North American Spine Society Journal (NASSJ) 19 (2024) 100514

Contents lists available at ScienceDirect

North American Spine Society Journal (NASSJ)

journal homepage: www.elsevier.com/locate/xnsj

Clinical Studies

Does hydrogen peroxide help mitigate the incidence of *Cutibacterium acnes* in cervical spine surgeries?

Maria Cecilia Madariaga, DO[a], Nicholas A. O'Malley, DO, MS[a,*], Hannah Groff, DO[a], Matthew Alben, DO[c], Aidan Papalia, DO, MBA[d], Joshua Fogel, PhD[b], Jeffrey Thompson, DO[a], Alexios Apazidis, MD[a]

[a] *Department of Orthopaedic Surgery, Nassau University Medical Center, East Meadow, NY 11554*
[b] *Department of Biostatistics, Nassau University Medical Center, East Meadow, NY 11554*
[c] *State University at Buffalo, Department of Orthopedic Surgery, Buffalo, NY*
[d] *Geisinger Health, Department of Orthopedic Surgery, Danville, PA*

ARTICLE INFO

Keywords:
Cutibacterium acnes
Cervical vertebrae
Infections
Hydrogen peroxide
ACDF
surgical site infection

ABSTRACT

Background: Surgical site infection (SSI) is a common yet serious complication of cervical spine surgery. While initially thought to be clinically insignificant, *Cutibacterium acnes* (*C. acnes)* is an important cause of infection. The purpose of this study was to investigate the ability of a hydrogen peroxide (H_2O_2) application during standard presurgical skin preparation to reduce the burden of *C. acnes* in patients undergoing cervical spine surgery.
Methods: This was a retrospective review of prospectively collected data. Subjects were randomly assigned to either standard surgical preparation plus H_2O_2 (experimental) or without H_2O_2 (control). Prescrub, postscrub, and dermal cultures were obtained to assess the *C. acnes* burden after cultures on an aerobic and anaerobic growth medium were held for 21 days. Multivariate analysis was conducted to determine factors associated with presence of *C. acnes*. Outcome measures included the results of intraoperative cultures and the development of a SSI within 90 days postoperatively.
Results: Patients (n=86) undergoing elective 2- or 3-level fusion via anterior approach were included. Prior to application of the antiseptic solution, 65% (28/43) of the experimental cohort and 77% (33/43) of the control cohort had positive *C. acnes* cultures (p=.34). Following application of antiseptic solution, there were no differences in positive *C. acnes* culture rates between the experimental and control cohorts in the epidermal (30% vs. 28%, p=1.00) or dermal (40% vs. 42%, p=1.00) cultures. No differences in the rates of *C. acnes* eradication from preantiseptic to postantiseptic application occurred for epidermal (p=1.00) or dermal (p=1.00) skin layers. None of the factors were associated with positive *C. acnes* epidermal cultures on multivariable logistic regression analysis (p>.05).
Conclusions: While there is potential for H_2O_2 to reduce the positive culture rate of *C. acnes* in cervical spine patients, no difference was seen when compared to standard surgical skin preparation.

Introduction

As cervical spine surgery continues to see an increasing trend in its utilization, these procedures are no more immune in their risk to postoperative complications than the other most commonly performed orthopedic surgeries [1–6]. Secondary to a higher prevalence of cervical spine operations conducted in our aging population, the associated presence of concomitant medical comorbidities further exacerbates the potential for such complications [6–9]. Specifically, a surgical site infection (SSI) following cervical spine surgery is among the most dreaded postoperative complications and is associated with an increased rate of morbidity and mortality [10–14]. With incidence rates ranging as high as 18%, such variability in the literature can be attributed to diagnostic methods improvements, differing criteria for physicians defining a SSI, as well as operative factors regarding instrumentation, case complexity, and the surgical approach used [10,11,15–20]. While *Staphylococcus aureus* is historically associated with postoperative infections, 1 bacteria, named *Cutibacterium acnes (C. acnes)*, has warranted particular concern in

FDA device/drug status: Not applicable.

Author disclosures: ***MCM:*** Nothing to disclose. ***NAOM:*** Nothing to disclose. ***HG:*** Nothing to disclose. ***MA:*** Nothing to disclose. ***AP:*** Nothing to disclose. ***JF:*** Nothing to disclose. ***JT:*** Nothing to disclose. ***AA:*** Nothing to disclose.

* Corresponding author. Department of Orthopedic Surgery, Nassau University Medical Center, 2201 Hempstead Turnpike, Suite 668, East Meadow, NY 11554
E-mail address: naomalley97@gmail.com (N.A. O'Malley).

https://doi.org/10.1016/j.xnsj.2024.100514
Received 16 April 2024; Received in revised form 6 June 2024; Accepted 25 June 2024
Available online 1 July 2024

orthopedic spine and shoulder surgery as the etiology for SSI, as it was previously discredited for pathological insignificance [10,12,13,16].

