PART III

SHOULDER

Prevention

1.1. PREVENTION: ANTIBIOTICS

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QUESTION 1: What are the optimal perioperative antibiotics for primary shoulder arthroplasty?

RECOMMENDATION: Patients undergoing primary shoulder arthroplasty should receive antibiotics that cover gram-positive and gram-negative organisms specific to the regionally encountered organisms. Peer-reviewed literature supports cefazolin dosing based on body weight (Table 1). Patients with methicillin-resistant *Staphylococcus aureus* (*S. aureus*), or MRSA, colonization should receive weight-adjusted glycopeptide, preferably in combination with cefazolin (Table 1). Patients who are believed to have an intolerance to beta-lactam antibiotics should be further evaluated to determine if they can receive cefazolin. Patients with a true hypersensitivity reaction or adverse reaction that precludes the use of cefazolin should receive vancomycin or clindamycin.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

A thorough search of the PubMed database for all available literature on the topic of optimal perioperative antibiotics for primary shoulder arthroplasty was undertaken. There are no prospective controlled studies comparing surgical antibiotic prophylaxis strategies for shoulder arthroplasty that adequately assess clinical outcomes. Studies measuring microbial burden (primarily *Cutibacterium acnes*) at the time of incision after surgical antimicrobial prophylaxis in the setting of shoulder surgery have been disappointing. One small randomized controlled study comparing preoperative doxycycline administration to placebo did not demonstrate a reduction in *Cutibacterium acnes* colonization [1]. The relevance of these findings with respect to surgical prophylaxis in the shoulder is not known. Surgical prophylaxis in total joint arthroplasty does reduce the burden of other cutaneous microorganisms and is recommended for all orthopaedic implant surgery [2–4].

Prophylaxis should target organisms most likely to cause prosthetic shoulder infection. The most common organisms to cause shoulder surgical site infection and periprosthetic joint infection (PJI) are coagulase-negative Staphylococcus species, *Cutibacterium acnes* and *S. aureus* [5–9]. In addition to antimicrobial spectrum, agents selected for prophylaxis should also achieve bactericidal tissue concentration at the time of incision. In the absence of shoulder-specific literature and recognizing the microbiology and other factors we believe it is reasonable to extrapolate from the non-shoulder arthroplasty literature. The agent most likely to provide optimal tissue concentrations for prophylaxis against these organisms is cefazolin, dosed based on patient body weight [10]. Vancomycin should be utilized when patients have a personal history of MRSA colonization or infection. Close attention to dosing based on body-weight and the earlier timing of prophylaxis when vancomycin is utilized is paramount [4,11]. Ideally, vancomycin should not be given alone, however, as studies have identified an increased risk of PJI and surgical site infection potentially due to the narrower spectrum of vancomycin when compared with cefazolin [12,13]. Combination therapy with vancomycin and cefazolin has not been prospectively demonstrated to reduce surgical site infection risk in

TABLE 1. Recommended antimicrobial prophylaxis for patients undergoing primary shoulder arthroplasty

Clinical Situation	Antimicrobial Recommended
No beta-lactam allergy	Cefazolin 2 gm IV (3 gm if patient weighs > 120 kg) starting within 30-60 minutes prior to incision; re-dose Q4 hours; postoperative doses not required and should not be given beyond 24 hours.
Personal history of MRSA infection or colonization	Vancomycin 15 mg/kg (max dose 2 gm) starting within 2 hours prior to incision; postoperative doses not required and should not be given beyond 24 hours. We favor the addition of cefazolin to vancomycin.
Proven, serious beta-lactam allergy	Vancomycin 15 mg/kg (max dose 2 gm) starting within 2 hours prior to incision; postoperative doses not required and should not be given beyond 24 hours.

MRSA, methicillin-resistant *Staphylococcus aureus*

arthroplasty over cefazolin alone, although two studies suggest a trend towards reduced infection [14,15]. Combination therapy may be associated with higher rates of nephrotoxicity than vancomycin alone [14]. However, the value of preventing prosthetic joint infections may still justify its use. Additional study to clarify risks and benefits of these strategies is warranted.

One of the most common causes for use of an alternative perioperative antibiotic other than cefazolin is beta-lactam allergy or intolerance. Most of these patients are not actually allergic and will be able to safely receive cefazolin after evaluation by an allergist [16]. Patients with a true hypersensitivity reaction or adverse reaction that prohibits cefazolin should receive vancomycin or clindamycin in agreement with the Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery [4].

REFERENCES

[1] 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;26:1495–1499. doi:10.1016/j.jse.2017.06.039.

[2] Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection 2017. JAMA Surg. 2017;152:784–791. doi:10.1001/jamasurg.2017.0904.

[3] Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis. 2016;16:e288–e303. doi:10.1016/S1473-3099(16)30402-9.

[4] Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70:195–283. doi:10.2146/ajhp120568.

[5] Koh CK, Marsh JP, Drinković D, Walker CG, Poon PC. Propionibacterium acnes in primary shoulder arthroplasty: rates of colonization, patient risk factors, and efficacy of perioperative prophylaxis. J Shoulder Elbow Surg. 2016;25:846–852. doi:10.1016/j.jse.2015.09.033.

[6] 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;24:844–847. doi:10.1016/j.jse.2014.10.016.

[7] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.

[8] Richards J, Inacio MCS, Beckett M, Navarro RA, Singh A, Dillon MT, et al. Patient and procedure-specific risk factors for deep infection after primary shoulder arthroplasty. Clin Orthop Relat Res. 2014;472:2809–2815. doi:10.1007/s11999-014-3696-5.

[9] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.

[10] Boyle KK, Duquin TR. Antibiotic prophylaxis and prevention of surgical site infection in shoulder and elbow surgery. Orthop Clin North Am. 2018;49:241–256. doi:10.1016/j.ocl.2017.11.011.

[11] Kheir MM, Tan TL, Azboy I, Tan DD, Parvizi J. Vancomycin prophylaxis for total joint arthroplasty: incorrectly dosed and has a higher rate of periprosthetic infection than cefazolin. Clin Orthop Relat Res. 2017;475:1767–1774. doi:10.1007/s11999-017-5302-0.

[12] Gupta K, Strymish J, Abi-Haidar Y, Williams SA, Itani KMF. Preoperative nasal methicillin-resistant Staphylococcus aureus status, surgical prophylaxis, and risk-adjusted postoperative outcomes in veterans. Infect Control Hosp Epidemiol. 2011;32:791–796. doi:10.1086/660362.

[13] Blumenthal KG, Ryan EE, Li Y, Lee H, Kuhlen JL, Shenoy ES. The Impact of a reported penicillin allergy on surgical site infection risk. Clin Infect Dis. 2018;66:329–336. doi:10.1093/cid/cix794.

[14] Branch-Elliman W, Ripollone JE, O'Brien WJ, Itani KMF, Schweizer ML, Perencevich E, et al. Risk of surgical site infection, acute kidney injury, and Clostridium difficile infection following antibiotic prophylaxis with vancomycin plus a beta-lactam versus either drug alone: a national propensity-score-adjusted retrospective cohort study. PLoS Med. 2017;14:e1002340. doi:10.1371/journal.pmed.1002340.

[15] Ponce B, Raines BT, Reed RD, Vick C, Richman J, Hawn M. Surgical site infection after arthroplasty: comparative effectiveness of prophylactic antibiotics: do surgical care improvement project guidelines need to be updated? J Bone Joint Surg Am. 2014;96:970–977. doi:10.2106/JBJS.M.00663.

[16] Park M, Markus P, Matesic D, Li JTC. Safety and effectiveness of a preoperative allergy clinic in decreasing vancomycin use in patients with a history of penicillin allergy. Ann Allergy Asthma Immunol. 2006;97:681–687. doi:10.1016/S1081-1206(10)61100-3.

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QUESTION 2: What are the optimal perioperative antibiotics for patients undergoing revision shoulder arthroplasty?

RECOMMENDATION: Patients undergoing revision shoulder arthroplasty should receive prophylactic antibiotics as discussed in Question 1. As addressed in Question 5, if there is suspicion for preexisting infection during surgery, consider oral amoxicillin or first-generation cephalosporin (or oral doxycycline if beta-lactam allergic) until cultures are finalized.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

After a thorough search of the PubMed database for studies evaluating the optimal perioperative antibiotic for patients undergoing revision shoulder arthroplasty, there are no prospective controlled studies comparing surgical antibiotic prophylaxis strategies for revision shoulder arthroplasty that adequately assess clinical outcomes.

Prophylaxis should target organisms most likely to cause prosthetic shoulder infection. The most common organisms to cause shoulder surgical site infection and PJI are coagulase-negative Staphylococcus species, *Cutibacterium acnes* (formerly known as *Proprionibacterium acnes*) and *Staphylococcus aureus* [1–3]. In the setting of revision surgery without an obvious reason for joint failure such as trauma, there may be a question of whether the patient's pain and/or stiffness may be caused by an occult perioperative joint infection (PJI) acquired during a prior case or joint injection. *C. acnes*, in particular, has emerged as a pathogen often cultivated from deep operative specimens in patients undergoing revision for pain and/or stiffness [4].

Unfortunately, inflammatory markers are often normal in these patients, and intraoperative evaluation is often benign-appearing, making it difficult to predict who will ultimately have substantially positive cultures after 14 days of incubation. Thus, surgeons may consider postoperative oral antibiotics to cover the most likely pathogen that may be detected after discharge—*C. acnes*—until cultures are finalized as negative [5]. This is distinctly different from the antibiotic prophylactic strategy for primary shoulder arthroplasty cases, which usually stops when the case concludes, certainly within 24

TABLE 1. Recommended antimicrobial prophylaxis for patients undergoing revision shoulder arthroplasty

Clinical Situation	Antimicrobial Recommended at Surgery (Note: Administer on time as usual, even if concerned about occult infection.)	Postoperative Antimicrobials to Consider if High Intraoperative Suspicion of Infection
No beta-lactam allergy	Cefazolin 2 gm IV (3 gm if patient weighs > 120 kg) starting within 30 minutes prior to incision; re-dose Q 4 hours; postoperative doses not required and should not be given beyond 24 hours.	Amoxicillin 500 mg PO Q 8 H or cefadroxil 500 mg PO BID x 14 days until operative cultures are reported negative. (Adjust for renal insufficiency.)
Personal history of MRSA infection or colonization	In **addition** to cefazolin above, add vancomycin 15 mg/kg (max dose 2 gm) starting within 1 hour prior to incision; postoperative doses are not required and should not be given beyond 24 hours.	Same as above, unless positive intraoperative gram stain or culture positive for MRSA (in which case, convert to treatment program with ID consultation).
Proven, serious beta-lactam allergy	Vancomycin 15 mg/kg (max dose 2 gm) starting within 1 hour prior to incision; postoperative doses are not required and should not be given beyond 24 hours.	Doxycycline 100 mg PO Q 12 H x 14 days until operative cultures are reported negative.

BID, twice daily; MRSA, methicillin-resistant *Staphylococcus aureus*; PO, orally; Q H., every hour

hours post-operatively [6]. Continuing antibiotics postoperatively carries risk of adverse events such as diarrhea, *C. difficile* infection, other side effects, toxicities, development of resistance and drug interactions.

In addition to antimicrobial spectrum, agents selected for prophylaxis should also achieve bactericidal tissue concentration at the time of incision. In the absence of shoulder-specific literature and recognizing the microbiology and other factors, we believe it is reasonable to extrapolate from the non-shoulder arthroplasty literature. The agent most likely to provide optimal tissue concentrations for prophylaxis against these organisms is cefazolin; with dosing based on patient body weight. Vancomycin can be added when patients have a personal history of MRSA colonization or infection, but, ideally, vancomycin should not be given alone. Studies have identified an increased risk of periprosthetic joint infection and surgical site infection, when prophylaxis with an agent other than cefazolin is used [7,8]. One of the most common causes for use of an alternative perioperative antibiotic other than cefazolin is a beta-lactam allergy or intolerance. Most of these patients are not actually allergic and will be able to safely receive cefazolin after evaluation by an allergist or the administration of a test-dose if the prior reaction was felt to be mild. Patients with a true hypersensitivity reaction or adverse reaction that prohibits cefazolin should receive vancomycin or clindamycin in agreement with the Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery [9].

Of note, timely administration of intravenous prophylactic antibiotics immediately before incision is unlikely to negatively impact the yield of deep cultures, if they are obtained [10].

Studies measuring microbial burden (primarily *C. acnes*) at the time of incision after surgical antimicrobial prophylaxis in the setting of shoulder surgery have been disappointing [11,12]. One small randomized controlled study comparing preoperative doxycycline administration to placebo did not demonstrate a reduction in *C. acnes* colonization [13]. The relevance of these findings with respect to surgical prophylaxis in the shoulder is not known. Surgical prophylaxis in total joint arthroplasty does reduce the burden of other cutaneous microorganisms and is recommended for all orthopaedic implant surgery [14].

REFERENCES

[1] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.

[2] Richards J, Inacio MCS, Beckett M, Navarro RA, Singh A, Dillon MT, et al. Patient and procedure-specific risk factors for deep infection after primary shoulder arthroplasty. Clin Orthop Relat Res. 2014;472:2809–2815. doi:10.1007/s11999-014-3696-5.

[3] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.

[4] Horneff JG, Hsu JE, Huffman GR. Propionibacterium acnes infections in shoulder surgery. Orthop Clin North Am. 2014;45:515–521. doi:10.1016/j.ocl.2014.06.004.

[5] Boyle KK, Duquin TR. Antibiotic prophylaxis and prevention of surgical site infection in shoulder and elbow surgery. Orthop Clin North Am. 2018;49:241–256. doi:10.1016/j.ocl.2017.11.011.

[6] Kheir MM, Tan TL, Azboy I, Tan DD, Parvizi J. Vancomycin prophylaxis for total joint arthroplasty: incorrectly dosed and has a higher rate of periprosthetic infection than cefazolin. Clin Orthop Relat Res. 2017;475:1767–1774. doi:10.1007/s11999-017-5302-0.

[7] Gupta K, Strymish J, Abi-Haidar Y, Williams SA, Itani KMF. Preoperative nasal methicillin-resistant Staphylococcus aureus status, surgical prophylaxis, and risk-adjusted postoperative outcomes in veterans. Infect Control Hosp Epidemiol. 2011;32:791–796. doi:10.1086/660362.

[8] Blumenthal KG, Ryan EE, Li Y, Lee H, Kuhlen JL, Shenoy ES. The impact of a reported Penicillin allergy on surgical site infection risk. Clin Infect Dis. 2018;66:329–336. doi:10.1093/cid/cix794.

[9] Park M, Markus P, Matesic D, Li JTC. Safety and effectiveness of a preoperative allergy clinic in decreasing vancomycin use in patients with a history of penicillin allergy. Ann Allergy Asthma Immunol. 2006;97:681–687. doi:10.1016/S1081-1206(10)61100-3.

[10] Pérez-Prieto D, Portillo ME, Puig-Verdié L, Alier A, Gamba C, Guirro P, et al. Preoperative antibiotic prophylaxis in prosthetic joint infections: not a concern for intraoperative cultures. Diagn Microbiol Infect Dis. 2016;86:442–445. doi:10.1016/j.diagmicrobio.2016.09.014.

[11] Koh CK, Marsh JP, Drinković D, Walker CG, Poon PC. Propionibacterium acnes in primary shoulder arthroplasty: rates of colonization, patient risk factors, and efficacy of perioperative prophylaxis. J Shoulder Elbow Surg. 2016;25:846–852. doi:10.1016/j.jse.2015.09.033.

[12] 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;24:844–847. doi:10.1016/j.jse.2014.10.016.

[13] 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;26:1495–1499. doi:10.1016/j.jse.2017.06.039.

[14] Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70:195–283. doi:10.2146/ajhp120568.

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QUESTION 3: Are there perioperative antibiotics that should be used for patients who have specific preoperative risk factors (e.g., patient sex and comorbidities) for shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: While risk of infection may be affected by demographics and comorbidities, outside of known methicillin-resistant *Staphylococcus aureus* (MRSA) colonization or true allergy, there are not patient-specific factors that justify a change in prophylaxis recommendations. Patients with MRSA colonization should receive a glycopeptide in addition to standard prophylaxis.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

The most common organisms to cause shoulder PJI are coagulase-negative staphylococcus species, *Cutibacterium acnes* and *Staphylococcus aureus* [1–7]. While the risk of shoulder PJI is impacted by comorbidities, and the prevalence of *Cutibacterium acnes* colonization is higher in men, there is no available data to support targeted modification of antimicrobial prophylaxis outside of the setting of known MRSA colonization. In the hip and knee arthroplasty setting, one study did not find that differential antimicrobial prophylaxis impacted surgical site infection risk when comorbidities were considered [8]. Studies have identified an increased risk of hip and knee PJI and surgical site infection when prophylaxis with an agent other than cefazolin is used [9,10].

REFERENCES

[1] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.
[2] Richards J, Inacio MCS, Beckett M, Navarro RA, Singh A, Dillon MT, et al. Patient and procedure-specific risk factors for deep infection after primary shoulder arthroplasty. Clin Orthop Relat Res. 2014;472:2809–2815. doi:10.1007/s11999-014-3696-5.
[3] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.
[4] 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 Joint Surg Am. 2015;97:957–963. doi:10.2106/JBJS.N.00784.
[5] Falconer TM, Baba M, Kruse LM, Dorrestijn O, Donaldson MJ, Smith MM, et al. Contamination of the surgical field with Propionibacterium acnes in primary shoulder arthroplasty. J Bone Joint Surg Am. 2016;98:1722–1728. doi:10.2106/JBJS.15.01133.
[6] Chuang MJ, Jancosko JJ, Mendoza V, Nottage WM. The incidence of Propionibacterium acnes in shoulder arthroscopy. Arthroscopy. 2015;31:1702–1707. doi:10.1016/j.arthro.2015.01.029.
[7] 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. doi:10.1016/j.jse.2014.09.042.
[8] Gupta K, Strymish J, Abi-Haidar Y, Williams SA, Itani KMF. Preoperative nasal methicillin-resistant Staphylococcus aureus status, surgical prophylaxis, and risk-adjusted postoperative outcomes in veterans. Infect Control Hosp Epidemiol. 2011;32:791–796. doi:10.1086/660362.
[9] Tan TL, Gomez MM, Kheir MM, Maltenfort MG, Chen AF. Should preoperative antibiotics be tailored according to patient's comorbidities and susceptibility to organisms? J Arthroplasty. 2017;32:1089-1094.e3. doi:10.1016/j.arth.2016.11.021.
[10] Kheir MM, Tan TL, Azboy I, Tan DD, Parvizi J. Vancomycin prophylaxis for total joint arthroplasty: incorrectly dosed and has a higher rate of periprosthetic infection than cefazolin. Clin Orthop Relat Res. 2017;475:1767–1774. doi:10.1007/s11999-017-5302-0.

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QUESTION 4: What is the optimal duration of perioperative antibiotics following primary or revision shoulder arthroplasty?

RECOMMENDATION: For primary shoulder arthroplasty, prophylactic intravenous (IV) antibiotics should be given within one hour prior to incision to decrease the risk of infection. Intravenous antibiotics may be continued for 24 hours postoperatively. For revision shoulder arthroplasty, intravenous antibiotics should be given within one hour prior to incision. While controversial, the current evidence suggests that prophylactic antibiotics should not be routinely held until tissue for culture is obtained (see Section 2.5. Diagnosis: Sampling, Question 7). Intravenous antibiotics should only be continued for 24 hours postoperatively, unless there is a concern for periprosthetic infection. Antibiotics can be continued up until final culture results are obtained in revision cases if there is some suspicion of infection while awaiting the final culture results.

LEVEL OF EVIDENCE: Moderate

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

RATIONALE

Primary Shoulder Arthroplasty

Prophylactic IV antibiotics should be started within one hour prior to incision to decrease the risk of infection [1–7]. IV antibiotics may be continued for 24 hours postoperatively [5–7].

However, recent recommendations from the Center for Disease Control and Prevention (CDC) suggest that prophylactic antibiotics should be administered such that a bactericidal concentration is present in the serum and tissues prior to incision and additional prophylactic antibiotic treatment should not be administered after the surgical incision is closed for clean and clean-contaminated procedures even in the presence of a drain [8]. Similar recommendations have recently been proposed by the World Health Organization advocating preoperative antibiotic prophylaxis without postoperative dosing [9].

Revision Shoulder Arthroplasty

IV antibiotics should be started within one hour prior to incision. There remains some controversy regarding whether or not to administer antibiotics prior to obtaining cultures in the revision setting. Based upon previous experience with revision shoulder arthroplasty [10], McGoldrick et al. recommended withholding prophylactic antibiotics until after tissue cultures have been obtained especially in cases "that have no overt preoperative evidence of clinical infection"[11]. Nevertheless, there is some evidence suggesting that withholding prophylactic IV antibiotics prior to revision for obvious or highly suspected infection is not needed, but this is mostly reported from the hip and knee arthroplasty literature [12,13]. Routine prophylactic IV antibiotics should only be continued for 24 hours postoperatively, unless there is a concern for periprosthetic infection in which case IV or oral antibiotics can be continued for up to 3 weeks postoperatively while awaiting the final culture results [12,14,15]. *C. acnes* may require 13-17 days to grow, necessitating antibiotics for 2 weeks following revision arthroplasty with a concern for periprosthetic joint infection [11,14–18].

Re-dosing of prophylactic antibiotics has been recommended for procedures lasting longer than 3-4 hours [19,20], although there are no shoulder arthroplasty studies on re-dosing of antibiotics.

Note: Despite appropriate skin prep and preoperative IV antibiotics, *C. acnes* can still be grown from the native tissue of the shoulder including within the glenohumeral joint in patients without prior surgery [17,21,22].

Shoulder Surgery Articles: 9 Studies
0 – Level I studies
0 – Prognostic Level II studies
4 – Retrospective Cohort Level III studies
3 – Case Series Level IV studies
2 – Level V opinion

TKA/THA/Other Surgical Articles: 12 Studies
1 – Level I studies
1 – Prognostic Level II studies
4 – Retrospective Cohort Level III studies
3 – Case Series Level IV studies
3 – Level V opinion

REFERENCES

[1] Bratzler DW, Houck PM, Surgical Infection Prevention Guidelines Writers Workgroup, American Academy of Orthopaedic Surgeons, American Association of Critical Care Nurses, American Association of Nurse Anesthetists, et al. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis. 2004;38:1706–1715. doi:10.1086/421095.

[2] Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med. 1992;326:281–286. doi:10.1056/NEJM199201303260501.

[3] Garey KW, Dao T, Chen H, Amrutkar P, Kumar N, Reiter M, et al. Timing of vancomycin prophylaxis for cardiac surgery patients and the risk of surgical site infections. J Antimicrob Chemother. 2006;58:645–650. doi:10.1093/jac/dkl279.

[4] Pauzenberger L, Grieb A, Hexel M, Laky B, Anderl W, Heuberer P. Infections following arthroscopic rotator cuff repair: incidence, risk factors, and prophylaxis. Knee Surg Sports Traumatol Arthrosc. 2017;25:595–601. doi:10.1007/s00167-016-4202-2.

[5] Stone HH, Hooper CA, Kolb LD, Geheber CE, Dawkins EJ. Antibiotic prophylaxis in gastric, biliary and colonic surgery. Ann Surg. 1976;184:443–452.

[6] Stowers MDJ, Lemanu DP, Coleman B, Hill AG, Munro JT. Review article: Perioperative care in enhanced recovery for total hip and knee arthroplasty. J Orthop Surg (Hong Kong). 2014;22:383–392. doi:10.1177/230949901402200324.

[7] van Kasteren MEE, Manniën J, Ott A, Kullberg B-J, de Boer AS, Gyssens IC. Antibiotic prophylaxis and the risk of surgical site infections following total hip arthroplasty: timely administration is the most important factor. Clin Infect Dis. 2007;44:921–927. doi:10.1086/512192.

[8] Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg. 2017;152:784–791. doi:10.1001/jamasurg.2017.0904.

[9] Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis. 2016;16:e288–e303. doi:10.1016/S1473-3099(16)30402-9.

[10] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[11] McGoldrick E, McElvany MD, Butler-Wu S, Pottinger PS, Matsen FA. Substantial cultures of Propionibacterium can be found in apparently aseptic shoulders revised three years or more after the index arthroplasty. J Shoulder Elbow Surg. 2015;24:31–35. doi:10.1016/j.jse.2014.05.008.

[12] Pérez-Prieto D, Portillo ME, Puig-Verdié L, Alier A, Gamba C, Guirro P, et al. Preoperative antibiotic prophylaxis in prosthetic joint infections: not a concern for intraoperative cultures. Diagn Microbiol Infect Dis. 2016;86:442–445. doi:10.1016/j.diagmicrobio.2016.09.014.

[13] Wouthuyzen-Bakker M, Benito N, Soriano A. The effect of preoperative antimicrobial prophylaxis on intraoperative culture results in patients with a suspected or confirmed prosthetic joint infection: a systematic review. J Clin Microbiol. 2017;55:2765–2774. doi:10.1128/JCM.00640-17.

[14] Padegimas EM, Lawrence C, Narzikul AC, Zmistowski BM, Abboud JA, Williams GR, et al. Future surgery after revision shoulder arthroplasty: the impact of unexpected positive cultures. J Shoulder Elbow Surg. 2017;26:975–981. doi:10.1016/j.jse.2016.10.023.

[15] Shirwaiker RA, Springer BD, Spangehl MJ, Garrigues GE, Lowenberg DW, Garras DN, et al. A clinical perspective on musculoskeletal infection treatment strategies and challenges. J Am Acad Orthop Surg. 2015;23 Suppl:S44-S54. doi:10.5435/JAAOS-D-14-00379.

[16] 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 Joint Surg Am. 2013;95:e1811-e1817. doi:10.2106/JBJS.L.01733.

[17] 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;24:844–847. doi:10.1016/j.jse.2014.10.016.

[18] Shields MV, Abdullah L, Namdari S. The challenge of Propionibacterium acnes and revision shoulder arthroplasty: a review of current diagnostic options. J Shoulder Elbow Surg. 2016;25:1034–1040. doi:10.1016/j.jse.2016.01.009.

[19] Scher KS. Studies on the duration of antibiotic administration for surgical prophylaxis. Am Surg. 1997;63:59–62.

[20] Steinberg JP, Braun BI, Hellinger WC, Kusek L, Bozikis MR, Bush AJ, et al. Timing of antimicrobial prophylaxis and the risk of surgical site infections: results from the Trial to Reduce Antimicrobial Prophylaxis Errors. Ann Surg. 2009;250:10–16. doi:10.1097/SLA.0b013e3181ad5fca.

[21] Falconer TM, Baba M, Kruse LM, Dorrestijn O, Donaldson MJ, Smith MM, et al. Contamination of the surgical field with Propionibacterium acnes in primary shoulder arthroplasty. J Bone Joint Surg Am. 2016;98:1722–1728. doi:10.2106/JBJS.15.01133.

[22] 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 Joint Surg Am. 2015;97:957–963. doi:10.2106/JBJS.N.00784.

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QUESTION 5: Is there a role for postoperative (pending culture results) antibiotics after revision shoulder arthroplasty without suspicion for infection?

RECOMMENDATION: In revision shoulder arthroplasty without clinical suspicion for infection, prolonged antibiotics are not routinely required.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

The prevalence of subclinical infections (unexpected positive culture (UPC)) is especially common with shoulder arthroplasty due to anatomic and demographic factors. The rate of positive cultures in primary and revision arthroplasty settings have been reported as high as 56% [1–3]. However, the significance and optimal treatment for UPCs remains unknown. There is limited data in the shoulder literature for or against any role for postoperative prophylactic/suppressive antibiotics after revision shoulder arthroplasty without clinical or radiographic signs of infection. While several studies described the use of prophylactic or suppressive antibiotics after revision shoulder arthroplasty, there was a lack of prospective randomized studies and none of the studies specifically evaluated their efficacy or included a comparative group.

Among published studies for outcomes specifically after revision shoulder arthroplasty with unexpected positive cultures, all were retrospective studies with differing and suboptimal methodologies [4–8]. None of the studies found a detrimental effect associated with not prescribing prolonged antibiotics postoperatively, although one study with no comparison group reported a 25% recurrence rate after UPC. For those studies that treated UPC with prolonged antibiotics, recurrence rates were low (0-3.5%). One systematic review confirmed a pooled true infection rate after UPC of 10.2% with antibiotic use not influencing the rate of occurrence of true infection after UPCs ($p = 0.498$) [9]. In the lower extremity arthroplasty literature, there was one randomized controlled study which found a limited benefit to prolonged oral antibiotic therapy after two-stage revision with negative cultures (5% versus 19%), although culture profiles from the reinfection tended to differ from the original infection organism profile [10].

One study used antibiotic cement and 24 hours of routine postoperative antibiotics with 1 superficial infection and no deep infections after revision shoulder arthroplasty [4]. Another study reported at least a 10% persistent infection rate after one-stage shoulder arthroplasty revision although antibiotic use and positive cultures did not influence the rate of true infections [5]. Another study reported a 23.9% UPC rate after revision shoulder arthroplasty with standardized UPC treatment of 6 weeks antibiotics or 2 weeks antibiotics at surgeon discretion. They found only 1 recurrent infection in the UPC group, 3.5% versus 3.4% in the non-UPC group [6]. Another study reported 8/28 (29%) UPC rate after revision shoulder arthroplasty and only treated one with antibiotics postoperatively for 4 weeks (due to superficial wound infection). Of 8 patients, 2 (25%) developed late clinical infection with *C. acnes* [7]. The last study reported a 49% positive culture rate after revision shoulder arthroplasty and treated patients based on a protocol of 6 weeks intravenous (IV) and 6 months of oral antibiotics if > 2 cultures were positive. No patients (0%) had recurrence of infection with this protocol for the positive culture group and negative culture groups [8]. Two studies reported a 19-42% complication side-effect rate from prolonged antibiotic use which was seen in both oral and IV medication use [4,8]. The vast majority (> 80%) of UPCs were *C. acnes* or Coagulase-negative *Staphlococcus* organisms and, therefore, meaningful comparisons to other more virulent organisms could not be performed.

Recent recommendations from the World Health Organization and the Centers for Disease Control and Prevention suggest a single perioperative dose is adequate for clean and clean-contaminated procedures [11,12]. One meta-analysis included 69 randomized controlled trials and did not demonstrate a difference in the odds of surgical site infection with a single intraoperative dose compared to multiple doses of postoperative surgical antimicrobial prophylaxis (odds ratio (OR) 0.89; 95% confidence interval (CI) 0.77–1.03) [12]. Encompassing concerns regarding the potential adverse consequences of antimicrobial use, in particular the risk of antimicrobial resistance, the panel made a strong recommendation, based on moderate quality evidence, that surgical antimicrobial prophylaxis should not be extended beyond the completion of the operation [12]. The applicability to unexpected positive cultures was not addressed in the studies.

In aggregate, these retrospective studies show no supporting evidence for routine use of prolonged antibiotic use over no prolonged antibiotic treatment in the setting of UPC after revision shoulder arthroplasty. Specifically, there is no identified evidence to demonstrate earlier preemptive treatment of UPC will ultimately alter outcomes. Patients without true infection may be unnecessarily exposed to a significant course of prolonged antimicrobials. There are well-reported risks of antibiotic-related side-effects and less obvious risks of antibiotic resistance with widespread prescribing. Additionally, there is no supporting evidence that suggests that antibiotic treatment should differ between UPC organisms.

A comprehensive literature review was performed to identify all studies on prophylactic/suppressive antibiotics after revision shoulder arthroplasty. Searches for the terms “shoulder replacement,” “infection,” “antibiotics,” “postoperative” and “joint replacement” were performed using the search engines PubMed and Google Scholar, which were searched through February 2018. Inclusion criteria for our systematic review were all English studies (Level I-IV evidence) that reported on antibiotic prophylaxis, or lack thereof, in cases of revision shoulder arthroplasty. Exclusion criteria were non-English language articles, nonhuman studies, retracted papers, case reports, review papers, studies with less than < 10 patients in the sample size, studies without clinical follow-up/infection rates and technique papers without patient data. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed. Thirty articles met inclusion and exclusion criteria and were reviewed.

REFERENCES

[1] 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. doi:10.1016/j.jse.2014.09.042.

[2] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[3] Brolin TJ, Hackett DJ, Abboud JA, Hsu JE, Namdari S. Routine cultures for seemingly aseptic revision shoulder arthroplasty: are they necessary? J Shoulder Elbow Surg. 2017;26:2060–2066. doi:10.1016/j.jse.2017.07.006.

[4] Grosso MJ, Sabesan VJ, Ho JC, Ricchetti ET, Iannotti JP. Reinfection rates after 1-stage revision shoulder arthroplasty for patients with unexpected positive intraoperative cultures. J Shoulder Elbow Surg. 2012;21:754–758. doi:10.1016/j.jse.2011.08.052.

[5] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:620–627. doi:10.1016/j.jse.2012.07.017.

[6] Padegimas EM, Lawrence C, Narzikul AC, Zmistowski BM, Abboud JA, Williams GR, et al. Future surgery after revision shoulder arthroplasty: the impact of unexpected positive cultures. J Shoulder Elbow Surg. 2017;26:975–981. doi:10.1016/j.jse.2016.10.023.

[7] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.

[8] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.

[9] Kim SJ, Kim JH. Unexpected positive cultures including isolation of Propionibacterium acnes in revision shoulder arthroplasty. Chin Med J. 2014;127:3975–3979.

[10] Frank JM et al. The Mark Coventry, MD, Award: oral antibiotics reduce reinfection after two-stage exchange: a multicenter, randomized controlled trial. Clin Orthop Relat Res. 2017;475(1):56-61.

[11] Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg. 2017;152:784–91. doi:10.1001/jamasurg.2017.0904.

[12] Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis. 2016;16:e288–e303. doi:10.1016/S1473-3099(16)30402-9.

1.2. PREVENTION: INTRAOPERATIVE

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QUESTION 1: Should antibiotic-impregnated cement be used during shoulder arthroplasty (primary and revision)?

RECOMMENDATION: There is insufficient evidence to determine whether antibiotic-impregnated cement should be used during primary or revision shoulder arthroplasty.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

A comprehensive review was performed to identify studies relating to the use of antibiotic impregnated cement in primary and revision shoulder arthroplasty. Searches for the terms "shoulder replacement," "shoulder arthroplasty," "prosthesis infection" and "postoperative infection" were undertaken using the search engines PubMed, Embase and Medline. Inclusion criteria included all systematic reviews, randomized controlled trials, cohort studies, case-controlled studies and case series with more than three patients with periprosthetic shoulder infections. Exclusion criteria consisted of case reports, case series with three or fewer patients with shoulder periprosthetic infection, expert opinions, articles relating to periprosthetic infections of joints other than the shoulder and publications not published in the English literature.

Periprosthetic joint infection (PJI) is relatively rare in shoulder arthroplasty (0.4–2.9%) but can be significantly higher in reverse shoulder arthroplasty [1]. PJI can have devastating implications for the patient and lead to significant cost and care provision challenges to the treating surgical teams. Minimizing the risk of infection is, therefore, imperative and optimization of cement fixation with the use of antibiotic-impregnated cement has been proposed as one such method [2]. Indeed, its use has long been suggested as an effective means of reducing the risk of lower limb arthroplasty infection [3].

In cemented primary shoulder arthroplasty, the choice of cement may be influential in the prevention of prosthetic joint infection. However, there is little reported in the literature on the effects of cement choice. Nowinski et al. [2] authored the only shoulder-specific publication in our literature review in which a primary reverse shoulder arthroplasty was cemented using either antibiotic loaded or plain cement. However, it was a retrospective study of 501 implants, divided into two groups (265 vs. 236), with four surgeons using three different antibiotic and cement combinations for differing primary pathologies. Deep infection was noted in 3% of the plain cement group, but none were reported in the antibiotic cement group. This was statistically significant ($p < 0.001$). However, there is a significant selection bias relating to these groups of patients as they were treated in different facilities by different surgeons, and there is, therefore, a substantial risk of confounding variables. In particular, the group without antibiotic-impregnated cement had over twice as many diagnoses of post-traumatic arthritis ($n = 37$) compared to the group in which antibiotics were used ($n = 16$). There were no cases of humeral loosening or osteolysis in the group with antibiotic-impregnated cement.

In revision shoulder arthroplasty, the revision procedure is often dictated by the cause of failure and the underlying pathology. There is no evidence regarding the use of antibiotic impregnated

cement in managing aseptic loosening with a one-stage prosthesis exchange. However, in the management of PJI, the role of antibiotic loaded cement choice may be dependent upon the type of operative revision: debridement and implant retention, one-stage revision, two-stage revision and resection arthroplasty.

Two publications [4,5] do report a series in which no recurrence of infection was noted following the use of antibiotic impregnated cement during one-stage revision of infected shoulder arthroplasty; however, the sample sizes were small with 16 patients in one cohort and 32 in the other. There was no comparative control group using plain cement, and, as all patients also underwent debridement and postoperative antibiotic therapy, no firm conclusions can be drawn regarding the independent relevance of the cement due to the presence of multiple confounding variables.

REFERENCES

[1] Bohsali KI, Bois AJ, Wirth MA. Complications of shoulder arthroplasty. J Bone Joint Surg Am. 2017;99:256–269. doi:10.2106/JBJS.16.00935.

[2] Nowinski RJ, Gillespie RJ, Shishani Y, Cohen B, Walch G, Gobezie R. Antibiotic-loaded bone cement reduces deep infection rates for primary reverse total shoulder arthroplasty: a retrospective, cohort study of 501 shoulders. J Shoulder Elbow Surg. 2012;21:324–328. doi:10.1016/j.jse.2011.08.072.

[3] Engesaeter LB, Lie SA, Espehaug B, Furnes O, Vollset SE, Havelin LI. Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22,170 primary hip replacements followed 0-14 years in the Norwegian Arthroplasty Register. Acta Orthop Scand. 2003;74:644–651. doi:10.1080/00016470310018135.

[4] Ince A, Seemann K, Frommelt L, Katzer A, Loehr JF. One-stage exchange shoulder arthroplasty for peri-prosthetic infection. J Bone Joint Surg Br. 2005;87:814–818. doi:10.1302/0301-620X.87B6.15920.

[5] Klatte TO, Kendoff D, Kamath AF, Jonen V, Rueger JM, Frommelt L, et al. Single-stage revision for fungal peri-prosthetic joint infection: a single-centre experience. Bone Joint J. 2014;96-B:492–496. doi:10.1302/0301-620X.96B4.32179.

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QUESTION 2: What is the role of topical intrawound antiseptics (dilute betadine lavage, acetic acid or antibiotics added to the irrigation solution) and antibiotic powder (such as vancomycin) during primary or revision shoulder arthroplasty?

RECOMMENDATION: Dilute povidone-iodine and/or vancomycin powder may have a role in patients considered at high-risk for periprosthetic joint infection (PJI) after primary or revision shoulder arthroplasty based on data extrapolated from other orthopaedic specialties.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

There is no data in the shoulder literature specific to the use of specific intrawound antiseptic agents, irrigation solutions or antibiotic powders. Because of this, expert recommendations will have to be inferred from data from spine surgery [1,2], elbow surgery [3] and lower extremity arthroplasty [4]. There are two randomized single-blinded studies that demonstrated the efficacy and safety of dilute betadine irrigation at reducing the risk of infection in spinal surgery [5,6]. Based on a review of this literature, there appear to be advantages associated with the utilization of dilute betadine and vancomycin powder in cases of primary surgery for prevention of surgical site infection and in cases of PJI treatment for prevention of recurrent PJI. However, the data does not consider the risks of development of antimicrobial resistance with use of vancomycin powder. Betadine may have a negative influence on osteoblast proliferation in vitro [7], and so utilization in cases of fracture may not be recommended. While data is lacking specifically for the shoulder, consensus from the hip/knee, trauma and spine groups provide the ability to make some generalized recommendations for primary and revision shoulder surgery.

TABLE 1. Characteristics of studies assessing intrawound agents, irrigation solutions or antiobiotic powders*

Study	Methods	Intrawound Product/Joint	Site	Result
Yan et al. [3]	Retrospective	Vancomycin powder	Elbow	Positive result: 6.4% SSI vs. 0% infection SSI
Riesgo et al. [4]	Retrospective	Dilute povidone-iodine lavage plus vancomycin powder	Lower extremity PJI	Positive result: 16.7% failed vs. 37% failed
Hey et al. [1]	Retrospective cohort comparative	Vancomycin powder	Spine	Positive result: 0.9% SSI vs. 6.3% SSI
Ghobrial et al. [2]	Meta-analysis	Vancomycin powder	Spine	Systematic review: confirms safety
Tomov et al. [8]	Retrospective	Vancomycin powder, betadine	Spine	Positive result: SSI rates were reduced by 50%

* None of these studies evaluated the shoulder specifically. SSI, surgical site infection; PJI, periprosthetic joint infection

A comprehensive literature review was performed to identify all studies examining the use of intrawound antiseptics and antibiotic powder in shoulder arthroplasty. Searches for the terms "intrawound antiseptics shoulder" (0/0), "antibiotic powder shoulder" (3/0), "betadine shoulder" (8/0), "irrigation solution shoulder" (18/1) and "shoulder irrigation infection" (81/0) were performed using the search engines PubMed and Scopus, which were searched through February 2018. Inclusion criteria for our systematic review were all English language studies (Level I-IV evidence) that reported on use of intrawound antiseptics or antibiotic powder in primary or revision shoulder surgery. Exclusion criteria were non-English language articles, nonhuman studies, retracted papers, case reports, review papers, studies with less than 10 patients in the sample size, studies without clinical follow-up/infection rates and technique papers without patient data. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed. We identified zero articles from PubMed and zero articles from Scopus that met all criteria. Given the limited number of articles identified with the search terms used, searches were separately performed to identify studies on intrawound antiseptic and antibiotics powder outside of the shoulder literature.

