek R, Sommer F, Kerwat M, Abdelkawi AF, Loos F, Gohlke F. *Propionibacterium acnes* in shoulder surgery: true infection, contamination, or commensal of the deep tissue? J Shoulder Elbow Surg 2014;23:1763-71. http://dx.doi.org/10.1016/j.jse.2014.05.024
11. Kelly JD 2nd, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res 2009;467:2343-8. http://dx.doi.org/10.1007/s11999-009-0875-x
12. Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA 3rd. *Propionibacterium* persists in the skin despite standard surgical preparation. J Bone Joint Surg Am 2014;96:1447-50. http://dx.doi.org/10.2106/JBJS.M.01474
13. Levy O, Iyer S, Atoun E, Peter N, Hous N, Cash D, et al. *Propionibacterium acnes:* an underestimated etiology in the pathogenesis of osteoarthritis? J Shoulder Elbow Surg 2013;22:505-11. http://dx.doi.org/10.1016/j.jse.2012.07.007
14. Leyden JJ. Effect of topical benzoyl peroxide/clindamycin versus topical clindamycin and vehicle in the reduction of *Propionibacterium acnes*. Cutis 2002;69:475-80.
15. Leyden JJ, Del Rosso JQ, Webster GF. Clinical considerations in the treatment of acne vulgaris and other inflammatory skin disorders: focus on antibiotic resistance. Cutis 2007;79(Suppl):9-25.
16. Matsen FA 3rd, Butler-Wu S, Carofino BC, Jette JL, Bertelsen A, Bumgarner R. Origin of propionibacterium in surgical wounds and evidence-based approach for culturing propionibacterium from surgical sites. J Bone Joint Surg Am 2013;95:e1811-7. http://dx.doi.org/10.2106/JBJS.L.01733
17. McLorinan GC, Glenn JV, McMullan MG, Patrick S. *Propionibacterium acnes* wound contamination at the time of spinal surgery. Clin Orthop Relat Res 2005:67-73.
18. Patel A, Calfee RP, Plante M, Fischer SA, Green A. *Propionibacterium acnes* colonization of the human shoulder. J Shoulder Elbow Surg 2009;18:897-902. http://dx.doi.org/10.1016/j.jse.2009.01.023

19. Pottinger P, Butler-Wu S, Neradilek MB, Merritt A, Bertelsen A, Jette JL, et al. Prognostic factors for bacterial cultures positive for *Propionibacterium acnes* and other organisms in a large series of revision shoulder arthroplasties performed for stiffness, pain, or loosening. J Bone Joint Surg Am 2012;94:2075-83. http://dx.doi.org/10.2106/JBJS.K.00861
20. Saltzman MD, Marecek GS, Edwards SL, Kalainov DM. Infection after shoulder surgery. J Am Acad Orthop Surg 2011;19:208-18.
21. Saltzman MD, Nuber GW, Gryzlo SM, Marecek GS, Koh JL. Efficacy of surgical preparation solutions in shoulder surgery. J Bone Joint Surg Am 2009;91:1949-53. http://dx.doi.org/10.2106/JBJS.H.00768
22. Sethi PM, Sabetta JR, Stuek SJ, Horine SV, Vadasdi KB, Greene RT, et al. Presence of *Propionibacterium acnes* in primary shoulder arthroscopy: results of aspiration and tissue cultures. J Shoulder Elbow Surg 2015;24:796-803. http://dx.doi.org/10.1016/j.jse.2014.09.042