C. acnes is a nonspore forming, gram positive, anaerobic bacilli regarded as an essential part of the normal microbiota where it resides on the skin, hair follicles, and sebaceous glands primarily concentrated in the back, neck, axilla, and chest wall [12,21,22]. Though its role in postoperative deep infections continues to be defined, *C. acnes* has been associated with up to 10%–20% of all infections following orthopedic surgery and is reported to be the primary source of postoperative infection in shoulder surgery [16,21,23–26]. *C. acnes* has been identified as an important pathogen in spine surgery, and specifically cervical spine surgery [27–29]. *C. acnes* was shown to cause as many as 21.6% of all disk infections and 37% of all spinal implant associated infections [29,30].

C. acnes has also been reported as an underlying etiology for patients with nonpyogenic intervertebral infection causing sciatica, Modic changes, and nonspecific lower back pain despite no index procedure predisposing one to bacterial seeding of the deep tissue layers [12,18,31–37]. Though controversial as some studies have failed to reproduce these findings, it is believed that damage to the disc renders it susceptible to bacterial seeding with ensuing inflammatory changes and damage to the encompassing vertebrae [12,18,32,38–40]. As more studies are needed to evaluate the role of *C. acnes* in SSIs and intervertebral disc degeneration, eradication of the organism from the surgical site is of particular interest to both spine and shoulder surgery.

Surgical disruption of follicles harboring *C. acnes* provides a means for direct inoculation of the surgical site, deeper tissue layers, instrumentation, and implants allowing for biofilm formation [10,16,17,41,42]. As *C. acnes* is a slow-growing commensal bacteria, SSI can often be difficult to diagnose due to its indolent nature and atypical presentation often lacking common signs or markers of an underlying infective process [12,20,21,26,42]. Despite advances in detection and management, no study has established a definitive means for eradication of *C. acnes* during surgical site preparation [17,21].

Colonizing as many as 10^5 *C. acnes* organisms per follicular pore, typical surgical site preparation methods using isopropyl alcohol, chlorhexidine gluconate (CHG), or Betadine (Purdue Pharma LP, Stam- ford, CT, USA), as well as intravenously administered preoperative antimicrobial prophylaxis have failed to show successful elimination from the surgical site [21,43–48]. Using a topical solution of 3% hydrogen peroxide (H_2O_2) has demonstrated to be an effective bactericidal agent against *C. acnes* both in vitro and clinically in the setting of shoulder surgery [21,49–51]. The purpose of this study was to investigate the ability of H_2O_2 application during standard sterile presurgical skin preparation to reduce the burden of *C. acnes* in patients undergoing cervical spine surgery. We sought to investigate what factors were predictive of a positive *C. acnes* epidermal culture. We hypothesize that H_2O_2 application will reduce the burden of *C. acnes* at the surgical site and male sex will show a greater propensity for a positive culture, and that the addition of H_2O_2 to skin preparation will lower the rate of infections, especially infections with *C. acnes* [16,26,49,52].

Methods

Ethics

Approval was granted for this study by the Nassau University Medical Center Institutional Review Board. All subjects provided informed consent prior to enrollment.

Study Design

This study was a retrospective review of prospectively collected data performed at a level 1 trauma center conducted between August 2020 and July 2022 in patients undergoing surgery by 3 fellowship trained orthopedic spine surgeons. Subjects were included in the study if they met the inclusion criteria of: (1) elected to undergo primary cervical spine surgery via anterior approach, (2) 18 years of age or older at time of surgery, and (3) no mental handicap precluding one's ability to provide informed consent. Subjects were excluded from our study if they failed to meet the aforementioned inclusion criteria or if they had a: (1) previous incision in the area of surgery or were undergoing a revision surgery, (2) traumatic etiology necessitating surgical treatment, (3) history of ongoing infection, (4) known use of antibiotics within 6 weeks prior to surgery, (5) known allergy to H_2O_2, benzoyl peroxide, or any of the other materials of standard sterile skin preparation, or (6) were undergoing primary or concomitant cervical spine surgery via a posterior approach. Inclusion criteria were similar to those seen in previous studies [53].

Sample acquisition

All patients were given weight-based Cefazolin IV 1 hour prior to surgery or Clindamycin if they were allergic to Cefazolin. If necessary, patients with hair at the anticipated area for surgical approach had hair removed using a battery powered hair clipper before any skin preparation was begun. The first culture, labeled "prescrub culture" was obtained prior to any preparation to determine the incidence of *C. acnes* in the normal skin flora of the respective patient's cervical region. In accordance with experimental protocol, all culture swabs were taken using a sterile cotton swab. The swab was then placed on the skin/dermis and rotated for 5 seconds, ensuring that all sides of the swab made contact with the skin/dermis. The swab was then placed in a sterile container. All participating surgeons were required to follow this swabbing protocol.

All surgeons participating in this study were required to follow the same protocol for both the experimental and control cohorts. In both treatment groups, 70% ethyl alcohol was applied to the appropriate area to clean the skin and remove any gross debris. Patients then underwent skin preparation with either Duraprep and 3% H_2O_2 (experimental) or Duraprep alone (control). Skin preparation included the application of four 1,010 drapes on the surgical site and then cleaning with either Duraprep or 3% H_2O_2 followed by Duraprep. A second culture stick was then used to swab over a 1-cm linear area near the incision site and labeled "skin culture." Formal draping was subsequently applied and Ioban (St. Paul, MN) draping was used to cover the incision site. The surgeon then made an incision with a third swab, labeled "dermal culture", taken in the dermal layer. A fourth culture was taken as a control and waved in the air during the start of the case and labeled "air culture."