Of note, the Centers for Disease Control and Prevention released a recommendation on the use of vancomycin in 1995. Due to concerns for development of antimicrobial resistance, routine utilization of vancomycin in prophylaxis has been discouraged. Instead, use of vancomycin is believed to be acceptable for "prophylaxis for major surgical procedures involving implantation of prosthetic materials or devices at institutions that have a high rate of infections caused by methicillin-resistant *Staphylococcus aureus* or methicillin-resistant *S. epidermidis*. A single dose of vancomycin administered immediately before surgery is sufficient unless the procedure lasts greater than six hours, in which case the dose should be repeated. Prophylaxis should be discontinued after a maximum of two doses." This position statement has not been updated recently or amended to include a discussion of vancomycin powder.

REFERENCES

[1] Hey HW, Thiam DW, Koh ZS, Thambiah JS, Kumar N, Lau LL, et al. Is intraoperative local vancomycin powder the answer to surgical site infections in spine surgery? Spine. 2017;42:267–274. doi:10.1097/BRS.0000000000001710.

[2] Ghobrial GM, Cadotte DW, Williams K, Fehlings MG, Harrop JS. Complications from the use of intrawound vancomycin in lumbar spinal surgery: a systematic review. Neurosurg Focus. 2015;39:E11. doi:10.3171/2015.7.FOCUS15258.

[3] Yan H, He J, Chen S, Yu S, Fan C. Intrawound application of vancomycin reduces wound infection after open release of post-traumatic stiff elbows: a retrospective comparative study. J Shoulder Elbow Surg. 2014;23:686–692. doi:10.1016/j.jse.2014.01.049.

[4] Riesgo AM, Park BK, Herrero CP, Yu S, Schwarzkopf R, Iorio R. Vancomycin povidone-iodine protocol improves survivorship of periprosthetic joint infection treated with irrigation and debridement. J Arthroplasty. 2018;33:847–850. doi:10.1016/j.arth.2017.10.044.

[5] Chang FY, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Can povidone-iodine solution be used safely in a spinal surgery? Eur Spine J. 2006;15:1005–1014. doi:10.1007/s00586-005-0975-6.

[6] Cheng MT, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery. Spine. 2005;30:1689–1693.

[7] Newton Ede MP, Philp AM, Philp A, Richardson SM, Mohammad S, Jones SW. Povidone-iodine has a profound effect on in vitro osteoblast proliferation and metabolic function and inhibits their ability to mineralize and form bone. Spine. 2016;41:729–734. doi:10.1097/BRS.0000000000001332.

[8] Tomov M, Mitsunaga L, Durbin-Johnson B, Nallur D, Roberto R. Reducing surgical site infection in spinal surgery with betadine irrigation and intrawound vancomycin powder. Spine. 2015;40:491–499. doi:10.1097/BRS.0000000000000789.

Authors: Jim Kelly, Vani Sabesan, Diego Lima, Michael Rozell

QUESTION 3: Do surgical drains influence the risk of infection in patients undergoing primary or revision shoulder arthroplasty?

RECOMMENDATION: There is no evidence to support routine use of closed-suction drains in patients undergoing shoulder arthroplasty for the prevention of periprosthetic joint infection (PJI).

LEVEL OF EVIDENCE: Limited

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

RATIONALE

We conducted literature search of PubMed for all articles published on closed surgical drains after anatomic total shoulder arthroplasty (TSA) and reverse total shoulder arthroplasty (RTSA) in the primary and revision settings. The exact search queries performed included the following keywords: "surgical drain in shoulder arthroplasty" in Medical Subject Headings (MeSH) Terms, "closed wound drainage in shoulder arthroplasty," "surgical wound drainage in shoulder arthroplasty" on Title/Abstract and in combination. The initial search produced five articles, including both shoulder and elbow arthroplasty, but after reviewing the elbow arthroplasty-related studies, all of these deemed to not provide information relevant for the purposes of this review and were excluded. This left two articles, both of which had their entire manuscripts analyzed thoroughly for relevance and inclusion.

There is a paucity of literature regarding the use of postoperative closed-suction drains and the relationship to infection and PJI after shoulder arthroplasty [1].

There are no current American Academy of Orthopaedic Surgeon (AAOS) clinical practice guidelines (CPG) which comment on the use of a postoperative drain following TSA or RTSA. While very limited literature is available regarding postoperative drain use in TSA or RTSA, there are several studies that have evaluated blood loss, change in hemoglobin, clinical outcomes and complication rates related to the use of drains after total knee arthroplasty (TKA) and total hip arthroplasty (THA) [1].

A level III, case-control study compared 64 patients who underwent TSH and RTSA without the use of a closed-suction drain to 304 patients that had a drain placed. This study found that drain usage was associated with lower postoperative hemoglobin, longer length of stay and lower postoperative simple shoulder test scores [1]. There was no clinically significant difference in the transfusion rates, superficial wound infections or deep infections. As is sometimes reported in the parallel TKA and THA literature evaluating closed suction drainage, there was no mention of hematoma

formation or analgesic requirements when comparing patients with and without drain use [1].

In 2007, a Cochrane Database Systematic Review evaluated 36 studies regarding the use of closed suction surgical wound drainage after orthopaedic surgery and reported only one study specific to shoulder surgeries by Gartsman et al. [2]. This level II, randomized trial evaluated length of hospital stay, wound dehiscence, infection, reoperation rates and hematomas in patients undergoing TSA, hemiarthroplasty, rotator cuff repair and anterior shoulder instability surgery and found no differences between patients who did or did not receive a drain [3].

Overall, there are few available studies, and these are not sufficiently powered to detect a difference in infection rates after shoulder arthroplasty.

REFERENCES

[1] Erickson BJ, Campbell K, Jain A, et al. Are post-operative drains beneficial in total and reverse total shoulder arthroplasty? Orthop Res Traumatol Open J. 2016;1(1):22-27.
[2] Gartsman GM, Milne JC, Russell JA. Closed wound drainage in shoulder surgery. J Shoulder Elbow Surg. 1997;6:288–290.
[3] Parker MJ, Livingstone V, Clifton R, McKee A. Closed suction surgical wound drainage after orthopaedic surgery. Cochrane Database Syst Rev. 2007:CD001825. doi:10.1002/14651858.CD001825.pub2.

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QUESTION 4: What is the role of tranexamic acid (TXA) during primary or revision shoulder arthroplasty (SA) in decreasing the risk of periprosthetic joint infection (PJI)?

RECOMMENDATION: There is no evidence to support routine use of TXA in patients undergoing shoulder arthroplasty for the prophylaxis of PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Patients undergoing SA may experience variable degrees of perioperative bleeding and blood loss, which in the most severe cases, may result in complications including hematoma formation [1], acute symptomatic anemia and the need for blood transfusions [2–4]. It has been suggested that there is an association between blood transfusion and wound hematomas with postoperative morbidity, including periprosthetic infection [5,6]. While hematomas requiring surgery are uncommon with a reported rate of 0.3% [5], blood transfusions are more common with a reported rate of 4.3% to 6.7%. [3,4,7,8] Besides the costs, allogeneic blood transfusion is associated with rare but serious complications, including allergic and immune-mediated reactions, hemodynamic overload and risk of blood borne infections [9]. In addition, allogeneic blood transfusions may have an immunomodulatory effect [10] that may predispose to increased risk of periprosthetic infection rate, as seen in total hip or total knee arthroplasty [11] as well as in SA [6].

TXA is a synthetic anti-fibrinolytic agent that has been shown to be a successful and cost-effective agent for reducing blood loss and transfusion requirements for patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA) [12]. Two recent meta-analyses [13,14] of TXA use in patients undergoing primary SA found that TXA is an effective intervention to decrease blood loss as measured by drain output, change in hemoglobin (Hb) and total calculated blood loss. Nevertheless, the effectiveness of TXA in reducing transfusion rates after SA has been conflicting. One meta-analysis reported a benefit of TXA [14] in reducing blood transfusion while a second reported no differences in the transfusion rate when TXA was used perioperatively [13]. Possible reasons for conflicting results are (1) the inclusion of non-randomized studies with biased methodology, (2) a high rate of included studies with zero events of transfusion that were excluded from the calculation of the pooling effect and (3) when there are findings that are not conclusive, there is a lack of an additional analysis to further determine the conclusiveness of the results given the low rate of events. As a result, in order to evaluate the effectiveness of TXA to reduce transfusion rates, we performed a new systematic review and meta-analysis that included only randomized controlled trials (RCT), which compared the use of TXA compared to placebo in patients undergoing SA. This meta-analysis considered the primary outcomes to be the effect of TXA upon transfusion rates, formation of hematomas and thromboembolic events. Secondary outcomes included blood loss as measured by drain output, change of Hb and calculated total blood loss.

Methods

The methodology described in the Cochrane Handbook for Systematic Reviews of Interventions [15] was followed to conduct this review and was reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [16]. Cochrane Central Register of Controlled Trials, Embase and Medline were searched up to March 15, 2018. Four RCTs [17–20] involving 375 patients undergoing primary SA were included. The risk of bias of the included studies was assessed and the pooled risk estimates were calculated with random-effect models. For the primary outcomes (transfusion rate and thromboembolic complications), as most of the trials had no events in the tranexamic acid or control group (zero-event studies), a 0.5 continuity correction was used to include data from those RCTs [21]. A trial sequence analysis was conducted to assist in the interpretation of the conclusiveness of the meta-analysis for the effect of TXA in the risk of blood transfusions. The quality of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results

This meta-analysis confirmed previous meta-analysis results and found that TXA is associated with significantly lower perioperative blood loss compared with placebo and that there is no higher risk of thromboembolic events with TXA (Table 1). However, this meta-analysis found that there was no significant difference for the risk of

TABLE 1. Summary of findings

Outcome No. of Participants (Studies)	Relative Effect (95% CI)	Anticipated Absolute Effects (95% CI)			Certainty
		Without TXA	With TXA	Difference	
Rate of blood transfusion (Transfusion) assessed with: Number of patients who received a postoperative transfusion of packed red blood cells No. of participants: 375 (4 RCTs)	**RR 0.53** (0.17 to 1.64)	**Study population**			⊕⊕ O O LOW [a,b]
		3.7%	**2.0%** (0.6% to 6.1%)	**1.8% fewer** (3.1% fewer to 2.4% more)	
		Low-risk transfusion patients*			
		1.0%	**0.5%** (0.2% to 1.6%)	**0.5% fewer** (0.8% fewer to 0.6% more)	
		High-risk transfusion patients*			
		15.0%	**8.0%** (2.6% to 24.6%)	**7.0% fewer** (12.4% fewer to 9.6% more)	
Thromboembolic complications (TEC) assessed with: Number of patients that developed a thromboembolic complication during follow-up (DVT, PE, Stroke) No. of participants: 375 (4 RCTs)	**RR 0.70** (0.11 to 4.38)	0.5%	**0.4%** (0.1% to 2.3%)	**0.2% fewer** (0.5% fewer to 1.8% more)	⊕⊕⊕O MODERATE
Total blood loss (TBL) assessed with: Estimation of total blood loss with Good's and Nadler's formula No. of participants: 264 (3 RCTs)	-	The mean total blood loss was **1344** ml	-	MD **279.5 ml lower** (411.7 ml lower to 147.3 ml lower)	⊕⊕⊕⊕ HIGH
Postoperative blood loss (PBL) assessed with: Drain output in milliliters (first 24 hours) follow up: mean 1 days No. of participants: 267 (3 RCTs)	-	The mean postoperative blood loss was **216** ml	-	MD **105.4 ml lower** (161.4 ml lower to 49.4 ml lower)	⊕⊕⊕⊕ HIGH
Decrease in hemoglobin (Hemoglobin change) assessed with: Change of preoperative versus lower postoperative hemoglobin (g/dL) No. of participants: 267 (3 RCTs)	-	The mean decrease in hemoglobin was **3.32** g/dL	-	MD **0.7 g/dL lower** (1 g/dL lower to 0.39 g/dL lower)	⊕⊕⊕⊕ HIGH

CI, confidence interval; RCT, randomized control trials; TXA, tranexamic acid

* These numbers were estimated from the literature, considering the rate of transfusion along with a low and high risk of transfusion.

a. The confidence interval crosses the clinical decision threshold between recommending and not recommending tranexamic acid (RR=1 meaning no difference in the rate of transfusion between tranexamic acid and placebo).

b. The accrued sample size of the meta-analysis is underpowered. The estimated optimal sample size with an alpha error of 5%, 80% of power and RRR of 57.4% with a basal risk of 3.7%, was 1555 patients.

Hematoma formation was assessed as an outcome, but it was not included in this table as there were only one trial that reported results.

blood transfusion after SA when comparing TXA with placebo (risk rate 0.53, 95% confidence interval 0.17 to 1.64). Due to the fact that the rate of transfusion after SA is low, the current data is too sparse to provide conclusive evidence for the effect of TXA on blood transfusions. In addition, there is insufficient evidence for the effect of TXA upon hematoma formation or other clinical outcomes after SA.

Conclusion

While this meta-analysis confirmed the effect of TXA in decreasing blood loss, the evidence for its effects on direct clinically important outcomes like rate of transfusions or hematoma formation was inconclusive. Blood loss is a surrogate outcome and there are no defined thresholds to associate a determined amount of blood loss to those clinically important outcomes.

The use of TXA in patients at high risk for transfusion or patients undergoing complex revision arthroplasty has not been adequately studied. Patients at high risk for transfusions include those with low preoperative Hb and hematocrit levels (Hb < 13 g/dL and hematocrit < 39.6%) [3,7,8,22,23], operative time longer than 5 hours [24], surgery with a diagnosis of posttraumatic or rheumatoid arthritis [2,3], and patients with diabetes or ischemic heart disease [8,24]. The use of TXA in these at-risk populations might be justified given the higher baseline risk of transfusion and the greater impact of blood loss. However, this is a recommendation that is weak and limited by the lack of direct evidence. Further study of TXA in these higher risk patients is warranted.

REFERENCES

[1] Cheung EV, Sperling JW, Cofield RH. Infection associated with hematoma formation after shoulder arthroplasty. Clin Orthop Relat Res. 2008;466:1363–1367. doi:10.1007/s11999-008-0226-3.

[2] Sperling JW, Duncan SFM, Cofield RH, Schleck CD, Harmsen WS. Incidence and risk factors for blood transfusion in shoulder arthroplasty. J Shoulder Elbow Surg. 2005;14:599–601. doi:10.1016/j.jse.2005.03.006.

[3] Padegimas EM, Clyde CT, Zmistowski BM, Restrepo C, Williams GR, Namdari S. Risk factors for blood transfusion after shoulder arthroplasty. Bone Joint J. 2016;98-B:224–228. doi:10.1302/0301-620X.98B2.36068.

[4] Ryan DJ, Yoshihara H, Yoneoka D, Zuckerman JD. Blood transfusion in primary total shoulder arthroplasty: incidence, trends, and risk factors in the United States from 2000 to 2009. J Shoulder Elbow Surg. 2015;24:760–765. doi:10.1016/j.jse.2014.12.016.

[5] Cheung EV, Sperling JW, Cofield RH. Infection associated with hematoma formation after shoulder arthroplasty. Clin Orthop Relat Res. 2008;466:1363–1367. doi:10.1007/s11999-008-0226-3.

[6] Grier AJ, Bala A, Penrose CT, Seyler TM, Bolognesi MP, Garrigues GE. Analysis of complication rates following perioperative transfusion in shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:1203–1209. doi:10.1016/j.jse.2016.11.039.

[7] Anthony CA, Westermann RW, Gao Y, Pugely AJ, Wolf BR, Hettrich CM. What are risk factors for 30-day morbidity and transfusion in total shoulder arthroplasty? A review of 1922 cases. Clin Orthop Relat Res. 2015;473:2099–2105. doi:10.1007/s11999-014-4107-7.

[8] Kandil A, Griffin J, Novicoff W, Brockmeier S. Blood transfusion after total shoulder arthroplasty: which patients are at high risk? Int J Shoulder Surg. 2016;10:72. doi:10.4103/0973-6042.180719.

[9] Nielsen HJ. Detrimental effects of perioperative blood transfusion. Br J Surg. 1995;82:582–587.

[10] Raghavan M, Marik PE. Anemia, allogenic blood transfusion, and immunomodulation in the critically ill. Chest. 2005;127:295–307. doi:10.1378/chest.127.1.295.

[11] Friedman R, Homering M, Holberg G, Berkowitz SD. Allogeneic blood transfusions and postoperative infections after total hip or knee arthroplasty. J Bone Joint Surg. 2014;96:272–278. doi:10.2106/JBJS.L.01268.

[12] Melvin JS, Stryker LS, Sierra RJ. Tranexamic acid in hip and knee. J Am Acad Orthop Surg. 2015;23(12):732–740. doi:10.5435/JAAOS-D-14-00223.

[13] Kirsch JM, Bedi A, Horner N, Wiater JM, Pauzenberger L, Koueiter DM, et al. Tranexamic acid in shoulder arthroplasty a systematic review and meta-analysis. JBJS Rev. 2017;5:1–11. doi:10.2106/JBJS.RVW.17.00021.

[14] Kuo LT, Hsu WH, Chi CC, Yoo JC. Tranexamic acid in total shoulder arthroplasty and reverse shoulder arthroplasty: a systematic review and meta-analysis. BMC Musculoskelet Disord. 2018;19:60. doi:10.1186/s12891-018-1972-3.

[15] Higgins JPT, Green S (editors). Cochrane handbook for systematic reviews of interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011.

[16] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009;6(7):e1000100. doi:10.1371/journal.pmed.1000100.

[17] Gillespie R, Shishani Y, Joseph S, Streit JJ, Gobezie R. Neer Award 2015: a randomized, prospective evaluation on the effectiveness of tranexamic acid in reducing blood loss after total shoulder arthroplasty. J Shoulder Elbow Surg. 2015;24:1679–1684. doi:10.1016/j.jse.2015.07.029.

[18] Vara AD, Koueiter DM, Pinkas DE, Gowda A, Wiater BP, Wiater JM. Intravenous tranexamic acid reduces total blood loss in reverse total shoulder arthroplasty: a prospective, double-blinded, randomized, controlled trial. J Shoulder Elbow Surg. 2017;26:1383–1389. doi:10.1016/j.jse.2017.01.005.

[19] Pauzenberger L, Domej MA, Heuberer PR, Hexel M, Grieb A, Laky B, et al. The effect of intravenous tranexamic acid on blood loss and early post-operative pain in total shoulder arthroplasty. Bone Joint J 2017;99-B:1073–1079. doi:10.1302/0301-620X.99B8.BJJ-2016-1205.R1.

[20] Cvetanovich GL, Fillingham YA, O'Brien M, Forsythe B, Cole BJ, Verma NN, et al. Tranexamic acid reduces blood loss after primary shoulder arthroplasty: a double-blind, placebo-controlled, prospective, randomized controlled trial. JSES Open Access. 2018;2(1):23–27. doi:10.1016/j.jses.2018.01.002.

[21] Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ Online. 2011;343:1–9. doi:10.1136/bmj.d5928.

[22] Millett PJ, Porramatikul M, Chen N, Zurakowski D, Warner JJP. Analysis of transfusion predictors in shoulder arthroplasty. J Bone Joint Surg Am. 2006;88:1223–1230. doi:10.2106/JBJS.E.00706.

[23] Makhni EC, Trofa DP, Watling JP, Bobman JT, Bigliani LU, Jobin CM, et al. Risk factors associated with blood transfusion after shoulder arthroplasty. JSES Open Access. 2017;1:10–14. doi:10.1016/j.jses.2017.03.004.

[24] Ahmadi S, Lawrence TM, Sahota S, Schleck CD, Harmsen WS, Cofield RH, et al. The incidence and risk factors for blood transfusion in revision shoulder arthroplasty: our institution's experience and review of the literature. J Shoulder Elbow Surg. 2014;23:43–48. doi:10.1016/j.jse.2013.03.010.

1.3. PREVENTION: PATIENT CHARACTERISTICS

Authors: Brent Morris, Joseph J. King

QUESTION 1: What is the role of medical comorbidities as potential risk factors for periprosthetic joint infection (PJI) following primary or revision total shoulder arthroplasty (TSA)?

RECOMMENDATION: Specific patient medical comorbidities and demographic factors are potential risk factors for shoulder PJI and appropriate preoperative evaluation and perioperative management should be standard practice.

LEVEL OF EVIDENCE: Moderate

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

RATIONALE

PJI after both primary and revision shoulder arthroplasty remains a challenging and costly problem. It is important to recognize medical comorbidities as well as demographic factors that may be risk factors for shoulder PJI. Medical comorbidities can negatively impact surgical outcomes and lead to an increased risk of complications; however, there is limited evidence specifically linking medical comorbidities and shoulder PJI. There are some helpful general measures of health, including American Society of Anesthesiologist (ASA) grading, Charlson Comorbidity Index (CCI) and Functional Comorbidity Index (FCI), among others. These indices can often be linked to surgical outcomes and PJI, including shoulder PJI [1].

A literature review was performed to identify all studies regarding medical comorbidities and demographic factors that may be risk factors for shoulder PJI. Search terms "shoulder replacement," "shoulder arthroplasty," "infection," "comorbidities" and "risk factors" were utilized for PubMed and Google Scholar searches through February 18, 2018. All abstracts were reviewed and full text article review was completed for screening of relevant articles. Ultimately, 13 studies were included for final analysis.

Medical comorbidities that have been shown to be potential risk factors for shoulder PJI include American Society of Anesthesiologists (ASA) grade III or higher [1], rheumatoid arthritis [2], long term corticosteroid use [2], current and former smokers [3], Hepatitis C virus [4], HIV-positive [5], weight loss/nutritional deficiency [6], drug abuse [6] and iron deficiency [7].

Increased body mass index greater than or equal to 35 kg/m^2 has been associated with increased superficial wound infection but was not shown to be associated with shoulder PJI [8]. Patient demographic factors that have been shown to be risk factors for shoulder PJI include younger age [6,7,9–11] and male gender [6,8–11].

There is a limited but growing body of literature to support medical comorbidities and demographic factors that are potential risk factors for shoulder PJI. It is important to recognize and treat potentially modifiable medical comorbidities as well as counsel patients regarding additional non-modifiable comorbidities and demographic factors.

REFERENCES

[1] Nagaya LH, Salles MJC, Takikawa LSC, Fregoneze M, Doneux P, Silva LA da, et al. Infections after shoulder arthroplasty are correlated with higher anesthetic risk score: a case-control study in Brazil. Braz J Infect Dis. 2017;21:613–619. doi:10.1016/j.bjid.2017.06.003.

[2] Everhart JS, Bishop JY, Barlow JD. Medical comorbidities and perioperative allogeneic red blood cell transfusion are risk factors for surgical site infection after shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:1922–1930. doi:10.1016/j.jse.2017.04.006.

[3] Hatta T, Werthel JD, Wagner ER, Itoi E, Steinmann SP, Cofield RH, et al. Effect of smoking on complications following primary shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:1–6. doi:10.1016/j.jse.2016.09.011.

[4] Cancienne JM, Dempsey IJ, Holzgrefe RE, Brockmeier SF, Werner BC. Is hepatitis C infection associated with a higher risk of complications after total shoulder arthroplasty? Clin Orthop Relat Res. 2016;474:2664–2669. doi:10.1007/s11999-016-4979-9.

[5] Bala A, Penrose CT, Visgauss JD, Seyler TM, Randell TR, Bolognesi MP, et al. Total shoulder arthroplasty in patients with HIV infection: complications, comorbidities, and trends. J Shoulder Elbow Surg. 2016;25:1971–1979. doi:10.1016/j.jse.2016.02.033.

[6] Padegimas EM, Maltenfort M, Ramsey ML, Williams GR, Parvizi J, Namdari S. Periprosthetic shoulder infection in the United States: incidence and economic burden. J Shoulder Elbow Surg. 2015;24:741–746. doi:10.1016/j.jse.2014.11.044.

[7] Morris BJ, O'Connor DP, Torres D, Elkousy HA, Gartsman GM, Edwards TB. Risk factors for periprosthetic infection after reverse shoulder arthroplasty. J Shoulder Elbow Surg. 2015;24:161–166. doi:10.1016/j.jse.2014.05.020.

[8] Wagner ER, Houdek MT, Schleck C, Harmsen WS, Sanchez-Sotelo J, Cofield R, et al. Increasing body mass index is associated with worse outcomes after shoulder arthroplasty. J Bone Joint Surg Am. 2017;99:929–937. doi:10.2106/JBJS.15.00255.

[9] Richards J, Inacio MCS, Beckett M, Navarro RA, Singh A, Dillon MT, et al. Patient and procedure-specific risk factors for deep infection after primary shoulder arthroplasty. Clin Orthop Relat Res. 2014;472:2809–2815. doi:10.1007/s11999-014-3696-5.

[10] Werthel JD, Hatta T, Schoch B, Cofield R, Sperling JW, Elhassan BT. Is previous nonarthroplasty surgery a risk factor for periprosthetic infection in primary shoulder arthroplasty? J Shoulder Elbow Surg. 2017;26:635–640. doi:10.1016/j.jse.2016.10.020.

[11] Singh JA, Sperling JW, Schleck C, Harmsen WS, Cofield RH. Periprosthetic infections after total shoulder arthroplasty: a 33-year perspective. J Shoulder Elbow Surg. 2012;21:1534–1541. doi:10.1016/j.jse.2012.01.006.

Authors: Mark Frankle, Jason Hsu

QUESTION 2: Does previous shoulder surgery (arthroscopic or open non-arthroplasty) increase the risk of periprosthetic joint infection (PJI)?

RECOMMENDATION: Previous ipsilateral non-arthroplasty shoulder surgery likely increases the risk of shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Due to the inability of skin preparation solutions [1–3] and antibiotics [3–5] to eradicate bacteria (e.g., *Cutiibacterium acnes*) living underneath the skin surface, transection of the dermal structures leads to inoculation of bacteria into the deep tissues [6]. Therefore, previous non-arthroplasty surgery theoretically may increase the risk of PJI.

To answer this question, we performed a systematic review using the following search phrase: ("previous" OR "history of") AND "shoulder arthroplasty" AND ("infection" OR "culture"). Thirty-nine results were filtered by title and abstract, and reference lists were reviewed for relevant studies. Studies were included for analysis if they compared infection rates for shoulder arthroplasty in a group of patients with and without history of previous non-arthroplasty surgery. Studies that included previous arthroplasty (rather than non-arthroplasty) surgery as a risk factor were excluded.

Two studies have addressed the question of whether previous non-arthroplasty surgery increased the risk for shoulder PJI. Werthel et al. [7] looked at non-arthroplasty surgery as a risk factor for PJI and found that previous non-arthroplasty surgery was a risk factor for deep infection after both a univariate ($p = 0.0094$) and a multivariate analysis ($p = 0.0390$). An increased number of previous surgeries was associated with a greater risk of deep infection ($p = 0.272$).

Florschütz et al. [8] also reported that patients undergoing primary total shoulder with history of previous non-arthroplasty surgery had a significantly higher (p = 0.016) rates of infection compared to patients with no previous surgery on the operative shoulder.

A few other studies not aimed directly at answering this question directly support this conclusion. Foruria et al. [9] studied 107 patients with unexpected positive cultures at revision shoulder arthroplasty and found that the number of previous surgeries was higher in patients deemed to have "true infections" compared to "contaminants" (p = 0.025) (it is unclear if these were arthroplasty or non-arthroplasty surgeries). Horneff et al. [10] found that patients undergoing revision arthroscopic surgery had a significantly higher rate of positive culture growth than those undergoing primary arthroscopic surgery (29.4% vs. 3.2%). Zavala et al. [11] reported on their experience with deep infection after reverse shoulder arthroplasty and found an overall infection rate of 6% and an infection rate of 12.9% for those who had previous failed cuff surgery.

REFERENCES

[1] Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA. Propionibacterium persists in the skin despite standard surgical preparation. J Bone Joint Surg Am. 2014;96:1447–1450. doi:10.2106/JBJS.M.01474.

[2] Saltzman MD, Nuber GW, Gryzlo SM, Marecek GS, Koh JL. Efficacy of surgical preparation solutions in shoulder surgery. J Bone Joint Surg Am. 2009;91:1949–1953. doi:10.2106/JBJS.H.00768.

[3] Phadnis J, Gordon D, Krishnan J, Bain GI. Frequent isolation of Propionibacterium acnes from the shoulder dermis despite skin preparation and prophylactic antibiotics. J Shoulder Elbow Surg. 2016;25:304–310. doi:10.1016/j.jse.2015.08.002.

[4] 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;26:1495–1499. doi:10.1016/j.jse.2017.06.039.

[5] 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;24:844–847. doi:10.1016/j.jse.2014.10.016.

[6] Falconer TM, Baba M, Kruse LM, Dorrestijn O, Donaldson MJ, Smith MM, et al. Contamination of the surgical field with Propionibacterium acnes in primary shoulder arthroplasty. J Bone Joint Surg Am. 2016;98:1722–1728. doi:10.2106/JBJS.15.01133.

[7] Werthel JD, Hatta T, Schoch B, Cofield R, Sperling JW, Elhassan BT. Is previous nonarthroplasty surgery a risk factor for periprosthetic infection in primary shoulder arthroplasty? J Shoulder Elbow Surg. 2017;26:635–640. doi:10.1016/j.jse.2016.10.020.

[8] Florschütz AV, Lane PD, Crosby LA. Infection after primary anatomic versus primary reverse total shoulder arthroplasty. J Shoulder Elbow Surg. 2015;24:1296–1301. doi:10.1016/j.jse.2014.12.036.

[9] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:620–627. doi:10.1016/j.jse.2012.07.017.

[10] Horneff JG, Hsu JE, Voleti PB, O'Donnell J, Huffman GR. Propionibacterium acnes infection in shoulder arthroscopy patients with postoperative pain. J Shoulder Elbow Surg. 2015;24:838–843. doi:10.1016/j.jse.2015.03.008.

[11] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. J Shoulder Elbow Surg. 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.

Authors: Mark Frankle, Jason Hsu

QUESTION 3: Does prior corticosteroid injection increase the risk of periprosthetic joint infection (PJI) after primary or revision shoulder arthroplasty?

RECOMMENDATION: An increased number of corticosteroid injections and a shorter interval between corticosteroid injection and shoulder arthroplasty may increase the risk for surgical site infection or shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

It is well-documented that usual skin preparation solutions do not adequately penetrate below the skin surface to eliminate bacteria, such as *Cutibacterium* [1,2]. Therefore, any instrument transecting the skin surface and sebaceous glands can theoretically inoculate the deep tissues [3].

To answer the question of whether corticosteroid injections increase the risk for surgical site infection/PJI, we performed a systematic review using the following search phrase: ("corticosteroid" OR "steroid" OR "cortisone") AND "shoulder" AND ("arthroplasty" OR "replacement"). Fifty-two results were filtered by title and abstract, and reference lists were reviewed for relevant studies. Studies were included for analysis if they were a study on primary or revision shoulder arthroplasty and studied preoperative injections as a risk factor.

A total of four studies have directly investigated the effect of previous steroid injection on the shoulder – one database study, one clinical study and two studies investigating deep cultures.

Werner et al. [4] performed a Medicare database study that compared three groups: arthroplasty within three months after injection, arthroplasty within three and 12 months after injection and a control group. Infection was defined by ICD-9 and CPT codes for both superficial and deep infection. The odds ratio for infection after arthroplasty was 2.0 at both three months (p = 0.007) and six months (p = 0.001) in patients who underwent injection within three months of arthroplasty and controls. No statistical difference was seen comparing those patients who underwent injection 3-12 months prior to arthroplasty and the control group. This study suggests that patients undergoing arthroplasty within three months after injection have a higher risk of infection.

Rashid et al. [5] performed a retrospective matched cohort study of 23 patients undergoing shoulder arthroplasty with history of preoperative intra-articular corticosteroid injection and 60 patients without a history of injection. None of the patients in either group had a superficial surgical site infection, and only one of the patients had a deep surgical site infection (defined as obvious purulence).

Two other studies have investigated the rate of positive deep cultures at the time of primary open shoulder surgery in patients that have and patients that have not had previous corticosteroid injections. Mook et al. [6] prospectively collected data on 104 patients undergoing open shoulder surgery at which time control

and pericapsular tissue samples were cultured. A history of two or more corticosteroid injections had a higher likelihood of bacterial growth than those with one or less injections ($p = 0.047$). Koh et al. [7] retrospectively analyzed 30 patients undergoing primary shoulder arthroplasty at which time superficial and deep wound swabs were taken. Steroid injection was not statistically significantly associated with positive deep cultures ($p = 0.14$), and the presence of hair in conjunction with previous steroid injection was not statistically significant ($p = 0.092$).

While the evidence in the hip arthroplasty literature is somewhat conflicting [8–10], multiple recent studies from the knee arthroplasty literature support the conclusion that corticosteroid injections before arthroplasty increase the risk for PJI [11,12].

REFERENCES

[1] Saltzman MD, Nuber GW, Gryzlo SM, Marecek GS, Koh JL. Efficacy of surgical preparation solutions in shoulder surgery. J Bone Joint Surg Am. 2009;91:1949–1953. doi:10.2106/JBJS.H.00768.

[2] Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA. Propionibacterium persists in the skin despite standard surgical preparation. J Bone Joint Surg Am. 2014;96:1447–1450. doi:10.2106/JBJS.M.01474.

[3] Falconer TM, Baba M, Kruse LM, Dorrestijn O, Donaldson MJ, Smith MM, et al. Contamination of the surgical field with Propionibacterium acnes in primary shoulder arthroplasty. J Bone Joint Surg Am. 2016;98:1722–1728. doi:10.2106/JBJS.15.01133.

[4] Werner BC, Cancienne JM, Burrus MT, Griffin JW, Gwathmey FW, Brockmeier SF. The timing of elective shoulder surgery after shoulder injection affects postoperative infection risk in Medicare patients. J Shoulder Elbow Surg. 2016;25:390–397. doi:10.1016/j.jse.2015.08.039.

[5] Rashid A, Kalson N, Jiwa N, Patel A, Irwin A, Corner T. The effects of pre-operative intra-articular glenohumeral corticosteroid injection on infective complications after shoulder arthroplasty. Shoulder Elbow. 2015;7:154–156. doi:10.1177/1758573214557149.

[6] 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 Joint Surg Am. 2015;97:957–963. doi:10.2106/JBJS.N.00784.

[7] Koh CK, Marsh JP, Drinković D, Walker CG, Poon PC. Propionibacterium acnes in primary shoulder arthroplasty: rates of colonization, patient risk factors, and efficacy of perioperative prophylaxis. J Shoulder Elbow Surg. 2016;25:846–852. doi:10.1016/j.jse.2015.09.033.

[8] McIntosh AL, Hanssen AD, Wenger DE, Osmon DR. Recent intraarticular steroid injection may increase infection rates in primary THA. Clin Orthop Relat Res. 2006;451:50–54. doi:10.1097/01.blo.0000229318.51254.79.

[9] Meermans G, Corten K, Simon J-P. Is the infection rate in primary THA increased after steroid injection? Clin Orthop Relat Res. 2012;470:3213–3219. doi:10.1007/s11999-012-2390-8.

[10] Pereira LC, Kerr J, Jolles BM. Intra-articular steroid injection for osteoarthritis of the hip prior to total hip arthroplasty: is it safe? a systematic review. Bone Joint J. 2016;98-B:1027–1035. doi:10.1302/0301-620X.98B8.37420.

[11] Bedard NA, Pugely AJ, Elkins JM, Duchman KR, Westermann RW, Liu SS, et al. The John N. Insall Award: do intraarticular injections increase the risk of infection after TKA? Clin Orthop Relat Res. 2017;475:45–52. doi:10.1007/s11999-016-4757-8.

[12] Cancienne JM, Werner BC, Luetkemeyer LM, Browne JA. Does timing of previous intra-articular steroid injection affect the post-operative rate of infection in total knee arthroplasty? J Arthroplasty. 2015;30:1879–1882. doi:10.1016/j.arth.2015.05.027.

1.4. PREVENTION: SKIN PREPARATION

Authors: Ben Clark, Vani Sabesan, Arjun Meiyappan

QUESTION 1: Is there a role for preoperative skin scrub (home scrubs and washes) prior to primary or revision shoulder arthroplasty?

RECOMMENDATION: Chlorhexidine gluconate (CHG) showers or cleansing wipes with at least two applications decreases the incidence of positive skin cultures prior to shoulder surgery. Pending further research, this protocol may provide a benefit.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

A systematic review of the published literature was performed on Scopus, PubMed and Cochrane databases that included any primary or secondary aims regarding preoperative skin prep for shoulder arthroplasty. A comprehensive review and list were accumulated and review was done to include all relevant studies that met these specific criteria.

Surgical site infections (SSIs) account for 14-16% of all nosocomial infections [1]. In an effort to reduce SSI's, protocols have incorporated whole body showering or bathing with CHG and other antiseptics. The aim is to cleanse the skin and reduce the cutaneous bacterial load prior to surgery. Previous studies have found reduced bacterial counts after use of chlorhexidine baths or washes with increased effect after multiple applications [2].

However, there has been much debate on this issue with various organizations expressing different views on the matter. The Centers for Disease Control and Prevention (CDC) has indicated that either soap or other antiseptic agents are equally efficacious as CHG. While the hospital infection control practice advisory committee – CDC recommend that patients shower at least one time with any kind antiseptic. Finally, the Institute for Healthcare Improvements – Project JOINTS recommends that patients should bathe or shower with CHG soap for at least three days prior to surgery [3].

Multiple interventional studies have investigated the use of preadmission CHG showers. Eiselt et al. focused on preoperative CHG cloths twice prior to total joint procedures and found that surgical site infections were significantly reduced from 3.19% to 2% when compared to a no wash group this was a significant reduction of 50.2% in SSIs [4]. Johnson et al. studied the use of at home chlorhexidine impregnated skin preparation cloth in decreasing the incidence of deep periprosthetic hip arthroplasty. Of the 1,134 studied, 157 complied with the preoperative chlorhexidine preparation protocol. There was no significant difference in the infection rates between the non-compliant and compliant groups (1.6% infection rate vs. 0% respectively; $p = 0.231$) [5]. Kapadia et al. evalu-

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].

REFERENCES

[1] Smyth ET, Emmerson AM. Surgical site infection surveillance. J Hosp Infect. 2000;45:173–184. doi:10.1053/jhin.2000.0736.

[2] Kaiser AB, Kernodle DS, Barg NL, Petracek MR. Influence of preoperative showers on staphylococcal skin colonization: a comparative trial of antiseptic skin cleansers. Ann Thorac Surg. 1988;45:35–38.

[3] Rubin C, Louthan RB, Wessels E, McGowan MB, Downer S, Maiden J. Chlorhexidine gluconate: to bathe or not to bathe? Crit Care Nurs Q. 2013;36:233–236. doi:10.1097/CNQ.0b013e31828404d1.

[4] Eiselt D. Presurgical skin preparation with a novel 2% chlorhexidine gluconate cloth reduces rates of surgical site infection in orthopaedic surgical patients. Orthop Nurs. 2009;28:141–145. doi:10.1097/NOR.0b013e3181a469db.

[5] Johnson AJ, Daley JA, Zywiel MG, Delanois RE, Mont MA. Preoperative chlorhexidine preparation and the incidence of surgical site infections after hip arthroplasty. J Arthroplasty. 2010;25:98–102. doi:10.1016/j.arth.2010.04.012.

[6] Kapadia BH, Johnson AJ, Daley JA, Issa K, Mont MA. Pre-admission cutaneous chlorhexidine preparation reduces surgical site infections in total hip arthroplasty. J Arthroplasty. 2013;28:490–493. doi:10.1016/j.arth.2012.07.015.

[7] Murray MR, Saltzman MD, Gryzlo SM, Terry MA, Woodward CC, Nuber GW. Efficacy of preoperative home use of 2% chlorhexidine gluconate cloth before shoulder surgery. J Shoulder Elbow Surg. 2011;20:928–933. doi:10.1016/j.jse.2011.02.018.

[8] Edmiston CE, Okoli O, Graham MB, Sinski S, Seabrook GR. Evidence for using chlorhexidine gluconate preoperative cleansing to reduce the risk of surgical site infection. AORN J. 2010;92:509–518. doi:10.1016/j.aorn.2010.01.020.

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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 15th, 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 ChloraPrep™ (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 ChloraPrep™ (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 (prosthe* or implant* or reconstruc* 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 antisepsis 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 (prosthe* or implant* or reconstruc* or replacement* or arthroplast* 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

REFERENCES

[1] Saltzman MD, Nuber GW, Gryzlo SM, Marecek GS, Koh JL. Efficacy of surgical preparation solutions in shoulder surgery. J Bone Joint Surg Am. 2009;91:1949–1953. doi:10.2106/JBJS.H.00768.

[2] Murray MR, Saltzman MD, Gryzlo SM, Terry MA, Woodward CC, Nuber GW. Efficacy of preoperative home use of 2% chlorhexidine gluconate cloth before shoulder surgery. J Shoulder Elbow Surg. 2011;20:928–933. doi:10.1016/j.jse.2011.02.018.

[3] Phadnis J, Gordon D, Krishnan J, Bain GI. Frequent isolation of Propionibacterium acnes from the shoulder dermis despite skin preparation and prophylactic antibiotics. J Shoulder Elbow Surg. 2016;25:304–310. doi:10.1016/j.jse.2015.08.002.

[4] Koh CK, Marsh JP, Drinković D, Walker CG, Poon PC. Propionibacterium acnes in primary shoulder arthroplasty: rates of colonization, patient risk factors, and efficacy of perioperative prophylaxis. J Shoulder Elbow Surg. 2016;25:846–852. doi:10.1016/j.jse.2015.09.033.

[5] 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;24:844–847. doi:10.1016/j.jse.2014.10.016.

[6] 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 Joint Surg Am. 2013;95:e1811-e1817. doi:10.2106/JBJS.L.01733.

[7] MacLean SBM, Phadnis J, Ling CM, Bain GI. Application of dermal chlorhexidine antisepsis is ineffective at reducing Proprionibacterium acnes colonization in shoulder surgery. Shoulder Elbow. 2018. doi:10.1177/1758573218755570.

[8] Lorenzetti AJ, Wongworawat MD, Jobe CM, Phipatanakul WP. Cyanoacrylate microbial sealant may reduce the prevalence of positive cultures in

revision shoulder arthroplasty. Clin Orthop Relat Res. 2013;471:3225–3229. doi:10.1007/s11999-013-2854-5.
[9] 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;26:1190–1195. doi:10.1016/j.jse.2017.03.003.
[10] Sabetta JR, Rana VP, Vadasdi KB, Greene RT, Cunningham JG, Miller SR, et al. Efficacy of topical benzoyl peroxide on the reduction of Propionibacterium acnes during shoulder surgery. J Shoulder Elbow Surg. 2015;24:995–1004. doi:10.1016/j.jse.2015.04.003.
[11] Scheer VM, Bergman Jungeström M, Lerm M, Serrander L, Kalén A. Topical benzoyl peroxide application on the shoulder reduces Propionibacterium acnes: a randomized study. J Shoulder Elbow Surg. 2018;27:957–961. doi:10.1016/j.jse.2018.02.038.
[12] Syed UAM, Seidl AJ, Hoffman RA, Bianchini J, Beredjiklian PK, Abboud JA. Preoperative sterilization preparation of the shoulder: a comparative study evaluating gauze sponge and commercially available applicator prep stick. Arch Bone Joint Surg. 2018;6:34–38.
[13] Marecek GS, Weatherford BM, Fuller EB, Saltzman MD. The effect of axillary hair on surgical antisepsis around the shoulder. J Shoulder Elbow Surg. 2015;24:804–808. doi:10.1016/j.jse.2014.10.007.

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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

cultures) of *C. acnes* skin colonization by day of surgery. The rate of positive cultures from the deep shoulder joint was 3.1% (2/65 patients) with preoperative BPO/C topical treatment, much lower than similar studies which described up to 19.6% positive deep cultures [9,15].

In summary, there is evidence that topical skin treatments can reduce bacterial loads, such as *C. acnes*. However, no studies examined the effect of skin preparations on the most clinically significant end-point—the rate of shoulder PJI. The use of topical BPO with or without clindamycin, whilst encouraging and warranting further study, cannot currently be fully endorsed as standard practice for prevention of shoulder PJI, until further data is available.

REFERENCES

[1] Parvizi J, Gehrke T, Chen AF. Proceedings of the International Consensus on Periprosthetic Joint Infection. Bone Joint J. 2013;95-B:1450–1452. doi:10.1302/0301-620X.95B11.33135.

[2] Richards J, Inacio MCS, Beckett M, Navarro RA, Singh A, Dillon MT, et al. Patient and procedure-specific risk factors for deep infection after primary shoulder arthroplasty. Clin Orthop Relat Res. 2014;472:2809–2815. doi:10.1007/s11999-014-3696-5.

[3] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[4] Koh CK, Marsh JP, Drinković D, Walker CG, Poon PC. Propionibacterium acnes in primary shoulder arthroplasty: rates of colonization, patient risk factors, and efficacy of perioperative prophylaxis. J Shoulder Elbow Surg. 2016;25:846–852. doi:10.1016/j.jse.2015.09.033.

[5] 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;24:844–847. doi:10.1016/j.jse.2014.10.016.

[6] Phadnis J, Gordon D, Krishnan J, Bain GI. Frequent isolation of Propionibacterium acnes from the shoulder dermis despite skin preparation and prophylactic antibiotics. J Shoulder Elbow Surg. 2016;25:304–310. doi:10.1016/j.jse.2015.08.002.

[7] 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(6):9–25.

[8] Seidler EM, Kimball AB. Meta-analysis comparing efficacy of benzoyl peroxide, clindamycin, benzoyl peroxide with salicylic acid, and combination benzoyl peroxide/clindamycin in acne. J Am Acad Dermatol. 2010;63:52–62. doi:10.1016/j.jaad.2009.07.052.

[9] Hsu JE, Bumgarner RE, Matsen FA. Propionibacterium in shoulder arthroplasty: what we think we know today. J Bone Joint Surg Am. 2016;98:597–606. doi:10.2106/JBJS.15.00568.

[10] 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;22:505–511. doi:10.1016/j.jse.2012.07.007.

[11] Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA. Propionibacterium persists in the skin despite standard surgical preparation. J Bone Joint Surg Am. 2014;96:1447–1450. doi:10.2106/JBJS.M.01474.

[12] MacLean SBM, Phadnis J, Ling CM, Bain GI. Application of dermal chlorhexidine antisepsis is ineffective at reducing Proprionibacterium acnes colonization in shoulder surgery. Shoulder Elbow. 2018. doi:10.1177/1758573218755570.

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

[14] Sabetta JR, Rana VP, Vadasdi KB, Greene RT, Cunningham JG, Miller SR, et al. Efficacy of topical benzoyl peroxide on the reduction of Propionibacterium acnes during shoulder surgery. J Shoulder Elbow Surg 2015;24:995–1004. doi:10.1016/j.jse.2015.04.003.

[15] 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;26:1190–1195. doi:10.1016/j.jse.2017.03.003.

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QUESTION 4: Should the subcutaneous and dermal tissues be disinfected during shoulder arthroplasty?

RECOMMENDATION: There is insufficient evidence for or against disinfection of the subcutaneous and dermal tissues during shoulder arthroplasty.

LEVEL OF EVIDENCE: No Evidence

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

RATIONALE

A review of PubMed "(subcutaneous OR irrigation OR disinfection OR topical OR local) AND shoulder AND arthroplasty)" and Google Scholar "shoulder arthroplasty subcutaneous irrigation disinfection topical local" was performed to identify articles comparing strategies for disinfection of the subcutaneous and dermal tissues during shoulder arthroplasty. No such literature was identified. In the absence of specific evidence, basic science research and research in other fields of surgery were reviewed.

Lee et al. [1] performed punch biopsy cultures from the shoulders of volunteers after standard surgical preparation of the skin. Seven of ten subjects revealed positive cultures for *Cutibacterium*. On this basis, the authors concluded that surgical preparation could leave bacteria under the surface of the skin, and further disinfection should be performed.

In a retrospective hip and knee arthroplasty series, Brown et al. [2] compared dilute betadine lavage prior to closure of total hip and knee arthroplasty incisions to controls. The deep infection rate was lower in the group undergoing betadine lavage compared to the control group. In contrast, a similar methodology using chlorhexidine gluconate (CHG) showed no difference between CHG irrigation groups and controls. However, the conclusions may have been confounded by the fact that povidone-iodine was also utilized in the control group [3]. A broader meta-analysis of randomized controlled trials across various surgical specialties found that lavage with dilute betadine reduced the occurrence of surgical site infections in the majority of trials with no reported complications [4].

An intra-articular injection of gentamicin [5] and the application of topical vancomycin powder [6] have also both been described as operative measures to reduce periprosthetic joint infection in shoulder arthroplasty. Although there was no clinical evidence for the use of vancomycin powder in the shoulder, recent literature in the field of spinal surgery has shown a significantly decreased risk of surgical site infection with the use of topical vancomycin

[7]. A retrospective review of 507 shoulder arthroplasty procedures compared 343 patients who received an intra-articular injection of 160 mg gentamycin at the end of surgery to 164 patients who did not; the infection rate in the control cohort was 3% (5 of 164) compared to 0.3% (1 of 343) in the gentamycin cohort [5]. However, the design of the study allowed for bias with confounding variables, including the use of antibiotic impregnated cement, which may have influenced outcomes.

It should be noted that the Centers for Disease Control and Prevention released a recommendation on the use of vancomycin in 1995. Due to concerns for development of antimicrobial resistance, routine utilization of vancomycin in prophylaxis has been discouraged. Instead, use of vancomycin is believed to be acceptable for "prophylaxis for major surgical procedures involving implantation of prosthetic materials or devices at institutions that have a high rate of infections caused by MRSA or methicillin-resistant S. epidermidis." This position statement has not been updated recently or amended to include a discussion of vancomycin powder.

REFERENCES

[1] Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA. Propionibacterium persists in the skin despite standard surgical preparation. J Bone Joint Surg Am. 2014;96:1447–1450. doi:10.2106/JBJS.M.01474.

[2] Brown NM, Cipriano CA, Moric M, Sporer SM, Della Valle CJ. Dilute betadine lavage before closure for the prevention of acute postoperative deep periprosthetic joint infection. J Arthroplasty. 2012;27:27–30. doi:10.1016/j.arth.2011.03.034.

[3] Frisch NB, Kadri OM, Tenbrunsel T, Abdul-Hak A, Qatu M, Davis JJ. Intraoperative chlorhexidine irrigation to prevent infection in total hip and knee arthroplasty. Arthroplasty Today. 2017;3:294–297. doi:10.1016/j.artd.2017.03.005.

[4] Chundamala J, Wright JG. The efficacy and risks of using povidone-iodine irrigation to prevent surgical site infection: an evidence-based review. Can J Surg. 2007;50:473–481.

[5] Lovallo J, Helming J, Jafari SM, Owusu-Forfie A, Donovan S, Minnock C, et al. Intraoperative intra-articular injection of gentamicin: will it decrease the risk of infection in total shoulder arthroplasty? J Shoulder Elbow Surg. 2014;23:1272–1276. doi:10.1016/j.jse.2013.12.016.

[6] Hatch MD, Daniels SD, Glerum KM, Higgins LD. The cost effectiveness of vancomycin for preventing infections after shoulder arthroplasty: a break-even analysis. J Shoulder Elbow Surg. 2017;26:472–477. doi:10.1016/j.jse.2016.07.071.

[7] Thompson GH, Poe-Kochert C, Hardesty CK, Son-Hing J, Mistovich RJ. Does vancomycin powder decrease surgical site infections in growing spine surgery?: a preliminary study. J Bone Joint Surg Am. 2018;100:466–4671. doi:10.2106/JBJS.17.00459.

Diagnosis

2.1. DIAGNOSIS: CULTURE SIGNIFICANCE

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QUESTION 1: What is the relevance of positive cultures in the evaluation for shoulder periprosthetic joint infection (PJI)? What defines a clinically relevant positive culture result(s) versus a culture contaminant?

RECOMMENDATION: Positive cultures in a patient with painful or failed shoulder prosthesis should be considered and treated appropriately based upon the clinical context and diagnostic criteria.

LEVEL OF EVIDENCE: Moderate

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

RATIONALE

A bacterial infection is most rigorously defined as "bacteria doing harm." This definition is not met by either (a) harm without the documentation of bacteria (e.g., a culture-negative draining sinus from fat necrosis or implant material allergy) or (b) bacteria in the absence of harm (e.g., *Cutibacterium* in the sebaceous glands of the normal dermis) [1,2].

Five factors need to be considered when evaluating the results of tissue and explant cultures in a case of suspected periprosthetic shoulder infection.

1. The importance of the denominator [3]; the chances of obtaining positive cultures rises with the number of specimens submitted for culture. For example, if the indication for treatment is two or more positive cultures and if one of three submitted specimens is culture positive, the criterion is not met. If, however, six specimens from the same shoulder are submitted, it is likely that two would be positive and the criterion would be met.
2. The source of the specimen affects the likelihood of a positive culture: explant and tissue specimens are more likely to be culture positive than joint fluid specimens from the same shoulder [4,5].
3. The media used in culturing of a specimen affect the likelihood of the specimen being culture positive. The use of multiple media, including broth and aerobic and anaerobic agar preparations is most likely to reveal the presence of bacteria [5].
4. Cultures are not simply "positive" or "negative." While some positive cultures grow out only one colony on a plate or are only positive in the broth, others have 2+ or more growth on agar plates, indicating a much greater bacterial load [6].

   Shoulders with higher bacterial loads are likely to have a higher percentage of specimens that are culture positive. Specimens with a high bacterial load are likely to have a shorter time to the point when the laboratory reports a positive culture result [7].
5. Cultures reveal the presence of live bacteria. It is important to consider the possibility that the specimen might have been contaminated from the operating room environment by inadvertent contact with the skin, unsterile instruments or accidental exposure in handling in the microbiology laboratory. Several precautions can be helpful in minimizing the risk of specimen contamination, including using new sterile instruments for each specimen, avoiding skin contact with the specimen and culturing sterile specimens (e.g., sponges or swabs opened in the operating room (OR)) to assess the rate of positive control cultures.

Mook et al. [8] reported a 13% positive control culture rate using a sterile sponge exposed to the air in the OR. Sabetta et al. reported a 4% culture positive rate for a cotton swab exposed to air as a control [9]. MacNiven et al. [10] found that 50 control swabs exposed to the air were all negative using a threshold Specimen Propionibacterium (*Cutibacterium*) Value (SPV) of ≥ 1. Because the rate of positivity of control samples obviously varies from center to center, it would seem essential that each shoulder service should periodically submit sterile specimens to determine its rate of positive control cultures.

REFERENCES

[1] 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;24:844–847. doi:10.1016/j.jse.2014.10.016.

[2] Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA. Propionibacterium persists in the skin despite standard surgical preparation. J Bone Joint Surg Am. 2014;96:1447–1450. doi:10.2106/JBJS.M.01474.

[3] Mook WR, Garrigues GE. Diagnosis and management of periprosthetic shoulder infections. J Bone Joint Surg Am. 2014;96:956–965. doi:10.2106/JBJS.M.00402.

[4] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[5] 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 Joint Surg Am. 2013;95:e1811-e1817. doi:10.2106/JBJS.L.01733.

[6] Ahsan ZS, Somerson JS, Matsen FA. Characterizing the Propionibacterium load in revision shoulder arthroplasty: a study of 137 culture-

positive cases. J Bone Joint Surg Am. 2017;99:150–154. doi:10.2106/JBJS.16.00422.
[7] Bossard DA, Ledergerber B, Zingg PO, Gerber C, Zinkernagel AS, Zbinden R, et al. Optimal length of cultivation time for isolation of Propionibacterium acnes in suspected bone and joint infections is more than 7 days. J Clin Microbiol. 2016;54:3043–3049. doi:10.1128/JCM.01435-16.
[8] 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 Joint Surg Am. 2015;97:957–963. doi:10.2106/JBJS.N.00784.
[9] Sabetta JR, Rana VP, Vadasdi KB, Greene RT, Cunningham JG, Miller SR, et al. Efficacy of topical benzoyl peroxide on the reduction of Propionibacterium acnes during shoulder surgery. J Shoulder Elbow Surg. 2015;24:995–1004. doi:10.1016/j.jse.2015.04.003.
[10] MacNiven I, Hsu JE, Neradilek MB, Matsen FAI. Preoperative skin-surface cultures can help to predict the presence of Propionibacterium in shoulder arthroplasty wounds. JBJS Open Access. 2018;3:e0052. doi:10.2106/JBJS.OA.17.00052.

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QUESTION 2: What is the relevance of unexpected positive cultures (UPC) in revision shoulder arthroplasty without clinical or radiographic signs of infection?

RECOMMENDATION: The relevance of unexpected positive cultures is unknown.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

A comprehensive literature review was performed to identify all studies on UPC in shoulders undergoing revision arthroplasty. Searches for the terms "unexpected," "infection," "positive culture," "indolent infection," "gram-positive bacterial infections," "prosthesis-related infections" and "shoulder joint," "shoulder," "arthroplasty," "total joint," "replacement," "periprosthetic," "peri-implant," "shoulder prosthesis" were performed using the search engines PubMed, Embase and Scopus. These searches were conducted on February 2, 2018 and include results published through that time. Inclusion criteria were patients undergoing revision shoulder arthroplasty, with no clinical or radiographic signs of infection, who had positive cultures taken from the shoulder undergoing the revision. Only studies that focused on the potential relevance of these UPCs were included. Only English-language studies that presented original data on more than five patients meeting inclusion criteria were included. For articles with both unexpected positive cultures and known septic revisions, the patients with UPC were included in the review if the data were reported such that patients meeting inclusion could be separated. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed. Fifteen articles met inclusion and exclusion criteria.

At the time of the writing of this document, the definition of a UPC in shoulder arthroplasty revisions has not been fully elucidated, nor has the role of *Cutibacterium acnes*, a commonly identified microorganism. Few studies have been designed to adequately capture this phenomenon as defined above by the inclusion and exclusion criteria, resulting in a challenge to draw any definitive conclusions. The results of studies that report the frequency of UPC and their characteristics are summarized in Table 1 [1–14]. An additional study [15] was also returned that does not provide data appropriate for Table 1, but nonetheless was relevant to this question and is discussed below.

Few studies fully meet the defined inclusion and exclusion criteria, and little consistency exists on the definitions of "unexpected" or even what constitutes a "true positive" culture. Without agreement on this definition, it is exceedingly challenging to compare studies reporting these rates. In some studies, "true positive" was defined as a shoulder that required re-revision whereas in other studies, evidence of an overt infection postoperatively was used. While both outcomes are clinically significant, the association of positive cultures with them cannot be conclusively characterized as causal.

The studies that identified UPC in shoulder arthroplasty revisions report a range from 9–56% of cases [5,6]. Combining the rates of UPCs in these studies yields an incidence of 22.5% (305 UPC out of 1,354 shoulder arthroplasty revisions). *C. acnes* was identified in 53.8% (164 of 305) [2,3,5,7,8,13,14]. The results presented by Pottinger et al. [6] were not included in these sums as the same data was included in Lucas et al. [13].

Other reports that did not evaluate UPCs in the setting of shoulder arthroplasty revision but did address the relevance and the baseline rate of positive *C. acnes* cultures in shoulders were included in our search results. Mook et al. found that 20.5% of shoulders undergoing open surgery for a variety of conditions had at least one positive culture (83.0% of which were *C. acnes*), but this rate was not significantly different from UPC rates from their control, "sterile" gauze cultures (13.0%) [16]. At this particular institution, the "false positive rate"—defined as the rate of positive cultures for "sterile" gauze sponges—was 20.5%, with the majority positive for *C. acnes*. These numbers should be compared with the overall rate of UPC in revision shoulder arthroplasty found in this review (22.5%) and with 53.8% positive for *C. acnes*. The detection of *C. acnes* on surgical equipment was replicated by Falconer et al. who, immediately after skin incision in shoulder without prior surgery, swabbed the subdermal layer, the surgeon's glove tip, the scalpel blades and the forceps to determine possible vectors for introduction of this bacteria to the deep shoulder. Where cultures are taken, *C. acnes* was detected on at least one of these cultures in 40% of their patients, with the subdermal layer being the most common origin of positive cultures, followed by the surgeon's glove and forceps. The fact that the within-subject positive culture rate of both of these sites was significantly correlated with positive subdermal cultures led the authors to suggest that it is the surgeon's manipulation of skin during a procedure that ultimately causes contamination of the deep shoulder with this organism [17]. Levy et al. similarly found *C. acnes* in 41.8% of shoulders undergoing primary shoulder arthroplasty for osteoarthritis following standard

chlorhexidine preparation and draping. Interestingly, in contrast to Falconer et al., Levy et al. concluded that this bacterium may not be a contaminant, but instead perhaps plays a role in the pathogenesis of glenohumeral arthritis [18].

To further determine if these positive results represent true positive or false positive results, we evaluated the rate of "true" infections using each author's own criteria. However, these definitions were not consistent across studies, presenting an obstacle that requires the clinician to use his or her judgment as to the most appropriate definition of true infection until a standard definition can be established. In some studies, repeat culture taken at either re-revision or as part of follow-up that demonstrates presence of the same organism was required to define a UPC as a true infection [7–9]. In other studies, signs or symptoms of infection post-revision were sufficient [5,14]. With this methodological caveat regarding the lack of a consistent definition for infection in mind, five studies [3,5,7,8,14] reported a "true" infection rate. When combined, only 18 of 168 total UPCs (10.7%) were considered "true," and, of those 18, 14 (77.8%) were *C. acnes*.

To determine the likelihood that UPCs represent a contaminant, McGoldrick et al. examined 148 cases to identify 14 shoulders with a UPC on revision that occurred at least 3 years following the initial arthroplasty with a mean time to revision of 8 years (range 4–12). They found that 79% of the 109 cultures they obtained grew *Cutibacterium* and concluded that a percentage this high implies that these cultures represent true infections of the shoulder and not contamination. McGoldrick et al. also pointed out that these positive cultures should truly be considered "unexpected" as many of the patients had factors well known to be correlated with positive *C. acnes* cultures, such as male gender, pain and stiffness [10].

Frangiamore et al. evaluated the time to positive culture in an attempt to differentiate "probable true positives" from "probable contaminants." Using their definitions, they found that the cultures of "probable true positives" grew bacteria by 11 days. Conversely, 44% of cultures of "probable contaminant" cases became positive after 11 days. The median time to growth among "probable true positives" was five days, compared to the nine days for the "probable contaminants." Their conclusion points out a potential downside to the increased sensitivity of long-hold cultures for *C. acnes* – this may also come with an increased risk of contamination and false positives. However, again, without a clear definition or a confirmatory test, it is not clear if the late growth cultures were really contaminants or simply had a lower inoculum of bacteria [9].

Pottinger et al. [6] evaluated potential risk factors for UPC in shoulder arthroplasty revisions across three phases of management: preoperative findings, gross intraoperative inspection upon entering the shoulder and histological examination. On multivariate analysis, they found that male sex (odds ratio (OR) 6.41, 95% confidence interval (CI) 3.10 – 14.42), and humeral osteolysis on X-ray (OR 12.85, 95% CI 2.92 – 92.53) were significantly more likely to grow *C. acnes,* while individuals with diabetes (OR 2.80, 95% CI 1.20 – 6.64), a history of smoking (OR 2.88, 95% CI 1.27-6.62) and glenoid loosening on X-ray (OR 3.07, 95% CI 1.50 – 6.40) had increased odds of positive cultures with non-*C. acnes* bacteria. In addition, the presence of a membrane and cloudy fluid were associated with *C. acnes,* while glenoid loosening and chronic inflammatory signs on histology were predictive of UPCs with other bacteria. Increased numbers of cultures taken were associated with UPCs of both *C. acnes* and other bacteria [6].

Factors that were not significant predictors of either type of UPC included local and systemic symptoms, age, white blood cell count, erythrocyte sedimentation rate, C-reactive protein, acne, diabetes and a number of other medical conditions [6]. The number of prior surgeries was not found to be a predictor of UPC [6]. These findings contrast with the findings of Foruria et al. that patients with "true infections" had undergone significantly more previous operations than their "contaminant" cohort [8]. Further complicating the interpretation of UPCs is the difference across studies between the requisite number of cultures with growth for the shoulder to be included in analysis. While some authors require at least two UPCs [4,10,12], others, such as Grosso et al. [5] and Foruria et al. [8], included patients with as few as one positive culture. However, they found that the number of positive cultures was not associated with rate of "true" infection, as they define it. Their data does demonstrate, though, that, when positive cultures are unexpected, the majority of the shoulders only grow out in just one culture (76 of 107 patients), although this finding is clouded by the wide variation in the total number of samples taken per patient (93 of the 107 patients had 1–3 samples taken) [8].

While some authors have conjectured that scenarios where only a small number of cultures grow *C. acnes*, especially with a delayed incubation time [9], are more likely to represent a contaminant [4,16], other authors have noted that these may simply represent a lower quantity of bacteria present. Ahsan et al. introduced a semi-quantitative approach to assessing the bacterial load in an attempt to define a threshold to differentiate "true" infections from "contaminant." They recommended calculating a "Shoulder Propi Value" to represent the amount of growth per culture, combining these values into "Shoulder Propi Scores" for each specimen location, and then calculating the "Average Shoulder Propi Scores." They did not observe a threshold above which one could be confident that a culture was a true positive, and they highlighted the wide variation in culture results across specimen locations [15].

When considering the relevance of UPCs in the context of "true infections," there are two potential areas of clinical significance: the UPC may have been a subclinical pathogenic cause of the revision during which it was uncovered, or the UPC may go on to cause sequelae post-revision. Lucas et al. analyzed the former question in a study evaluating cultures taken from several sites within the shoulder. When considering UPCs from explanted glenoid components of the original arthroplasty, more of these components were loose at revision than were not. However, when considering all the cultures taken from a shoulder, there was no difference between the positive culture rates between the loose and not loose glenoid component groups [13]. In a study examining patients with glenoid component loosening but no evidence of infection otherwise, Cheung et al. evaluated the significance of UPCs both as potentially correlated with the need for the index revision where the UPC was identified and as potentially correlated with the need for future revision. They found that culture results were not associated with the need for the index revision, but they did note a trend towards a positive effect between UPCs and the need for further re-operation, though this did not reach significance ($p = 0.09$) [2].

There is no consistent definition that determines whether a positive culture represents a "true infection" or a "contaminant." One additional state exists; a positive culture could represent "commensal organisms"—present but not causing pain or pathology. Furthermore, while *C. acnes* represents the majority of positive UPC cultures, it is not clear if the relevance of a UPC with one bacterium differs from a UPC with another. The debate regarding the relevance of unexpected positive long-hold cultures will continue until a definition or confirmatory test allows clinicians and researchers to properly categorize these findings.

TABLE 1. Summary of studies examining unexpected positive cultures in shoulder arthroplasty revisions

Author, Year	Proportion of Shoulders with UPC at Revision	*C. acnes* among Patients with UPC	"True" Infections	Definition of "True" Infection	"True" Infection with *C. acnes*	Follow-up (revision/clinical failure) and Organism at that Time
Topolski 2006 [1]	75 UPC reviewed. Total population size is not described.	45/75 (60%)	10/75 (13%)	Required re-revision.	5/10 (50%)	10 total patients required re-revision for pain, instability, dislocation and infection.
Cheung 2008 [2]	20/68 (29%)	14/20 (70%)	Not described	Not described	Not described	Trend toward positive cultures predicting increased likelihood of surgery ($p = 0.09$) in group that did not have glenoid reimplantation. Organism at follow-up not described.
Kelly 2009 [3]	8/28 (29%)	6/8 (75%)	2/8 (25%)	Subsequent infection at minimum 1-year follow-up.	2/2 (100%)	Both infections treated with resection and placement of antibiotic cement spacer. Additional follow-up not described.
Dodson 2010 [4]	6 UPC in retrospective review of 11 patients with positive cultures. Total population size is not described.	6/6 (100%)	3/6 (50%)	Acute and chronic inflammation and granulation consistent with infection on pathology.	3/6 (50%)	All patients chose medical management, but long-term follow-up is not described.
Grosso 2012 [5]	17/187 (9%)	10/17 (59%)	1/17 (6%)	Recurrence with erythema and swelling.	0/1 (0%)	In only patient to develop post-revision infection, irrigation and debridement followed by > 5 weeks of antibiotic therapy successfully maintained aseptic shoulder for at least 5 years. Offending organism was the same as original positive culture, *Staphylococcus epidermidis*.
Pottinger 2012 [6]	108/193 (56%)	75/108 (69%)	Not described	Not described	Not described	Not described
Lorenzetti 2013 [7]	8/55 (15%)	6/8 (75%)	3/8 (38%)	Positive cultures and/or purulence at re-revision.	1/3 (33%)	Of three post-revision infections, all from the control group, *C. acnes* was confirmed in one and underwent re-revision.
Foruria 2013 [8]	107/678 (15%)	68/107 (64%)	11/107 (10%)	Positive culture with same organism as initial culture, taken post-revision, obtained via aspiration or during re-revision.	10/11 (91%)	8 of the 11 true infections underwent re-revision.

TABLE 1. Summary of studies examining unexpected positive cultures in shoulder arthroplasty revisions (*Cont.*)

Author, Year	Proportion of Shoulders with UPC at Revision	*C. acnes* among Patients with UPC	"True" Infections	Definition of "True" Infection	"True" Infection with *C. acnes*	Follow-up (revision/clinical failure) and Organism at that Time
Frangiamore 2015 [9]	26 UPC of 46 studied shoulders, all of which had positive cultures. Total population size is not described.	26/26 (100%)*	17/26 (65%) described as probable true positive	Probable true infection among UPC defined as > 1 positive culture.	17/17 (100%) *	Not described
McGoldrick 2015 [10]	14 UPC at revision at least 3 years after index arthroplasty. Total population size is not described.	14/14 (100%) **	Not described	Not described	Not described	Not described
Piggot 2015 [11]	8 UPC of 24 studied shoulders, all of which had positive cultures. Total population size is not described.	8/8 (100%)*	1/8 (13%)	For UPC, definite infection is defined as at least 2 positive cultures with no other organisms.	1/1 (100%)*	4/8 (50%) UPC had favorable clinical outcome; 3/8 (38%) did not have a favorable clinical outcome, and 1/8 (13%) was lost to follow-up.
Hsu 2016 [12]	27/55 (49%), where "positive" was defined as at least 2 positive Propionibacterium cultures.	27/27 (100%) **	Not described	Not described	Not described	No difference between revision rate, functional or pain scores between positive-culture and control cohorts. 3 from culture-positive cohort underwent re-revision and all cultures were negative at that time.
Lucas 2016 [13] ***	117/221 (53%)	45/117 (38%)	Not described	Not described	Not described	Not described
Padegimas 2017 [14]	28/117 (24%)	15/28 (57%)	1/28 (3.6%)	Recurrent infection	1/1 (100%) ****	No statistically significant difference in re-operation rates between UPC and non-UPC patients.

UPC, unexpected positive culture
* Only *C. acnes* cultures were studied.
** Only *Cutibacterium* were studied.
***This study is an addition of 137 cases to the cases already described in Pottinger et al. (6).
****Only 1/6 cultures for this patient grew *C. acnes*

REFERENCES

[1] Topolski MS, Chin PYK, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: the value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006;15:402–406. doi:10.1016/j.jse.2005.10.001.

[2] Cheung EV, Sperling JW, Cofield RH. Revision shoulder arthroplasty for glenoid component loosening. J Shoulder Elbow Surg. 2008;17:371–375. doi:10.1016/j.jse.2007.09.003.

[3] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.

[4] Dodson CC, Craig EV, Cordasco FA, Dines DM, Dines JS, Dicarlo E, et al. Propionibacterium acnes infection after shoulder arthroplasty: a diagnostic challenge. J Shoulder Elbow Surg. 2010;19:303–307. doi:10.1016/j.jse.2009.07.065.

[5] Grosso MJ, Sabesan VJ, Ho JC, Ricchetti ET, Iannotti JP. Reinfection rates after 1-stage revision shoulder arthroplasty for patients with unexpected positive intraoperative cultures. J Shoulder Elbow Surg. 2012;21:754–758. doi:10.1016/j.jse.2011.08.052.

[6] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[7] Lorenzetti AJ, Wongworawat MD, Jobe CM, Phipatanakul WP. Cyanoacrylate microbial sealant may reduce the prevalence of positive cultures in revision shoulder arthroplasty. Clin Orthop Relat Res. 2013;471:3225–3229. doi:10.1007/s11999-013-2854-5.

[8] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:620–627. doi:10.1016/j.jse.2012.07.017.

[9] Frangiamore SJ, Saleh A, Grosso MJ, Alolabi B, Bauer TW, Iannotti JP, et al. Early versus late culture growth of Propionibacterium acnes in revision shoulder arthroplasty. J Bone Joint Surg Am. 2015;97:1149–1158. doi:10.2106/JBJS.N.00881.

[10] McGoldrick E, McElvany MD, Butler-Wu S, Pottinger PS, Matsen FA. Substantial cultures of Propionibacterium can be found in apparently

aseptic shoulders revised three years or more after the index arthroplasty. J Shoulder Elbow Surg. 2015;24:31–35. doi:10.1016/j.jse.2014.05.008.
[11] Piggott DA, Higgins YM, Melia MT, Ellis B, Carroll KC, McFarland EG, et al. Characteristics and treatment outcomes of Propionibacterium acnes prosthetic shoulder infections in adults. Open Forum Infect Dis. 2016;3:ofv191. doi:10.1093/ofid/ofv191.
[12] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.
[13] Lucas RM, Hsu JE, Whitney IJ, Wasserburger J, Matsen FA. Loose glenoid components in revision shoulder arthroplasty: is there an association with positive cultures? J Shoulder Elbow Surg. 2016;25:1371–1375. doi:10.1016/j.jse.2015.12.026.
[14] Padegimas EM, Lawrence C, Narzikul AC, Zmistowski BM, Abboud JA, Williams GR, et al. Future surgery after revision shoulder arthroplasty: the impact of unexpected positive cultures. J Shoulder Elbow Surg. 2017;26:975–981. doi:10.1016/j.jse.2016.10.023.
[15] Ahsan ZS, Somerson JS, Matsen FA. Characterizing the Propionibacterium load in revision shoulder arthroplasty: a study of 137 culture-positive cases. J Bone Joint Surg Am. 2017;99:150–154. doi:10.2106/JBJS.16.00422.
[16] 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 Joint Surg Am. 2015;97:957–963. doi:10.2106/JBJS.N.00784.
[17] Falconer TM, Baba M, Kruse LM, Dorrestijn O, Donaldson MJ, Smith MM, et al. Contamination of the surgical field with Propionibacterium acnes in primary shoulder arthroplasty. J Bone Joint Surg Am. 2016;98:1722–1728. doi:10.2106/JBJS.15.01133.
[18] 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;22:505–511. doi:10.1016/j.jse.2012.07.007.

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QUESTION 3: What is the treatment (if any) for unexpected positive cultures (UPC) in revision shoulder arthroplasty without clinical or radiographic signs of infection?

RECOMMENDATION: Unknown. Few publications offer protocols for addressing unexpected positive cultures. Of these, the most common options include antibiotics, re-operation and withholding any treatment. The lack of comparative data on outcomes of these therapy regimens makes it difficult to conclusively determine optimal management.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

A comprehensive literature review was performed to identify all studies on unexpected positive cultures (UPC) in shoulders undergoing revision arthroplasty. Searches for the terms "unexpected," "infection," "positive culture," "indolent infection," "gram-positive bacterial infections," "prosthesis-related infections" and "shoulder joint," "shoulder," "arthroplasty," "total joint," "replacement," "periprosthetic," "peri-implant," "shoulder prosthesis" were performed using the search engines PubMed, Embase and Scopus. These searches were conducted in February 2, 2018 and include results published through that time. Inclusion criteria included patients undergoing revision shoulder arthroplasty, with no clinical or radiographic signs of infection, who had positive cultures taken from the shoulder undergoing the revision. Only studies that focused on the potential treatment of these UPCs were included. Only English-language studies that presented original data on more than five patients meeting inclusion criteria were included. For articles with both unexpected positive cultures and known septic revisions, the patients with UPC were included in the review if the data was reported such that the patients meeting inclusion criteria could be separated. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed. Eight articles met inclusion and exclusion criteria.

Of the eight studies [1–8] returned that allude to treatment of UPCs, only six described their treatment protocol, but these do not allow for definitive conclusions to be drawn regarding the effect of each treatment type on outcomes, if any were reported (see Table 1) [1–6]. Despite neither providing a methodology for treatment assignment, nor results that were not in aggregate, Foruria et al. [3] noted that their duration of antibiotic treatment (range: 8-700 days) was not associated with the likelihood of a second positive culture during follow-up [3]. In the study by Hsu et al. [5], a more standardized treatment protocol was developed and applied to their sample of 55 patients. However, this study was limited by the use of a control cohort (that received a different treatment course) that may have had a single positive culture, thus making it challenging to answer the question of the best treatment for UPCs using these data. These investigators found that three patients in both the culture-positive cohort (defined as at least two UPC, n = 27) and the control cohort (zero or one UPC, n = 28) required a subsequent procedure. None of these three culture-positive cohort patients, who received the extended antibiotic regimen, had subsequent positive cultures at their revision, while one of three control cohort patients did [5]. Two studies do present this data, but it is not robust [7,8]. Few studies fully meet the defined inclusion and exclusion criteria, and many of these report results in an aggregate. Only two studies compare different treatment options using non-aggregated outcomes.

Padegimas et al. [7] compared individuals undergoing shoulder arthroplasty revision, 28 of which had UPC and 89 who did not. They noted that all patients received the authors' standard, postoperative empirical oral antibiotics for two weeks and then may continue to receive antibiotics for an additional six weeks depending on culture results, presentation and intraoperative findings. One of the 10 patients who did not receive the additional 6-week regimen had reinfection. Of note though, there were three other patients who did not have UPCs who developed reinfection as well. A higher percentage of UPC patients underwent reoperation (20.2%) than those without UPC (7.1%), but this difference did not reach statistical significance ($p = 0.109$) [7].

In the study by Piggot et al. [8], 8 shoulders of the 24 with positive *C. acnes* cultures that they studied were "unexpected" as defined by our inclusion criteria. The primary outcome used in this study was termed "a favorable clinical outcome," which was defined as a post-treatment improvement in pain and function and a lack of additional operations. This metric was assessed at the latest possible clinical visit. Four of these eight UPC patients met the favorable clinical outcome endpoint; three did not, and one was lost to follow-up. The antibiotics that each of these eight patients received varied by clinical judgment and susceptibility

TABLE 1. Summary of studies offering limited data on treatment and outcomes

Author	Number of Patients with UPC	Treatment Protocols	Outcomes
Kelly [1]	8	1 patient received 4 weeks of oral doxycycline for unrelated infection; 7 received nothing	2 late clinical infections, unclear if patient who received doxycycline was among them.
Dodson [2]	6	IV cefazolin for 36 hours postoperatively and clindamycin or penicillin upon culture result of *C. acnes* in all patients; oral ampicillin for 8-10 weeks in 5 patients; oral suppressive therapy for 24 months in 1 patient.	Patient on oral suppressive therapy had no signs of infection at time authors were writing. Outcomes not otherwise reported.
Foruria [3]	107	Variable; 34 patients were treated with antibiotic regimen (range 8-700 days) postoperatively; 19 were treated with chronic antibiotic suppression; 54 did not receive antibiotics other than preoperative prophylaxis.	Variable results mostly reported in aggregate; authors noted that duration of antibiotic regiment had no effect on likelihood of a repeat positive culture during follow-up.
Grosso [4]	17	13 patients received tobramycin or gentamicin impregnated cement; all received IV antibiotics for 24 hours postoperatively; no additional therapy following culture results.	1 clinical infection at 6 weeks postoperatively, confirmed as superficial wound infection during irrigation and debridement.
Hsu [5]	55 patients total; 27 were considered culture-positive with at least 2 positive cultures; 28 were considered the control cohort with 0 or 1 positive cultures	Variable; high-suspicion of infection patients received intravenous ceftriaxone for a minimum of 3 weeks; low-suspicion patients received oral amoxicillin and clavulanate for same minimum duration. If a patient became a culture-positive patient when more than 2 cultures became positive, the regimen was changed to intravenous ceftriaxone or vancomycin plus oral rifampin for 6 weeks followed by doxycycline or amoxicillin with clavulanate for a minimum of 6 weeks.	3 in the culture positive cohort required additional procedures, but none had positive cultures at re-revision; 3 in the control cohort also required subsequent procedures, and 1 of these 3 had a single positive culture. Further details about treatment duration on a patient-by-patient basis, beyond the general protocol already described, were not reported.
Topolski [6]	75	Variable; 54 patients received only the standard 2-3 doses of intravenous postoperative antibiotics and nothing further; 14 received additional, unspecified antibiotics (range 1-6 weeks); 7 received only oral, unspecified antibiotics.	10 required re-revision, 7 of which had positive cultures at that time, 5 of which were *C. acnes*. Further details about treatment duration on a patient-by-patient-basis were not reported.

UPC, unexpected positive culture

and is not well-reported. The addition of rifampin, and its duration, however, is well-documented. Of the four patients who had a favorable outcome, rifampin was added to the unspecified antibiotic regimen for each one with an average duration of 608.5 days (range 126–1,540 days). Of the three patients without a favorable clinical outcome, one received unspecified antibiotics plus rifampin for 196 days; one received unspecified antibiotics alone for 189 days, and one underwent surgery [8].

There is a clear need for additional research into treatment options for UPC. The comparative studies are weak and underpowered and a dearth of randomized controlled trials of medical management is apparent. No conclusion can be made at this time as to what treatment option, if any, is appropriate for UPCs.

REFERENCES

[1] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.

[2] Dodson CC, Craig EV, Cordasco FA, Dines DM, Dines JS, Dicarlo E, et al. Propionibacterium acnes infection after shoulder arthroplasty: a diagnostic challenge. J Shoulder Elbow Surg. 2010;19:303–307. doi:10.1016/j.jse.2009.07.065.

[3] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:620–627. doi:10.1016/j.jse.2012.07.017.
[4] Grosso MJ, Sabesan VJ, Ho JC, Ricchetti ET, Iannotti JP. Reinfection rates after 1-stage revision shoulder arthroplasty for patients with unexpected positive intraoperative cultures. J Shoulder Elbow Surg. 2012;21:754–758. doi:10.1016/j.jse.2011.08.052.
[5] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.
[6] Topolski MS, Chin PYK, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: the value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006;15:402–406. doi:10.1016/j.jse.2005.10.001.
[7] Padegimas EM, Lawrence C, Narzikul AC, Zmistowski BM, Abboud JA, Williams GR, et al. Future surgery after revision shoulder arthroplasty: the impact of unexpected positive cultures. J Shoulder Elbow Surg. 2017;26:975–981. doi:10.1016/j.jse.2016.10.023.
[8] Piggott DA, Higgins YM, Melia MT, Ellis B, Carroll KC, McFarland EG, et al. Characteristics and treatment outcomes of Propionibacterium acnes prosthetic shoulder infections in adults. Open Forum Infect Dis. 2016;3:ofv191. doi:10.1093/ofid/ofv191.