All 4 cultures were taken to the microbiology laboratory and grown in the appropriate media with incubation for 21 days to evaluate for *C. acnes*. Though the surgeon knew what skin preparation was used, this is a single blinded study, as neither the patient nor the microbiology lab was aware of the perioperative preparation.

Data collection

Chart review was conducted independently. Factors evaluated were based on their relevance to the literature pertaining to SSI in spine surgery in general, as well as *C. acnes* specific infections in patients undergoing spine surgery. These factors included: sex, age, body mass index (BMI), medical comorbidities such as diabetes, hypertension, hyperlipidemia, smoking status (never vs current smoker), Hispanic vs. non-Hispanic heritage, and invasiveness of procedure relative to size of the incision (2 vs. 3 vertebral level surgery) [14,20,38,48,50–52]. Similarly, culture results for each patient were obtained by chart review upon final growth determination after a 21-day incubation period. Finally, patient charts were reviewed for the development of SSI, defined as return to the operating room for irrigation and debridement within 90-days of the index procedure.

Table 1
Patient demographics.

		Overall, n=86	Traditional, n=43	Hydrogen peroxide, n=43	p-value
Demographics	Age	43.0 (12.5)	42.3 (13.4)	43.7 (11.6)	.61
	Male	28 (32.6)	12 (27.9)	16 (37.2)	.49
	BMI	29.6 (6.1)	29.7 (6.1)	29.6 (6.3)	.99
	African	22 (25.6)	11 (25.6)	11 (25.6)	.976
	Hispanic	34 (39.5)	18 (41.9)	16 (37.2)	
	White	15 (17.4)	7 (16.3)	8 (18.6)	
	Other	15 (17.4)	7 (16.3)	8 (18.6)	
Levels fused	II	69 (80.2)	37 (86.0)	32 (74.4)	.28
	III	17 (19.8)	6 (14.0)	11 (25.6)	
Other	Diabetes	11 (12.8)	7 (16.3)	4 (9.3)	.52
	Hypertension	15 (17.4)	7 (16.3)	8 (18.6)	1.00
	Hyperlipidemia	5 (5.8)	3 (7.0)	2 (4.7)	1.000
	Smoking	15 (17.4)	8 (18.6)	7 (16.3)	1.000
	Revision	0 (0)	0 (0)	0 (0)	1.000

BMI, body mass index.

Statistical analysis

All statistical analysis was performed via Jupyter Notebook Version 6.4.8 (Open Source) using Python programming language (Willmington, DE) [52,54]. A priori power analysis was performed with G*Power Version 3.1.9.7 (Dusseldorf, Germany) using an effect size of 0.3 in positive culture rates as previously described in the literature as the threshold for clinical significance [53,55]. With the goal of achieving a minimum of 80% power with alpha level of 0.05, it was determined that 36 patients were needed per each cohort. Chi-square or the Fisher's exact test were used for analysis of categorical variables and continuous variables were analyzed using the 2-sample t-test.

Multivariable logistic regression analysis was performed to evaluate factors predictive of a positive *C. acnes* culture while controlling for covariates (age and BMI). The primary outcome evaluated was presence of Duraprep and 3% H_2O_2 scrub vs. Duraprep. Possible confounding variables assessed included sex (male vs. female), comorbidities (diabetes, hypertension, and hyperlipidemia), smoking status (never vs. ever smoker), Hispanic heritage, and invasiveness of procedure (2-level vs. 3-level fusion). For all analyses, a p-value $\leq$.05 was determined to be statistically significant. All analyses were 2-tailed.

Results

A total of 86 patients were enrolled in this study upon application of the inclusion and exclusion criteria. Subjects were divided into an experimental and a control cohort each consisting of 43 patients, making our study powered to determine significant differences as defined by our power analysis. Cohorts were similar with respect to age (43.7 ± 11.6 vs. 42.3 ± 13.4, p=.61), male sex (37% (16/43) vs. 27% (12/43), p=.49), BMI (29.6 ± 6.3 vs. 29.7 ± 6.1, p=.61) when comparing the experimental and control cohorts, respectively. A complete comparison of patient demographics between cohorts is available in Table 1.

Prior to application of the antiseptic solution, 65% (28/43) of patients in the experimental cohort and 77% (33/43) of patients in the control cohort had positive *C. acnes* cultures (p=.34). Following application of antiseptic solution, there were no differences in positive *C. acnes* culture rates in the epidermal (30% (13/43) vs. 28% (12/43), p=.81) or dermal (40% (17/43) vs. 42% (18/43), p=.83) cultures for the experimental vs. control cohorts, respectively. There were no differences in the rates of *C. acnes* eradication from preantiseptic to postantiseptic application for epidermal (61% (17/43) vs. 70% (23/43), p=1.00) or dermal (61% (17/43) vs. 70% (23/43), p=1.00) skin layers for the experimental vs. control cohorts, respectively. A complete comparison of positive *C. acnes* cultures rates can be seen in Table 2. After controlling for covariates (age and BMI), none of the factors evaluated demonstrated a significant association with positive *C. acnes* epidermal cultures on multivariable logistic regression analysis (p>.05). A comprehensive list of factors evaluated are seen in Table 3.

Table 2
Positive *Cutibacterium acnes* cultures.

	Prescrub	Postscrub	Dermal	Eradicated
Traditional, n=43	33 (76.7)	12 (27.9)	18 (41.9)	23 (69.7)
Hydrogen peroxide, n=43	28 (65.1)	13 (30.2)	17 (39.5)	17 (60.7)
p-value	.24	.81	.83	.46

Positive culture rates at baseline, following presurgical skin preparation, and upon dermal incision, as well as count of positive bacteria cultures which were eradicated between pre and postscrub.

Table 3
Multivariable logistic regression analysis for factors predictive of positive *Cutibacterium acnes* epidermal culture.

Factors	*OR*	*95%* Confidence Interval	p-value
Male vs. female	0.65	0.23–1.83	.42
Diabetes	1.92	0.33–11.08	.46
Hypertension	0.49	0.13–1.86	.29
Hyperlipidemia	1.73	0.15–19.23	.66
Never vs. ever smoker	0.81	0.23–2.84	.75
Hispanic vs. vs. non-Hispanic	1.27	0.44–3.63	.66
Hydrogen peroxide vs. control	0.60	0.22–1.60	.31
II vs. III Levels	0.81	0.22–2.86	.75

Odds ratios and 95% confidence intervals for patient factors assessed with multivariate analysis, controlling for age and body mass index.

Table 4
Results of chi-square for surgical site infection.

	No SSI	*SSI*	p
Traditional, n=43	43 (100.0%)	0 (0%)	.31
Hydrogen Peroxide, n=43	42 (97.7%)	1 (2.3%)	

Table 4. Results of chi-square analysis comparing the development of SSI within 90 days postoperatively between the traditional skin preparation cohort and the hydrogen peroxide treated cohort.
SSI, surgical site infection.

With regard to the development of surgical site infection within 90 days postoperatively, infection rates in the total cohort were low (1/86 = 1.16%). The 1 infection was noted in the control cohort. Chi-square analysis demonstrated no significance between the 2 cohorts (Duraprep and 3% H_2O_2 0% vs. Duraprep 2.33%, p=.31) (Table 4).

Discussion

This is the first study to investigate the application of H_2O_2 preoperatively during standard surgical site preparation in patients undergoing elective primary cervical spine surgery via an anterior approach.

When comparing the incidence of *C. acnes* at baseline (p=.34), postscrub (p=.81), or upon dermal incision (p=.82) between our study cohorts, no difference was found. Furthermore, no difference between the experimental and control cohort was noted when comparing eradication of *C. acnes* following presurgical skin preparation on the epidermal (p=1.00) or dermal (p=1.00) cultures. When examining factors associated with a positive presurgical culture, neither sex, medical comorbidities (diabetes, hypertension, hyperlipidemia), ethnicity, or invasiveness of procedure were predictive. Further, there was no statistically significant difference in development of SSI between the treatment and control groups. Age, positive preoperative cultures, and male sex were analyzed as these factors have been shown to be highly associated with C. acnes colonization [49,50,53]. Medical comorbidities and ethnicity were analyzed as these have been shown to predict SSI [8,14].

Acting by free radical generation to induce oxidative stress to disrupt the cellular processes of bacteria, H_2O_2 is an inexpensive antimicrobial agent having shown effectiveness at a 3% concentration in reducing *C. acnes* from the surgical site [13,21,41,49–51,53,56]. While potential risk for contact dermatitis, skin blanching, or blistering has been described, no adverse reactions were observed in our sample or in related literature [21,53,57,58]. Moreover, the potential clinical application outweighs these rare and typically transient symptoms, as standard skin preparation methods of ChloraPrep, DuraPrep, and Povidone-Iodine scrub have proven inadequate for eradicating *C. acnes* from the surgical site [13,53,59]. As the investigation of concomitant application of H_2O_2 presurgically has primarily been the focus of shoulder surgery, our study is the first to investigate its impact in the setting of the cervical spine.

Though our study showed no difference between our control and experimental cohorts, several studies have reported on the potential for H_2O_2 application presurgically. In vitro studies by Hernandez et al. [51] and Ohlin et al. [56] showed a bactericidal effect of H_2O_2 against *C. acnes* after 5 minutes of application and its potential use in eradicating bacteria from seeding the surgical site by pretreating implants with H_2O_2, respectively. Notably, these studies used lab isolates of *C. acnes* and did not examine clinical variants of the pathogen. This may account for some of the difference noted between our study and theirs. Topical use of benzoyl peroxide or its active product H_2O_2 prior to shoulder surgery has supported these findings by showing up to 50% reduction in positive *C. acnes* skin cultures with an even greater effect on deep cultures when combined with topical clindamycin [21,53,57,60]. These studies likely have positive results due to differing methodologies. Kolakowski et al., compared *C. acnes* derived their eradication rates based on the difference between contralateral sides of the same patient, 1 side treated with benzoyl peroxide and the other chlorhexidine gluconate [21]. This limits the generalizability of the study as it limits comparison across clinical variants of *C. acnes*. In another example, Stull et al., used punch biopsy as opposed culture swabs. [53] Both Sabetta et al. [60] and Dizay et al. [57] allowed for more extended periods of application and penetration of benzoyl peroxide, thus allowing for greater efficacy. Thus, many of these observed differences were due to methodology.