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QUESTION 4: What is the role of quantitative evaluation (e.g., density of bacteria, cuti (propi) score) of positive cultures from the shoulder?

RECOMMENDATION: Semi-quantitative and quantitative reporting of bacterial culture results may have clinical utility for the diagnosis of shoulder periprosthetic joint infection (PJI) and may be used to interpret the relevance of positive cultures.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

Introduction

Approaches to quantifying the bacterial load at the time of revision shoulder arthroplasty.

Infection is an especially problematic and potentially devastating complication of elective major joint arthroplasty. There is extensive recent interest in PJI of knee and hip arthroplasty leading to protocols for prevention, evaluation and management of PJI. Investigation of PJI of the shoulder has lagged in part due to the limited numbers of primary shoulder arthroplasty cases, the relatively infrequent recognition of PJI, and the difficulty in applying the traditional criteria for hip and knee PJI to the shoulder due to the issue of "stealth" presentation of *Propionibacterium,* frequently occurring at times long after the index procedure.

The diagnosis and management of a prosthetic joint infection is dependent upon identifying the pathogen. Prior to the recognition of *Cutibacterium* as a definite pathogen, it was not uncommon for cases of shoulder PJI to be unrecognized. More recent studies have attempted to determine the optimal approach to evaluation of potential shoulder PJI. This includes specific approaches to specimen harvest, culturing method and culture observation appropriate for identifying *Cutibacterium.*

While the results of a specimen culture are often reported as being "positive" or "negative," it is now apparent that the degree of positivity – that is the number of bacteria in the specimen – can vary widely. Quantitative cultures have been used by clinicians to estimate the threshold above which the bacterial burden will likely be of clinical significance [1]. Low levels of bacterial growth from a specimen may be of less clinical significance than high levels. In determining the clinical importance of any level of bacterial growth, it is also important to know the degree to which control specimens (i.e., a sterile sponge opened in the operating room (OR) without contact with the patient's tissue) demonstrate bacterial growth [2,3].

Quantitative culture results have been used to evaluate wound infection, urinary tract infections and bronchial brushings. In the case of urine the actual colony count of a urine specimen is necessary (one colony equals one colony-forming unit or CFU) and a positive culture with 100,000 CFU is considered to be indicative of a urinary tract infection [4]. A number of studies have investigated the relevance of bacterial count to wound healing. Bacterial counts above 10,000 to 100,000 are thought to be indicative of infection and delayed healing [5]. More recent work supports this concept but suggests that there is little to no benefit of quantitative biopsy analyses or quantitative wound surface cultures, with several studies finding a low correlation of culture to infection. The problem with any threshold, such as 100,000 CFU is that there can be no clinically significant difference between a count of 100,010 and 99,990.

Most standard bacterial cultures are evaluated using a semi-quantitative technique in which cultures are inoculated onto medium using a sterile loop that sequentially dilutes the specimen from the first area or quadrant of the medium to the last area or quadrant. Results are often reported as 1+, 2+, 3+ or 4+ (or as text, using such terms as "trace," "few," "moderate" or "abundant"), depending on which areas or quadrants demonstrate bacterial growth [1,6,7].

Bacterial load, the virulence of the organism, variations in host response and wound environment all may contribute to determining the effect of the bacteria in the wound. Despite this, the literature on shoulder PJI suggests wide variability in culture practice and rarely considers semi-quantitative or quantitative culture results [8]. The purpose of this systematic review was to identify information regarding quantitative evaluation of bacterial cultures and to relate this to the evaluation and management of shoulder PJI.

Methods

A Scopus search was performed with the query "(shoulder OR "upper extremity") AND (arthroplasty OR replacement OR revision) AND (culture OR microbiologic OR microbiology)." The resulting titles, abstracts and full text (127) from this query were reviewed for relevance to the question of number of samples for culture, specimen type and anatomic locations. All pertinent articles were then fully reviewed and any other pertinent citations in these gathered articles were obtained and reviewed. Based upon the findings of this review and review of the manuscript reference lists, an additional

search was performed on PubMed using the term "quantitative culture."

Results

The initial search identified 127 articles. After review of these articles, 11 were included in the final summary. Due to the nature of the available data, it was not possible to perform a meta-analysis. Thus, this is a narrative report of the findings.

Kallstrom, in a review article, discussed the role of quantitative cultures in determining if a nonhealing wound is infected [1]. Despite early work that emphasized the importance of quantitative wound tissue cultures, the current thought is that there is little to no benefit of quantitative biopsy analyses or quantitative wound surface cultures, with several studies finding a low correlation of culture to infection. Quantitative wound cultures of tissue is challenging, as the tissue must be accurately weighed, homogenized and serially diluted prior to inoculation of media for each dilution under aerobic and anaerobic conditions. Variations in biopsy collection processing and inoculation can often confuse the interpretation of quantitative wound culture results. The delay in reporting results from quantitative cultures makes clinical management difficult, so direct Gram staining has been used as a surrogate to determine bacterial loads in wounds. Early advocates of quantitative wound cultures were correct in realizing that clinical infection was influenced by an imbalance in the bacterial load, variations in the host response and wound type.

Ashan et al. studied a cohort of 137 patients who underwent revision shoulder arthroplasty and had at least one positive culture [6]. The subjects all had pain, stiffness or component loosening but did not have obvious clinical evidence of infection. The authors excluded subjects that did not have at least four culture specimens. The focus of the study was to use the semi-quantitative culture results to determine a measure of bacterial burden specific to *C. acnes*. They assigned numerical values (Specimen Propi Values) to the semi-quantitative Propionibacterium (now *Cutibacterium*) culture results: 0.1 (broth only), 0.1 (1 colony), 1, 2, 3, and 4 (1+, 2+, 3+, or 4+, respectively) and referred to this number as the "degree of positivity" for each specimen with the idea that this value "roughly" reflected the amount of bacterial growth [9]. They also calculated the sum for each type of specimen (humeral stem explant, humeral head explant, glenoid explant, collar membrane [between the modular head and stem], humeral membrane [between the humeral stem and humeral bone], other soft tissue, fluid, or "other") from each shoulder. The Specimen Propi Values for all of the specimens from a particular shoulder were summed to derive the Shoulder Propi Score for that shoulder. In order to account for the number of culture specimens in each case they calculated the Average Shoulder Propi Score, which they defined as the Shoulder Propi Score divided by the total number of specimens from that shoulder submitted for culture.

They reported that the average Specimen Propi Value for fluid (0.35 ± 0.89) was significantly lower than that for soft tissue (0.92 ± 1.50) and explant specimens (0.66 ± 0.90) ($p < 0.001$). Men had a significantly higher mean Shoulder Propi Score (3.56 ± 3.74) than women (1.22 ± 3.11) ($p < 0.001$), and men had a significantly higher Average Shoulder Propi Score (0.53 ± 0.51) than women (0.19 ± 0.43) ($p < 0.001$). Patient age did not have a significant effect on either score.

They further reported that, although the Shoulder Propi Score and Average Shoulder Propi Score varied among the shoulders that were culture-positive for Propionibacterium (now *Cutibacterium*), they could not identify a clear threshold above which they could be confident that a positive culture result represented a clinical infection, as opposed to contamination or commensal presence of an organism. The findings of this study clearly demonstrate that the identification of *C. acnes* is highly dependent upon the source of the culture specimen. The findings of this work have limitations, because the authors did not clearly determine what level of *C. acnes* burden constitutes a periprosthetic infection. Thus, true the value of semi-quantitative reporting of cultures is not clearly delineated. However, if one considers that the clinical manifestations of an infection are the result of an interaction between a host and a pathogen, then it is logical to consider that the amount of bacterial burden is important.

In a separate publication, Hsu and co-workers studied the results of epidermal, dermal and deep cultures obtained from subjects undergoing revision shoulder arthroplasty [7]. Based upon their data, they calculated that four different specimens would need to be cultured to have a 95% chance of detecting the organism and that, in order to achieve 95% of the positive cultures, the cultures need to be held for at least 14 days.

Carli et al. studied a mouse model of acute periprosthetic knee infection [10]. The experimental animals were inoculated with *S. aureus*. The infected animals demonstrated clinical signs of infection with impaired gait, implant loosening and elevated inflammatory markers. Viable *S. aureus* was quantified from the retrieved implant surfaces, and the infected animals had greater than 10^6 CFUs at 2 weeks and greater than 10^5 CFUs at 6 weeks.

Esteban et al. used quantitative culture analysis to study cases of PJI in which antibiotic loaded cement spacer was used during two-stage revision reconstruction [11]. Culture specimens were obtained from sonicated implants. Infection was defined by having one of the following criteria: (1) fistulae or wound dehiscence at the time of the second-stage surgery, (2) persistent pain around the joint associated with elevated C-reactive protein or (3) clinical appearance of infected tissue during surgery according to the surgeon. Thirteen of 50 specimens had positive sonicate cultures, 9 from infected cases and 4 from non-infected ones ($p = 0.001$, Fisher's exact test). The presence of high colony counts or a different isolate individually showed a strong statistical association with infection.

Grosso et al. studied implant sonication culture for the diagnosis of shoulder periprosthetic infection [12]. They defined infection according to their published guidelines that included four groups: definite infection, probable infection, probable contaminant or no evidence for infection. Their culture technique report quantified the number of CFUs for each specimen. Prior work by Trampuz et al. suggested that sonication fluid cultures of hip and knee arthroplasty implants had greater sensitivity than periprosthetic tissue cultures [13]. In contrast, Grosso et al. reported that there was no significant benefit to the shoulder implant sonication culture technique compared with standard intraoperative cultures. Using the cutoff value of > 20 CFU/mL to exclude contaminants, implant sonication culture had a low sensitivity (56%) but high specificity (93%). While without a cutoff value, implant sonication culture had a high sensitivity (96%) but low specificity (64%). Standard intraoperative cultures (tissue and fluid) had a better overall performance compared with the cutoff and non-cutoff sonication results.

Piper et al. also studied the role of sonication of shoulder implants and evaluated the relevance of quantitative reporting of the culture results [14]. In their previous work on hip and knee implants, they used a cutoff of 5 CFU per plate of sonicated fluid culture. In the study of shoulder implants they found that a cutoff of 20 CFU per plate with concentrated sonicate fluid resulted in a sensitivity and a specificity similar to those in their hip and knee work. In contrast to Grosso et al., they concluded that sonicate fluid culture is useful for diagnosing shoulder PJI.

Discussion

The clinical manifestations of an infection are the results of the interaction between a pathogen and the host. Kravitz wrote that "we

think of infection in terms of bioburden, which refers to the presence of bacteria in a wound and the number of microorganisms that contaminate an object" and subdivided bioburden into 4 categories: (1) contamination-bacteria within a wound without host reaction, (2) colonization-bacteria within the wound that multiply or initiate a host reaction, (3) critical colonization-bacteria that multiply to cause a delay in wound healing, often with increased pain but not with an acute host reaction and (4) infection-bacteria that multiply and cause a host reaction [15]. It seems logical that the presence of greater numbers of bacteria would correlate with the presence and severity of a periprosthetic shoulder infection. The results of this systematic review point out the paucity of available information, knowledge and understanding of the role of quantitative culture in the evaluation and management of shoulder PJI.

The limited data available suggests that standard fluid and tissue cultures are better than sonication cultures for diagnosis of shoulder PJI. However, there is insufficient experience and study of this technique to make definitive evidenced based recommendations. From a practical standpoint sonication is not readily available in all institutions. However, it seems that if sonication is used the quantitative culture results should reported.

New culture independent techniques and assays employed to identify the presence of bacteria including polymerase chain reaction, next generation sequencing and labeling techniques hold promise to aid both in the actual diagnosis of shoulder PJI as well as reduce the time to diagnosis. Nevertheless, the results of culture remain an important means to identify and characterize pathogenic microorganisms, to determine antibiotic susceptibility and to confirm the results of culture-independent methods. Previous experience demonstrates that the actual presence of bacteria does not always correlate with clinical manifestations of infection and that a number of pathogen and host factors must be considered in the diagnosis and management of shoulder PJI.

In summary, the results of prior studies in other specialties suggest that determining bacterial load with semi-quantitative and quantitative culture assessment in shoulder arthroplasty is of value in the evaluation and management of cases in which PJI is suspected. The application of these semi-quantitative and quantitative culture results to the evaluation of a failed shoulder arthroplasty requires (1) a standardized approach to harvesting specimens (source, number and technique), (2) using standardized culturing protocols designed to detect the presence of *Cutibacterium*, (3) standardized approach to reporting of the semi-quantitative or quantitative results and (4) documentation of the semi-quantitative or quantitative results of control specimens from the OR that have not been in contact with the patient.

REFERENCES

[1] Kallstrom G. Are quantitative bacterial wound cultures useful? J Clin Microbiol. 2014;52:2753–2756. doi:10.1128/JCM.00522-14.

[2] 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 Joint Surg Am. 2015;97:957–963. doi:10.2106/JBJS.N.00784.

[3] MacNiven I, Hsu JE, Neradilek MB, Matsen FAI. Preoperative skin-surface cultures can help to predict the presence of Propionibacterium in shoulder arthroplasty wounds. JBJS Open Access. 2018;3:e0052. doi:10.2106/JBJS.OA.17.00052.

[4] Laboratory Quality Assurance Program. n.d. https://www.cps.sk.ca/imis/CPSS/Programs_and_Services/Laboratory_Quality_Assurance.aspx?LabQualityCCO=Laboratory%20Quality%20Assurance%20Program%20Overview (accessed August 31, 2018).

[5] Bowler PG, Duerden BI, Armstrong DG. Wound microbiology and associated approaches to wound management. Clin Microbiol Rev. 2001;14:244–269. doi:10.1128/CMR.14.2.244-269.2001.

[6] Ahsan ZS, Somerson JS, Matsen FA. Characterizing the Propionibacterium load in revision shoulder arthroplasty: a study of 137 culture-positive cases. J Bone Joint Surg Am. 2017;99:150–154. doi:10.2106/JBJS.16.00422.

[7] Hsu JE, Neradilek MB, Russ SM, Matsen FA. Preoperative skin cultures are predictive of Propionibacterium load in deep cultures obtained at revision shoulder arthroplasty. J Shoulder Elbow Surg. 2018;27:765–770. doi:10.1016/j.jse.2018.01.021.

[8] Hsu JE, Somerson JS, Vo KV, Matsen FA. What is a "periprosthetic shoulder infection"? A systematic review of two decades of publications. Int Orthop. 2017;41:813–822. doi:10.1007/s00264-017-3421-6.

[9] 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 Joint Surg Am. 2013;95:e1811-e1817. doi:10.2106/JBJS.L.01733.

[10] Carli AV, Bhimani S, Yang X, Shirley MB, de Mesy Bentley KL, Ross FP, et al. Quantification of peri-implant bacterial load and in vivo biofilm formation in an innovative, clinically representative mouse model of periprosthetic joint infection. J Bone Joint Surg Am. 2017;99:e25. doi:10.2106/JBJS.16.00815.

[11] Esteban J, Gadea I, Pérez-Jorge C, Sandoval E, García-Cañete J, Fernandez-Roblas R, et al. Diagnosis of spacer-associated infection using quantitative cultures from sonicated antibiotics-loaded spacers: implications for the clinical outcome. Eur J Clin Microbiol Infect Dis. 2016;35:207–213. doi:10.1007/s10096-015-2531-6.

[12] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.

[13] Trampuz A, Piper KE, Hanssen AD, Osmon DR, Cockerill FR, Steckelberg JM, et al. Sonication of explanted prosthetic components in bags for diagnosis of prosthetic joint infection is associated with risk of contamination. J Clin Microbiol. 2006;44:628–631. doi:10.1128/JCM.44.2.628-631.2006.

[14] Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR, et al. Microbiologic diagnosis of prosthetic shoulder infection by use of implant sonication. J Clin Microbiol. 2009;47:1878–1884. doi:10.1128/JCM.01686-08.

[15] Kravitz S. Infection: are we defining it accurately? Adv Skin Wound Care. 2006;19:176.

2.2. DIAGNOSIS: CULTURE TECHNIQUE

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QUESTION 1: What is the optimal culture technique (e.g., culture medium, days of incubation) in evaluating patients for shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Current evidence suggests that culture of tissue samples for the diagnosis of shoulder PJI is best performed using both aerobic and anaerobic conditions. For solid culture media, diagnostic accuracy may be improved by using enrichment media. Fourteen days is the most common culture duration cited.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

PJI of the shoulder is a common indication for revision surgery [1]. The organisms that are most commonly responsible include *Staphylococcus* and *Cutibacterium acnes* (formally *Propionibacterium acnes*). Culture techniques and interpretation of culture results for the former are well established, but *C. acnes* is a ubiquitous skin commensal in humans. Therefore, the distinction between it being a contaminant versus pathogen is challenging. This is complicated by the fact that *C. acnes* is often associated with few local or systemic signs of inflammation and is often slow to grow in the laboratory. Defining the optimal culture technique for diagnosis of shoulder PJI is, therefore, important. However, even if this were achieved, cultures are likely to yield a proportion of false positive results, and, therefore, the inclusion of a confirmatory test in the diagnostic pathway is critically needed for the interpretation and corroboration of culture results. There are three main variables relating to culture conditions for the diagnosis of shoulder PJI.

Duration of Culture

In order to optimize detection of all organisms, including *C. acnes,* in upper limb PJI, most authors advise prolonged incubation, although the ideal duration has yet to be established. An incubation time which is too short may limit the sensitivity; an incubation time which is too long results in the isolation of non-diagnostic isolates or contaminants, thereby limiting the specificity.

Zappe et al. [2], in a retrospective analysis of 139 cases of PJI, suggest that *Cutibacterium* associated infection occurs at a frequency comparable to many other pathogens and that the median time to culture positivity is 8 days. They advise that tissue samples should be incubated for 14 days.

Schäfer et al. [3] likewise suggested that prolongation of the incubation period was associated with an increase in the proportion and diversity of positive samples. They recommended an incubation period of up to 14 days based especially on late recovery of aerobic gram-positive rods and *Cutibacterium* species.

Similarly, Butler-Wu et al. [4] estimated the median time to positivity using standard bacteriological methods to be 6 days with a range of 2-15.

Based on such studies, many authors advise a minimum incubation period of 14 days [5–8] while some advise at least 21 days [1,9].

However, prolonged incubation of cultures increases the risk of generating false positive results due to sample contamination and, therefore, may adversely affect the specificity of the test. A retrospective study by Frangiamore et al. [10] suggested that, amongst 46 cases, median time to *C. acnes* growth in the probable true-positive group was 5 days as compared to 9 days in the probable contaminant group ($p = 0.002$).

Peel et al. [11] demonstrated that, in 117 cases of proven PJI as defined by the Infectious Disease Society of America (IDSA) criteria, the median time to positivity using blood culture bottles was around 24 hours. Extending anaerobic incubation beyond 7 days yielded a diagnosis of PJI in only five additional subjects who fulfilled the IDSA diagnostic criteria and anaerobic blood culture bottles detected pathogen growth more rapidly than agar or thioglycolate broth.

Minassian et al. [12] prospectively analyzed 332 revision arthroplasty patients whose surgical samples were processed using both blood culture bottles and conventional media. Amongst 66 who had microbiologically confirmed PJI, 65 cases were identified as culture positive within 3 days and one at day 8.

Anaerobic and Aerobic Culture

PJI caused by strictly anaerobic pathogens is rare but mandates careful selection of antimicrobials for optimal therapy. While *C. acnes* is an anaerobic organism, many strains are aerotolerant and Butler-Wu et al. [4] suggested a significant and clinically important improvement in yield by using aerobic and anaerobic culture conditions. Peel et al. [11], however, suggest little advantage of prolonged aerobic cultures specifically for the diagnosis of *C. acnes* but reported benefit from extended anaerobic culture.

Choice of Culture Medium

Conventionally, the laboratory diagnosis of PJI has relied upon culture of tissue specimens on solid media (agar) and broth cultures. Unless they become visibly turbid, the latter are terminally subcultured onto agar to detect any non-visible growth in the broth. This is time consuming, cumbersome and provides no advantage over automated techniques.

Butler-Wu et al. [4] analyzed the accuracy of *C. acnes* PJI diagnosis in 198 revision arthroplasty procedures using four different culture media (blood agar, chocolate agar, Brucella agar and brain-heart infusion (BHI) broth). They found that recovery of *C. acnes* from blood agar was exclusively associated with the presence of infection (16 specimens), but all specimens positive for growth of *C. acnes* on blood agar were also positive for growth on at least one additional culture medium. BHI yielded the highest number false positive results and Brucella agar yielded the highest number of true positive results. They suggest that isolation of *C. acnes* from clinically proven infected cases were 6.3 times more likely to have two media positive for growth as compared to unproven cases of infection ($p = 0.002$).

Hughes et al. [13] prospectively compared conventional culture media and blood culture medium in 849 separate specimens from 178 patients undergoing arthroplasty revision. They estimated the sensitivity and specificity of blood culture medium to be 87% and 98% respectively. By comparison, the sensitivity of direct plates and cooked meat broth culture were 39% and 83%

Motwani et al. [14] found that, in 60 cases of pediatric septic arthritis caused by any organism, incubation of clinical samples in BACTEC blood culture bottles, as compared to conventional agar plates, increased the yield from 42% to 71%.

A prospective study of 369 adults by Peel et al. [11] similarly showed that use of blood culture bottles improved bacterial yield in comparison to conventional agar and broth culture (92.1% versus 62.6%, respectively).

REFERENCES

[1] Fink B, Sevelda F. Periprosthetic joint infection of shoulder arthroplasties: diagnostic and treatment options. BioMed Res Int. 2017;2017:4582756. doi:10.1155/2017/4582756.

[2] Zappe B, Graf S, Ochsner PE, Zimmerli W, Sendi P. Propionibacterium spp. in prosthetic joint infections: a diagnostic challenge. Arch Orthop Trauma Surg. 2008;128:1039–1046. doi:10.1007/s00402-007-0454-0.

[3] Schäfer P, Fink B, Sandow D, Margull A, Berger I, Frommelt L. Prolonged bacterial culture to identify late periprosthetic joint infection: a promising strategy. Clin Infect Dis. 2008;47:1403–1409. doi:10.1086/592973.

[4] Butler-Wu SM, Burns EM, Pottinger PS, Magaret AS, Rakeman JL, Matsen FA, et al. Optimization of periprosthetic culture for diagnosis of Propionibacterium acnes prosthetic joint infection. J Clin Microbiol. 2011;49:2490–2495. doi:10.1128/JCM.00450-11.

[5] Parvizi J, Gehrke T, International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. J Arthroplasty. 2014;29:1331. doi:10.1016/j.arth.2014.03.009.

[6] Fink B, Makowiak C, Fuerst M, Berger I, Schäfer P, Frommelt L. The value of synovial biopsy, joint aspiration and C-reactive protein in the diagnosis of late peri-prosthetic infection of total knee replacements. J Bone Joint Surg Br 2008;90:874–8. doi:10.1302/0301-620X.90B7.20417.

[7] Ince A, Rupp J, Frommelt L, Katzer A, Gille J, Löhr JF. Is "aseptic" loosening of the prosthetic cup after total hip replacement due to nonculturable bacterial pathogens in patients with low-grade infection? Clin Infect Dis. 2004;39:1599–1603. doi:10.1086/425303.

[8] Nodzo SR, Boyle KK, Bhimani S, Duquin TR, Miller AO, Westrich GH. Propionibacterium acnes host inflammatory response during periprosthetic infection is joint specific. HSS J. 2017;13:159–164. doi:10.1007/s11420-016-9528-2.
[9] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.
[10] Frangiamore SJ, Saleh A, Grosso MJ, Alolabi B, Bauer TW, Iannotti JP, et al. Early versus late culture growth of Propionibacterium acnes in revision shoulder arthroplasty. J Bone Joint Surg Am. 2015;97:1149–1158. doi:10.2106/JBJS.N.00881.
[11] Peel TN, Dylla BL, Hughes JG, Lynch DT, Greenwood-Quaintance KE, Cheng AC, et al. Improved diagnosis of prosthetic joint infection by culturing periprosthetic tissue specimens in blood culture bottles. MBio. 2016;7:e01776–e01715. doi:10.1128/mBio.01776-15.
[12] Minassian AM, Newnham R, Kalimeris E, Bejon P, Atkins BL, Bowler ICJW. Use of an automated blood culture system (BD BACTEC™) for diagnosis of prosthetic joint infections: easy and fast. BMC Infect Dis. 2014;14:233. doi:10.1186/1471-2334-14-233.
[13] Hughes HC, Newnham R, Athanasou N, Atkins BL, Bejon P, Bowler ICJW. Microbiological diagnosis of prosthetic joint infections: a prospective evaluation of four bacterial culture media in the routine laboratory. Clin Microbiol Infect. 2011;17:1528–1530. doi:10.1111/j.1469-0691.2011.03597.x.
[14] Motwani G, Mehta R, Aroojis A, Vaidya S. Current trends of microorganisms and their sensitivity pattern in paediatric septic arthritis: a prospective study from tertiary care level hospital. J Clin Orthop Trauma. 2017;8:89–92. doi:10.1016/j.jcot.2016.09.001.

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QUESTION 2: Should *Cutibacterium acnes* (formerly known as *Propionibacterium acnes*) isolated in samples from the shoulder be sub-typed?

RECOMMENDATION: *Cutibacterium acnes* isolated in samples from the shoulder should not be routinely sub-typed.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

The survey of the studies was conducted by searching PubMed since January 1, 2000 in the best match sort order with the following query ((Propionibacterium acnes OR Cutibacterium acnes OR P acnes)) AND (strain OR types OR typing OR phylogenetic OR orthopedic infection OR prosthetic joint OR arthroplasty OR shoulder OR implant OR instrumentation) AND (("2000/01/01"[PDat]: "3000/12/31"[PDat]) AND Humans[Mesh]).

Cutibacterium acnes (formerly known as *Propionibacterium acnes* [1]) is a member of the normal human skin microbiota and is associated with various infections and clinical conditions. It is frequently isolated from prosthetic joints (particularly shoulder arthroplasties) and the spine, mainly due to the proximity of these sites to areas of skin rich in pilosebaceous glands, where *C. acnes* reside [2,3].

C. acnes is one of the most frequent microorganisms isolated in shoulder periprosthetic joint infection (PJI). In contrast to the knee and hip joints, *C. acnes* has been isolated in 17.6% to 60% of periprosthetic shoulder infection cases [4–7]. However, its role in pathogenesis has been questioned [8], as up to 60% of patients that grow *C. acnes* from a prosthetic joint have no evidence of acute inflammation in histopathology [9]. Besides that, *C. acnes* has been present in culture specimens during primary shoulder surgery [10–12], and it has been identified as a common contaminant of the surgical field [13]. One possible explanation for these observations is that standard skin surface preparation cannot eliminate *C. acnes* in a high percentage of individuals, thus favoring inoculation from the more superficial dermal structures into the deep tissues during surgery [14].

Within the last 10 years, phylogenetic studies based on single and multilocus gene sequencing, as well as whole-genome analyses have provided valuable insights into the genetic population structure of *C. acnes*, particularly in the context of health and disease. The bacterium has an overall clonal structure, and its isolates can be classified into a number of phylogroups designated types IA1, IA2, IB, IC, II and III [15–17]. These types appear to display differences in associations with specific types of infections and vary in the production of putative virulence determinants, inflammatory potential, antibiotic resistances, aggregative properties and morphological characteristics. However, uncertainty still exists regarding the exact clinical relevance of these phylogroups, as well as the wider issue of whether isolates recovered from different clinical samples are truly representative of infection in all contexts or are simply skin contaminants or passive bystanders within a sample [15].

Since *C. acnes* can be isolated as a pathogen or a contaminant, it can be difficult to interpret clinical significance simply based on its isolation. In addition, subacute and chronic shoulder PJI typically present with low-grade, indolent clinical features and normal laboratory inflammatory markers, which further confounds this distinction [15–17]. Microbial characteristics that indicate whether the isolated *C. acnes* is a likely cause of orthopaedic implant infection versus a colonizing agent would be clinically useful. In a prospective study conducted by Sampedro et al. [18], the phylotype of *Cutibacterium* had no clear association with infection or colonization of failed orthopaedic implants [10]. To date, no clear association between phylotypes and infection/colonization or outcome of infection has been reported [13].

Considering this uncertainty over clinical relevance and utility and considering the high costs and limited availability in clinical microbiology laboratories, we suggest that *Cutibacterium acnes* isolated in samples from the shoulder should not be routinely specified according to phylogroups. Rather, these techniques should be reserved for research purposes. Studies focusing on the determination of phylotypes and identification of virulence factors associated with deep infection should be encouraged, since these tools may become useful to improve diagnosis by means of the development of new techniques to identify target strains that can cause infection [3].

REFERENCES

[1] Scholz CFP, Kilian M. The natural history of cutaneous propionibacteria, and reclassification of selected species within the genus Propionibacterium to the proposed novel genera Acidipropionibacterium gen. nov., Cutibacterium gen. nov. and Pseudopropionibacterium gen. nov. Int J Syst Evol Microbiol. 2016;66:4422–4432. doi:10.1099/ijsem.0.001367.

[2] Bémer P, Corvec S, Tariel S, Asseray N, Boutoille D, Langlois C, et al. Significance of Propionibacterium acnes-positive samples in spinal instrumentation. Spine. 2008;33:E971-E976. doi:10.1097/BRS.0b013e31818e28dc.
[3] Hsu JE, Bumgarner RE, Matsen FA. Propionibacterium in shoulder arthroplasty: what we think we know today. J Bone Joint Surg Am. 2016;98:597–606. doi:10.2106/JBJS.15.00568.
[4] Grosso MJ, Frangiamore SJ, Ricchetti ET, Bauer TW, Iannotti JP. Sensitivity of frozen section histology for identifying Propionibacterium acnes infections in revision shoulder arthroplasty. J Bone Joint Surg Am. 2014;96:442–447. doi:10.2106/JBJS.M.00258.
[5] Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR, et al. Microbiologic diagnosis of prosthetic shoulder infection by use of implant sonication. J Clin Microbiol. 2009;47:1878–1884. doi:10.1128/JCM.01686-08.
[6] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.
[7] Sabesan VJ, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. Clin Orthop Relat Res. 2011;469:2538–2543. doi:10.1007/s11999-011-1774-5.
[8] Mollerup S, Friis-Nielsen J, Vinner L, Hansen TA, Richter SR, Fridholm H, et al. Propionibacterium acnes: disease-causing agent or common contaminant? Detection in diverse patient samples by next-generation sequencing. J Clin Microbiol. 2016;54:980–987. doi:10.1128/JCM.02723-15.
[9] Burnham JP, Shupe A, Burnham CD, Warren DK. Utility of strain typing of Propionibacterium acnes in central nervous system and prosthetic joint infections to differentiate contamination from infection: a retrospective cohort. Eur J Clin Microbiol Infect Dis. 2017;36:2483–2489. doi:10.1007/s10096-017-3090-9.
[10] 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 Joint Surg Am. 2015;97:957–963. doi:10.2106/JBJS.N.00784.
[11] 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;23:1763–1771. doi:10.1016/j.jse.2014.05.024.
[12] 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;22:505–511. doi:10.1016/j.jse.2012.07.007.
[13] Falconer TM, Baba M, Kruse LM, Dorrestijn O, Donaldson MJ, Smith MM, et al. Contamination of the surgical field with Propionibacterium acnes in primary shoulder arthroplasty. J Bone Joint Surg Am. 2016;98:1722–1728. doi:10.2106/JBJS.15.01133.
[14] Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA. Propionibacterium persists in the skin despite standard surgical preparation. J Bone Joint Surg Am. 2014;96:1447–1450. doi:10.2106/JBJS.M.01474.
[15] Barnard E, Nagy I, Hunyadkürti J, Patrick S, McDowell A. Multiplex touchdown PCR for rapid typing of the opportunistic pathogen Propionibacterium acnes. J Clin Microbiol. 2015;53:1149–1155. doi:10.1128/JCM.02460-14.
[16] McDowell A, Valanne S, Ramage G, Tunney MM, Glenn JV, McLorinan GC, et al. Propionibacterium acnes types I and II represent phylogenetically distinct groups. J Clin Microbiol. 2005;43:326–334. doi:10.1128/JCM.43.1.326-334.2005.
[17] McDowell A, Perry AL, Lambert PA, Patrick S. A new phylogenetic group of Propionibacterium acnes. J Med Microbiol. 2008;57:218–224. doi:10.1099/jmm.0.47489-0.
[18] Sampedro MF, Piper KE, McDowellA, Patrick S, Mandrekar JN, Rouse MS, et al. Species of Propionibacterium and Propionibacterium acnes phylotypes associated with orthopedic implants. Diagn Microbiol Infect Dis. 2009 Jun;64(2):138-45. doi: 10.1016/j.diagmicrobio.2009.01.024.

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QUESTION 3: Is there a role for Polymerase chain reaction/next generation sequencing (PCR/NGS) technique in the diagnosis of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There is not sufficient data to support the use of PCR or NGS in diagnosis of shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

A comprehensive literature review was performed to identify all studies on use of PCR or NGS in diagnosis of shoulder PJI. Searches for the terms "polymerase chain reaction shoulder arthroplasty," "polymerase chain reaction shoulder replacement," "next generation sequencing shoulder arthroplasty" and "next generation sequencing shoulder replacement" were performed using the search engines PubMed and Scopus, which were searched through February 2018. Inclusion criteria for our systematic review were all English studies (Level I-IV evidence) that reported on PCR or NGS in diagnosis of shoulder PJI. Exclusion criteria were non-English language articles, nonhuman studies, retracted papers, case reports, review papers, studies with less than 10 patients in the sample size, studies without clinical follow-up/infection rates and technique papers without patient data. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed. After removal of duplicates, 12 titles were evaluated and zero studies met full inclusion and exclusion criteria to allow for analysis.

There is limited data in the shoulder literature specific to the use of PCR or NGS to diagnose periprosthetic joint infection. Holmes et al. won the Neer Award in 2017 for their investigation of a polymerase chain reaction-restriction fragment length polymorphism (RFLP) approach that sensitively and specifically identifies *C. acnes* in tissue specimens within a 24-hour period [1]. Samples from five surgical biopsies were tested with the PCR-RFLP assay, and samples from two patients undergoing revision shoulder arthroplasty for culture-positive *C. acnes* infection both yielded a positive result by PCR. Additionally, samples from 3 patients undergoing revision shoulder arthroplasty for aseptic indications tested negative with the PCR-RFLP assay. A recent study from the hip and knee arthroplasty literature demonstrated the potential for NGS to diagnose PJI. Tarabichi et al. performed a prospective evaluation of 65 revision hip and knee arthroplasties [2]. In 28 revisions, the cases were considered to be infected; cultures were positive in 17 cases (60.7%), and NGS was positive in 25 cases (89.3%), with concordance between NGS and culture in 15 cases. Among the 11 cases of culture-negative PJI, NGS was able to identify an organism in 9 cases (81.8%). This data indicates that NGS may provide additional information in cases of potential PJI. There is currently no published data on NGS in the shoulder. An unpublished study from the Rothman Institute indicates that some cases of monomicrobial shoulder PJI may have additional organisms that escape detection when culture is used, which may be detected by NGS. Further research will be needed to determine whether NGS has a role in shoulder PJI diagnosis.

REFERENCES

[1] Holmes S, Pena Diaz AM, Athwal GS, Faber KJ, O'Gorman DB. Neer Award 2017: A rapid method for detecting Propionibacterium acnes in surgical biopsy specimens from the shoulder. J Shoulder Elbow Surg. 2017;26:179–185. doi:10.1016/j.jse.2016.10.001.

[2] Tarabichi M, Shohat N, Goswami K, Alvand A, Silibovsky R, Belden K, et al. Diagnosis of periprosthetic joint infection: the potential of next-generation sequencing. J Bone Joint Surg Am. 2018;100:147–154. doi:10.2106/JBJS.17.00434.

2.3. DIAGNOSIS: DIAGNOSTIC CRITERIA

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QUESTION 1: What clinical signs (e.g., gross wound changes (swelling, erythema or drainage)) are concerning for shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: The presence of a sinus tract is the only clinical sign that can be considered highly specific for shoulder PJI. Other clinical signs of shoulder PJI include unexpected wound drainage.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Infections after shoulder arthroplasty often involve lower virulence bacteria such as *Cutibacterium acnes* and *Staphylococcus epidermidis*, and, as a consequence, the usual obvious signs of infection are frequently absent. In the case of subacute and late shoulder PJI (again, with inconsistently defined timing), the clinical presentation may be limited to a painful and stiff shoulder, which can lead to confusion with aseptic causes of prosthetic failure [1-3]. In these cases, clinical signs are not considered specific enough, and further investigations are needed for the diagnosis of infection.

A PubMed search was performed with the keywords "Shoulder" (Title) AND "Infection" (Title/Abstract). Among the 570 entries, we selected only the articles involving shoulder prostheses and focused on clinical studies only. We excluded the studies that did not report the initial presentation (one study focusing on the second stage of two-stage revision only). We found no meta-analysis reporting the initial clinical features at presentation. Twenty-five studies were included in the final full-text review for this analysis.

Among the 25 published series of shoulder periprosthetic infection, we identified in the literature [1–25], clinical symptoms were constantly cited as an important part of the diagnostic process. Despite this, clinical presentation was not always precisely reported in the published series [26], and this allowed only a limited analysis: 9 series did not give any information about clinical signs [2-4,7,15,18,21,22,25], and, in the 16 others, the clinical description was incomplete in most of the cases. Furthermore, the clinical criteria were never stratified by timing of presentation (acute, subacute, chronic), and, when they were, the definitions of these timings varied, making it impossible to draw conclusions regarding the utility of clinical features depending on timing of presentation.

Sinus Tract

The presence of a sinus tract has always been recognized among the major clinical criterion for the diagnosis of infection and is one of the criteria published by the Musculoskeletal Infection Society in 2009 [27]. Eleven of the 25 series reviewed reported on the presence or absence of a sinus tract at the time of diagnosis, accounting for 264 shoulders [5,9,10, 12-14,16,17,19,20,24]. A sinus tract was reported in 110 cases (41.7%). In each of these cases, infection was considered obvious, even in the absence of other clinical, laboratory (white blood cell count, C-reactive protein, erythrocyte sedimentation rate) or microbiological findings. In addition to a sinus tract formation, the development of unexpected wound drainage (drainage outside of the immediate postoperative period) is highly suspicious for the development of shoulder PJI. Kelly et al. [28] specifically utilized "wound drainage" in their definition of shoulder PJI. The inflammatory process leading to wound drainage from a previously dry, healing wound has limited etiologies and should significantly raise the suspicion for PJI.

Local Tissue Inflammation

The presence of erythema and swelling is mentioned in only 7 studies (187 shoulders) and reported in 71 cases (38%) [4,5,9,11,17,19,20]. Although very suggestive of infection, these symptoms are not usually considered specific enough to reach with certainty a diagnosis of infection. In fact, a certain degree of erythema and swelling can be seen in cases of hematoma, allergy or other acute aseptic problem (i.e., periprosthetic fracture or aseptic loosening).

Fever

Systemic signs of infection such as fever are rarely reported in association with shoulder PJI. Only 4 studies specified if fever was present at the time of diagnosis; 14 cases among 132 patients (10.6%) [14,16,19,20]. It is impossible to ascertain why fever was not reported in the other literature reviewed and whether it was not present or if it was an omission. The presence of fever in association with shoulder PJI suggests a more fulminant process. Fever in the absence of other clinical signs of shoulder infection may indicate another unrelated process.

Pain and Impaired Function

Although nonspecific, shoulder pain and dysfunction are the most frequent signs/symptoms associated with shoulder PJI. Shoulder arthroplasty, when performed for the proper indications,

is highly effective at pain relief. In many cases of late shoulder PJI, including those with unexpected positive cultures, a change in patient pain and dysfunction are often the only clinical manifestation. On the other hand, when pain does not normally diminish in the early recovery period after surgery (first few weeks), PJI should also be suspected. Two hundred fifty patients among 276 (90.6%) reported in 10 studies [1,5,6,8,10,14,19,20,23,24], suffered from shoulder pain and impairment at the time of diagnosis, making pain a sensitive symptom. Pain can be associated with other local signs (inflammatory wound, swelling, collection, fistula), or may be present in isolation. In the case of a painful shoulder arthroplasty, establishing a diagnosis of infection is often difficult and should be based on further investigation. Nevertheless, infection should be strongly considered in the case of a painful shoulder arthroplasty. In less than 10% of cases, an infected shoulder prosthesis can be painless, but in these cases, there is always local evidence for an infection (inflammatory wound, swelling, collection, fistula).

Stiffness

Limited range of motion is classically associated with shoulder periprosthetic infection, but was specifically reported in only one study (30 out of 44 patients; 68.2%) [5]. It frequently occurs in conjunction with pain, another nonspecific symptom.

REFERENCES

[1] Braman JP, Sprague M, Bishop J, Lo IK, Lee EW, Flatow EL. The outcome of resection shoulder arthroplasty for recalcitrant shoulder infections. J Shoulder Elbow Surg. 2006;15:549–553. doi:10.1016/j.jse.2005.11.001.

[2] Buchalter DB, Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Two-stage revision for infected shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:939–947. doi:10.1016/j.jse.2016.09.056.

[3] Jawa A, Shi L, O'Brien T, Wells J, Higgins L, Macy J, et al. Prosthesis of antibiotic-loaded acrylic cement (PROSTALAC) use for the treatment of infection after shoulder arthroplasty. J Bone Joint Surg Am. 2011;93:2001–2009. doi:10.2106/JBJS.J.00833.