Furthermore, our study found that overall rates of infection were low. Our total cohort SSI incidence of 1.16% matches that described in the literature. [61] While no significant difference was noted between the H_2O_2-treated group and the control group, interestingly the singular infection found among the total sample was only in the control group. More research is needed to further confirm this pattern.

Though determining the optimal presurgical treatment to mitigate the risk of a SSI is paramount, identifying what factors increase the risk of a positive *C. acnes* culture is prudent as well. In general, obesity, smoking, alcohol abuse, steroid use, malnutrition, medical comorbidities, extremes of age, and surgical approach all play a role in SSI development [10,11,14,62] Specific to *C. acnes*, men have been found to have up to a 5-fold greater incidence of *C. acnes,* while geography and ethnicity have shown variations in the skin microbiome composition [26,47–49,52,63–65].

While no factors evaluated in our study were associated with a positive *C. acnes* culture at baseline when controlling for confounding factors, understanding what factors predispose to a greater biologic burden and facilitate early intraoperative colonization are of the utmost importance in patients electing to undergo spinal surgery. Thus, it is important to also discuss the limitations of our study and possible further areas of study. While our study sought to evaluate the impact of H_2O_2 on reducing *C. acnes* burden in patients undergoing cervical spine surgery, each subject in our sample underwent surgery via an anterior approach. This limits the generalizability of our findings as different surgical approaches and locations are inherently subject to their own respective risk of SSI, as well as *C. acnes* burden [10,11,14,21,53,62]. Despite this restraint on external validity, we sought to provide the foundation for understanding the implication behind the use of H_2O_2 in patients undergoing cervical spine surgery. Similar to the findings in the shoulder literature, future studies may wish to investigate the effect of application of H_2O_2 with or without topical antibiotics as this may yield a difference in culture rates [21,53,57,60].

Another possible limitation of our study was that implant design and composition data was not collected. A study by Garcia et al. found polyether ether ketone implants to show the greatest biologic burden for rapid biofilm formation for *C. acnes* in the first 24 hours from exposure [66]. This constitutes a potential future direction and further research should address this topic. The inclusion of 3 surgeons in this study is another possible limitation, as there could be some variance in preparation methods. However, this was mitigated by necessitating that all participating surgeons follow the above outlined protocols. This study was also limited by its limited follow-up. Finally, this study was limited by its inclusion of only a single-center, limiting the generalizability of the results as rates of SSI and *C. acnes* colonization vary between locations.

Conclusion

While there is potential for H_2O_2 to reduce the positive culture rate of *C. acnes* in cervical spine patients, no difference was seen when compared to standard surgical skin preparation. Future studies are necessary to determine if there is an optimal duration of application or different combination of skin preparations, or whether the addition of antibiotics to skin preparation might help to reduce *C. acnes* burden.

Funding

No funding was received for the conduct of this research. The authors have no other relevant conflicts of interest to disclose.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. MCM: Nothing to disclose. NAO: Nothing to disclose. HG: Nothing to disclose. JF: Nothing to disclose. JT: Nothing to disclose. AA:Nothing to disclose.

References

[1] Oglesby M, Fineberg SJ, Patel AA, Pelton MA, Singh K. Epidemiological trends in cervical spine surgery for degenerative diseases between 2002 and 2009. Spine 2013;38(14):1226–32. doi:10.1097/BRS.0b013e31828be75d.

[2] Saifi C, Fein AW, Cazzulino A, et al. Trends in resource utilization and rate of cervical disc arthroplasty and anterior cervical discectomy and fusion throughout the United States from 2006 to 2013. Spine J 2018;18(6):1022–9. doi:10.1016/j.spinee.2017.10.072.

[3] Marquez-Lara A, Nandyala SV, Fineberg SJ, Singh K. Current trends in demographics, practice, and in-hospital outcomes in cervical spine surgery: a national database analysis between 2002 and 2011. Spine 2014;39(6):476–81. doi:10.1097/BRS.0000000000000165.

[4] Arshi A, Wang C, Park HY, et al. Ambulatory anterior cervical discectomy and fusion is associated with a higher risk of revision surgery and perioperative complications: an analysis of a large nationwide database. Spine J 2018;18(7):1180–7. doi:10.1016/j.spinee.2017.11.012.

[5] Ziino C, Bala A, Cheng I. Utilization and reimbursement trends based on certificate of need in single-level cervical discectomy. J Am Acad Orthop Surg 2021;29(10):e518–22. doi:10.5435/JAAOS-D-19-00224.

[6] Bernstein DN, Thirukumaran C, Saleh A, Molinari RW, Mesfin A. Complications and readmission after cervical spine surgery in elderly patients: an analysis of 1786 patients. World Neurosurg 2017;103:859–868.e8. doi:10.1016/j.wneu.2017.04.109.

[7] Wilson LA, Fiasconaro M, Liu J, et al. Trends in comorbidities and complications among patients undergoing inpatient spine surgery. Spine 2020;45(18):1299–308. doi:10.1097/BRS.0000000000003280.

[8] Katz AD, Mancini N, Karukonda T, Cote M, Moss IL. Comparative and predictor analysis of 30-day readmission, reoperation, and morbidity in patients undergoing multilevel ACDF versus single and multilevel ACCF using the ACS-NSQIP dataset. Spine 2019;44(23):E1379–87. doi:10.1097/BRS.0000000000003167.

[9] Wada K, Tamaki R, Inoue T, Hagiwara K, Okazaki K. Postoperative complications and survival rate in hemodialysis-dependent patients undergoing cervical spine surgery. Spine Surg Relat Res 2022;6(3):233–9. doi:10.22603/ssrr.2021-0173.

[10] Chahoud J, Kanafani Z, Kanj SS. Surgical site infections following spine surgery: eliminating the controversies in the diagnosis. Front Med 2014;1:E1–E10. doi:10.3389/fmed.2014.00007.

[11] Dowdell J, Brochin R, Kim J, et al. Postoperative spine infection: diagnosis and management. Glob Spine J 2018;8(4_suppl) 37S–43S. doi:10.1177/2192568217745512.

[12] Khalil JG, Gandhi SD, Park DK, Fischgrund JS. Cutibacterium acnes in spine pathology: pathophysiology, diagnosis, and management. J Am Acad Orthop Surg 2019;27(14):e633–40. doi:10.5435/JAAOS-D-17-00698.

[13] Dockery DM, Allu S, Vishwanath N, et al. Review of pre-operative skin preparation options based on surgical site in orthopedic surgery. Surg Infect 2021;22(10):1004–13. doi:10.1089/sur.2021.085.

[14] Yao R, Zhou H, Choma TJ, Kwon BK, Street J. Surgical site infection in spine surgery: who is at risk? Glob Spine J 2018;8(4_suppl) 5S–30S. doi:10.1177/2192568218799056.

[15] Chaudhary SB, Vives MJ, Basra SK, Reiter MF. Postoperative spinal wound infections and postprocedural diskitis. J Spinal Cord Med 2007;30(5):441–51. doi:10.1080/10790268.2007.11753476.

[16] Lavergne V, Malo M, Gaudelli C, et al. Clinical impact of positive Propionibacterium acnes cultures in orthopedic surgery. Orthop Traumatol Surg Res 2017;103(2):307–14. doi:10.1016/j.otsr.2016.12.005.

[17] Achermann Y, Goldstein EJC, Coenye T, Shirtliff ME. Propionibacterium acnes: from commensal to opportunistic biofilm-associated implant pathogen. Clin Microbiol Rev 2014;27(3):419–40. doi:10.1128/CMR.00092-13.

[18] Chen Z, Cao P, Zhou Z, Yuan Y, Jiao Y, Zheng Y. Overview: the role of Propionibacterium acnes in nonpyogenic intervertebral discs. Int Orthop 2016;40(6):1291–8. doi:10.1007/s00264-016-3115-5.

[19] LaGreca J, Hotchkiss M, Carry P, et al. Bacteriology and risk factors for development of late (greater than one year) deep infection following spinal fusion with instrumentation. Spine Deform 2014;2(3):186–90. doi:10.1016/j.jspd.2013.12.004.

[20] Caseris M, Ilharreborde B, Doit C, et al. Is Cutibacterium acnes early surgical site infection rate related to the duration of antibiotic prophylaxis in adolescent idiopathic scoliosis surgery? Eur Spine J 2020;29(7):1499–504. doi:10.1007/s00586-020-06427-2.

[21] Kolakowski L, Lai JK, Duvall GT, et al. Neer Award 2018: benzoyl peroxide effectively decreases preoperative Cutibacterium acnes shoulder burden: a prospective randomized controlled trial. J Shoulder Elbow Surg 2018;27(9):1539–44. doi:10.1016/j.jse.2018.06.012.

[22] Allhorn M, Arve S, Brüggemann H, Lood R. A novel enzyme with antioxidant capacity produced by the ubiquitous skin colonizer Propionibacterium acnes. Sci Rep 2016;6(1):36412. doi:10.1038/srep36412.

[23] Wang B, Toye B, Desjardins M, Lapner P, Lee C. A 7-year retrospective review from 2005 to 2011 of Propionibacterium acnes shoulder infections in Ottawa, Ontario, Canada. Diagn Microbiol Infect Dis 2013;75(2):195–9. doi:10.1016/j.diagmicrobio.2012.10.018.

[24] Portillo ME, Corvec S, Borens O, Trampuz A. *Propionibacterium acnes* : an underestimated pathogen in implant-associated infections. BioMed Res Int 2013;2013:1–10. doi:10.1155/2013/804391.

[25] Zhang AL, Feeley BT, Schwartz BS, Chung TT, Ma CB. Management of deep postoperative shoulder infections: is there a role for open biopsy during staged treatment? J Shoulder Elbow Surg 2015;24(1):e15–20. doi:10.1016/j.jse.2014.04.007.

[26] Mook WR, Klement MR, Green CL, Hazen KC, Garrigues GE. The incidence of Propionibacterium acnes in open shoulder surgery: a controlled diagnostic study. J Bone Jt Surg 2015;97(12):957–63. doi:10.2106/JBJS.N.00784.

[27] Oyama R, Iida K, Saiwai H, Matsumoto Y, Nakashima Y. Destructive cervical spondylitis due to Cutibacterium acnes with synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome: a case report. Mod Rheumatol Case Rep 2023;7(1):267–70. doi:10.1093/mrcr/rxac035.