[4] Achermann Y, Sahin F, Schwyzer H, Kolling C, Wüst J, Vogt M. Characteristics and outcome of 16 periprosthetic shoulder joint infections. Infection. 2013;41:613–620. doi:10.1007/s15010-012-0360-4.

[5] Amaravathi RS, Kany J, Melet M, Katz D, Sauzieres P, Valenti P, et al. Analysis of infection in shoulder arthroplasty: a multicentre study. Eur J Orthop Surg Traumatol. 2012;22:145–150. doi:10.1007/s00590-011-0806-x.

[6] Assenmacher AT, Alentorn-Geli E, Dennison T, Baghdadi YMK, Cofield RH, Sánchez-Sotelo J, et al. Two-stage reimplantation for the treatment of deep infection after shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:1978–1983. doi:10.1016/j.jse.2017.05.005.

[7] Beekman PDA, Katusic D, Berghs BM, Karelse A, De Wilde L. One-stage revision for patients with a chronically infected reverse total shoulder replacement. J Bone Joint Surg Br. 2010;92:817–822. doi:10.1302/0301-620X.92B6.23045.

[8] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.

[9] Cuff DJ, Virani NA, Levy J, Frankle MA, Derasari A, Hines B, et al. The treatment of deep shoulder infection and glenohumeral instability with debridement, reverse shoulder arthroplasty and postoperative antibiotics. J Bone Joint Surg Br. 2008;90-B:336–342. doi:10.1302/0301-620X.90B3.19408.

[10] Dennison T, Alentorn-Geli E, Assenmacher AT, Sperling JW, Sánchez-Sotelo J, Cofield RH. Management of acute or late hematogenous infection after shoulder arthroplasty with irrigation, débridement, and component retention. J Shoulder Elbow Surg. 2017;26:73–78. doi:10.1016/j.jse.2016.05.018.

[11] Dodson CC, Craig EV, Cordasco FA, Dines DM, Dines JS, Dicarlo E, et al. Propionibacterium acnes infection after shoulder arthroplasty: a diagnostic challenge. J Shoulder Elbow Surg. 2010;19:303–307. doi:10.1016/j.jse.2009.07.065.

[12] Ghijselings S, Stuyck J, Debeer P. Surgical treatment algorithm for infected shoulder arthroplasty: a retrospective analysis of 17 cases. Acta Orthop Belg. 2013;79:626–635.

[13] Ince A, Seemann K, Frommelt L, Katzer A, Loehr JF. One-stage exchange shoulder arthroplasty for peri-prosthetic infection. J Bone Joint Surg Br. 2005;87:814–818. doi:10.1302/0301-620X.87B6.15920.

[14] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.

[15] Jerosch J, Schneppenheim M. Management of infected shoulder replacement. Arch Orthop Trauma Surg. 2003;123:209–214. doi:10.1007/s00402-003-0497-9.

[16] Klatte TO, Junghans K, Al-Khateeb H, Rueger JM, Gehrke T, Kendoff D, et al. Single-stage revision for peri-prosthetic shoulder infection: outcomes and results. Bone Joint J. 2013;95-B:391–395. doi:10.1302/0301-620X.95B3.30134.

[17] Levy JC, Triplet J, Everding N. Use of a functional antibiotic spacer in treating infected shoulder arthroplasty. Orthopedics. 2015;38:e512–e519. doi:10.3928/01477447-20150603-60.

[18] Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Definitive treatment of infected shoulder arthroplasty with a cement spacer. Orthopedics. 2016;39:e924–930. doi:10.3928/01477447-20160623-07.

[19] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.

[20] Romanò CL, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. Int Orthop. 2012;36:1011–1017. doi:10.1007/s00264-012-1492-y.

[21] Sabesan VJ, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. Clin Orthop Relat Res. 2011;469:2538–2543. doi:10.1007/s11999-011-1774-5.

[22] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.

[23] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. J Bone Joint Surg Br. 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.

[24] Weber P, Utzschneider S, Sadoghi P, Andress H-J, Jansson V, Müller PE. Management of the infected shoulder prosthesis: a retrospective analysis and review of the literature. Int Orthop. 2011;35:365–373. doi:10.1007/s00264-010-1019-3.

[25] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. J Shoulder Elbow Surg. 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.

[26] Hsu JE, Somerson JS, Vo KV, Matsen FA. What is a "periprosthetic shoulder infection"? A systematic review of two decades of publications. Int Orthop. 2017;41:813–822. doi:10.1007/s00264-017-3421-6.

[27] Parvizi J, Gehrke T, International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. J Arthroplasty. 2014;29:1331. doi:10.1016/j.arth.2014.03.009.

[28] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467(9):2343–2348. doi:10.1007/s11999-009-0875-x

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QUESTION 2: What radiographic findings are concerning for shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Radiographic findings concerning for shoulder PJI include component loosening or migration, radiolucent lines, osteolysis, endosteal scalloping and new bone formation. Specifically, humeral loosening should significantly raise the suspicion for shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

A formal comprehensive literature search was performed to address this subject. PubMed, conference proceedings and Google scholar were searched using the following terms and keywords: infection, periprosthetic, prosthesis, arthroplasty, low-grade, total shoulder, shoulder arthroplasty, radiology, X-rays and imaging.

Plain Radiographs

The typical clinical presentation of an acutely infected shoulder arthroplasty includes (1) local symptoms, such as shoulder pain, decreased range of motion, erythema, swelling, wound drainage, draining sinus, purulence and warmth; and (2) systemic symptoms, such as fever, chills and malaise and positive markers (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)). In the presence of these obvious signs of infection, any radiographic change will be attributed to periprosthetic shoulder infection (PSI). However, depending on the virulence of the infecting organisms and the intensity of the host immune response, an infected arthroplasty can have subtle or even no clinical signs. This is true of most subacute and chronic PSI and almost universally true in revision of cases of apparently aseptic failure that are subsequently determined to be infected. Plain radiographs may help to determine the diagnosis of PSI. If any of the following are present, infection should be considered: non-traumatic periprosthetic fracture, fracture of the arthroplasty material, implant loosening, osteolysis without loosening, periosteal new bone formation, subluxation due to cuff failure from infection or dislocation.

Detection of periprosthetic lucency, loosening of the prosthesis components, effusion, adjacent soft tissue gas or fluid collection, or periosteal new bone formation around the hip arthroplasty may suggest infection, but none are either sensitive or specific [1]. A study of 65 patients with painful hip arthroplasties found that the presence of either lucency or periosteal new bone formation was 75% sensitive but only 28% specific for diagnosis of PJI [2]. Periosteal new bone formation alone was 100% specific but occurred in only 16% of patients with PJI. Serial radiographs with progressively expanding lucency over several months may also suggest PJI.

Plain radiographs are essential for the evaluation of any painful shoulder arthroplasty but are neither sensitive nor specific for the diagnosis of low-grade indolent infection. Typical radiographic findings that suggest periprosthetic infection include radiolucent lines around the components, osteolysis, bone erosion, endosteal scalloping, new periosteal bone formation and shift of the components. These findings are, however, often absent in indolent or low-grade infection.

In a review of 193 revision shoulder arthroplasty patients without obvious clinical evidence of infection, Pottinger et al. [3] reported a 56% incidence of unexpected positive intraoperative culture, with *C. acnes* being identified most commonly in 69% of the positive cultures. They found that humeral component loosening and humeral osteolysis on plain radiographs were associated with 3-fold and 10-fold increases, respectively, in the risk of a positive *C. acnes* culture.

Radiolucent lines around the glenoid component have been reported to be common even in the immediate postoperative period [4–6]. Interpretation of these radiolucent lines in the absence of clinical symptoms or signs should be done with caution so as not to inappropriately assume that there is an infection. However, radiolucent lines that appear relatively early after surgery and those that are significant enough to cause loosening of the component should always raise a high index of suspicion of infection, especially in the presence of pain or stiffness.

Computed Tomography (CT) Scans

CT scans are often used in revision shoulder arthroplasty for evaluation of the remaining bone stock, implant position and loosening, glenoid component wear, soft tissue swelling, fluid collection, and rotator cuff tendon and muscle pathology. However, the value of CT scan as a direct diagnostic modality for infection is limited to the identification of the same structural changes as observed in plain radiographs, and the metal artifact from the implants can make the interpretation difficult.

If there is a need for computed tomography arthrography, such as for evaluation of rotator cuff integrity or glenoid loosening, a joint aspiration can be performed concomitantly for synovial fluid analysis and culture.

CT has the advantages of high spatial resolution and allows for the evaluation of signs of infection in the periprosthetic tissues. One study found that detection of joint distention upon CT imaging was highly sensitive (83%) and specific (96%) for suspected hip arthroplasty infection [2]. However, the added benefit of these findings beyond history, physical examination and plain radiographs is unclear. The same study found no difference in the evaluation of the bony structures compared to the use of plain radiographs.

Magnetic Resonance Imaging (MRI)

MRI is of little value in the diagnosis of infection because of metal artifact from implants and is seldom used. Adjustments in the image acquisition parameters can lessen but not eliminate these artifacts. The metal artifact reduction sequence (MARS) can be helpful is some occasions. The MARS technique allows visualization of structures adjacent to metal implants and may improve visualisation of periprosthetic bone and soft-tissue structures near total shoulder arthroplasty [7,8].

Nuclear imaging

Currently, little is known about the diagnostic accuracy of nuclear imaging for indolent or low-grade periprosthetic shoulder joint infection (PSJI). It is reported to have a limited direct role in diagnosis of lower extremity PJI [9,10].

Technetium Tc99m bone scintigraphy is sensitive for identifying a failed arthroplasty but cannot differentiate between infection and aseptic failure. Neither periprosthetic uptake patterns nor performance of the test as a 3-phase study significantly improves the accuracy, which is only about 50% to 70% [9].

Three-phase bone scintigraphy is one of the most widely utilized imaging techniques in the diagnosis of PJI. The intensity of uptake following injection of the radiopharmaceutical is measured at three different time points, corresponding to blood flow (immediate), blood pool (at 15 min) and late (at 2 to 4 h) time points [11,12]. Uptake at the prosthesis interfaces at the blood pool and late time points suggests PJI. A limitation of this technique is the lack of specificity.

Asymptomatic patients frequently have uptake detected by delayed-phase imaging in the first year or two after implantation [13]. Given that many PJI occur within this time period, this lack of specificity, reportedly as low as 18%, is a limitation for the use of this technology. However, three-phase bone scintigraphy may be more useful for PJI occurring late after arthroplasty.

A study of 92 patients undergoing evaluation for revision of hip arthroplasty at mean of 9 years after implantation found that increased uptake at both the second and third phases provided sensitivity and specificity for making an accurate diagnosis of 68% and 76%, respectively [14]. The fact that only a minority of these patients underwent revision limits comparison to a true diagnostic gold standard. Another study reported a sensitivity of 88% and a specificity of 90% for detecting PJI in 46 patients at a mean of 8.5 years after hip arthroplasty [15].

Other imaging modalities may be performed in conjunction with bone scintigraphy in an effort to increase specificity. Radioactive Indium (In111) is used to label autologous leukocytes, which are then re-injected with images being obtained 24 hours later. A positive scan is typically considered when there is uptake on the labeled leukocyte image, with absent or decreased uptake at the same location on the late-phase bone scan [16]. A late-phase bone scan combined with a 111In leukocyte scan was 64% sensitive and 70% specific for detection of PJI in 166 revision knee or hip arthroplasties at a median of 7 years after implantation [17].

Indium In 111-labeled white blood cell (WBC) scan has been regarded as the gold standard technique for diagnosis of infectious conditions that involve local accumulation of leucocytes (usually pyogenic organisms) [18]; however, the accuracy for PSJI is reported to be poor. In a study of 17 patients with verified PSJI, Strickland et al. [19] reported that 111In-labeled WBC count scan was obtained in eight shoulders and all scans were negative. Variable and often poor sensitivity and specificity of nuclear imaging in diagnosis of PSJI make the interpretation of the findings difficult [20].

Other studies using slightly different technologies have reported somewhat higher accuracies, with sensitivities ranging from 77 to 100% and specificities ranging from 86 to 91% [16,21,22]. Fluoro-2-deoxyglucose [^{18}F-FDG] positron emission tomography (FDG-PET) is widely used in cancer care and treatment and has emerged as a diagnostic modality for PJI. A meta-analysis of 11 studies involving 635 prosthetic hip and knee arthroplasties found that FDG-PET had pooled sensitivity and specificity values of 82.1% and 86.6%, respectively, for the diagnosis of PJI [23–27].

While several nuclear imaging techniques [28] have been used to diagnosis PJI, the most accurate and cost-effective technique has yet to be elucidated. Furthermore, with the high cost of performing and analyzing nuclear imaging, its role in the workup for PJI should be limited. As such, there is rare utility for nuclear imaging with the multitude of more cost-effective measures.

REFERENCES

[1] Tigges S, Stiles RG, Roberson JR. Appearance of septic hip prostheses on plain radiographs. AJR Am J Roentgenol. 1994;163:377–380. doi:10.2214/ajr.163.2.8037035.

[2] Cyteval C, Hamm V, Sarrabère MP, Lopez FM, Maury P, Taourel P. Painful infection at the site of hip prosthesis: CT imaging. Radiology. 2002;224:477–483. doi:10.1148/radiol.2242010989.

[3] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[4] Vavken P, Sadoghi P, von Keudell A, Rosso C, Valderrabano V, Müller AM. Rates of radiolucency and loosening after total shoulder arthroplasty with pegged or keeled glenoid components. J Bone Joint Surg Am. 2013;95:215–221. doi:10.2106/JBJS.L.00286.

[5] Klepps S, Chiang AS, Miller S, Jiang CY, Hazrati Y, Flatow EL. Incidence of early radiolucent glenoid lines in patients having total shoulder replacements. Clin Orthop Relat Res. 2005:118–125.

[6] Lazarus MD, Jensen KL, Southworth C, Matsen FA. The radiographic evaluation of keeled and pegged glenoid component insertion. J Bone Joint Surg Am. 2002;84-A:1174–1182.

[7] Olsen RV, Munk PL, Lee MJ, Janzen DL, MacKay AL, Xiang QS, et al. Metal artifact reduction sequence: early clinical applications. Radiographics. 2000;20:699–712. doi:10.1148/radiographics.20.3.g00ma10699.

[8] Lohmann CH, Rampal S, Lohrengel M, Singh G. Imaging in peri-prosthetic assessment: an orthopaedic perspective. EFORT Open Rev. 2017;2:117–125. doi:10.1302/2058-5241.2.160058.

[9] Love C, Marwin SE, Palestro CJ. Nuclear medicine and the infected joint replacement. Semin Nucl Med. 2009;39:66–78. doi:10.1053/j.semnuclmed.2008.08.007.

[10] Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Orthop Res. 2014;32 Suppl 1:S98–S107. doi:10.1002/jor.22553.

[11] Glaudemans AWJM, Galli F, Pacilio M, Signore A. Leukocyte and bacteria imaging in prosthetic joint infection. Eur Cell Mater. 2013;25:61–77.

[12] Erba PA, Glaudemans AWJM, Veltman NC, Sollini M, Pacilio M, Galli F, et al. Image acquisition and interpretation criteria for 99mTc-HMPAO-labelled white blood cell scintigraphy: results of a multicentre study. Eur J Nucl Med Mol Imaging. 2014;41:615–623. doi:10.1007/s00259-013-2631-4.

[13] Rosenthall L, Lepanto L, Raymond F. Radiophosphate uptake in asymptomatic knee arthroplasty. J Nucl Med. 1987;28:1546–1549.

[14] Reinartz P, Mumme T, Hermanns B, Cremerius U, Wirtz DC, Schaefer WM, et al. Radionuclide imaging of the painful hip arthroplasty: positron-emission tomography versus triple-phase bone scanning. J Bone Joint Surg Br. 2005;87:465–470. doi:10.1302/0301-620X.87B4.14954.

[15] Nagoya S, Kaya M, Sasaki M, Tateda K, Yamashita T. Diagnosis of peri-prosthetic infection at the hip using triple-phase bone scintigraphy. J Bone Joint Surg Br. 2008;90:140–144. doi:10.1302/0301-620X.90B2.19436.

[16] Love C, Marwin SE, Tomas MB, Krauss ES, Tronco GG, Bhargava KK, et al. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection 18F-FDG and 111In-labeled leukocyte/99mTc-sulfur colloid marrow imaging. J Nucl Med. 2004;45:1864–1871.

[17] Teller RE, Christie MJ, Martin W, Nance EP, Haas DW. Sequential indium-labeled leukocyte and bone scans to diagnose prosthetic joint infection. Clin Orthop Relat Res. 2000:241–247.

[18] Gemmel F, Van den Wyngaert H, Love C, Welling MM, Gemmel P, Palestro CJ. Prosthetic joint infections: radionuclide state-of-the-art imaging. Eur J Nucl Med Mol Imaging. 2012;39:892–909. doi:10.1007/s00259-012-2062-7.

[19] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. J Bone Joint Surg Br. 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.

[20] Saltzman MD, Marecek GS, Edwards SL, Kalainov DM. Infection after shoulder surgery. J Am Acad Orthop Surg. 2011;19:208–218.

[21] Love C, Tomas MB, Marwin SE, Pugliese PV, Palestro CJ. Role of nuclear medicine in diagnosis of the infected joint replacement. Radiographics. 2001;21:1229–1238. doi:10.1148/radiographics.21.5.g01se191229.

[22] Scher DM, Pak K, Lonner JH, Finkel JE, Zuckerman JD, Di Cesare PE. The predictive value of indium-111 leukocyte scans in the diagnosis of infected total hip, knee, or resection arthroplasties. J Arthroplasty. 2000;15:295–300.

[23] Kwee TC, Kwee RM, Alavi A. FDG-PET for diagnosing prosthetic joint infection: systematic review and metaanalysis. Eur J Nucl Med Mol Imaging. 2008;35:2122–2132. doi:10.1007/s00259-008-0887-x.

[24] Kwee TC, Basu S, Torigian DA, Zhuang H, Alavi A. FDG PET imaging for diagnosing prosthetic joint infection: discussing the facts, rectifying the unsupported claims and call for evidence-based and scientific approach. Eur J Nucl Med Mol Imaging. 2013;40:464–466. doi:10.1007/s00259-012-2319-1.

[25] Kwee TC, Basu S, Alavi A. Should the nuclear medicine community continue to underestimate the potential of 18F-FDG-PET/CT with present generation scanners for the diagnosis of prosthetic joint infection? Nucl Med Commun. 2015;36:756–757. doi:10.1097/MNM.0000000000000318.

[26] Kwee TC, Basu S, Alavi A. The ongoing misperception that labeled leukocyte imaging is superior to 18F-FDG PET for diagnosing prosthetic joint infection. J Nucl Med. 2017;58:182. doi:10.2967/jnumed.116.181461.

[27] Palestro CJ. Radionuclide imaging of musculoskeletal infection: a review. J Nucl Med. 2016;57:1406–1412. doi:10.2967/jnumed.115.157297.

[28] Gyftopoulos S, Rosenberg ZS, Roberts CC, Bencardino JT, Appel M, Baccei SJ, et al. ACR appropriateness criteria imaging after shoulder arthroplasty. J Am Coll Radiol. 2016;13:1324–1336. doi:10.1016/j.jacr.2016.07.028.

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QUESTION 3: What intraoperative findings are concerning for shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: The presence of humeral stem loosening and cloudy synovial fluid should raise suspicion for shoulder PJI. Gross intra-articular pus (without a mechanical or rheumatologic explanation) or the presence of a sinus tract, communicating with the implant, are pathognomonic for periprosthetic shoulder infection.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

Each specific clinical question was queried via input of keywords into the PubMed search engine. Appropriate references were reviewed to summarize findings and determine the level of evidence. The bibliographies of selected articles were scanned for additional references that may be applicable to the question. The findings of applicable studies were synthesized to formulate recommendations.

Synovial Fluid Analysis

The presence of "cloudy" fluid noted intraoperatively is associated with *C. acnes* culture positive prosthetic shoulder revisions. When combined with other patient demographics (male), radiographic features (humeral osteolysis and glenoid loosening) and the presence of a humeral membrane, cloudy fluid was associated with a 3-6 fold increase in the risk of shoulder PJI [1,2]. The presence of cloudy fluid suggests an elevated white blood cell (WBC) count. However, what constitutes "cloudy fluid" is subjective. Additionally, the threshold value for an elevated WBC for shoulder PJI is unknown and may be lower than accepted levels for other prosthetic joint infections given the lower virulence of *C. acnes*. *C. acnes* infections have been associated with relative increases in lymphocytes and plasma cells rather than polymorphonuclear leukocyte (PMN) [3]. The currently accepted white blood cell count thresholds of > 1100-3000 cells/cc with a > 80% PMN differential for chronic hip and knee arthroplasty infections [4,5] are likely not relevant for the diagnosis of shoulder PJI due to the less vigorous inflammatory response elicited by common shoulder bacterial pathogens. However, given the potential for infection by bacterial species other than *C. acnes*, a synovial fluid WBC with differential is a potentially valuable initial screening test for shoulder PJI.

Gross Biofilm

There is weak evidence linking the presence of increased biofilm, specifically humeral membrane, to the presence of bacterial infection, notably *C. acnes* [1,2]. The presence of biofilm formation is common with bacterial infections and not specific to *C. acnes*. Humeral membrane can also be present in cases of aseptic humeral loosening. The amount of biofilm formation that would be considered pathologic or indicative of infection is subjective and not known.

Furthermore, biofilm formation present in infected cases may not be macroscopically detectable. The absence of increased biofilm visually does not rule out a bacterial infection. The presence of biofilm (membrane) alone does not accurately diagnose an infection but may be used as an adjunct finding.

Sinus Tract

See Shoulder: Section 2.3. Diagnosis: Diagnositic Criteria, Question 1 for discussion of sinus tract as diagnostic marker for PJI.

Humeral Stem Loosening

See Shoulder: Section 2.3. Diagnosis: Diagnostic Criteia, Question 5 for discussion of the association between humeral component loosening and PJI.

REFERENCES

[1] Hou C, Gupta A, Chen M, Matsen FA. How do revised shoulders that are culture positive for Propionibacterium differ from those that are not? J Shoulder Elbow Surg. 2015;24:1427–1432. doi:10.1016/j.jse.2015.01.003.

[2] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[3] 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;22:505–511. doi:10.1016/j.jse.2012.07.007.

[4] Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Arthroplasty. 2014;29:77–83. doi:10.1016/j.arth.2013.09.040.

[5] Parvizi J, Ghanem E, Sharkey P, Aggarwal A, Burnett RSJ, Barrack RL. Diagnosis of infected total knee: findings of a multicenter database. Clin Orthop Relat Res. 2008;466:2628–2633. doi:10.1007/s11999-008-0471-5.

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QUESTION 4: What is the role for periprosthetic frozen section and permanent histology in evaluation of a shoulder arthroplasty for periprosthetic joint infection (PJI)?

RECOMMENDATION: Frozen sections or histology, reviewed by an experienced pathologist, may be useful in revision shoulder arthroplasty to evaluate for periprosthetic joint infection. The detection of infection with less virulent organisms, which make up a significant percentage of shoulder PJI, may be less reliable.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 95%, Disagree: 5%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Histologic analysis is well-established as a valuable tool for diagnosing lower extremity PJI [1–4]. Multiple studies of lower extremity revision arthroplasty have shown that frozen section has an accuracy in establishing PJI equivalent to that of permanent histologic analysis [2,5]. This led to the inclusion of frozen section in the American Academy of Orthopedic Surgeons (AAOS) clinical guidelines for the diagnosis of PJI [6], the Musculoskeletal Infection Society (MSIS) definition of PJI [7], and the first International Consensus Meeting on Periprosthetic Joint Infection definition of PJI in 2013 [8].

Intraoperative assessment of periprosthetic inflammation can serve as a quickly available tool in the evaluation for PJI. Despite the extensive evidence supporting its utility in the evaluation of lower extremity arthroplasty, the literature on histologic analysis in shoulder arthroplasty is very limited. Because *Cutibacterium acnes*, a less virulent pathogen, is the predominant cause of shoulder PJI a reassessment of standard markers for PJI is necessary [9–12]. For this purpose, a systematic review of histologic analysis for shoulder PJI was undertaken on Scopus [13] with the query, "(shoulder OR 'upper extremity') AND (arthroplasty OR replacement) AND (infection OR infected) AND ('frozen section' OR histology OR histologic)."

This query identified two articles directly evaluating the use of frozen section in revision shoulder arthroplasty [14,15]. First, Topolski et al. [15] evaluated the utility of frozen section histopathology in patients with unexpected positive cultures (UPC) during revision shoulder arthroplasty. In 75 patients undergoing revision shoulder arthroplasty who had occult infection defined as positive intraoperative cultures, 92% (67/73) had a negative result on frozen section—with a positive result defined as at least five neutrophils on any high-powered field. In this study, there was a single case with a discrepancy between frozen section (negative) and permanent histology (positive). This study demonstrated that most patients with unexpected positive cultures did not have a strong periprosthetic inflammatory response. They concluded that frozen section analysis was not helpful in cases of UPC when using the criteria of Mirra et al. [16].

The second study, Grosso et al., evaluated the results of frozen section in forty-five revision total shoulder arthroplasties [14]. Based upon their definition for infection, the cohort was divided into non-infected (n = 15), infected (n = 12), and *C. acnes* infection (n = 18). Using the threshold from Moraweitz et al. [17], 23 neutrophils over five high-powered fields, frozen section had sensitivity and specificity of 67% and 100% for the infected group and 56% and 100%, respectively, for the *C. acnes* group. Re-evaluating the threshold for positive frozen section with a receiver operating characteristic (ROC) curve found that five high powered fields with a sum of at least ten neutrophils improved the overall sensitivity to 73% without sacrificing specificity. At that institution, with the aid of an experienced pathologist, these authors were able to demonstrate that a lowered threshold for these less-virulent infections can improve the accuracy and utility of frozen section analysis for diagnosing PJI during revision shoulder arthroplasty.

While these two studies are the only shoulder-specific analyses of frozen section for shoulder PJI, their developed thresholds have not been widely adopted by clinical pathologists. In fact, one of the two institutions noted above has since abandoned the clinical use of their published criteria. Therefore, utilization of the standard thresholds from the lower extremity arthroplasty community may be the most prudent currently.

Multiple studies of histologic analysis during lower extremity revision arthroplasty have demonstrated that the concordance between frozen section and permanent histology is very high. Thus, it is expected that the same difficulties with detection of infection by less virulent organisms in shoulder PJI would apply to both permanent, as well as frozen section, histology [2,5,18].

Histologic analysis is also used to evaluate for persistent infection during reimplantation of a hip or knee undergoing two-stage exchange [19–21]. These analyses found poor sensitivity but high specificity in identifying persistent PJI. Such analysis has not been completed in the shoulder and further work is required in this regard.

REFERENCES

[1] Feldman DS, Lonner JH, Desai P, Zuckerman JD. The role of intraoperative frozen sections in revision total joint arthroplasty. J Bone Joint Surg Am. 1995;77:1807–1813.
[2] Kwiecien G, George J, Klika AK, Zhang Y, Bauer TW, Rueda CAH. Intraoperative frozen section histology: matched for musculoskeletal infection society criteria. J Arthroplasty. 2017;32:223–227. doi:10.1016/j.arth.2016.06.019.
[3] Lonner JH, Desai P, Dicesare PE, Steiner G, Zuckerman JD. The reliability of analysis of intraoperative frozen sections for identifying active infection during revision hip or knee arthroplasty. J Bone Joint Surg Am. 1996;78:1553–1558.
[4] Spangehl MJ, Masri BA, O'Connell JX, Duncan CP. Prospective analysis of preoperative and intraoperative investigations for the diagnosis of infection at the sites of two hundred and two revision total hip arthroplasties. J Bone Joint Surg Am. 1999;81:672–683.
[5] Stroh DA, Johnson AJ, Naziri Q., Mont MA. How do frozen and permanent histopathologic diagnoses compare for staged revision after periprosthetic hip infections? J Arthroplasty. 2012;27:1663–1668.e1. doi:10.1016/j.arth.2012.03.035.
[6] Della Valle C, Parvizi J, Bauer TW, DiCesare PE, Evans RP, Segreti J, et al. American Academy of Orthopaedic Surgeons clinical practice guideline on: the diagnosis of periprosthetic joint infections of the hip and knee. J Bone Joint Surg Am. 2011;93:1355–1357. doi:10.2106/JBJS.9314ebo.
[7] Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, et al. New definition for periprosthetic joint infection: from the workgroup of the musculoskeletal infection society. Clin Orthop Relat Res. 2011;469:2992–2994. doi:10.1007/s11999-011-2102-9.

[8] Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Orthop Res. 2014;32 Suppl 1:S98-S107. doi:10.1002/jor.22553.
[9] Ahsan ZS, Somerson JS, Matsen FA. Characterizing the Propionibacterium load in revision shoulder arthroplasty: a study of 137 culture-positive cases. J Bone Joint Surg Am. 2017;99:150–154. doi:10.2106/JBJS.16.00422.
[10] Dodson CC, Craig EV, Cordasco FA, Dines DM, Dines JS, Dicarlo E, et al. Propionibacterium acnes infection after shoulder arthroplasty: a diagnostic challenge. J Shoulder Elbow Surg. 2010;19:303–307. doi:10.1016/j.jse.2009.07.065.
[11] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:620–627. doi:10.1016/j.jse.2012.07.017.
[12] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.
[13] Scopus preview - Scopus - Welcome to Scopus n.d. https://www.scopus.com/home.uri (accessed February 7, 2018).
[14] Grosso MJ, Frangiamore SJ, Ricchetti ET, Bauer TW, Iannotti JP. Sensitivity of frozen section histology for identifying Propionibacterium acnes infections in revision shoulder arthroplasty. J Bone Joint Surg Am. 2014;96:442–447. doi:10.2106/JBJS.M.00258.
[15] Topolski MS, Chin PYK, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: the value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006;15:402–406. doi:10.1016/j.jse.2005.10.001.
[16] Mirra JM, Marder RA, Amstutz HC. The pathology of failed total joint arthroplasty. Clin Orthop Relat Res. 1982:175–183.
[17] Morawietz L, Tiddens O, Mueller M, Tohtz S, Gansukh T, Schroeder JH, et al. Twenty-three neutrophil granulocytes in 10 high-power fields is the best histopathological threshold to differentiate between aseptic and septic endoprosthesis loosening. Histopathology. 2009;54:847–853. doi:10.1111/j.1365-2559.2009.03313.x.
[18] Miyamae Y, Inaba Y, Kobayashi N, Choe H, Yukizawa Y, Ike H, et al. Different diagnostic properties of C-reactive protein, real-time PCR, and histopathology of frozen and permanent sections in diagnosis of periprosthetic joint infection. Acta Orthop. 2013;84:524–529. doi:10.3109/17453674.2013.862460.
[19] Della Valle CJ, Bogner E, Desai P, Lonner JH, Adler E, Zuckerman JD, et al. Analysis of frozen sections of intraoperative specimens obtained at the time of reoperation after hip or knee resection arthroplasty for the treatment of infection. J Bone Joint Surg Am. 1999;81:684–689.
[20] George J, Kwiecien G, Klika AK, Ramanathan D, Bauer TW, Barsoum WK, et al. Are frozen sections and MSIS criteria reliable at the time of reimplantation of two-stage revision arthroplasty? Clin Orthop Relat Res. 2016;474:1619–1626. doi:10.1007/s11999-015-4673-3.
[21] George J, Zhang Y, Jawad M, Faour M, Klika AK, Bauer TW, et al. Diagnostic utility of histological analysis for detecting ongoing infection during two-stage revision prthroplasty in patients with inflammatory arthritis. J Arthroplasty. 2017;33(7S):S219–S223. doi:10.1016/j.arth.2017.12.021.

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QUESTION 5: What are the diagnostic criteria of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: See International Consensus Meeting (ICM) definition of shoulder PJI below.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 88%, Disagree: 12%, Abstain: 0% (Super Majority, Strong Consensus)

INTERNATIONAL CONSENSUS MEETING (ICM) FOR PERIPROSTHETIC JOINT INFECTION: DEFINITION, CATEGORIZATION AND SCORING SYSTEM FOR SHOULDER PJI

Definite PJI

Meeting one of the following criteria is diagnostic of **definite** periprosthetic shoulder infection:

- A sinus tract communicating with the prosthesis is present
- Gross intra-articular pus
- Two positive cultures with phenotypically-identical virulent organisms

Evaluation Scoring

Weighted values for all positive tests performed as part of the diagnostic evaluation of a failed shoulder arthroplasty are summed (Table 1).

- Six or greater with identified organism = **probable PJI**
- Six or greater *without* identified organism = **possible PJI**
- Six or less
  - single positive culture virulent organism = **possible PJI**
  - two positive cultures low-virulence organism = **possible PJI**
  - negative cultures or only single positive culture for low virulent organism = **PJI unlikely**

RATIONALE

The need for a consensus definition of shoulder PJI cannot be understated. A clear definition serves two purposes: (1) to aid in clinical decision making and (2) to provide a framework for consistent future research reporting. Furthermore, acceptance of a definition is a necessary first step in providing a well-tested diagnostic algorithm. As Hsu et al. demonstrated [1], the shoulder research community has used disparate definitions of PJI—likely leading to variable and inconsistent conclusions about the diagnosis and management. Adoption of a uniform definition of PJI for the lower extremity quickly led to hundreds of publications evaluating prevention, diagnosis and treatment of PJI based upon the same consistent diagnostic criteria [2,3]. This task is even more urgent in regard to shoulder arthroplasty due to the unique microbiologic and the ambiguity presented by high rates of positive intraoperative cultures in revision cases that otherwise appear aseptic [4–9]. In order to discuss diagnosis and evaluation of shoulder PJI, it is imperative that the shoulder community begin with a standardized and accepted definition of shoulder PJI.

TABLE 1. Weighted values for all positive tests performed as part of the diagnostic evaluation of a failed shoulder arthroplasty

Minor Criteria	Weight
Unexpected wound drainage	4
Single positive tissue culture (virulent organism)	3
Single positive tissue culture (low-virulence organism)	1
Second positive tissue culture (identical low-virulence organism)	3
Humeral loosening	3
Positive frozen section (5 PMN in at least 5 high-power fields)	3
Positive preoperative aspirate culture (low or high-virulence)	3
Elevated synovial neutrophil percentage (> 80%)*	2
Elevated Synovial WBC (> 3,000 cells / µL)*	2
Elevated ESR (> 30 mm/hr)*	2
Elevated CRP (> 10 mg/L)*	2
Elevated synovial alpha-defensin	2
Cloudy fluid	2

PMN, polymorphonuclear leukocyte; WBC, white blood cell; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein
*Beyond six weeks from recent surgery

Committee Goals

1. Define criteria that establish a diagnosis of shoulder PJI.
2. Provide a common language for research reporting and clinical decision making.
3. The definition should be flexible enough to include the "obvious" suppurative, shoulder PJI, as well as the subtler "stealth" infections and cases where the clinical scenario is unclear.
4. Incorporate the best available evidence in this field.
5. That the definition of shoulder PJI should generally be similar to the Musculoskeletal Infection Society (MSIS) hip and knee definition, but differ according to specific characteristics unique to the shoulder.
    a. Less weight put on positive cultures with low-virulence organisms given the data on this phenomenon in the shoulder.
    b. A larger "grey area" of "possible PJI" to recognize that there are a large number of cases where, given the current state of the field, it is not possible to define as clearly infected or uninfected.
    c. Include a scoring system in order to potentially create objective criteria for sorting these "possible PJI" cases.

Committee Process

The process undertaken to formulate this definition was a consensus effort relying upon the clinical expertise of numerous shoulder and elbow surgeons who routinely treat shoulder periprosthetic joint infection. First, a systematic review as undertaken to evaluate the definitions in use for shoulder PJI and the evidence for each (this is included in Appendix A). Second, over a year-long process, the 69 ICM delegates (experts in shoulder PJI and infectious disease from 11 countries) performed 75 separate, parallel systematic reviews evaluating aspects of prevention, diagnosis and management of shoulder PJI. Following a Delphi process these reviews were disseminated, discussed and then refined in-person at the Second ICM in Philadelphia (July 2018) where delegates voted on each statement. Each of these 75 reports was used by the definition committee in addition to their own experience to discuss potential definition options. These were refined, voted upon and ultimately accepted at the ICM meeting in Philadelphia. The original MSIS criteria have gone through multiple iterations as the consensus definition has been refined through testing and further research. The definition of shoulder PJI is no different, and we fully expect that as researchers begin to adopt this definition the criteria and weightings may change, as our knowledge and understanding of the evaluation and management of shoulder PJI evolves.

Rationale for the Definition

While there remains controversy and uncertainty about the definition and management of shoulder PJI, there are cases that are considered to be unquestionably infected. Therefore, a subgroup of "Definite PJI" shoulder PJI was defined to identify these cases. This included the presence of a sinus tract (as discussed Section 2:3, Question 1), gross intra-articular pus, or two separate positive cultures with identical virulent pathogens (as discussed in Section 2:1, Question 1). While specific evidence for these criteria is lacking, a strong consensus existed that if any of these criteria were met, an infection was undoubtedly present. When assessing intra-articular purulence, consideration must be given to other less common inflammatory conditions, including rheumatologic disease and

reactions to metal or other foreign bodies, which rarely incite a process that produces debris or aseptic purulence in shoulder arthroplasty.

As discussed in Section 2:1, Question 1 and Section 2:5, Question 8, the significance of a positive culture may depend upon the number of cultures sent and the degree of growth. Therefore, as discussed in "Diagnosis: Sampling" Question 8, it is recommended that "five deep tissue specimens for culture be obtained from various surgical sites (e.g., capsule, humeral canal, and periprosthetic membranes in the proximal humerus and glenoid)." This should provide sufficient sensitivity for bacterial growth while minimizing the risk of false positives, as discussed in Section 2:1, Question 1. Furthermore, when reporting results we recommend that the number of positive cultures should be reported as a fraction of the total cultures sent (x/y where x = number of positive cultures and y = total number of cultures sampled) and/or the "Shoulder propi score" Section 2:1, Question 2). Lastly, as discussed in Section 2:2, Question 1, cultures should be held for fourteen days to optimize detection of pathogens.

The lack of these defining signs certainly does not exclude the diagnosis of PJI. Therefore, in these less distinct scenarios three categories were established: "Probable PJI," "Possible PJI" and "PJI unlikely." Given the lack of strong evidence defining the clinical significance of low-virulence positive cultures, this stratification allows for clinical guidance and classification of cases for research purposes without grouping heterogenous cases. For classification of these cases, minor criteria were proposed and edited by the group at large. Many of these minor criteria have been discussed in other questions (Table 1). As the significance of a positive result for these minor criteria varies, each criterion was weighted. It was agreed that a threshold score of six would serve as a marker of the increased likelihood of a shoulder PJI, though the committee fully expects that as this definition is tested and refined, the weightings and the thresholds will be improved.

To apply weight for each of these minor criteria, a score was applied to each criterion independently by every member of the shoulder group in attendance. These scores were then averaged and discussed further, resulting in the weighting reported here. To further test the definition, clinical scenarios were proposed and evaluated with the definition (Table 2). In each case, the ICM diagnostic criteria gave a result which the delegates felt, with consensus, described their own clinical conclusions.

Inflammatory markers (synovial fluid white blood cell count and differential, serum erythrocyte sedimentation rate, and serum C-reactive protein) are often elevated during the early postoperative period, and, thus, use in the diagnostic evaluation was limited to beyond six weeks from a recent surgery. There have been multiple studies in the lower extremity demonstrating the impact of surgery on these inflammatory markers [10,11]. Normal thresholds for inflammatory markers in the acute postoperative period after shoulder arthroplasty have not been established.

The formation of this definition provides an important step in improving the care for patients with and understanding of shoulder PJI. Adoption of this definition by those performing research of shoulder PJI will allow for uniform evaluation of study outcomes as researchers, reviewers and readers will all be using the same language. Lastly, we want to emphasize this definition is a first iteration. As the understanding of shoulder PJI evolves and each diagnostic test is further evaluated, it will be necessary to revisit this definition as a community.

APPENDIX A

Search Strategy and Study Selection

Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we conducted a systematic review to identify all studies concerning diagnosis and treat-

TABLE 2. ICM questions discussing each minor criterion in greater detail

Minor Criteria	Question
Unexpected wound drainage	Section 2:3, Question 1
Single positive tissue culture (virulent organism)	Section 2:1, Question 1
Single positive tissue culture (low-virulence organism)	Section 2:1, Question 1
Second positive tissue culture (identical low-virulence organism)	Section 2:1, Question 1
Humeral loosening	Section 2:3, Question 2
Positive frozen section (5 PMN in at least 5 high-power fields)	Section 2:3, Question 4
Positive preoperative aspirate culture (low or high-virulence)	Section 2:5, Question 8 Section 2:4, Question 9
Elevated synovial neutrophil percentage (> 80%)	Section 2:4, Question 3
Elevated Synovial WBC (> 3,000 cells / µL)	Section 2:4, Question 3
Elevated ESR (> 30 mm/hr)	Section 2:4,Question 1
Elevated CRP (> 10 mg/L)	Section 2:4, Question 1
Elevated synovial alpha-defensin	Section 2:4, Question 7
Cloudy fluid	Section 2:3, Question 3

PMN, polymorphonuclear leukocyte; WBC, white blood cell; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

TABLE 3. Clinical scenarios of the ICM diagnostic criteria in practice

#	Scenario	Definition
1	Painful shoulder arthroplasty: • Positive aspirate culture (*C. acnes*): 3 points • 1/5 intraoperative cultures positive (*C. acnes*): 1 point • Humeral loosening: 3 points	Probable PJI
2	Painful shoulder arthroplasty: • No aspirate completed • Persistent unexpected wound drainage: 4 points • 2/5 intraoperative cultures positive (*C. acnes*): 1 + 3 = 4 points	Probable PJI
3	Painful shoulder arthroplasty: • Dry aspirate • 2/5 intraoperative cultures positive (MSSA) • Elevated ESR • Elevated CRP	Definite PJI
4	Painful shoulder arthroplasty: • Well-fixed components • 2/5 intraoperative cultures positive (*C. acnes*): 1 + 3 = 4 points • All other tests negative	Possible PJI
5	Painful shoulder arthroplasty: • Persistent unexpected wound drainage: 4 points • 1/5 intraoperative cultures positive (*C. acnes*): 1 point • All other tests negative	Unlikely PJI
6	Painful shoulder arthroplasty: • Persistent unexpected wound drainage: 4 points • 1/5 intraoperative cultures positive (MSSA): 3 point • All other tests negative	Probable PJI

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MSSA, methicillin-sensitive *S. aureus*

ment of "infection" at the time of revision shoulder arthroplasty. We searched for all studies published in English using the terms (("revision" OR "failed") AND "shoulder" AND ("arthroplasty" OR "replacement")) limited to dates between January 1, 1996 and February 3, 2018.