[28] Xia MAM, Winder MJ. M6-C cervical disc replacement failure associated with late onset infection. J Spine Surg Hong Kong 2019;5(4):584–8. doi:10.21037/jss.2019.11.06.

[29] Grossi O, Lamberet R, Longis PM, et al. Risk factors for Cutibacterium acnes spinal implant-associated infection: a case-case-control study. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis 2020;26(6):743–7. doi:10.1016/j.cmi.2019.10.018.

[30] Ganko R, Rao PJ, Phan K, Mobbs RJ. Can bacterial infection by low virulent organisms be a plausible cause for symptomatic disc degeneration? A systematic review. Spine 2015;40(10):E587–92. doi:10.1097/BRS.0000000000000832.

[31] Stirling A, Worthington T, Rafiq M, Lambert PA, Elliott TS. Association between sciatica and Propionibacterium acnes. The Lancet 2001;357(9273):2024–5. doi:10.1016/S0140-6736(00)05109-6.

[32] Yuan Y, Zhou Z, Jiao Y, et al. Histological identification of *Propionibacterium acnes* in nonpyogenic degenerated intervertebral discs. BioMed Res Int 2017;2017:1–7. doi:10.1155/2017/6192935.

[33] Agarwal R, Gupta A, Gupta S. The impact of tort reform on defensive medicine, quality of care, and physician supply: a systematic review. Health Serv Res 2019;54(4):851–9. doi:10.1111/1475-6773.13157.

[34] Arndt J, Charles YP, Koebel C, Bogorin I, Steib JP. Bacteriology of degenerated lumbar intervertebral disks. J Spinal Disord Tech 2012;25(7):E211–16. doi:10.1097/BSD.0b013e318269851a.

[35] Albert HB, Lambert P, Rollason J, et al. Does nuclear tissue infected with bacteria following disc herniations lead to Modic changes in the adjacent vertebrae? Eur Spine J 2013;22(4):690–6. doi:10.1007/s00586-013-2674-z.

[36] Zhou Z, Chen Z, Zheng Y, et al. Relationship between annular tear and presence of Propionibacterium acnes in lumbar intervertebral disc. Eur Spine J 2015;24(11):2496–502. doi:10.1007/s00586-015-4180-y.

[37] Chen Z, Zheng Y, Yuan Y, et al. Modic Changes and Disc Degeneration Caused by Inoculation of *Propionibacterium acnes* inside Intervertebral Discs of Rabbits: A Pilot Study. BioMed Res Int 2016;2016:1–7. doi:10.1155/2016/9612437.

[38] Ben-Galim P, Rand N, Giladi M, et al. Association between sciatica and microbial infection: true infection or culture contamination? Spine 2006;31(21):2507–9. doi:10.1097/01.brs.0000238657.13263.b2.

[39] Fritzell P, Bergström T, Welinder-Olsson C. Detection of bacterial DNA in painful degenerated spinal discs in patients without signs of clinical infection. Eur Spine J 2004;13(8):702–6. doi:10.1007/s00586-004-0719-z.

[40] Gilligan CJ, Cohen SP, Fischetti VA, Hirsch JA, Czaplewski LG. Chronic low back pain, bacterial infection and treatment with antibiotics. Spine J 2021;21(6):903–14. doi:10.1016/j.spinee.2021.02.013.

[41] Sagkrioti M, Glass S, Arealis G. Evaluation of the effectiveness of skin preparation methods for the reduction of *Cutibacterium acnes* (formerly *Propionibacterium acnes*) in shoulder surgery: a systematic review. Shoulder Elb 2022;14(6):583–97. doi:10.1177/17585732211032523.

[42] Sanderson BR, Saini A, Chiang E, Linton K, Brien EW. Short-term clinical outcomes of unexpected culture-positive Cutibacterium acnes (formerly Propionibacterium acnes) in open orthopaedic surgery. JAAOS Glob Res Rev 2022;6(7):e.22.00010. doi:10.5435/JAAOSGlobal-D-22-00010.

[43] Heckmann N, Sivasundaram L, Heidari KS, et al. Propionibacterium acnes persists despite various skin preparation techniques. Arthrosc J Arthrosc Relat Surg 2018;34(6):1786–9. doi:10.1016/j.arthro.2018.01.019.

[44] Casey A, Itrakjy A, Birkett C, et al. A comparison of the efficacy of 70% v/v isopropyl alcohol with either 0.5% w/v or 2% w/v chlorhexidine gluconate for skin preparation before harvest of the long saphenous vein used in coronary artery bypass grafting. Am J Infect Control 2015;43(8):816–20. doi:10.1016/j.ajic.2015.03.034.

[45] George J, Klika AK, Higuera CA. Use of chlorhexidine preparations in total joint arthroplasty. J Bone Jt Infect 2017;2(1):15–22. doi:10.7150/jbji.16934.

[46] Namdari S, Nicholson T, Parvizi J, Ramsey M. Preoperative doxycycline does not decolonize Propionibacterium acnes from the skin of the shoulder: a randomized controlled trial. J Shoulder Elbow Surg 2017;26(9):1495–9. doi:10.1016/j.jse.2017.06.039.

[47] Matsen FA, 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 Jt Surg 2013;95(23):e181. doi:10.2106/JBJS.L.01733.