A total of 2,354 studies were identified. We reviewed the titles and abstracts of all studies and excluded studies that (1) included patients with shoulder infection without arthroplasty, (2) reported on patients with positive cultures not considered infection or that were "unexpected," as a strict definition of infection in these studies was not applied, or (3) included patients with arthroplasty of joints other than the shoulder. The reference lists for all included studies were searched for any additional references and three references were added to our list. A total of 25 studies met inclusion criteria and were included in the final analysis.

Data Collection

Relevant data were extracted from the selected publications, including the definition of infection used by the authors and the components it involved. Factors involved in the definition of infection included (1) clinical symptoms (erythema, sinus tract formation, drainage, systemic symptoms), (2) preoperative laboratory serology, (3) radiologic tests for infection, (4) preoperative aspiration laboratory results, (5) preoperative aspiration culture results, (6) intraoperative frozen section results and (7) intraoperative culture results.

Results

See Appendix A, Table 1 below. An explicit statement describing how infection was defined was not present in 6 of 25 studies. A classification system was used in 5 of 25 of the studies, including three that utilized the Musculoskeletal Infection Society definition described by Parvizi et al. [2], one that utilized a definition reported by Spangehl et al. [12] for total hip arthroplasty, and one that utilized the classification described by Grosso et al. [13]. The remaining 14 studies used author-defined combinations of clinical symptoms, laboratory tests, radiographic characteristics, findings on aspiration, and results of cultures of specimens harvested at the time of revision.

Workup for Periprosthetic Infection

Utilization of clinical signs and symptoms, preoperative serology, radiographic loosening and preoperative aspiration to workup and define infection was highly variable in the studies reviewed (Table 1). Of the 19 studies that provided a definition for infection, all used clinical examination findings as part of their definition, 14 used serum laboratory results, 6 utilized preoperative shoulder joint aspirate laboratory values, 10 used an intraoperative gram stain or frozen section and 6 used radiographic findings to aid in diagnosis. While all studies performed either preoperative aspiration or intraoperative tissue sampling for culture, intraoperative culture results were utilized in the definition of infection in only 10 studies.

APPENDIX A: TABLE 1. Definition of infection in included studies

Author	Year	Definition Provided	Clinical Exam	Serum Lab Values	Aspirate Values	Aspirate Culture	Surgical Specimen Culture	Intraoperative Frozen / Gram Stain	Radiographic Findings
Previously described criteria									
Ghijselings [14]	2013	"criteria proposed by Parvizi et al."	✓	✓	✓	✓	✓	✓	X
Grubhofer [15]	2018	"according to the Musculoskeletal Infection Society (MSIS) PJI criteria"	✓	✓	✓	✓	✓	✓	X
Jacquot [16]	2015	"according to the Musculoskeletal Infection Society criteria"	✓	✓	✓	✓	✓	✓	X
Lee [17]	2017	"probable or definite infection as the criteria for periprosthetic shoulder infection [by Grosso et al.]"	✓	X	X	X	✓	✓	X
Romanò [18]	2012	"criteria established by Spangehl et al."	✓	✓	X	✓	✓	✓	X
Combined definition									
Achermann [19]	2013	"(1) visible purulence of a preoperative aspirate or intraoperative periprosthetic tissue, (2) presence of a sinus tract communicating with the prosthesis, (3) microbial growth in a preoperative joint aspirate, intraoperative periprosthetic tissue or sonication fluid of the removed implant, or (4) synovial fluid with > 1,700 leukocytes/ul or > 65% granulocytes."	✓	X	✓	✓	✓	X	X
Amaravathi [20]	2012	"based on a combination of symptoms, laboratory tests, and findings of physical examinations such as draining sinus, radiological evidence of loosening of prosthesis, and analysis of intraoperative specimen."	✓	✓	X	X	✓	X	✓
Beekman [21]	2010	"clinical picture… swelling, redness, or a sinus… and laboratory tests… or fistula without altered laboratory tests"	✓	✓	X	X	X	X	X
Buchalter [22]	2017	"clinical, laboratory, radiographic, and operative evaluations"	✓	✓	X	✓	X	✓	✓

TABLE 1. Definition of infection in included studies (*Cont.*)

Author	Year	Definition Provided	Clinical Exam	Serum Lab Values	Aspirate Values	Aspirate Culture	Surgical Specimen Culture	Intraoperative Frozen / Gram Stain	Radiographic Findings
Coste [23]	2004	"1) the presence of a sinus; 2) serum leucocyte count; 3) erythrocyte sedimentation rate; 4) C-reactive protein (CRP); 5) preoperative and peroperative joint aspiration cultures and cultures of surgical specimens; 6) loosening of the components on standard radiographs and periosteal reaction; and 7) three-phase bone isotope scanning."	✓	✓	X	✓	✓	X	✓
Jawa [24]	2011	"combination of symptoms, physical findings, and laboratory tests"	✓	✓	X	X	X	X	X
Jerosch [25]	2003	"clinical symptoms associated with positive blood tests… intra-articular aspirates with WBC over 30,000 cells or positive bacterial growth"	✓	✓	✓	✓	X	X	X
Kelly [6]	2009	"associated skin erythema, wound drainage, or obvious purulence or tissue synovitis at the time of surgery… clinical aspiration yielding a positive Gram stain or culture was considered infected… positive intraoperative Gram stain or frozen section showing more than five polymorphonuclear leukocytes per high-powered field was considered infected."	✓	X	X	✓	✓	✓	X
Levy [26]	2015	"clinical evaluation, radiographs, and laboratory test results"	✓	✓	X	X	X	X	✓
Mahure [27]	2016	"combination of clinical, radiographic, and laboratory tests"	✓	✓	✓	✓	X	✓	✓
Sabesan [28]	2011	"clinical suspicion, positive intraoperative frozen sections, positive culture treated at an outside referring institution, positive preoperative aspiration cultures, or positive intraoperative tissue cultures"	✓	X	X	✓	✓	✓	X
Sperling [29]	2001	"patient's clinical course, the observation of purulence at the time of surgery, and a sinus that communicated directly with the joint"	✓	X	X	X	X	X	X

TABLE 1. Definition of infection in included studies (*Cont.*)

Author	Year	Definition Provided	Clinical Exam	Serum Lab Values	Aspirate Values	Aspirate Culture	Surgical Specimen Culture	Intraoperative Frozen / Gram Stain	Radiographic Findings
Stone [30]	2017	"history of previous infection, findings on physical examination (i.e., skin erythema, swelling, draining sinus), laboratory tests (white blood cell count, erythrocyte sedimentation rate, and C-reactive protein) when obtained, and positive intraoperative findings, including purulence, intraoperative frozen section showing more than 5 polymorphonuclear leukocytes per high-powered field for 5 fields, and cultures"	✓	✓	X	X	✓	✓	X
Weber [31]	2011	"...to substantiate the clinical suspicion, laboratory analysis and radiological examination with blood tests including CRP and WBC. In patients with fistula, microbiological swabs were taken before the procedure and in other patients the joint itself was aspirated. In the case of remaining doubt about the infection, an indium-labelled white blood cell scan was performed."	✓	✓	X	✓	X	X	✓
No clear definition provided									
Braman [32]	2006	"No objective grading criteria were used."							
Ince [33]	2005	None							
Klatte [34]	2013	None							
Ortmaier [35]	2014	None							
Strickland [36]	2008	No explicit definition							
Zavala [37]	2012	None							
Overall	✓= Component of definition		19	14	6	12	11	10	6
	X = Not considered		0	5	13	7	8	9	13

This search methodology, results and table have been adopted and updated from Hsu et al. [1].
CRP, C-reactive protein; MSIS, Musculoskeletal Infection Society; PJI, periprosthetic joint infection; WBC, white blood cell

REFERENCES

[1] Hsu JE, Somerson JS, Vo KV, Matsen FA. What is a "periprosthetic shoulder infection"? A systematic review of two decades of publications. Int Orthop. 2017;41(4):813–822. doi:10.1007/s00264-017-3421-6

[2] Parvizi J, Zmistowski B, Berbari EF, et al. New definition for periprosthetic joint infection: from the workgroup of the musculoskeletal infection society. Clin Orthop Relat Res. 2011;469(11):2992–2994. doi:10.1007/s11999-011-2102-9

[3] Zmistowski B, Della Valle C, Bauer TW, et al. Diagnosis of periprosthetic joint infection. J Orthop Res. 2014;32 Suppl 1:S98–S107. doi:10.1002/jor.22553

[4] Ahsan ZS, Somerson JS, Matsen FA. Characterizing the Propionibacterium load in revision shoulder arthroplasty: a study of 137 culture-positive cases. J Bone Joint Surg Am. 2017;99(2):150–154. doi:10.2106/JBJS.16.00422

[5] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22(5):620–627. doi:10.1016/j.jse.2012.07.017

[6] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467(9):2343–2348. doi:10.1007/s11999-009-0875-x

[7] Lucas RM, Hsu JE, Whitney IJ, Wasserburger J, Matsen FA. Loose glenoid components in revision shoulder arthroplasty: is there an association with positive cultures? J Shoulder Elbow Surg. 2016;25(8):1371–1375. doi:10.1016/j.jse.2015.12.026

[8] McGoldrick E, McElvany MD, Butler-Wu S, Pottinger PS, Matsen FA. Substantial cultures of Propionibacterium can be found in apparently aseptic shoulders revised three years or more after the index arthroplasty. J Shoulder Elbow Surg. 2015;24(1):31–35. doi:10.1016/j.jse.2014.05.008

[9] Topolski MS, Chin PYK, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: The value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006;15(4):402–406. doi:10.1016/j.jse.2005.10.001

[10] Bedair H, Ting N, Jacovides C, et al. The Mark Coventry Award: diagnosis of early postoperative TKA infection using synovial fluid analysis. Clin Orthop Relat Res. 2010;469(1):34–40. doi:10.1007/s11999-010-1433-2

[11] Christensen CP, Bedair H, Della Valle CJ, Parvizi J, Schurko B, Jacobs CA. The natural progression of synovial fluid white blood-cell counts and the percentage of polymorphonuclear cells after primary total knee arthroplasty: a multicenter study. J Bone Joint Surg Am. 2013;95(23):2081–2087. doi:10.2106/JBJS.L.01646

[12] Spangehl MJ, Masri BA, O'Connell JX, Duncan CP. Prospective analysis of preoperative and intraoperative investigations for the diagnosis of infection at the sites of two hundred and two revision total hip arthroplasties. J Bone Joint Surg Am 1999;81:672–683.

[13] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.

[14] Ghijselings S, Stuyck J, Debeer P. Surgical treatment algorithm for infected shoulder arthroplasty: a retrospective analysis of 17 cases. Acta Orthop Belg. 2013;79:626–635.

[15] Grubhofer F, ImamMD MA, Wieser K, Achermann Y, Meyer DC, Gerber C. Staged revision with antibiotic spacers for shoulder prosthetic joint infections yields high infection control. Clin Orthop Relat Res. 2018;476:146–152. doi:10.1007/s11999.0000000000000049.

[16] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.

[17] Lee SH, Kim SJ, Kook SH, Kim JW. Two-stage revision of infected shoulder arthroplasty using prosthesis of antibiotic-loaded acrylic cement: minimum three-year follow-up. Int Orthop 2018;42:867–874. doi:10.1007/s00264-017-3699-4.

[18] Romanò CL, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. Int Orthop. 2012;36:1011–1017. doi:10.1007/s00264-012-1492-y.

[19] Achermann Y, Sahin F, Schwyzer HK, Kolling C, Wüst J, Vogt M. Characteristics and outcome of 16 periprosthetic shoulder joint infections. Infection. 2013;41:613–620. doi:10.1007/s15010-012-0360-4.

[20] Amaravathi RS, Kany J, Melet M, Katz D, Sauzieres P, Valenti P, et al. Analysis of infection in shoulder arthroplasty: a multicentre study. Eur J Orthop Surg Traumatol. 2012;22:145–150. doi:10.1007/s00590-011-0806-x.

[21] Beekman PDA, Katusic D, Berghs BM, Karelse A, De Wilde L. One-stage revision for patients with a chronically infected reverse total shoulder replacement. J Bone Joint Surg Br. 2010;92:817–822. doi:10.1302/0301-620X.92B6.23045.

[22] Buchalter DB, Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Two-stage revision for infected shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:939–947. doi:10.1016/j.jse.2016.09.056.

[23] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.

[24] Jawa A, Shi L, O'Brien T, Wells J, Higgins L, Macy J, et al. Prosthesis of antibiotic-loaded acrylic cement (PROSTALAC) use for the treatment of infection after shoulder arthroplasty. J Bone Joint Surg Am. 2011;93:2001–2009. doi:10.2106/JBJS.J.00833.

[25] Jerosch J, Schneppenheim M. Management of infected shoulder replacement. Arch Orthop Trauma Surg. 2003;123:209–214. doi:10.1007/s00402-003-0497-9.

[26] Levy JC, Triplet J, Everding N. Use of a functional antibiotic spacer in treating infected shoulder arthroplasty. Orthopedics. 2015;38:e512–e519. doi:10.3928/01477447-20150603-60.

[27] Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Definitive treatment of infected shoulder arthroplasty with a cement spacer. Orthopedics. 2016;39:e924–e930. doi:10.3928/01477447-20160623-07.

[28] Sabesan VJ, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. Clin Orthop Relat Res. 2011;469:2538–2543. doi:10.1007/s11999-011-1774-5.

[29] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.

[30] Stone GP, Clark RE, O'Brien KC, Vaccaro L, Simon P, Lorenzetti AJ, et al. Surgical management of periprosthetic shoulder infections. J Shoulder Elbow Surg. 2017;26:1222–1229. doi:10.1016/j.jse.2016.11.054.

[31] Weber P, Utzschneider S, Sadoghi P, Andress H-J, Jansson V, Müller PE. Management of the infected shoulder prosthesis: a retrospective analysis and review of the literature. Int Orthop. 2011;35:365–373. doi:10.1007/s00264-010-1019-3.

[32] Braman JP, Sprague M, Bishop J, Lo IK, Lee EW, Flatow EL. The outcome of resection shoulder arthroplasty for recalcitrant shoulder infections. J Shoulder Elbow Surg. 2006;15:549–553. doi:10.1016/j.jse.2005.11.001.

[33] Ince A, Seemann K, Frommelt L, Katzer A, Loehr JF. One-stage exchange shoulder arthroplasty for peri-prosthetic infection. J Bone Joint Surg Br. 2005;87:814–818. doi:10.1302/0301-620X.87B6.15920.

[34] Klatte TO, Junghans K, Al-Khateeb H, Rueger JM, Gehrke T, Kendoff D, et al. Single-stage revision for peri-prosthetic shoulder infection: outcomes and results. Bone Joint J. 2013;95-B:391–395. doi:10.1302/0301-620X.95B3.30134.

[35] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.

[36] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. J Bone Joint Surg Br. 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.

[37] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. J Shoulder Elbow Surg. 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.

2.4. DIAGNOSIS: INFLAMMATORY MARKERS

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QUESTION 1: What is the role for serum erythrocyte sediment rate (ESR), C-reactive protein (CRP), or white blood cell (WBC) count in the evaluation of a shoulder arthroplasty for periprosthetic joint infection (PJI)?

RECOMMENDATION: Serum ESR, CRP or WBC count have poor sensitivity for the diagnosis of shoulder PJI. Although they should be obtained as part of a standard workup for infection, normal values do not rule out infection.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 4%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

A comprehensive literature search for periprosthetic shoulder infection was performed of the PubMed/Medline, Cochrane, Google Scholar and Embase databases through February 2018. The search terms used were "periprosthetic joint infection," "revision shoulder arthroplasty," "CRP," "ESR," "WBC." The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was followed for this review. Studies (Level II-IV evidence) in which at least one of ESR, CRP and WBC count were recorded in patients with periprosthetic shoulder infection or in patients with positive intraoperative culture were included in the study. Exclusion criteria were case reports, studies on non-prosthetic shoulder implants, studies with missing patient data, papers where the cutoff value is not specified for ESR, CRP and WBC, and non-English language papers.

The diagnosis and the treatment of shoulder PJI can be difficult [1,2]. *Cutibacterium acnes*, which causes indolent infection, is the most common causative agent of shoulder PJI [3–5]. In the case of infection caused by this agent that has low virulence, inflammatory markers such as ESR, CRP and WBC, are generally not elevated [6]. On the other hand, immunosuppression secondary to rheumatoid arthritis or systemic lupus erythematosus is the leading cause of the increased risk of infection in this group of patients [7]. The presence of high CRP and ESR values in the natural course of these diseases may lead to confusion in interpreting these parameters in terms of infection.

There is a paucity of literature regarding serum ESR, CRP or WBC count in the evaluation of a shoulder arthroplasty for PJI [3,8]. The most comprehensive meta-analysis regarding laboratory parameters in shoulder periprosthetic infection was performed by Nelson et al. [8]. The authors reported a mean ESR of 27.6 mm/h (in 231 patients), a mean WBC count of 7472 cells/μL (in 418 patients) and a mean CRP of 2.6 mg/dL (in 279 patients). Only 6.8% of patients who were treated for shoulder PJI had an elevated WBC, 37.6% of the patients had an elevated CRP while elevated ESR was reported in 62.1% of the patients (Table 1).

Whereas in the series of Pottinger et al. [9], these values were reported to be 8%, 20%, and 17%, respectively. In a study by Topolski et al. [3], it has been reported that 93% had a normal WBC count, 86% had a normal ESR and 75% had a normal CRP level.

The limited literature focuses on the sensitivity and specificity of laboratory tests [1,10–12]. Berbari et al. [10] reported sensitivities of ESR and CRP of only 16% and 42% in the shoulder, and 75% and 88% in the lower extremity, respectively. A few authors reported that the sensitivity of ESR was 12-45% and the specificity was 65-98% in detecting shoulder PJI [1,11,12]. For CRP, the sensitivity was reported as 0-46% and the specificity as 84-95%. Due to considerable heterogeneity, those indexes were not deemed suitable to be pooled (I^2 for the sensitivity of CRP was 97.7% and for the sensitivity of ESR was 91.5%).

In a majority of the studies, WBC was normal and CRP was usually increased in the shoulder PJI [3,5,13]. Piper et al. [1] have investigated the role of CRP and ESR in shoulder PJI since CRP and ESR are a useful diagnostic tool for knee and hip PJI. According to this, they stated that CRP was an effective parameter in distinguishing aseptic failure and infection of shoulder arthroplasty, whereas ESR was not. In the diagnosis of the shoulder PJI, while a CRP > 10 mg/L had a sensitivity of 42% and specificity of 84%, an ESR > 30 mm/h had a sensitivity of 16% and specificity of 98%.

Recently, optimized cutoff values of CRP and ESR for shoulder PJI have been published [1]. Optimized ESR cutoff for shoulder arthroplasty was 26 mm/h. This ESR cutoff value had a sensitivity of 32% and specificity of 93% for the shoulder PJI. Optimized CRP cutoff was 7 mg/L, and this value had a sensitivity of 63% and specificity of 73% for the shoulder PJI [1].

In a retrospective study using national insurance database by Chalmers et al., laboratory tests to diagnose infection in the setting of revision shoulder arthroplasty have been examined. In that study involving 1392 patients, the best diagnostic performance was attributed to the combination of ESR, CRP, and WBC (sensitivity = 7-42%, specificity = 92%, positive predictive value = 45%, negative predictive value = 91%, accuracy = 84-85%).[14]

REFERENCES

[1] Piper KE, Fernandez-Sampedro M, Steckelberg KE, Mandrekar JN, Karau MJ, Steckelberg JM, et al. C-reactive protein, erythrocyte sedimentation rate and orthopedic implant infection. PloS One. 2010;5:e9358. doi:10.1371/journal.pone.0009358.

[2] Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. N Engl J Med. 2004;351(16):1645–1654. doi:10.1056/NEJMra040181.

[3] Topolski MS, Chin PYK, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: the value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006;15:402–406. doi:10.1016/j.jse.2005.10.001.

[4] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.

[5] Dodson CC, Craig EV, Cordasco FA, Dines DM, Dines JS, Dicarlo E, et al. Propionibacterium acnes infection after shoulder arthroplasty: a diagnostic challenge. J Shoulder Elbow Surg. 2010;19:303–307. doi:10.1016/j.jse.2009.07.065.

[6] Grosso MJ, Sabesan VJ, Ho JC, Ricchetti ET, Iannotti JP. Reinfection rates after 1-stage revision shoulder arthroplasty for patients with unexpected positive intraoperative cultures. J Shoulder Elbow Surg. 2012;21:754–758. doi:10.1016/j.jse.2011.08.052.

[7] Bohsali KI, Wirth MA, Rockwood CA. Complications of total shoulder arthroplasty. J Bone Joint Surg Am. 2006;88:2279–2292. doi:10.2106/JBJS.F.00125.

[8] Nelson GN, Davis DE, Namdari S. Outcomes in the treatment of periprosthetic joint infection after shoulder arthroplasty: a systematic review. J Shoulder Elbow Surg. 2016;25:1337–1345. doi:10.1016/j.jse.2015.11.064.

[9] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[10] Berbari E, Mabry T, Tsaras G, Spangehl M, Erwin PJ, Murad MH, et al. Inflammatory blood laboratory levels as markers of prosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2010;92:2102–2109. doi:10.2106/JBJS.I.01199.

[11] Grosso MJ, Frangiamore SJ, Saleh A, Kovac MF, Hayashi R, Ricchetti ET, et al. Poor utility of serum interleukin-6 levels to predict indolent periprosthetic shoulder infections. J Shoulder Elbow Surg. 2014;23:1277–1281. doi:10.1016/j.jse.2013.12.023.

TABLE 1. Mean values and rates of elevation in ESR, CRP and WBC values in the study by Nelson et al.

	Number	Mean Values	Rates of Elevation
ESR	231	27.6 mm/h	62.1%
CRP	279	2.6 mg/dL	37.6%
WBC	418	7,472 cells /μL	6.8%

ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; WBC, white blood cell

[12] Villacis D, Merriman JA, Yalamanchili R, Omid R, Itamura J, Rick Hatch GF. Serum interleukin-6 as a marker of periprosthetic shoulder infection. J Bone Joint Surg Am. 2014;96:41–45. doi:10.2106/JBJS.L.01634.
[13] Lutz M-F, Berthelot P, Fresard A, Cazorla C, Carricajo A, Vautrin A-C, et al. Arthroplastic and osteosynthetic infections due to Propionibacterium acnes: a retrospective study of 52 cases, 1995-2002. Eur J Clin Microbiol Infect Dis. 2005;24:739–744. doi:10.1007/s10096-005-0040-8.
[14] Chalmers PN, Sumner S, Romeo AA, Tashjian RZ. Do elevated inflammatory markers associate with infection in revision shoulder arthroplasty? J Shoulder Elb Arthroplasty. 2018;2:2471549217750465. doi:10.1177/2471549217750465.

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QUESTION 2: Is there a role for (a) synovial or (b) serum IL-6 in the diagnosis of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: (a) There is a potential role for synovial fluid IL-6 in the diagnosis of shoulder PJI, both as an individual marker and when interpreted in combination with other synovial fluid markers. (b) Although its specificity is high, serum IL-6 does not appear to provide additional information beyond the more readily available serum markers (erythrocyte sedimentation rate (ESR), C-reative protein (CRP), white blood cell (WBC) count).

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 92%, Disagree: 0%, Abstain: 8% (Super Majority, Strong Consensus)

RATIONALE

(a) Synovial

Several meta-analyses [1,2] have been performed on synovial biomarkers in the hip and knee PJI literature, with multiple markers showing very good diagnostic test characteristics, including synovial interleukin (IL)-6. Lee et al. [1] found that the sensitivity, specificity, diagnostic odds ratio (DOR) and area under the curve (AUC) for synovial IL-6 was 0.81, 0.94, 4.38, and 0.95, respectively, in one of these recent meta-analyses. The results for studies specifically of shoulder PJI are also very promising,[3,4] but with diagnostic test performance that is slightly lower compared to the hip and knee findings, likely due to the indolent nature and lower virulence of the common infecting organisms in the shoulder, *Cutibacterium acnes* (*C. acnes*) and coagulase-negative *Staphylococcus* species (CNSS).

Frangiamore et al. [3] prospectively examined intraoperative levels of synovial IL-6 in 35 cases of revision shoulder arthroplasty; 15 cases categorized as infected and 20 as not infected based on perioperative criteria (Table 1). Using a cut-off level of 359.3 pg/mL based on ROC analysis, synovial fluid IL-6 was found to have an AUC of 0.891, with a high sensitivity (87%) and high specificity (90%) and a positive

TABLE 1. Periprosthetic shoulder infection criteria

Category	Criteria
Definite Infection	At least 1 positive preoperative or intraoperative finding of infection* and more than 1 positive culture (preoperative or intraoperative) *or* One positive preoperative culture (aspirate) and 1 positive intraoperative culture with the same organism
Probable Infection	At least 1 positive preoperative or intraoperative finding of infection* and one positive culture (preoperative or intraoperative *or* No preoperative or intraoperative findings of infection* and more than one positive culture (preoperative or intraoperative)
Probably Contaminant	No preoperative or intraoperative findings of infection* and one positive culture (preoperative or intraoperative)
No Evidence for Infection	No preoperative or intraoperative findings of infection* and no positive cultures (preoperative or intraoperative)

*Preoperative or intraoperative findings of infection:
- Preoperative clinical signs (swelling, sinus tract, redness, drainage).
- Positive result on serum erythrocyte sedimentation rate or C-reactive protein analysis. Intraoperative gross findings (purulent drainage, necrosis).
- Positive intraoperative frozen section.

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and negative likelihood ratio of 8.45 and 0.15, respectively, for diagnosis of infection. Synovial fluid IL-6 was also significantly elevated in cases classified as infected in cases with *C. acnes* culture growth and in cases with a positive intraoperative frozen section compared to those with no positive frozen sections. Synovial fluid IL-6 significantly positively correlated with the total number (and percentage) of positive cultures per case.

In a second study that investigated the role of synovial fluid IL-6 in the diagnosis of shoulder PJI, Frangiamore et al. [4] prospectively examined intraoperative levels of 9 synovial fluid cytokines (IL-6, granulocyte macrophage colony-stimulating factor (GM-CSF), IL-1β, IL-12, IL-2, IL-8, interferon (IFN)-γ, IL-10, tumor necrosis factor (TNF)-α) in 75 cases of revision shoulder arthroplasty; 28 cases categorized as infected and 47 as not infected based on perioperative criteria (Table 1). The most commonly cultured bacteria was *C. acnes* (67% of cases), with CNSS the second most frequently cultured bacteria (25% of cases). Synovial IL-6, GM-CSF, IFN-γ, IL-1β, IL-2, IL-8 and IL-10 were significantly elevated in cases classified as infected; while IL-6, IL-1β, IL-2, IL-8 and IL-10 were significantly elevated in cases with *C. acnes* culture growth. Levels of all cytokines except TNF-α were significantly higher in revision cases with at least one positive intraoperative frozen section compared to those with no positive frozen sections, and moderately and significantly positively correlated (r = 0.41-0.68) with the total number (and percentage) of positive cultures per case, including IL-6. Individually, IL-6, IL-1β, IL-8 and IL-10 showed the best combined sensitivity and specificity for predicting infection (Table 2) with synovial IL-6 found to have an AUC of 0.87 with a high sensitivity (82%) and high specificity (87%) and a positive and negative likelihood ratio of 6.4 and 0.20, respectively, using a cut-off level of 453.6 pg/mL based on ROC analysis.

While IL-6 performed well as an individual diagnostic marker, it also performed well in combination with other synovial cytokines. A statistical model consisting of IL-6, TNF-α and IL-2 was found to have the optimal predictive power and showed better diagnostic test characteristics than any synovial cytokine alone with an AUC, sensitivity, specificity, positive and negative predictive value (NPV, PPV), and positive and negative likelihood ratio (LR+, LR-) of 0.87, 0.80, 0.93, 0.87, 0.89, 12.0 and 0.21, respectively (Table 2). A nomogram of the statistical model was developed and used to predict likelihood of infection for a patient.

(b) Serum

Several meta-analyses [5,6] have been performed on serum IL-6 in the hip and knee PJI literature with good diagnostic test characteristics reported, including sensitivity and specificity ranging from 72-97% and 89-91%, respectively. However, these results have not been replicated in the shoulder, likely due to the indolent nature and lower virulence of the common infecting organisms in the shoulder such as *C. acnes* and CNSS.

Villacis et al. [7] prospectively examined serum IL-6 levels in 34 cases of revision shoulder arthroplasty. Infection was defined as at least one positive intraoperative culture of peri-implant tissue with 14 cases categorized as infected and 20 as not infected. The most commonly cultured bacteria was *C. acnes* (64% of cases) with CNSS as the second most frequently cultured bacteria (29% of cases). There was no significant difference in the serum IL-6 levels between patients with and without infection. Serum IL-6 was found to have a sensitivity, specificity, positive predictive value, negative predictive

TABLE 2. Synovial fluid cytokine diagnostic test characteristic for infection

Cytokine	AUC*	Optimal Cut-off* (pg/mL)	Sensitivity	Specificity	PPV	NPV	LR+	LR-
IL-6	0.87	453.6	0.82	0.87	0.79	0.89	6.4	0.20
GM-CSF	0.70	1.5	0.54	0.85	0.68	0.75	3.6	0.55
IFN-γ	0.69	4.9	0.60	0.80	0.62	0.78	3.0	0.50
IL-1β	0.80	3.6	0.71	0.87	0.77	0.84	5.6	0.33
IL-12	0.60	6.0	0.36	0.94	0.77	0.71	5.6	0.69
IL-2	0.70	1.6	0.54	0.87	0.71	0.76	4.2	0.53
IL-8	0.78	1502.4	0.71	0.79	0.67	0.82	3.4	0.36
IL-10	0.76	28.1	0.72	0.82	0.69	0.84	4.0	0.34
TNF-α	0.60	4.5	0.92	0.33	0.43	0.88	1.4	0.24
Combined†	0.87	0.4	0.80	0.93	0.87	0.89	12.0	0.21

+, positive; -, negative; AUC, area under the curve; GM-CSF, granulocyte macrophage colony-stimulating factor; IFN, interferon; IL, interleukin; LR, likelihood ration; NPV, negative predictive value; PPV, positive predictive value; TNF, tumor necrosis factor.

* AUC and optimal cutoff were determined using receiver operating characteristics curves. Sensitivity, specificity, PPV, NPV, LR+, and LR were determined from the receiver operating chararteristic curve analysis.

† Represents the diagnostic test characteristics of the combined 3-cytokine (IL-6, TNF-α, IL-2) model found to have the optimal predictive power. Reprinted with permission [4].

TABLE 3. Criteria for infection categories

Category	Criteria
No infection	All negative cultures (tissue or aspirate) and no preoperative or intraoperative* findings of infection
Possible infection	Negative preoperative or intraoperative* finding *and* 1 positive intraoperative culture
Probably infection	>1 positive intraoperative culture *and* negative preoperative or intraoperative* findings *or* At least 1 positive preoperative or intraoperative finding *and* 1 positive culture
Definite infection	At least 1 positive preoperative or intraoperative* finding of infection *and* >1 positive intraoperative culture *or* 1 positive preoperative (aspirate) culture *and* 1 positive intraoperative culture

Note: Positive preoperative aspirate has its own category because it is more definitive than these findings.

*Preoperative or intraoperative findings of infection: preoperative clinical signs (swelling, sinus tract, redness, drainage); positive ESR or CRP; positive frozen section; intraoperative gross findings (e.g., pus, drainage, necrosis).

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value and accuracy of 0.14, 0.95, 0.67, 0.61 and 0.62, respectively, using a cut-off level of 10 pg/mL.

Subsequently, Grosso et al. [8] prospectively examined serum IL-6 levels in 69 cases of revision shoulder arthroplasty; 24 cases categorized as infected and 45 as not infected based on perioperative criteria (Table 3). The most commonly cultured bacteria was *C. acnes* (83% of cases) with CNSS the second most frequently cultured bacteria (16% of cases). Only 6 cases in the study had an elevated serum IL-6 level, 3 in the infected group and 3 in the not infected group. Serum IL-6 was found to have a sensitivity and specificity of 12% and 93%, respectively, using a cut-off level of 5 pg/mL.

REFERENCES

[1] Lee YS, Koo KH, Kim HJ, Tian S, Kim TY, Maltenfort MG, et al. Synovial fluid biomarkers for the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2017;99:2077–2084. doi:10.2106/JBJS.17.00123.

[2] Saleh A, Ramanathan D, Siqueira MBP, Klika AK, Barsoum WK, Rueda CAH. The diagnostic utility of synovial fluid markers in periprosthetic joint infection: a systematic review and meta-analysis. J Am Acad Orthop Surg. 2017;25:763–772. doi:10.5435/JAAOS-D-16-00548.

[3] Frangiamore SJ, Saleh A, Kovac MF, Grosso MJ, Zhang X, Bauer TW, et al. Synovial fluid interleukin-6 as a predictor of periprosthetic shoulder infection. J Bone Joint Surg Am. 2015;97:63–70. doi:10.2106/JBJS.N.00104.

[4] Frangiamore SJ, Saleh A, Grosso MJ, Farias Kovac M, Zhang X, Daly TM, et al. Neer Award 2015: analysis of cytokine profiles in the diagnosis of periprosthetic joint infections of the shoulder. J Shoulder Elbow Surg. 2017;26:186–196. doi:10.1016/j.jse.2016.07.017.

[5] Berbari E, Mabry T, Tsaras G, Spangehl M, Erwin PJ, Murad MH, et al. Inflammatory blood laboratory levels as markers of prosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2010;92:2102–2109. doi:10.2106/JBJS.I.01199.

[6] Xie K, Dai K, Qu X, Yan M. Serum and synovial fluid Interleukin-6 for the diagnosis of periprosthetic joint infection. Sci Rep. 2017;7(1):1496. doi:10.1038/s41598-017-01713-4.

[7] Villacis D, Merriman JA, Yalamanchili R, Omid R, Itamura J, Rick Hatch GF. Serum interleukin-6 as a marker of periprosthetic shoulder infection. J Bone Joint Surg Am. 2014;96:41–45. doi:10.2106/JBJS.L.01634.

[8] Grosso MJ, Frangiamore SJ, Saleh A, Kovac MF, Hayashi R, Ricchetti ET, et al. Poor utility of serum interleukin-6 levels to predict indolent periprosthetic shoulder infections. J Shoulder Elbow Surg. 2014;23:1277–1281. doi:10.1016/j.jse.2013.12.023.

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QUESTION 3: Is there a role for synovial fluid white blood cell (WBC) count and differential in the diagnosis of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There may be a role, but synovial fluid cell count and differential currently lacks diagnostic thresholds from shoulder-specific literature.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

WBC count and polymorphonuclear leukocyte (PMN) percentage in synovial fluid continue to be used as parameters in the diagnosis of PJI [1–10]. As an indirect marker, synovial fluid WBC count and differential has been used as a reliable tool for diagnosing PJI of the lower

extremity [3,8,11]. However, shoulder-specific data is limited. The shoulder presents a unique challenge in diagnosis due to frequent culture growth of low-virulent organisms [12–14].

To evaluate the existing literature for use of synovial WBC and differential in the diagnosis of shoulder PJI, a PubMed search was undertaken with the query: "(periprosthetic OR PJI) AND shoulder AND (white OR WBC) AND (synovial OR aspirate)." This search provided three articles for review of which one was pertinent [15].

In a multicenter analysis of *C. acnes* PJI cases (as defined by original Musculoskeletal Infection Society (MSIS) criteria [16]), Nodzo et al. described the characteristics of the host inflammatory response in 18 knees, 12 hips and 35 shoulders [15]. They identified a significantly lower mean value for synovial WBC count for the shoulder (750 cells/ mm^3) compared to the knee (19,950 cells/ mm^3). This was, however, similar to the average reported for the infected hips (500 cells/ mm^3). Interestingly, the neutrophil percentage was similar between shoulders (90%) and knees (92.5%), while significantly lower for hips (61.0%). Unfortunately, while providing some insight into the inflammatory response to a low-virulent pathogen, this limited dataset was unable to calculate a diagnostic threshold or calculate sensitivity and specificity of synovial WBC for diagnosing PJI. As this analysis demonstrates a response commiserate with low-virulent infections of the hip, the diagnostic values reported for hip PJI (3,000 cells / mm^3 and 80% PMN) [3] may be the best current alternative.

WBC count and PMN percentage can remain high up to three months after arthroplasty. This limits the test utility in the first six postoperative weeks as a modified threshold has not been identified for the shoulder [17,18].

Compounding the uncertainty about the WBC count and PMN percentages as metrics that indicate shoulder PJI is the fact that shoulder synovial fluid aspirations frequently yield little to no fluid, a high percentage of "dry taps" [19,20].

REFERENCES

[1] Ahmad SS, Shaker A, Saffarini M, Chen AF, Hirschmann MT, Kohl S. Accuracy of diagnostic tests for prosthetic joint infection: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2016;24:3064–3074. doi:10.1007/s00167-016-4230-y.

[2] Ghanem E, Parvizi J, Burnett RSJ, Sharkey PF, Keshavarzi N, Aggarwal A, et al. Cell count and differential of aspirated fluid in the diagnosis of infection at the site of total knee arthroplasty. J Bone Joint Surg Am. 2008;90:1637–1643. doi:10.2106/JBJS.G.00470.

[3] Higuera CA, Zmistowski B, Malcom T, Barsoum WK, Sporer SM, Mommsen P, et al. Synovial fluid cell count for diagnosis of chronic periprosthetic hip infection. J Bone Joint Surg Am. 2017;99:753–759. doi:10.2106/JBJS.16.00123.

[4] Jacovides CL, Parvizi J, Adeli B, Jung KA. Molecular markers for diagnosis of periprosthetic joint infection. J Arthroplasty. 2011;26:99–103.e1. doi:10.1016/j.arth.2011.03.025.

[5] Parvizi J, Alijanipour P, Berbari E, Hickok N, Phillips KS, M Shapiro I, et al. Novel developments in the prevention, diagnosis, and treatment of periprosthetic joint infections. J Am Acad Orthop Surg. 2015;23 Suppl:S32–S43. doi:10.5435/JAAOS-D-14-00455.

[6] Collins I, Wilson-MacDonald J, Chami G, Burgoyne W, Vineyakam P, Berendt T, et al. The diagnosis and management of infection following instrumented spinal fusion. Eur Spine J. 2008;17:445–450. doi:10.1007/s00586-007-0559-8.

[7] Lee YS, Koo K-H, Kim HJ, Tian S, Kim T-Y, Maltenfort MG, et al. Synovial fluid biomarkers for the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2017;99:2077–2084. doi:10.2106/JBJS.17.00123.

[8] Mason JB, Fehring TK, Odum SM, Griffin WL, Nussman DS. The value of white blood cell counts before revision total knee arthroplasty. J Arthroplasty. 2003;18:1038–1043.

[9] Saleh A, Ramanathan D, Siqueira MBP, Klika AK, Barsoum WK, Rueda CAH. The diagnostic utility of synovial fluid markers in periprosthetic joint infection: a systematic review and meta-analysis. J Am Acad Orthop Surg. 2017;25:763–772. doi:10.5435/JAAOS-D-16-00548.

[10] Kevin Ko J-W, Namdari S. The diagnosis and management of periprosthetic joint infections of the shoulder. Oper Tech Orthop. 2016;26. doi:10.1053/j.oto.2015.12.001.

[11] Ricchetti E, Frangiamore S, Grosso M, Alolabi B, Saleh A, W. Bauer T, et al. Diagnosis of periprosthetic infection after shoulder arthroplasty: a critical analysis review. JBJS Rev. 2013;1:e3. doi:10.2106/JBJS.

[12] 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;24:844–847. doi:10.1016/j.jse.2014.10.016.

[13] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.

[14] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.

[15] Nodzo SR, Boyle KK, Bhimani S, Duquin TR, Miller AO, Westrich GH. Propionibacterium acnes host inflammatory response during periprosthetic infection is joint specific. HSS J. 2017;13:159–164. doi:10.1007/s11420-016-9528-2.

[16] Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, et al. New Definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res. 2011;469:2992–2994. doi:10.1007/s11999-011-2102-9.