[48] Matsen FA, Russ SM, Bertelsen A, Butler-Wu S, Pottinger PS. Propionibacterium can be isolated from deep cultures obtained at primary arthroplasty despite intravenous antimicrobial prophylaxis. J Shoulder Elbow Surg 2015;24(6):844–7. doi:10.1016/j.jse.2014.10.016.

[49] Grewal G, Polisetty T, Boltuch A, Colley R, Tapia R, Levy JC. Does application of hydrogen peroxide to the dermis reduce incidence of Cutibacterium acnes during shoulder arthroplasty: a randomized controlled trial. J Shoulder Elbow Surg 2021;30(8):1827–33. doi:10.1016/j.jse.2021.03.144.

[50] Chalmers PN, Beck L, Stertz I, Tashjian RZ. Hydrogen peroxide skin preparation reduces Cutibacterium acnes in shoulder arthroplasty: a prospective, blinded, controlled trial. J Shoulder Elbow Surg 2019;28(8):1554–61. doi:10.1016/j.jse.2019.03.038.

[51] Hernandez P, Sager B, Fa A, Liang T, Lozano C, Khazzam M. Bactericidal efficacy of hydrogen peroxide on *Cutibacterium acnes*. Bone Jt Res 2019;8(1):3–10. doi:10.1302/2046-3758.81.BJR-2018-0145.R1.

[52] Pottinger P, Butler-Wu S, Neradilek MB, 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 Jt Surg-Am Vol. 2012;94(22):2075–83. doi:10.2106/JBJS.K.00861.

[53] Stull JD, Nicholson TA, Davis DE, Namdari S. Addition of 3% hydrogen peroxide to standard skin preparation reduces Cutibacterium acnes–positive culture rate in shoulder surgery: a prospective randomized controlled trial. J Shoulder Elbow Surg 2020;29(2):212–16. doi:10.1016/j.jse.2019.09.038.

[54] Kluyver T, Ragan-Kelley B, Pérez F, et al. Jupyter Notebooks—a Publishing Format For Reproducible Computational Workflows. IOS Press; 2016. p. 87–90. doi:10.3233/978-1-61499-649-1-87.

[55] Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007;39(2):175–91. doi:10.3758/BF03193146.

[56] Ohlin A, Mattsson E, Mörgelin M, et al. Titanium granules pre-treated with hydrogen peroxide inhibit growth of bacteria associated with post-operative infections in spine surgery. Eur Spine J 2018;27(10):2463–8. doi:10.1007/s00586-018-5619-8.

[57] Dizay HH, Lau DG, Nottage WM. Benzoyl peroxide and clindamycin topical skin preparation decreases Propionibacterium acnes colonization in shoulder arthroscopy. J Shoulder Elbow Surg 2017;26(7):1190–5. doi:10.1016/j.jse.2017.03.003.
[58] Murphy EC, Friedman AJ. Hydrogen peroxide and cutaneous biology: translational applications, benefits, and risks. J Am Acad Dermatol 2019;81(6):1379–86. doi:10.1016/j.jaad.2019.05.030.
[59] Saltzman MD, Marecek GS, Edwards SL, Kalainov DM. Infection after shoulder surgery. Am Acad Orthop Surg 2011;19(4):208–18. doi:10.5435/00124635-201104000-00005.
[60] Sabetta JR, Rana VP, Vadasdi KB, et al. Efficacy of topical benzoyl peroxide on the reduction of Propionibacterium acnes during shoulder surgery. J Shoulder Elbow Surg 2015;24(7):995–1004. doi:10.1016/j.jse.2015.04.003.
[61] Aleem IS, Tan LA, Nassr A, Riew KD. Infection prevention in cervical spine surgery. J Spine Surg Hong Kong 2020;6(1):334–9. doi:10.21037/jss.2020.01.13.
[62] Smith JS, Shaffrey CI, Sansur CA, et al. Rates of infection after spine surgery based on 108,419 procedures: a report from the Scoliosis Research Society Morbidity and Mortality Committee. Spine 2011;36(7):556–63. doi:10.1097/BRS.0b013e3181eadd41.
[63] Scheer VM, Jungeström MB, Serrander L, Kalén A, Scheer JH. Benzoyl peroxide treatment decreases Cutibacterium acnes in shoulder surgery, from skin incision until wound closure. J Shoulder Elbow Surg 2021;30(6):1316–23. doi:10.1016/j.jse.2020.12.019.
[64] Gupta VK, Paul S, Geography Dutta C. Ethnicity or subsistence-specific variations in human microbiome composition and diversity. Front Microbiol 2017;8:1162. doi:10.3389/fmicb.2017.01162.
[65] Lin ZX, Steed LL, Marculescu CE, Slone HS, Woolf SK. *Cutibacterium acnes* infection in orthopedics: microbiology, clinical findings, diagnostic strategies, and management. Orthopedics 2020;43(1):52–61. doi:10.3928/01477447-20191213-02.
[66] Garcia D, Mayfield CK, Leong J, et al. Early adherence and biofilm formation of Cutibacterium acnes (formerly Propionibacterium acnes) on spinal implant materials. Spine J 2020;20(6):981–7. doi:10.1016/j.spinee.2020.01.001.