[17] Christensen CP, Bedair H, Della Valle CJ, Parvizi J, Schurko B, Jacobs CA. The natural progression of synovial fluid white blood-cell counts and the percentage of polymorphonuclear cells after primary total knee arthroplasty: a multicenter study. J Bone Joint Surg Am. 2013;95:2081–2087. doi:10.2106/JBJS.L.01646.

[18] Bedair H, Ting N, Jacovides C, Saxena A, Moric M, Parvizi J, et al. The Mark Coventry Award: diagnosis of early postoperative TKA infection using synovial fluid analysis. Clin Orthop Relat Res. 2010. doi:10.1007/s11999-010-1433-2.

[19] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.

[20] Millett PJ, Yen Y-M, Price CS, Horan MP, van der Meijden OA, Elser F. Propionibacterium acnes infection as an occult cause of postoperative shoulder pain: a case series. Clin Orthop Relat Res. 2011;469:2824–2830. doi:10.1007/s11999-011-1767-4.

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QUESTION 4: Is there a role for synovial cytokines in the diagnosis of shoulder periprosthetic (PJI)?

RECOMMENDATION: While not yet widely available, evaluation of cytokine levels in synovial fluid shows promise in clarifying the probability of shoulder PJI. See Questions 2 and 5 (Section 1.2. Prevention: Intraoperative) for discussion of specific cytokine evaluations.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Although the majority of previous literature on the use of cytokines for PJI diagnosis was focused on hip and knee arthroplasty [1–4], there are a number of recent publications regarding shoulder PJI [5–13]. It is established that shoulder PJI is often caused by less viru-

lent organisms than those in the hip or knee [5,7,12,14] with the most common microorganisms being- *Cutibacterium acnes* and coagulase negative Staph. Therefore, even though shoulder PJI might share some common characteristics to hip and knee PJI, a direct comparison is not suitable and more research specific to shoulder PJI is needed to establish concrete guidelines for the role of cytokines in these diagnoses [2,8,12].

Literature regarding cytokines (including interleukins IL-2, IL-4, IL-6, IL-8, IL-10) shows consensus that IL-6 is the most relevant cytokine biomarker for predicting shoulder PJI. Evidence supports that IL-6 has a sensitivity and specificity of approximately 90% and 95% respectively, as well as improved diagnostic accuracy when combined with IL-8 and IL-10 [7,9,11,15]. However, there remains some controversy regarding the use of IL-6 to determine resolution of infection after antibiotic and surgical treatment of PJI [16,17]. Applying this to current Musculoskeletal Infection Society criteria, IL-6 may be a useful adjunct however for diagnosis of resolution of infection although determination of resolution of infection still requires negative cultures and return of C-reactive protein and erythrocyte sedimentation rate to normal levels [11]. Cytokines were found to have the highest correlations with positive frozen sections [7], suggesting that the combination of cytokines and frozen sections may be a possible avenue for recommendations. The use of lateral flow immunoassay technique (QuickLine IL-6 Test) for IL-6 during surgery allows for rapid assessment of synovial fluid (17), but while it provides an acceptable specificity (97.6%), it has a weaker sensitivity (46.9%) [6].

Several published reports [7,9] describe cytokines as a strong predictor for shoulder PJI: one study with level 2 evidence [9], two level 3 [7,16], one level 4 [18], and one of level 5 [17]. The cutoffs for what constitutes a positive test are not well established and based on the frequently minimal inflammatory response to shoulder PJI, as suggested by Frangiamore et al., cytokine values for the diagnosis of shoulder PJI will likely be lower than those established for hip or knee infections. It also must be considered that there are studies reporting no infection with a cutoff under 10,000 pq; making imperative the need for other diagnostic tools for the assessment of shoulder PJI.

Although synovial fluid cytokines show promise as a preoperative or intraoperative tool to diagnose shoulder PJI, further validation is needed in the setting of shoulder PJI specifically, appropriate cutoff values must be further defined, and the tests must become rapid, affordable and widely available in order to truly impact clinical care.

REFERENCES

[1] Grosso MJ, Frangiamore SJ, Saleh A, Kovac MF, Hayashi R, Ricchetti ET, et al. Poor utility of serum interleukin-6 levels to predict indolent periprosthetic shoulder infections. J Shoulder Elbow Surg. 2014;23:1277–1281. doi:10.1016/j.jse.2013.12.023.

[2] Randau TM, Friedrich MJ, Wimmer MD, Reichert B, Kuberra D, Stoffel-Wagner B, et al. Interleukin-6 in serum and in synovial fluid enhances the differentiation between periprosthetic joint infection and aseptic loosening. PloS One. 2014;9:e89045. doi:10.1371/journal.pone.0089045.

[3] Wimmer MD, Ploeger MM, Friedrich MJ, Bornemann R, Roessler PP, Gravius S, et al. The QuickLine IL-6 lateral flow immunoassay improves the rapid intraoperative diagnosis of suspected periprosthetic joint infections. Technol Health Care. 2016;24:927–932. doi:10.3233/THC-161247.

[4] Bauer TW, Parvizi J, Kobayashi N, Krebs V. Diagnosis of periprosthetic infection. J Bone Joint Surg Am. 2006;88:869–882. doi:10.2106/JBJS.E.01149.

[5] Ahmad SS, Shaker A, Saffarini M, Chen AF, Hirschmann MT, Kohl S. Accuracy of diagnostic tests for prosthetic joint infection: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2016;24:3064–3074. doi:10.1007/s00167-016-4230-y.

[6] Ricchetti ET, Frangiamore SJ, Grosso MJ, Alolabi B, Saleh A, Bauer TW, et al. Diagnosis of periprosthetic infection after shoulder arthroplasty: a critical analysis review. JBJS Rev. 2013;1. doi:10.2106/JBJS.RVW.M.00055.

[7] Frangiamore SJ, Saleh A, Grosso MJ, Farias Kovac M, Zhang X, Daly TM, et al. Neer Award 2015: analysis of cytokine profiles in the diagnosis of periprosthetic joint infections of the shoulder. J Shoulder Elbow Surg. 2017;26:186–196. doi:10.1016/j.jse.2016.07.017.

[8] Marschall J, Lane MA, Beekmann SE, Polgreen PM, Babcock HM. Current management of prosthetic joint infections in adults: results of an Emerging Infections Network survey. Int J Antimicrob Agents. 2013;41:272–277. doi:10.1016/j.ijantimicag.2012.10.023.

[9] Frangiamore SJ, Saleh A, Kovac MF, Grosso MJ, Zhang X, Bauer TW, et al. Synovial fluid interleukin-6 as a predictor of periprosthetic shoulder infection. J Bone Joint Surg Am. 2015;97:63–70. doi:10.2106/JBJS.N.00104.

[10] Jacovides CL, Parvizi J, Adeli B, Jung KA. Molecular markers for diagnosis of periprosthetic joint infection. J Arthroplasty. 2011;26:99–103.e1. doi:10.1016/j.arth.2011.03.025.

[11] Parvizi J, Alijanipour P, Berbari E, Hickok N, Phillips KS, M Shapiro I, et al. Novel developments in the prevention, diagnosis, and treatment of periprosthetic joint infections. J Am Acad Orthop Surg. 2015;23 Suppl:S32–S43. doi:10.5435/JAAOS-D-14-00455.

[12] Kevin Ko J-W, Namdari S. The diagnosis and management of periprosthetic joint infections of the shoulder. Oper Tech Orthop. 2016;26. doi:10.1053/j.oto.2015.12.001.

[13] Rahmi H, Burkhead W, Itamura J. Current treatments in periprosthetic shoulder infections. Curr Orthop Pract. 2017;28:524. doi:10.1097/BCO.0000000000000567.

[14] Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Orthop Res. 2014;32 Suppl 1:S98–S107. doi:10.1002/jor.22553.

[15] Xie K, Dai K, Qu X, Yan M. Serum and synovial fluid interleukin-6 for the diagnosis of periprosthetic joint infection. Sci Rep. 2017;7:1496. doi:10.1038/s41598-017-01713-4.

[16] Saleh A, Ramanathan D, Siqueira MBP, Klika AK, Barsoum WK, Rueda CAH. The diagnostic utility of synovial fluid markers in periprosthetic joint infection: a systematic review and meta-analysis. J Am Acad Orthop Surg. 2017;25:763–772. doi:10.5435/JAAOS-D-16-00548.

[17] Frangiamore SJ, Siqueira MBP, Saleh A, Daly T, Higuera CA, Barsoum WK. Synovial cytokines and the MSIS criteria are not useful for determining infection resolution after periprosthetic joint infection explantation. Clin Orthop Relat Res. 2016;474:1630–1639. doi:10.1007/s11999-016-4710-x.

[18] Ricchetti ET, Frangiamore SJ, Grosso MJ, Alolabi B, Saleh A, Bauer TW, et al. Diagnosis of periprosthetic infection after shoulder arthroplasty: a critical analysis review. JBJS Rev. 2013;1. doi:10.2106/JBJS.RVW.M.00055.

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QUESTION 5: Is there a role for synovial fluid tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-2 in the diagnosis of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There is a potential role for synovial fluid TNF-α and IL-2 in the diagnosis of shoulder PJI when interpreted in combination with other synovial fluid markers. TNF-α and IL-2 may not be as useful individually.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

Several meta-analyses have been performed on synovial biomarkers in the hip and knee PJI literature, but with limited reports specifically on IL-2 and TNF-α [1,2]. In the only published article in the literature investigating the role for synovial fluid TNF-α and IL-2 in the diagnosis of shoulder PJI, Frangiamore et al. [3] prospectively examined intraoperative levels of 9 synovial fluid cytokines (IL-6, GM-CSF, IL-1β, IL-12, IL-2, IL-8, IFN-γ, IL-10, TNF-α) in 75 cases of revision shoulder arthroplasty; 28 cases categorized as infected and 47 as not infected based on perioperative criteria (Table 1). The most commonly cultured bacteria was *C. acnes* (67% of cases), with coagulase-negative Staphylococcus spp (CNSS) as the second most frequently cultured bacteria (25% of cases). Synovial IL-6, GM-CSF, IFN-γ, IL-1β, IL-2, IL-8 and IL-10 were significantly elevated in cases classified as infected; while IL-6, IL-1β, IL-2, IL-8 and IL-10 were significantly elevated in cases with *C. acnes* culture growth. Levels of all cytokines, except TNF-α, were significantly higher in revision cases, with at least one positive

TABLE 1. Periprosthetic shoulder infection criteria

Category	Criteria
Definite Infection	At least 1 positive preoperative or intraoperative finding of infection* and more than 1 positive culture (preoperative or intraoperative) *or* One positive preoperative culture (aspirate) and 1 positive intraoperative culture with the same organism
Probable Infection	At least 1 positive preoperative or intraoperative finding of infection* and one positive culture (preoperative or intraoperative *or* No preoperative or intraoperative findings of infection* and more than one positive culture (preoperative or intraoperative)
Probably Contaminant	No preoperative or intraoperative findings of infection* and one positive culture (preoperative or intraoperative)
No Evidence for Infection	No preoperative or intraoperative findings of infection* and no positive cultures (preoperative or intraoperative)

*Preoperative or intraoperative findings of infection:

- Preoperative clinical signs (swelling, sinus tract, redness, drainage).
- Positive result on serum erythrocyte sedimentation rate or C-reactive protein analysis. Intraoperative gross findings (purulent drainage, necrosis).
- Positive intraoperative frozen section.

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intraoperative frozen section compared to those with no positive frozen sections, and moderately and significantly positively correlated (r = 0.41-0.68) with the total number (and percentage) of positive cultures per case. Individually, IL-6, IL-1β, IL-8 and IL-10 showed the best combined sensitivity and specificity for predicting infection (Table 2). TNF-α was found to have an area under the curve (AUC) of 0.60 with a high sensitivity (92%) and low specificity (33%), while IL-2 was found to have an AUC of 0.70 with a low sensitivity (54%) and high specificity (87%).

While TNF-α and IL-2 did not perform as well as some of the other markers when assessed individually, combinations of synovial cytokines were also assessed for diagnostic performance using logistic regression analysis. A statistical model consisting of IL-6, TNF-α and IL-2 was found to have the optimal predictive power and showed better diagnostic test characteristics than any synovial cytokine alone with an AUC, sensitivity, specificity, positive and negative predictive value, and positive and negative likelihood ratio of 0.87, 0.80, 0.93, 0.87, 0.89, 12.0 and 0.21, respectively (Table 2). A nomogram of the statistical model was developed and used to predict likelihood of infection for a patient.

While testing synovial fluid cytokine levels intraoperatively hold promise, these assays are not widely available at the present time and further study is needed.

REFERENCES

[1] Lee YS, Koo KH, Kim HJ, Tian S, Kim TY, Maltenfort MG, et al. Synovial fluid biomarkers for the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2017;99:2077–2084. doi:10.2106/JBJS.17.00123.

[2] Saleh A, Ramanathan D, Siqueira MBP, Klika AK, Barsoum WK, Rueda CAH. The diagnostic utility of synovial fluid markers in periprosthetic joint infection: a systematic review and meta-analysis. J Am Acad Orthop Surg. 2017;25:763–772. doi:10.5435/JAAOS-D-16-00548.

[3] Frangiamore SJ, Saleh A, Grosso MJ, Farias Kovac M, Zhang X, Daly TM, et al. Neer Award 2015: analysis of cytokine profiles in the diagnosis of periprosthetic joint infections of the shoulder. J Shoulder Elbow Surg. 2017;26:186–196. doi:10.1016/j.jse.2016.07.017.

TABLE 2. Synovial fluid cytokine diagnostic test characteristic for infection

Cytokine	AUC*	Optimal Cut-off* (pg/mL)	Sensitivity	Specificity	PPV	NPV	LR+	LR-
IL-6	0.87	453.6	0.82	0.87	0.79	0.89	6.4	0.20
GM-CSF	0.70	1.5	0.54	0.85	0.68	0.75	3.6	0.55
IFN-γ	0.69	4.9	0.60	0.80	0.62	0.78	3.0	0.50
IL-1β	0.80	3.6	0.71	0.87	0.77	0.84	5.6	0.33
IL-12	0.60	6.0	0.36	0.94	0.77	0.71	5.6	0.69
IL-2	0.70	1.6	0.54	0.87	0.71	0.76	4.2	0.53
IL-8	0.78	1502.4	0.71	0.79	0.67	0.82	3.4	0.36
IL-10	0.76	28.1	0.72	0.82	0.69	0.84	4.0	0.34
TNF-α	0.60	4.5	0.92	0.33	0.43	0.88	1.4	0.24
Combined†	0.87	0.4	0.80	0.93	0.87	0.89	12.0	0.21

+, positive; -, negative; AUC, area under the curve; GM-CSF, granulocyte macrophage colony-stimulating factor; IFN, interferon; IL, interleukin; LR, likelihood ration; NPV, negative predictive value; PPV, positive predictive value; TNF, tumor necrosis factor.

* AUC and optimal cutoff were determined using receiver operating characteristics curves. Sensitivity, specificity, PPV, NPV, LR+, and LR were determined from the receiver operating chararteristic curve analysis.

† Represents the diagnostic test characteristics of the combined 3-cytokine (IL-6, TNF-α, IL-2) model found to have the optimal predictive power.

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QUESTION 6: Is there a role for synovial fluid leukocyte esterase strip testing in the diagnosis of shoulder periprosthetic joint injection (PJI)?

RECOMMENDATION: Given the current evidence, there is no role for synovial fluid leukocyte esterase (LE) strip testing in the diagnosis of shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Several meta-analyses [1–5] have been performed on synovial biomarkers in the hip and knee PJI literature, with multiple markers showing very good diagnostic test characteristics, including synovial LE strip testing. Lee et al. [1] found that the sensitivity, specificity, diagnostic odds ratio (DOR) and area under the curve (AUC) for synovial LE strip testing was 0.77, 0.95, 4.57 and 0.92, respectively, in one of these recent meta-analyses. Wyatt et al. [4] found that the sensitivity, specificity and AUC for synovial LE strip testing was 0.81, 0.97, and 0.97, respectively, in another of these recent meta-analyses. However, these results have not been replicated in the shoulder, likely due to the indolent nature of the common infecting organisms in the shoulder, *Cutibacterium acnes* (*C. acnes*) and coagulase-negative *Staphylococcus* species (CNSS).

In the only published article in the literature investigating the role for synovial fluid LE strip testing in the diagnosis of shoulder PJI, Nelson et al. [5] prospectively performed leukocyte esterase strip testing in 45 cases of primary shoulder arthroplasty and 40 cases of revision shoulder arthroplasty. Diagnosis of PJI was made based on Musculoskeletal Infection Society criteria. Ten patients (all revisions) met criteria for true PJI (n = 7) or potential PJI (n = 3). The sensitivity of LE strip testing, when including all of these patients as meeting the diagnosis of PJI, was only 30% and the specificity was only 67%. Positive predictive value was 43% and negative predictive value was 83%. When looking just at the presence of positive cultures, LE strip testing still had only a sensitivity of 25% and specificity of 75% for predicting a positive culture in the revision cases. In addition, a significant proportion of samples in the study were considered indeterminate (13.3% of primary samples and 22.5% of revision samples) because the aspirate was too bloody to interpret even after centrifugation. The authors concluded from this study that LE strip testing is an unreliable diagnostic test in shoulder PJI and should not be routinely used in the shoulder.

REFERENCES

[1] Lee YS, Koo KH, Kim HJ, Tian S, Kim TY, Maltenfort MG, et al. Synovial fluid biomarkers for the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2017;99:2077–2084. doi:10.2106/JBJS.17.00123.

[2] Saleh A, George J, Faour M, Klika AK, Higuera CA. Serum biomarkers in periprosthetic joint infections. Bone Joint Res. 2018;7:85–93. doi:10.1302/2046-3758.71.BJR-2017-0323.

[3] Shahi A, Tan TL, Kheir MM, Tan DD, Parvizi J. Diagnosing periprosthetic joint infection: and the winner is? J Arthroplasty. 2017;32:S232–S235. doi:10.1016/j.arth.2017.06.005.

[4] Wyatt MC, Beswick AD, Kunutsor SK, Wilson MJ, Whitehouse MR, Blom AW. The Alpha-defensin immunoassay and leukocyte esterase colorimetric strip test for the diagnosis of periprosthetic infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2016;98:992–1000. doi:10.2106/JBJS.15.01142.

[5] Nelson GN, Paxton ES, Narzikul A, Williams G, Lazarus MD, Abboud JA. Leukocyte esterase in the diagnosis of shoulder periprosthetic joint infection. J Shoulder Elbow Surg. 2015;24:1421–1426. doi:10.1016/j.jse.2015.05.034.

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QUESTION 7: Is there a role for synovial fluid alpha-defensin in the diagnosis of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Synovial alpha-defensin may aid in the diagnosis of shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Alpha-defensin is an antimicrobial peptide that is released by neutrophils in response to bacterial or fungal pathogens. The presence of alpha-defensin in synovial fluid has been thoroughly investigated as a biomarker for PJI following hip and knee arthroplasty with a reported 98% sensitivity and 100% specificity [1–11]. However, there is limited evidence regarding the use of alpha defensin as a biomarker for infection in shoulder arthroplasty.

Thirteen studies in the past three years have demonstrated the efficacy of this test in the diagnosis of hip and knee PJI, and better prognostic results have been reported compared to leukocyte esterase [3,6,9,11–14]. However, the role of alpha-defensin in diagnosing shoulder PJI is less well known. The literature contains only one study that specifically evaluated alpha defensin in shoulder arthroplasty. In this study by Frangiamore et al, alpha-defensin levels were obtained in 33 patients at the time of revision shoulder arthroplasty [6]. Patients were classified as infected or not infected by a standard criteria based on clinical evaluation, laboratory studies, histology and culture results. The area under the curve, sensitivity, specificity and positive and negative likelihood ratios for alpha-defensin in the diagnosis of infection were 0.78, 63%, 95%, 12.1 and 0.38, respectively. There was a significant difference in the median alpha-defensin level between the infection and no infection groups (3.2 [.21-4.74] versus .21 [.19-.23] p = .006). The authors concluded that alpha-defensin may be an appropriate test in the evaluation of infection in the painful shoulder arthroplasty.

A point of care device is now available for direct assessment of alpha-defensin in synovial fluid during surgical procedures (lateral flow immunoassay) [9,13]. Initial reports with this device report a 92% sensitivity and 100% specificity for the diagnosis of PJI in hip and knee arthroplasty [16]. However, some studies have concluded that the point of care lateral flow assay has a lower sensitivity and specificity when compared with the laboratory-based alpha-defensin test (sensitivity 77%, specificity 91%) [9,13,15]. This device has not been evaluated for the diagnosis of shoulder PJI.

Although the clinical presentation and diagnostic challenges are different in shoulder PJI than in hip and knee PJI, detection of high levels of alpha-defensin in synovial fluid in the shoulder could be a good predictor of infection. However, the cut-off values are not well defined, with authors reporting a range from 5.20-7.72 mg/L [16–18]. Further research and validation of alpha-defensin as a marker for PJI in shoulders is required.

REFERENCES

[1] Ahmad SS, Shaker A, Saffarini M, Chen AF, Hirschmann MT, Kohl S. Accuracy of diagnostic tests for prosthetic joint infection: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2016;24:3064–3074. doi:10.1007/s00167-016-4230-y.

[2] Bingham J, Clarke H, Spangehl M, Schwartz A, Beauchamp C, Goldberg B. The alpha defensin-1 biomarker assay can be used to evaluate the potentially infected total joint arthroplasty. Clin Orthop Relat Res. 2014;472:4006–4009. doi:10.1007/s11999-014-3900-7.

[3] Bonanzinga T, Zahar A, Dütsch M, Lausmann C, Kendoff D, Gehrke T. How reliable is the alpha-defensin immunoassay test for diagnosing periprosthetic joint infection? A prospective study. Clin Orthop Relat Res. 2017;475:408–415. doi:10.1007/s11999-016-4906-0.

[4] Deirmengian C, Kardos K, Kilmartin P, Cameron A, Schiller K, Parvizi J. Diagnosing periprosthetic joint infection: has the era of the biomarker arrived? Clin Orthop Relat Res. 2014;472:3254–3262. doi:10.1007/s11999-014-3543-8.

[5] Frangiamore SJ, Gajewski ND, Saleh A, Farias-Kovac M, Barsoum WK, Higuera CA. α-Defensin accuracy to diagnose periprosthetic joint infection-best available test? J Arthroplasty. 2016;31:456–460. doi:10.1016/j.arth.2015.09.035.

[6] Kasparek MF, Kasparek M, Boettner F, Faschingbauer M, Hahne J, Dominkus M. Intraoperative diagnosis of periprosthetic joint infection using a novel alpha-defensin lateral flow assay. J Arthroplasty. 2016;31:2871–2874. doi:10.1016/j.arth.2016.05.033.

[7] Frangiamore SJ, Saleh A, Grosso MJ, Kovac MF, Higuera CA, Iannotti JP, et al. α-Defensin as a predictor of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2015;24:1021–1027. doi:10.1016/j.jse.2014.12.021.

[8] Saleh A, Ramanathan D, Siqueira MBP, Klika AK, Barsoum WK, Rueda CAH. The diagnostic utility of synovial fluid markers in periprosthetic joint infection: a systematic review and meta-analysis. J Am Acad Orthop Surg. 2017;25:763–772. doi:10.5435/JAAOS-D-16-00548.

[9] Gehrke T, Lausmann C, Citak M, Bonanzinga T, Frommelt L, Zahar A. The accuracy of the alpha defensin lateral flow device for diagnosis of periprosthetic joint infection: comparison with a gold standard. J Bone Joint Surg Am. 2018;100:42–48. doi:10.2106/JBJS.16.01522.
[10] Xie K, Qu X, Yan M. Procalcitonin and α-defensin for diagnosis of periprosthetic joint infections. J Arthroplasty. 2017;32:1387–1394. doi:10.1016/j.arth.2016.10.001.
[11] Bauer TW, Parvizi J, Kobayashi N, Krebs V. Diagnosis of periprosthetic infection. J Bone Joint Surg Am. 2006;88:869–882. doi:10.2106/JBJS.E.01149.
[12] Lee YS, Koo K-H, Kim HJ, Tian S, Kim T-Y, Maltenfort MG, et al. Synovial fluid biomarkers for the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2017;99:2077–2084. doi:10.2106/JBJS.17.00123.
[13] Suen K, Keeka M, Ailabouni R, Tran P. Synovasure "quick test" is not as accurate as the laboratory-based α-defensin immunoassay: a systematic review and meta-analysis. Bone Joint J. 2018;100-B:66–72. doi:10.1302/0301-620X.100B1.BJJ-2017-0630.R1.
[14] Deirmengian C, Kardos K, Kilmartin P, Gulati S, Citrano P, Booth RE. The alpha-defensin test for periprosthetic joint infection responds to a wide spectrum of organisms. Clin Orthop Relat Res. 2015;473:2229–2235. doi:10.1007/s11999-015-4152-x.
[15] Sigmund IK, Holinka J, Gamper J, Staats K, Böhler C, Kubista B, et al. Qualitative α-defensin test (Synovasure) for the diagnosis of periprosthetic infection in revision total joint arthroplasty. Bone Joint J. 2017;99-B:66C72. doi:10.1302/0301-620X.99B1.BJJ-2016-0295.R1.
[16] Fink B, Sevelda F. Periprosthetic joint infection of shoulder arthroplasties: diagnostic and treatment options. BioMed Res Int. 2017;2017:4582756. doi:10.1155/2017/4582756.
[17] Ricchetti ET, Frangiamore SJ, Grosso MJ, Alolabi B, Saleh A, Bauer TW, et al. Diagnosis of periprosthetic infection after shoulder arthroplasty: a critical analysis review. JBJS Rev. 2013;1. doi:10.2106/JBJS.RVW.M.00055.
[18] Parvizi J, Alijanipour P, Barberi EF, Hickok NJ, Phillips KS, Shapiro IM, et al. Novel developments in the prevention, diagnosis, and treatment of periprosthetic joint infections. J Am Acad Orthop Surg. 2015;23 Suppl:S32–S43. doi:10.5435/JAAOS-D-14-00455.

Author: Anders Ekelund

QUESTION 8: Is there a role for serum D-dimer in the evaluation of periprosthetic joint injection (PJI) following shoulder arthroplasty?

RECOMMENDATION: Unknown. There is currently only limited evidence related to the evaluation of hip and knee PJI and no study to date evaluating its use in shoulder PJI.

LEVEL OF EVIDENCE: No Evidence

DELEGATE VOTE: Agree: 96%, Disagree: 4%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

A literature review (Medline, PubMed) was performed to identify relevant studies on the role for serum D-dimer in shoulder arthroplasty infections. Terms used included "periprosthetic infection," shoulder infection," "D-dimer," "diagnosing PJI," "serum biomarkers PJI." D-dimer is a fibrin degradation product, a small protein present in the blood after a blood clot is degraded. The D-dimer test has been used for diagnosing thrombosis, pulmonary embolus and disseminated intravascular coagulation (DIC). Lippi et al. [1] found that in an urban population the most common reason for an elevated D-dimer was infection (15%).

There has been a growing interest in the use of serum biomarkers to diagnose periprosthetic joint infections, especially given the imperfect nature of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) tests. A literature search found no studies regarding D-dimer and shoulder arthroplasty. There are however, reports in the hip and knee arthroplasty literature. Lee et al. [2] studied the postoperative levels of D-dimer after elective total hip arthroplasty. Only one paper was found regarding D-dimer as a diagnostic test for periprosthetic infection. Shahi et al. [3] reported on a prospective study of 245 patients undergoing primary arthroplasty (23), revision for aseptic failure (86), revision of PJI (57), reimplantation (29) and infection in a site other than a joint (50) (urinary tract infection, pneumonia, upper respiratory infection). The study included only hip and knee arthroplasties. The median serum D-dimer was significantly higher for patients with PJI and the 850 ng/mL was determined as the optimal threshold value for serum D-dimer for the diagnosis of a PJI. The sensitivity (89%) and specificity (93%) for serum D-dimer was better than for ESR, CRP and ESR & CRP combined. An interesting finding was that D-dimer was elevated in cases of *C. acnes* infection, a common pathogen in the shoulder which typically does not cause elevation in serum ESR or CRP. The authors concluded that serum D-dimer is a promising marker for the diagnosis of PJI.

REFERENCES

[1] Lippi G, Bonfanti L, Saccenti C, Cervellin G. Causes of elevated D-dimer in patients admitted to a large urban emergency department. Eur J Intern Med. 2014;25:45–48. doi:10.1016/j.ejim.2013.07.012.
[2] Lee YS, Lee YK, Han SB, Nam CH, Parvizi J, Koo K-H. Natural progress of D-dimer following total joint arthroplasty: a baseline for the diagnosis of the early postoperative infection. J Orthop Surg. 2018;13:36. doi:10.1186/s13018-018-0730-4.
[3] Shahi A, Kheir MM, Tarabichi M, Hosseinzadeh HRS, Tan TL, Parvizi J. Serum D-dimer test is promising for the diagnosis of periprosthetic joint infection and timing of reimplantation. J Bone Joint Surg Am. 2017;99:1419–1427. doi:10.2106/JBJS.16.01395.

Authors: Jonathon Levy; Samer S. Hasan

QUESTION 9: Is there a role for preoperative joint aspiration in the evaluation of a shoulder arthroplasty for periprosthetic joint infection (PJI)?

RECOMMENDATION: Glenohumeral joint aspiration has a role as part of the investigation for shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Synovial fluid obtained from joint aspiration in the evaluation for PJI can be analyzed to determine nucleated cell count, culture and sensitivity, and various inflammatory markers (interleukin (IL)-6, tumor necrosis factor-α, and alpha defensin). Aspiration for culture is commonly performed. Controversy remains regarding the role of preoperative aspiration in the diagnosis of shoulder PJI. While multiple Level III and IV studies report using preoperative aspiration to evaluate a suspected shoulder PJI, many studies discuss the challenges of obtaining an adequate sample [1–3] as well as a variable incidence of false negative cultures [4,5]. In addition, the unique bacteriology of shoulder PJI, with a preponderance of the non-planktonic organism *C. acnes*, impacts the utility of shoulder aspiration in some clinical settings. No large study has adequately explored the predictive value of preoperative joint aspiration for synovial fluid culture in the diagnosis of shoulder PJI. Thus, there is limited evidence to support routine preoperative aspiration during the workup of a suspected shoulder PJI.

Millett et al. [6] reported on a series of 10 patients presenting with chronic shoulder pain arising after shoulder surgery. In all cases, a preoperative aspiration was carried out, but, in many cases, the tap was dry even after saline lavage. Infection was subsequently determined by positive bacterial culture from a sub-deltoid specimen [6].

In a retrospective multicenter review of infected reverse shoulder arthroplasties, Jacquot et al. [7] reported that preoperative joint aspiration was carried out in 14/32 (44%) cases and was positive in 12/14 (85%). They advocated joint aspiration before any single stage revision shoulder arthroplasty to determine the infective organism and antibiotic sensitivity that would allow selection of an appropriate antibiotic to include in the polymethylmethacrylate cement. Klatte et al. [8] reported on a series of 35 patients undergoing single stage exchange arthroplasty for shoulder PJI. All of the patients had preoperative joint aspiration. Antibiotics were withheld for two weeks prior to joint aspiration. Culture samples were incubated for 14 days, and the results were used to guide the choice of antibiotic added to cement at time of single stage revision. They felt their high cure rate after single stage treatment of shoulder PJI was due, in part, to the isolation of the infective organisms from the preoperative joint aspiration and the ability to add the appropriate antibiotics to polymethyl methacrylate cement as well as initiate the antibiotic treatment.

Ince et al. [4] reported on a series of patients undergoing single stage revision shoulder arthroplasty for shoulder PJI. Preoperative aspiration was performed in all patients and antibiotics were withheld for one week prior to aspiration. The authors were able to identify the infecting organism in 13/16 (83%) of the cases. Intraoperative biopsy and culture was needed to identify the infecting organism in the other three cases. Cultures were routinely held for 14 days to improve sensitivity.

Dilisio et al. [9] in a retrospective study compared the culture results of preoperative joint aspiration prior to arthroscopy to the results of intraoperative arthroscopic tissue biopsy. Fourteen of nineteen cases undergoing joint aspiration underwent fluoroscopic guidance with contrast to confirm intra-articular placement of aspiration needle. Only 1 of 14 patients (7%) had positive cultures. In contrast, 9 of 19 arthroscopic tissue biopsy cultures were positive. The authors reported that the sensitivity, specificity, positive predictive value and negative predictive value for arthroscopic biopsy was uniformly 100%. In contrast, preoperative aspiration had a sensitivity of 17%, a specificity of 100%, a positive predictive value of 100% and a negative predictive value of 58%. The authors concluded that arthroscopic biopsy is better than preoperative aspiration for identifying shoulder PJI.

Ghijselings et al. [10] reported on 17 patients with shoulder PJI. The authors noted that 15 patients had preoperative cultures, but only 6 patients had undergone joint aspiration. Given the lack of a consistent protocol regarding preoperative joint aspiration, the authors did not comment on any recommended indication for joint aspiration. Sabesan et al. [11] reported on a retrospective review of 27 patients treated with two-stage revision for shoulder PJI. The authors recommended preoperative aspiration, if there was a high suspicion for infection. Twelve of 17 patients underwent aspiration. Fluid was available in 10/12 (83%) patients, and 6 of these had positive cultures.

Other reports have commented on the low yield of preoperative joint aspiration because of the high incidence of dry taps and/or false negative results. Sperling et al. [12] reported that preoperative joint aspiration was possible for only 56% of patients and that *P. acnes* was identified in less than 30%. Codd et al. [13] reported that aspiration was positive in only 39% of shoulders and that cultures were positive in about 29%. Romanó et al. [14] and Coste et al. [15] also reported that the preoperative joint aspiration was diagnostic in only 34-50% of the cases. Strickland et al. [5] reported that joint aspiration for shoulder PJI yielded a 34% false negative rate.

Finally, two review articles merit mention. Hsu et al. [16] evaluated 14 studies that attempted to define shoulder PJI. Of these, 4 used preoperative aspiration to identify the infective organisms. Mook and Garrigues [17] published a review article opining that preoperative serologies, synovial fluid cultures and synovial leukocyte count lacked the necessary specificity and sensitivity for diagnosis of shoulder PJI, especially those caused by *C. acnes* and other slow growing organisms. The authors conceded that, "There are no rigorous large-scale investigations available that address the following questions: (1) When is it appropriate to diagnostically aspirate a prosthetic shoulder joint? (2) If the decision is made to aspirate the shoulder prior to, or during, revision arthroplasty, what values of the synovial fluid leukocyte count are predictive of infection?" The authors add that guidelines for interpreting the results of joint aspirate are borrowed from hip and knee and are largely left up to surgeon judgment.

Based on our evaluation of the shoulder arthroplasty literature and consideration of data on hip and knee arthroplasty, we believe that aspiration of the shoulder joint being investigated for PJI may provide important information and should be attempted, when possible. We realize that a substantial number of these joint aspirations are likely to be dry or yield inadequate synovial fluid to allow all analyses. We also realize that shoulder joint aspiration can be performed with minimal risk and could provide critical information regarding the infective organism(s) and allow determination of the antibiotic sensitivity prior to surgical intervention.

REFERENCES

[1] Horneff JG, Hsu JE, Huffman GR. Propionibacterium acnes infections in shoulder surgery. Orthop Clin North Am. 2014;45:515–521. doi:10.1016/j.ocl.2014.06.004.

[2] Kevin Ko JW, Namdari S. The diagnosis and management of periprosthetic joint infections of the shoulder. Oper Tech Orthop. 2016;26. doi:10.1053/j.oto.2015.12.001.

[3] Ricchetti E, Frangiamore S, Grosso M, Alolabi B, Saleh A, W. Bauer T, et al. Diagnosis of periprosthetic infection after shoulder arthroplasty a critical analysis review. JBJS Rev. 2013;1:e3. doi:10.2106/JBJS.

[4] Ince A, Seemann K, Frommelt L, Katzer A, Loehr JF. One-stage exchange shoulder arthroplasty for peri-prosthetic infection. J Bone Joint Surg Br. 2005;87:814–818. doi:10.1302/0301-620X.87B6.15920.

[5] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. J Bone Joint Surg Br. 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.

[6] Millett PJ, Yen YM, Price CS, Horan MP, van der Meijden OA, Elser F. Propionibacterium acnes infection as an occult cause of postoperative shoulder pain: a case series. Clin Orthop Relat Res. 2011;469:2824–2830. doi:10.1007/s11999-011-1767-4.

[7] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.

[8] Klatte TO, Kendoff D, Kamath AF, Jonen V, Rueger JM, Frommelt L, et al. Single-stage revision for fungal peri-prosthetic joint infection: a single-centre experience. Bone Joint J. 2014;96-B:492–496. doi:10.1302/0301-620X.96B4.32179.

[9] Dilisio MF, Miller LR, Warner JJP, Higgins LD. Arthroscopic tissue culture for the evaluation of periprosthetic shoulder infection. J Bone Joint Surg Am. 2014;96:1952–1958. doi:10.2106/JBJS.M.01512.

[10] Ghijselings S, Stuyck J, Debeer P. Surgical treatment algorithm for infected shoulder arthroplasty: a retrospective analysis of 17 cases. Acta Orthop Belg. 2013;79:626–635.

[11] Sabesan VJ, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. Clin Orthop Relat Res. 2011;469:2538–2543. doi:10.1007/s11999-011-1774-5.

[12] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.

[13] Codd TP, Yamaguchi K, Pollock RG, Flatow EL, Bigliani LU. Infected shoulder arthroplasties: treatment with staged reimplantation vs resection arthroplasty. Orthop Trans. 1996;20:59.

[14] Romanò CL, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. Int Orthop. 2012;36:1011–1017. doi:10.1007/s00264-012-1492-y.

[15] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86(1):65–69.

[16] Hsu JE, Somerson JS, Vo KV, Matsen FA. What is a "periprosthetic shoulder infection"? A systematic review of two decades of publications. Int Orthop. 2017;41:813–822. doi:10.1007/s00264-017-3421-6.

[17] Mook WR, Garrigues GE. Diagnosis and management of periprosthetic shoulder infections. J Bone Joint Surg Am. 2014;96:956–965. doi:10.2106/JBJS.M.00402.

2.5. DIAGNOSIS: SAMPLING

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QUESTION 1: Should tissue samples be obtained for culture in all revision shoulder arthroplasties?

RECOMMENDATION: Tissue samples should be obtained for culture in all revision shoulder arthroplasties when there is suspicion for infection.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

Prosthetic ioint infection (PJI) is a devastating complication following shoulder arthroplasty and varies between 0-5% with increasing risk in revision arthroplasty [1,2]. As such, organism identification and appropriate antibiotic administration is essential.

The failure to address infection without the relevant antimicrobial therapy results in poor outcomes with Coste et al. [3], reporting 30% residual infection when infected shoulder arthroplasty was treated with resection arthroplasty alone and 60% residual infection when purely antibiotic treatment was advocated. The appropriate surgical procedure, combined with the relevant antibiotic therapy, is therefore integral to the effective management of revision shoulder arthroplasty.

Aseptic loosening can be indistinguishable from acute infection and unexpected positive cultures are not uncommon and can be as high as 29% [4,5]. This is particularly relevant when considering the indolent nature of *Cutibacterium acnes*, a common shoulder pathogen, which can be isolated in as high as 60% of revision shoulder arthroplasties in which there were no positive preoperative or intraoperative investigations suggesting infection [5]. Tissue samples for culture should therefore be undertaken at the time of the procedure to both diagnose and confirm infection. Indeed, even in the presence of known infection, alternative organisms can be reported at the time of revision, which can also influence postoperative antibiotic therapy.

Interpreting positive cultures in a previously regarded aseptic revision can, however, be difficult due to false positives from contaminates. False negative results can also prove a challenge, particularly with regard to *Cutibacterium*, which can take 8-10 days to grow [6]. Extended culture incubation for a minimum of 10-14 days is, therefore, recommended [6,7]. Notwithstanding this, the multifocal and low-grade nature of chronic infection can lead to false negative cultures, and sampling bias must, therefore, be considered as a cause for negative cultures.

Mathematical modelling techniques have been utilised to mitigate the risk of false negatives, and it has been proposed that, following five or six specimens in predominantly revision hip and knee arthroplasty, infection can be diagnosed in the presence of three or more positive cultures [8]. In shoulder specific publications a minimum of four specimens have been advocated [9]. Furthermore, aseptic sampling techniques are imperative to minimize the risks of false positives [7,8,10].

Despite this, however, the staged treatment of infected shoulder arthroplasty can still result in residual infection with persistent infection reported in up to 22% of two-stage revisions which had completed implant explantation, debridement, antibiotic spacer and intravenous antibiotics for six weeks [11]. Tissue sampling and culture at the second stage of a two-stage revision shoulder arthroplasty is, therefore, still recommended to ensure optimal outcomes.

REFERENCES

[1] Franceschini V, Chillemi C. Periprosthetic shoulder infection. Open Orthop J. 2013;7:243–249. doi:10.2174/1874325001307010243.

[2] Cofield RH, Edgerton BC. Total shoulder arthroplasty: complications and revision surgery. Instr Course Lect. 1990;39:449–462.

[3] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.

[4] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.

[5] Topolski MS, Chin PYK, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: the value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006;15:402–406. doi:10.1016/j.jse.2005.10.001.

[6] Dodson CC, Craig EV, Cordasco FA, Dines DM, Dines JS, Dicarlo E, et al. Propionibacterium acnes infection after shoulder arthroplasty: a diagnostic challenge. J Shoulder Elbow Surg. 2010;19:303–307. doi:10.1016/j.jse.2009.07.065.

[7] Maccioni CB, Woodbridge AB, Balestro J-CY, Figtree MC, Hudson BJ, Cass B, et al. Low rate of Propionibacterium acnes in arthritic shoulders undergoing primary total shoulder replacement surgery using a strict specimen collection technique. J Shoulder Elbow Surg. 2015;24:1206–1211. doi:10.1016/j.jse.2014.12.026.

[8] Atkins BL, Athanasou N, Deeks JJ, Crook DWM, Simpson H, Peto TEA, et al. Prospective evaluation of criteria for microbiological diagnosis of prosthetic-joint infection at revision arthroplasty. J Clin Microbiol. 1998;36:2932–2939.

[9] Ahsan ZS, Somerson JS, Matsen FA. Characterizing the Propionibacterium load in revision shoulder arthroplasty: a study of 137 culture-positive cases. J Bone Joint Surg Am. 2017;99:150–154. doi:10.2106/JBJS.16.00422.

[10] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.

[11] 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:e15–e20. doi:10.1016/j.jse.2014.04.007.

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QUESTION 2: Is there a role for obtaining tissue cultures when performing an irrigation and debridement (I&D) for hematoma after shoulder (primary or revision) arthroplasty?

RECOMMENDATION: Deep tissue samples should be routinely obtained and sent for culture when performing an I&D for hematoma after shoulder (primary or revision) arthroplasty.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 64%, Disagree: 28%, Abstain: 8% (Super Majority, Weak Consensus)

RATIONALE

A literature search of PubMed and Medline using the terms "shoulder" and "hematoma" resulted in 337 citations. After review of the abstracts, 11 articles that pertained to the topic of hematoma after shoulder arthroplasty were identified for full review. Due to the limited literature on hematoma and shoulder arthroplasty, references on the management of hematoma after total hip and knee arthroplasty were used in the development of this recommendation.

Postoperative hematoma is a known risk factor for prosthetic joint infection following hip and knee arthroplasty [1–3]. Although the supporting literature is scant, hematoma is often cited as a risk factor for the development of deep infection following shoulder arthroplasty as well [4–9]. A study by Cheung et al. retrospectively reviewed 3,541 primary and 606 revision shoulder arthroplasties and found that hematoma formation following shoulder arthroplasty was often accompanied by positive intraoperative cultures [9]. However, only 12 patients (30%) required hematoma evacuation. Nine of these patients had intraoperative cultures sent, and the cultures were positive in six patients. Two of the 12 patients ultimately required resection arthroplasty for deep infection.

In a case-control study Nagaya et al. found that patients with local hematoma formation after total shoulder arthroplasty and hemiarthroplasty had an increased risk for prosthetic joint infection (odds ratio (OR) = 7.10, 95% confidence interval (CI) 1.09-46.09, p = .04) on univariate analysis [10]. This association was lost in the multivariate analysis likely secondary to the low reported infection rate, although a trend towards significance persisted (OR = 6.51. 95% CI .84-50.70, p = .074).

While multiple other studies examining risk factors for the development of prosthetic joint infection following shoulder arthroplasty have been published, most do not specifically address the issue of hematoma formation. Some studies simply did not systemically collect data pertaining to hematoma formation [11–13] or, if they did, did not explore the statistical relationship between hematoma formation and subsequent prosthetic joint infection [8,14–19]. A few studies combined hematoma formation with other complications (e.g., wound dehiscence, superficial infection) when determining statistical associations with infection, making it difficult to determine the specific impact of hematoma formation alone [20,21].

Werner et al. reported on 58 consecutive patients undergoing reverse total shoulder arthroplasty and found that of the 12 patients (20%) requiring treatment for postoperative hematoma none developed any further complications requiring revision [22]. The rate of hematoma formation in the latter study, however, appeared to be very high compared to other reports, which may limit the generaliz-

ability of their results. In comparison, a prospective registry of 301 patients undergoing reverse total shoulder arthroplasty reported only one patient developing hematoma (0.33%) [23]. A systematic review of the literature, comprising 19,262 shoulder arthroplasty cases, found hematoma developed in only 0.51% of revision shoulder arthroplasty cases and 0.09% of total shoulder arthroplasty cases [24].

The presence of infection can be difficult to exclude based on gross findings at the time of hematoma evacuation. Based on the experience reported with arthroplasty of the hip and knee and the small amount of available literature specific to shoulder arthroplasty, we recommend that deep tissue samples be sent for culture routinely when performing an I&D for hematoma after shoulder arthroplasty. The data obtained from these culture samples are useful and can aid the treating orthopaedic surgeons in consultation with infectious disease specialists to determine the optimal management of these patients.

REFERENCES

[1] Saleh K, Olson M, Resig S, Bershadsky B, Kuskowski M, Gioe T, et al. Predictors of wound infection in hip and knee joint replacement: results from a 20 year surveillance program. J Orthop Res. 2002;20:506–515. doi:10.1016/S0736-0266(01)00153-X.

[2] Parvizi J, Ghanem E, Joshi A, Sharkey PF, Hozack WJ, Rothman RH. Does "excessive" anticoagulation predispose to periprosthetic infection? J Arthroplasty. 2007;22:24–28. doi:10.1016/j.arth.2007.03.007.

[3] Galat DD, McGovern SC, Hanssen AD, Larson DR, Harrington JR, Clarke HD. Early return to surgery for evacuation of a postoperative hematoma after primary total knee arthroplasty. J Bone Joint Surg Am. 2008;90:2331–2336. doi:10.2106/JBJS.G.01370.

[4] Farshad M, Gerber C. Reverse total shoulder arthroplasty-from the most to the least common complication. Int Orthop. 2010;34:1075–1082. doi:10.1007/s00264-010-1125-2.

[5] Saltzman MD, Marecek GS, Edwards SL, Kalainov DM. Infection after shoulder surgery. J Am Acad Orthop Surg. 2011;19:208–218.

[6] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.

[7] Mook WR, Garrigues GE. Diagnosis and management of periprosthetic shoulder infections. J Bone Joint Surg Am. 2014;96:956–965. doi:10.2106/JBJS.M.00402.

[8] Groh GI, Groh GM. Complications rates, reoperation rates, and the learning curve in reverse shoulder arthroplasty. J Shoulder Elbow Surg. 2014;23:388–394. doi:10.1016/j.jse.2013.06.002.

[9] Cheung EV, Sperling JW, Cofield RH. Infection associated with hematoma formation after shoulder arthroplasty. Clin Orthop Relat Res. 2008;466:1363–1367. doi:10.1007/s11999-008-0226-3.

[10] Nagaya LH, Salles MJC, Takikawa LSC, Fregoneze M, Doneux P, Silva LA da, et al. Infections after shoulder arthroplasty are correlated with higher anesthetic risk score: a case-control study in Brazil. Braz J Infect Dis. 2017;21:613–619. doi:10.1016/j.bjid.2017.06.003.

[11] Richards J, Inacio MCS, Beckett M, Navarro RA, Singh A, Dillon MT, et al. Patient and procedure-specific risk factors for deep infection after primary shoulder arthroplasty. Clin Orthop Relat Res. 2014;472:2809–2815. doi:10.1007/s11999-014-3696-5.

[12] Nelson GN, Davis DE, Namdari S. Outcomes in the treatment of periprosthetic joint infection after shoulder arthroplasty: a systematic review. J Shoulder Elbow Surg. 2016;25:1337–1345. doi:10.1016/j.jse.2015.11.064.

[13] Achermann Y, Sahin F, Schwyzer HK, Kolling C, Wüst J, Vogt M. Characteristics and outcome of 16 periprosthetic shoulder joint infections. Infection. 2013;41:613–620. doi:10.1007/s15010-012-0360-4.

[14] Schairer WW, Zhang AL, Feeley BT. Hospital readmissions after primary shoulder arthroplasty. J Shoulder Elbow Surg. 2014;23:1349–1355. doi:10.1016/j.jse.2013.12.004.

[15] Stechel A, Fuhrmann U, Irlenbusch L, Rott O, Irlenbusch U. Reversed shoulder arthroplasty in cuff tear arthritis, fracture sequelae, and revision arthroplasty. Acta Orthop. 2010;81:367–372. doi:10.3109/17453674.2010.487242.

[16] Streubel PN, Simone JP, Sperling JW, Cofield R. Thirty and ninety-day reoperation rates after shoulder arthroplasty. J Bone Joint Surg Am. 2014;96:e17. doi:10.2106/JBJS.M.00127.

[17] Boileau P, Watkinson D, Hatzidakis AM, Hovorka I. Neer Award 2005: The Grammont reverse shoulder prosthesis: results in cuff tear arthritis, fracture sequelae, and revision arthroplasty. J Shoulder Elbow Surg. 2006;15:527–540. doi:10.1016/j.jse.2006.01.003.

[18] Lovy AJ, Keswani A, Beck C, Dowdell JE, Parsons BO. Risk factors for and timing of adverse events after total shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:1003–1010. doi:10.1016/j.jse.2016.10.019.

[19] Alentorn-Geli E, Samitier G, Torrens C, Wright TW. Reverse shoulder arthroplasty. Part 2: systematic review of reoperations, revisions, problems, and complications. Int J Shoulder Surg. 2015;9:60–67. doi:10.4103/0973-6042.154771.

[20] Farshad M, Grögli M, Catanzaro S, Gerber C. Revision of reversed total shoulder arthroplasty. Indications and outcome. BMC Musculoskelet Disord. 2012;13:160. doi:10.1186/1471-2474-13-160.

[21] Singh JA, Sperling JW, Schleck C, Harmsen WS, Cofield RH. Periprosthetic infections after total shoulder arthroplasty: a 33-year perspective. J Shoulder Elbow Surg. 2012;21:1534–1541. doi:10.1016/j.jse.2012.01.006.

[22] Werner CML, Steinmann PA, Gilbart M, Gerber C. Treatment of painful pseudoparesis due to irreparable rotator cuff dysfunction with the Delta III reverse-ball-and-socket total shoulder prosthesis. J Bone Joint Surg Am. 2005;87:1476–1486. doi:10.2106/JBJS.D.02342.

[23] Morris BJ, O'Connor DP, Torres D, Elkousy HA, Gartsman GM, Edwards TB. Risk factors for periprosthetic infection after reverse shoulder arthroplasty. J Shoulder Elbow Surg. 2015;24:161–166. doi:10.1016/j.jse.2014.05.020.

[24] Bohsali KI, Bois AJ, Wirth MA. Complications of shoulder arthroplasty. J Bone Joint Surg Am. 2017;99:256–269. doi:10.2106/JBJS.16.00935.

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QUESTION 3: Should tissue cultures be obtained in primary shoulder arthroplasty (SA) cases with history of prior surgery (arthroscopic, open, open reduction and internal fixation (ORIF), or another non-arthroplasty surgery)?

RECOMMENDATION: Obtaining tissue samples for culture in patients with history of prior non-arthroplasty surgery may be indicated in select cases.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Primary SA in patients with history of prior surgery in the affected shoulder is common. The reported prevalence is between 18%-23% [1,2], being higher in primary reverse shoulder arthroplasty (32% to 48%) [1,2] than in primary anatomic arthroplasty (11% to 14%) [1,2].

There is evidence demonstrating that prior surgery on a shoulder undergoing primary SA significantly increases the risk that a periprosthetic joint infection (PJI) will develop. Florschütz et al. [1] found that shoulders with prior surgery undergoing primary

SA demonstrated a significantly higher (p = 0.016) infection rate (4.3%) compared with shoulders with no prior surgery (1.3%), exhibiting a 3.35-times higher risk (95% confidence interval (CI), 1.28-8.81) for infection development. Werthel et al. [2] confirmed this finding in a cohort of 4,577 patients treated with primary SA. Of the 813, patients who had undergone prior surgery, 20 (2.46%) developed PJI. In contrast, of the 3,764 patients who did not have prior shoulder surgery only 48 patients (1.28%) developed PJI. This difference was significant in both the univariate (hazard ratio (HR), 2.08; 95% CI, 1.27-3.45; p = .0094 p = .0094) and multivariate analyses (HR, 1.81; 95% CI, 1.03-3.05 p = .0390). Additionally, a higher number of previous surgeries (HR, 1.68 per surgery) and SA for traumatic etiology (HR 4.49) were also significantly associated with an increased risk of PJI.

The mechanism by which prior surgery increases the risk of PJI is unknown. Possibilities include deep tissues open to the environment with increased operative time both during the index surgery and the arthroplasty [3]; altering the ability to combat infection by affecting lymphatic drainage and blood supply of periarticular tissues [3]; or perhaps, organisms, such as *Cutibacterium Acnes,* may colonize the shoulder and the hardware at the time of the index surgery and remain quiescent or as a low-grade infection until an arthroplasty is performed, which provides a larger surface area of prosthetic material for establishment of a biofilm [2]. There is evidence of subclinical low-grade infections without overt signs of infection by *C. acnes* after arthroscopic and open non-arthroplasty surgery [4–7]. Therefore, while we can make no definitive recommendation given the lack of data in patients undergoing SA subsequent to prior non-arthroplasty surgery, it is reasonable to consider sending intraoperative tissue samples for culture to screen for possible low-grade subclinical infections or wound contaminations.

A comprehensive review of the literature on cultures from tissue samples in primary arthroplasty with history of prior surgery was performed and did not find any prospective or randomized studies. While there is lack of evidence for positive cultures in patients with history of prior surgery, there are a number of studies that investigate patients undergoing primary arthroplasty without prior surgery. Levy et al. [8] isolated *C. acnes* from the synovial fluid and tissue prior to prophylactic antibiotics in 41.5% of shoulders undergoing shoulder replacement for osteoarthritis. In this study, *C. acnes* infection was defined as a positive culture in 50% or more of specimens collected (swab or tissue). Maccioni et al. [9] reported positive tissue cultures for *C. acnes* in 3.1% of cases . Matsen et al. [10] collected 50 tissue samples from 10 patients undergoing primary SA without a history of prior surgery after aggressive prophylactic antibiotic and skin preparation and reported that 14% were positive for *C. acnes*. Falconer et al. [11] evaluated the contamination of the surgical field by *C. acnes* in patients undergoing primary SA without history of prior surgery. The rate of one or more positive swab cultures was 33%. The most common site of growth of *C. acnes* was the subdermal layer. Koh et al. [12] assessed the rate of *C. acnes* colonization in patients undergoing primary shoulder arthroplasty. Patients with prior surgery were excluded. Thirteen patients (43%) had positive deep swab cultures on entering the glenohumeral joint. While in these studies there is variability of the reported rates that might reflect the heterogeneity in the culture techniques and the different definitions used to define a positive culture, there is a consistent finding of positive cultures in primary arthroplasties without a history of prior surgery. The clinical relevance of positive cultures from shoulder undergoing primary surgery is unclear.

In light of reports of positive tissue cultures from shoulders without prior surgery, the utility of intraoperative tissue cultures in patients undergoing primary SA with a history of prior surgery is unclear. Further research into the results of cultures in primary arthroplasty with history of prior surgery using standardized culture techniques and better methods to interpret the results is warranted.

Given the lack of evidence, the use of intraoperative tissue samples for cultures in patients undergoing primary SA with history of prior surgery as a screening infection test should be used at the discretion of the treating surgeon. No universal recommendation can be made at this time. However, considering that low-grade infections actually occur after arthroscopic and open shoulder surgeries and that prior surgery is a demonstrated risk factor for PJI, a screening strategy involving a selected group of patients based on the presence of risk factors (multiple prior surgeries; prior failed ORIF; male gender; younger patients may be prudent [1,2,13,14].

REFERENCES

[1] Florschütz AV, Lane PD, Crosby LA. Infection after primary anatomic versus primary reverse total shoulder arthroplasty. J Shoulder Elbow Surg. 2015;24:1296–1301. doi:10.1016/j.jse.2014.12.036.

[2] Werthel JD, Hatta T, Schoch B, Cofield R, Sperling JW, Elhassan BT. Is previous nonarthroplasty surgery a risk factor for periprosthetic infection in primary shoulder arthroplasty? J Shoulder Elbow Surg. 2017;26:635–640. doi:10.1016/j.jse.2016.10.020.

[3] Marmor S, Kerroumi Y. Patient-specific risk factors for infection in arthroplasty procedure. Orthop Traumatol Surg Res. 2016;102:S113–S119. doi:10.1016/j.otsr.2015.05.012.

[4] Millett PJ, Yen Y-M, Price CS, Horan MP, van der Meijden OA, Elser F. Cutibacterium acnes infection as an occult cause of postoperative shoulder pain: a case series. Clin Orthop Relat Res. 2011;469:2824–2830. doi:10.1007/s11999-011-1767-4.

[5] Klatte TO, Junghans K, Al-Khateeb H, Rueger JM, Gehrke T, Kendoff D, et al. Single-stage revision for peri-prosthetic shoulder infection: outcomes and results. Bone Joint J. 2013;95-B:391–395. doi:10.1302/0301-620X.95B3.30134.

[6] Vasso M, Schiavone Panni A. Low-grade periprosthetic knee infection: diagnosis and management. J Orthop Traumatol. 2015;16:1–7. doi:10.1007/s10195-014-0294-y.

[7] Horneff JG, Hsu JE, Voleti PB, O'Donnell J, Huffman GR. Cutibacterium acnes infection in shoulder arthroscopy patients with postoperative pain. J Shoulder Elbow Surg. 2015;24:838–843. doi:10.1016/j.jse.2015.03.008.

[8] Levy JC, Triplet J, Everding N. Use of a functional antibiotic spacer in treating infected shoulder arthroplasty. Orthopedics. 2015;38:e512–e519. doi:10.3928/01477447-20150603-60.

[9] Maccioni CB, Woodbridge AB, Balestro J-CY, Figtree MC, Hudson BJ, Cass B, et al. Low rate of Cutibacterium acnes in arthritic shoulders undergoing primary total shoulder replacement surgery using a strict specimen collection technique. J Shoulder Elbow Surg. 2015;24:1206–1211. doi:10.1016/j.jse.2014.12.026.

[10] Matsen FA, Russ SM, Bertelsen A, Butler-Wu S, Pottinger PS. Cutibacterium can be isolated from deep cultures obtained at primary arthroplasty despite intravenous antimicrobial prophylaxis. J Shoulder Elbow Surg. 2015;24:844–847. doi:10.1016/j.jse.2014.10.016.

[11] Falconer TM, Baba M, Kruse LM, Dorrestijn O, Donaldson MJ, Smith MM, et al. Contamination of the surgical field with Cutibacterium acnes in primary shoulder arthroplasty. J Bone Joint Surg Am. 2016;98:1722–1728. doi:10.2106/JBJS.15.01133.

[12] Koh CK, Marsh JP, Drinković D, Walker CG, Poon PC. Cutibacterium acnes in primary shoulder arthroplasty: rates of colonization, patient risk factors, and efficacy of perioperative prophylaxis. J Shoulder Elbow Surg. 2016;25:846–852. doi:10.1016/j.jse.2015.09.033.

[13] Singh JA, Sperling JW, Schleck C, Harmsen WS, Cofield RH. Periprosthetic infections after total shoulder arthroplasty: a 33-year perspective. J Shoulder Elbow Surg. 2012;21:1534–1541. doi:10.1016/j.jse.2012.01.006.

[14] Padegimas EM, Maltenfort M, Ramsey ML, Williams GR, Parvizi J, Namdari S. Periprosthetic shoulder infection in the United States: incidence and economic burden. J Shoulder Elbow Surg. 2015;24:741–746. doi:10.1016/j.jse.2014.11.044.

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QUESTION 4: Is there a role for preoperative open or arthroscopic tissue biopsy in the evaluation prior to initial revision shoulder arthroplasty?

RECOMMENDATION: Arthroscopic or open biopsy prior to initial revision shoulder arthroplasty can aid in the diagnosis of suspected shoulder periprosthetic joint infection (PJI).

LEVEL OF EVIDENCE: Limited

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

RATIONALE

PubMed and Embase were searched from 1980 to January 2018 to identify studies evaluating preoperative open or arthroscopic tissue biopsy prior to revision shoulder arthroplasty. A secondary search of the references of included studies was also conducted. Three articles were selected for inclusion. Articles regarding hip and knee arthroplasty were excluded.

Morman et al. described one case in which arthroscopy was used in the evaluation of shoulder PJI prior to revision [1]. The patient presented with pain and glenoid loosening three years after total shoulder arthroplasty (TSA), underwent arthroscopic tissue biopsy that grew *C. acnes*, and went on to undergo successful two-stage revision for shoulder PJI.

Dilisio et al. reported on a series of 19 cases from a series of 350 painful shoulder arthroplasties who underwent arthroscopic biopsy prior to revision [2]. At revision shoulder arthroplasty, 41% had positive cultures, all for *C. acnes*. Arthroscopic biopsy prior to revision was exactly consistent with the final revision cultures with 100% sensitivity, specificity, positive predictive value and negative predictive value. The authors also reported that fluoroscopically guided glenohumeral aspiration prior to revision was inferior to arthroscopic biopsy with 16.7% sensitivity, 100% specificity, 100% positive predictive value and 58.3% negative predictive value. There are potential limitations including selection bias in this study without well-defined criteria by which the 19 patients out of 350 painful TSAs were selected to undergo arthroscopy. Thus, it is unclear what features of the presentation led the treating surgeon to continue to have a high index of suspicion for infection in these particular cases. Furthermore, cultures were held following revision surgery for only 7 days, whereas many authors advocate for longer incubation times (most frequently 14 days) for the fastidious and slow-growing *C. acnes*.

Tashjian et al. reported on a series of 77 patients who had revision TSA, and pre-revision biopsy was performed in 17 cases considered "at-risk" for infection [3]. Specifically, this included patients with abnormal erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) with no growth on shoulder aspiration, as well as patients with normal ESR/CRP and a dry aspirate. Patients that were grossly infected, those with positive aspiration culture, as well as those with normal ESR/CRP and negative aspiration culture were not biopsied. Open biopsy was performed for cases of known deficient rotator cuff via the proximal 3cm of the prior deltopectoral incision. Arthroscopic biopsy was performed with anatomic TSA with intact rotator cuff via a posterior viewing portal and anterior rotator interval portal for obtaining biopsy specimens. Two to three samples were obtained during biopsy and again at the time of revision TSA, and cultures were held for 14 days. Revision arthroplasty was performed at least three weeks after biopsy. They found that the prerevision biopsy resulted in 75% sensitivity, 60% specificity, 82% positive predictive value and 50% negative predictive value for the prediction of positive culture at the time of revision TSA. For diagnosis of infection, sensitivity was 90%, specificity 85%, positive predictive value 90% and negative predictive value 86%. The study limitations include a mixture of open and arthroscopic biopsies prior to revision TSA, a small sample size, and the use of two biopsy samples in some patients and three in others. There was also no comparison between open and arthroscopic biopsy and no comparison to other diagnostic tests.

Overall, the limited available literature suggests that biopsy prior to revision TSA can improve the diagnosis of shoulder PJI in cases without obvious objective evidence of infection, where the clinician remains suspicious of occult infection. While not well studied, many clinicians have used this technique as a method to confirm an aseptic environment before implantation of a prosthetic in cases where there is a distant history of apparently fully treated infection after shoulder surgery. Future research must report which history, demographic, physical exam, radiographic or laboratory features can guide a clinician to continue to be suspicious of occult infection. There is no evidence for a role in cases that are obviously infected or cases without suspicion for infection (e.g., loosening after trauma or loosening after many years of successfully functioning shoulder arthroplasty where labs are normal and radiographs do not suggest infection). Specific indications for arthroscopic biopsy remain to be further defined due to the limited available literature at present. Perhaps the main advantage of pre-revision biopsy for culture is that if the cultures are positive one might make the definitive decision to perform two-stage revision and have a better understanding of appropriate antibiotic management. However, it also remains unclear if this would be the appropriate decision given the good track record of one-stage revision TSA in cases of unexpected positive cultures for *C. acnes*. In addition, the cost-effectiveness of adding an arthroscopic biopsy to the treatment algorithm for revision shoulder arthroplasty remains unknown.

REFERENCES

[1] Morman M, Fowler RL, Sanofsky B, Sanosky B, Higgins LD. Arthroscopic tissue biopsy for evaluation of infection before revision arthroplasty. J Shoulder Elbow Surg. 2011;20:e15–e22. doi:10.1016/j.jse.2010.11.015.

[2] Dilisio MF, Miller LR, Warner JJP, Higgins LD. Arthroscopic tissue culture for the evaluation of periprosthetic shoulder infection. J Bone Joint Surg Am. 2014;96:1952–1958. doi:10.2106/JBJS.M.01512.

[3] Tashjian RZ, Granger EK, Zhang Y. Utility of prerevision tissue biopsy sample to predict revision shoulder arthroplasty culture results in at-risk patients. J Shoulder Elbow Surg. 2017;26:197–203. doi:10.1016/j.jse.2016.07.019.

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QUESTION 5: Does the sampling technique (number of samples, anatomic locations) of the tissue obtained in the evaluation for shoulder periprosthetic joint infection (PJI) affect the result of frozen section and permanent histology?

RECOMMENDATION: Obtaining samples from multiple locations—most importantly from the prosthetic interface membranes—may optimize accuracy if performing frozen section or permanent histology as part of a workup for periprosthetic shoulder infection.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 91%, Disagree: 0%, Abstain: 9% (Super Majority, Strong Consensus)

RATIONALE

Frozen section histology can be useful in the diagnosis of shoulder PJI [1]. Two studies have specifically assessed the use of frozen section in revision shoulder arthroplasty [1,2]. These analyses did not offer specific guidance on the tissue sampling technique for histologic analysis in the shoulder. Topolski et al. stated only that "a biopsy specimen from the synovial surface that appears most inflamed is usually sent for histologic evaluation of frozen sections" [2]. Alternatively, Grosso et al. suggested sampling deep periprosthetic tissue—specifically tissue obtained from the membranes of the glenoid or humeral components [1].

Due to the lack of evidence addressing the optimal sampling technique in shoulder-specific literature, a broad systematic review of all arthroplasty literature was undertaken. A search was performed on Scopus [3] with the query, "(joint OR hip OR knee OR shoulder) AND (arthroplasty OR replacement) AND (infection OR infected) AND ('frozen section' OR histology OR histologic)." This provided thirty-eight articles of interest to this topic. Twenty-five of these articles reported the number of samples obtained and/or their anatomic location—most of which described obtaining samples from multiple sites, including the prosthetic membrane interface and inflamed-appearing synovium. Two articles resulting from this query, however, provide specific analysis of intraoperative sampling technique for histologic analysis.

Wu et al. performed a review of lower-extremity revision arthroplasty cases with specific focus on histologic analysis using a non-standard definition of PJI (based upon purulence, culture-results and histologic analysis) as the gold-standard [4]. This analysis found increased sensitivity for frozen section when increasing the number of samples (76%, 86% and 86% for three, five, and seven samples, respectively) with decreasing specificity (97%, 96% and 92%). From this, the authors concluded that the most accurate use of frozen section is sampling of five sites with a single positive sample (using Feldman's adoption of Mirra's criteria [5,6]) deemed as diagnostic of PJI. Unfortunately, the authors did not clarify if this sub-analysis was performed as a simulation and how samples were excluded.

Bori et al. investigated the association between anatomic location of the tissue sample and the accuracy of frozen section analysis [7]. In their review of 69 revision hip arthroplasties, they found that frozen section of tissue taken from the prosthetic interface membrane compared to pseudocapsule had improved sensitivity (83% versus 42%) with identical specificity (98%). Unfortunately, these authors used a non-standard definition of PJI. They also excluded patients who were ultimately diagnosed with PJI based upon intraoperative testing and appearance but were presumed to have aseptic loosening preoperatively.

While limited, the two lower extremity arthroplasty studies suggest that the most accurate utilization of intraoperative frozen section is conferred by obtaining multiple frozen sections from the prosthetic interface membrane [4,7]. This is in concert with the single study finding benefit of frozen section in the setting of shoulder revision arthroplasty [1]. Further evidence is necessary to confirm this recommendation.

REFERENCES

[1] Grosso MJ, Frangiamore SJ, Ricchetti ET, Bauer TW, Iannotti JP. Sensitivity of frozen section histology for identifying Propionibacterium acnes infections in revision shoulder arthroplasty. J Bone Joint Surg Am. 2014;96:442–447. doi:10.2106/JBJS.M.00258.

[2] Topolski MS, Chin PYK, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: the value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006;15:402–406. doi:10.1016/j.jse.2005.10.001.

[3] Kasten MD, Skinner HB. Total elbow arthroplasty. An 18-year experience. Clin Orthop Relat Res. 1993:177–188.

[4] Wu C, Qu X, Mao Y, Li H, Dai K, Liu F, et al. Utility of intraoperative frozen section in the diagnosis of periprosthetic joint infection. PloS One. 2014;9:e102346. doi:10.1371/journal.pone.0102346.

[5] Feldman DS, Lonner JH, Desai P, Zuckerman JD. The role of intraoperative frozen sections in revision total joint arthroplasty. J Bone Joint Surg Am. 1995;77:1807–1813.

[6] Mirra JM, Amstutz HC, Matos M, Gold R. The pathology of the joint tissues and its clinical relevance in prosthesis failure. Clin Orthop Relat Res. 1976:221–240.

[7] Bori G, Muñoz-Mahamud E, Garcia S, Mallofre C, Gallart X, Bosch J, et al. Interface membrane is the best sample for histological study to diagnose prosthetic joint infection. Mod Pathol. 2011;24:579–584. doi:10.1038/modpathol.2010.219.

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QUESTION 6: Is there a role for sonication of retrieved shoulder implants in the diagnosis of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There is currently no evidence to support routine sonication of the retrieved shoulder implant in the diagnosis of shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

PubMed and Embase were searched from 1980 to January 2018 to identify studies evaluating the role of sonication of retrieved implants in shoulder PJI. A secondary search of the references of included studies was also conducted. Prior work has evaluated the role of sonication of retrieved implants in hip and knee arthroplasty. In some of these scenarios, sonication of implants has been used to improve PJI culture sensitivity via disruption of bacterial biofilms (see Hip and Knee, Section 2.4. Pathogen Isolation, Culture Related Matters, Question 6 for full discussion of available literature and recommendations from the International Consensus Meeting (ICM) on musculoskeletal infection) [1–7]. Our search identified two studies that have evaluated the role of implant sonication specifically in the setting of shoulder PJI [3,5].

Piper et al. compared periprosthetic tissue culture and implant sonication followed by sonicate fluid culture from 136 shoulder arthroplasty revisions performed for any indication between 2004 and 2008 [5]. For the sonicate fluid culture, a cutoff of > 20 colony forming units per milliliter was used to exclude contaminants. Thirty-three cases had a definite shoulder PJI and 2 had probable shoulder PJI. The sonicate fluid culture showed slightly better sensitivity for detecting shoulder PJI compared with periprosthetic tissue culture (66.7% vs. 54.5%, p = 0.046). There was no difference in specificity (98% vs. 95.1%, p = 0.26). The authors concluded that sonication improved the diagnosis of shoulder PJI.

Grosso et al. compared intraoperative tissue and fluid culture to sonication fluid culture for 53 revision total shoulder arthroplasty procedures, of which 25 were identified as shoulder PJI [3]. The sensitivity and specificity of the intraoperative cultures were 96% and 75%, respectively. Using a cutoff of > 20 colony forming units per milliliter, the sonication fluid culture had sensitivity and specificity of 56% and 93%, respectively. While the sensitivity was greater for intraoperative culture than sonication (p = 0.001), there was no difference in specificity (p = 0.07). The authors concluded that implant sonication had no benefit in comparison to standard intraoperative cultures for shoulder PJI diagnosis.

The Piper et al. and Grosso et al. studies differed in several ways including the diagnostic criteria for shoulder PJI (2 positive cultures vs. 1 positive culture with other signs of infection), length of culture (7 days vs. 12 to 14 days) and the sonication methods. Overall, the conflicting results of these two limited studies make it unclear whether sonication can improve diagnosis of shoulder PJI.

REFERENCES

[1] Achermann Y, Vogt M, Leunig M, Wüst J, Trampuz A. Improved diagnosis of periprosthetic joint infection by multiplex PCR of sonication fluid from removed implants. J Clin Microbiol. 2010;48:1208–1214. doi:10.1128/JCM.00006-10.

[2] Esteban J, Alvarez-Alvarez B, Blanco A, Fernández-Roblas R, Gadea I, Garcia-Cañete J, et al. Prolonged incubation time does not increase sensitivity for the diagnosis of implant-related infection using samples prepared by sonication of the implants. Bone Joint J. 2013;95-B:1001–1006. doi:10.1302/0301-620X.95B7.31174.

[3] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.

[4] Holinka J, Bauer L, Hirschl AM, Graninger W, Windhager R, Presterl E. Sonication cultures of explanted components as an add-on test to routinely conducted microbiological diagnostics improve pathogen detection. J Orthop Res. 2011;29:617–622. doi:10.1002/jor.21286.

[5] Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR, et al. Microbiologic diagnosis of prosthetic shoulder infection by use of implant sonication. J Clin Microbiol. 2009;47:1878–1884. doi:10.1128/JCM.01686-08.

[6] Sharma K, Meena RK, Aggarwal A, Chhabra R. Multiplex PCR as a novel method in the diagnosis of spinal tuberculosis-a pilot study. Acta Neurochir (Wien). 2017;159:503–507. doi:10.1007/s00701-016-3065-0.

[7] Prieto-Borja L, Auñón Á, Blanco A, Fernández-Roblas R, Gadea I, García-Cañete J, et al. Evaluation of the use of sonication of retrieved implants for the diagnosis of prosthetic joint infection in a routine setting. Eur J Clin Microbiol Infect Dis. 2018;37:715–722. doi:10.1007/s10096-017-3164-8.

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QUESTION 7: Should preoperative antibiotics be held until after cultures are obtained in revision shoulder arthroplasty (RSA)?

RECOMMENDATION: Recent studies have shown that preoperative antibiotic prophylaxis does not adversely affect intraoperative culture results. We do not recommend routinely holding preoperative antibiotics in RSA.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

In a systematic review using the Cochrane Library, Medline, Embase and CINAHL (Cumulative Index to Nursing and Allied Health Literature) databases, it has been reported that intravenous antibiotic prophylaxis reduces the risk of absolute infection by 8% and the risk of relative infection by 81% in patients who underwent a primary or revision total hip replacement or total knee replacement [1]. On the other hand, it has been shown that the identification of pathogen and pathogen-specific antibiotic therapy are extremely important in the treatment of periprosthetic joint infection (PJI) [2,3]. In the Report of the Third International Consensus Meeting, withholding preoperative antibiotics was not routinely recommended for the operative treatment of the knee and hip PJI [4,5]. However, it has been stated that antibiotics might be held in cases where the pathogen is not identified preoperatively [4]. In contrast to bacteria with high antigenicity that cause suppurative infection and sepsis clinically, low virulence *C. acnes* (*Cutibacterium acnes*) is responsible for the majority of shoulder PJI [6,7]. The culture sensitivity is poor for this pathogen [6]. It may be helpful to utilize implant sonication [8], next-generation sequencing and polymerase chain reaction (PCR) technologies to increase the sensitivity of detecting this low-virulence bacterium [3]. However, those techniques are not used routinely in current clinical practice due to fact that they are not cost-effective and require additional equipment [9]. Given these difficulties, it is important to anticipate whether preoperative intravenous antibiotic prophylaxis will reduce culture sensitivity. Pottinger et al. [10] evaluated the effects of antibiotic prophylaxis on the culture positivity in patients who underwent RSA with a diagnosis of shoulder PJI (at least 2 cultures being positive). In the patient group for which antibiotics were held, the cultures were more than twice as likely to be positive for *C. acnes* and other organisms versus the group of patients where antibiotics had not been held. However, this is a retrospective study and the decision to hold antibiotics was dependent on the operating surgeon. There might be bias on holding antibiotics for a case that the operating surgeon thought might be infected rather than not. There is insufficient literature in this regard with limited evidence. In the majority of RSA studies, although the effect of antibiotic prophylaxis on culture positivity has not been directly examined, it has been observed that clinicians have a tendency to hold preoperative antibiotic prophylaxis in revision shoulder arthroplasty [10–13]. However, in the Clinical Practice Guideline issued by the Infectious Diseases Society of America, the importance of evaluating preop PJI risk was emphasized in the decision to hold antibiotic prophylaxis. If the history, examination, erythrocyte sedimentation rate, C-reactive protein level and preoperative aspiration suggest that the risk of PJI is low, preoperative antibiotic holding is not recommended. Preoperative antibiotic holding is only recommended in cases where the infection is strongly suspected [14].

A study directly examining the effect of preoperative antibiotics on culture results in RSA was performed recently by Anagnostopoulos et al. The authors assessed the influence of antibiotic prophylaxis within 30 to 60 minutes before surgery on time to positivity of intraoperative cultures and the proportion of positive intraoperative cultures [15]. One-hundred-ten patients who underwent revision shoulder, hip or knee arthroplasty were included in the study. Seventy-two patients underwent RSA and the culture of *C. acnes* was evaluated directly. Among the 64 patients with *C. acnes* infection, the proportion of culture positivity was 71.6% (95% confidence interval (CI) 64.1-79.1) in the patients without perioperative prophylaxis, whereas the proportion of culture positivity was 65.9% (95% CI 55.3-76.5) in the patients with perioperative prophylaxis. This was not a statistically significant difference ($p = 0.39$).

In a study by Matsen et al. [16], intraoperative positive cultures for *C. acnes* could be obtained even when using intravenous antibiotic prophylaxis in the setting of a primary shoulder replacement. Similar to Matsen et al., Phadnis et al. [17] reported obtaining positive culture for *C. acnes* from the shoulder dermis despite skin preparation and prophylactic antibiotics.

Based on the available limited literature, considering that the importance of protecting the newly implanted hardware and avoiding surgical field infection are of utmost importance, we recommend that preoperative antibiotics should not be held until after cultures are obtained in RSA.

REFERENCES

[1] AlBuhairan B, Hind D, Hutchinson A. Antibiotic prophylaxis for wound infections in total joint arthroplasty: a systematic review. J Bone Joint Surg Br. 2008;90:915–919. doi:10.1302/0301-620X.90B7.20498.

[2] Bedenčič K, Kavčič M, Faganeli N, Mihalič R, Mavčič B, Dolenc J, et al. Does preoperative antimicrobial prophylaxis influence the diagnostic potential of periprosthetic tissues in hip or knee infections? Clin Orthop Relat Res. 2016;474:258–264. doi:10.1007/s11999-015-4486-4.

[3] Tarabichi M, Shohat N, Goswami K, Alvand A, Silibovsky R, Belden K, et al. Diagnosis of periprosthetic joint infection: the potential of next-generation sequencing. J Bone Joint Surg. Am 2018;100:147–154. doi:10.2106/JBJS.17.00434.

[4] Ghanem E, Parvizi J, Clohisy J, Burnett S, Sharkey PF, Barrack R. Perioperative antibiotics should not be withheld in proven cases of periprosthetic infection. Clin Orthop Relat Res. 2007;461:44–47. doi:10.1097/BLO.0b013e3180656780.

[5] Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Orthop Res. 2014;32 Suppl 1:S98–S107. doi:10.1002/jor.22553.

[6] Dodson CC, Craig EV, Cordasco FA, Dines DM, Dines JS, Dicarlo E, et al. Propionibacterium acnes infection after shoulder arthroplasty: a diagnostic challenge. J Shoulder Elbow Surg. 2010;19:303–307. doi:10.1016/j.jse.2009.07.065.

[7] Achermann Y, Sahin F, Schwyzer HK, Kolling C, Wüst J, Vogt M. Characteristics and outcome of 16 periprosthetic shoulder joint infections. Infection. 2013;41:613–620. doi:10.1007/s15010-012-0360-4.

[8] Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR, et al. Microbiologic diagnosis of prosthetic shoulder infection by use of implant sonication. J Clin Microbiol. 2009;47:1878–1884. doi:10.1128/JCM.01686-08.

[9] Ricchetti ET, Frangiamore SJ, Grosso MJ, Alolabi B, Saleh A, Bauer TW, et al. Diagnosis of periprosthetic infection after shoulder arthroplasty: a critical analysis review. JBJS Rev. 2013;1. doi:10.2106/JBJS.RVW.M.00055.

[10] Grosso MJ, Frangiamore SJ, Ricchetti ET, Bauer TW, Iannotti JP. Sensitivity of frozen section histology for identifying Propionibacterium acnes infections in revision shoulder arthroplasty. J Bone Joint Surg Am. 2014;96:442–447. doi:10.2106/JBJS.M.00258.

[11] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.

[12] Lucas RM, Hsu JE, Whitney IJ, Wasserburger J, Matsen FA. Loose glenoid components in revision shoulder arthroplasty: is there an association with positive cultures? J Shoulder Elbow Surg. 2016;25:1371–1375. doi:10.1016/j.jse.2015.12.026.

[13] Lutz M-F, Berthelot P, Fresard A, Cazorla C, Carricajo A, Vautrin A-C, et al. Arthroplastic and osteosynthetic infections due to Propionibacterium acnes: a retrospective study of 52 cases, 1995-2002. Eur J Clin Microbiol Infect Dis. 2005;24:739–744. doi:10.1007/s10096-005-0040-8.

[14] Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013;56:e1–e25. doi:10.1093/cid/cis803.

[15] Anagnostopoulos A, Bossard DA, Ledergerber B, Zingg PO, Zinkernagel AS, Gerber C, et al. Perioperative antibiotic prophylaxis has no effect on time to positivity and proportion of positive samples: a cohort study of 64 Cutibacterium acnes bone and joint infections. J Clin Microbiol. 2018;56. doi:10.1128/JCM.01576-17.

[16] 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;24:844–847. doi:10.1016/j.jse.2014.10.016.

[17] Phadnis J, Gordon D, Krishnan J, Bain GI. Frequent isolation of Propionibacterium acnes from the shoulder dermis despite skin preparation and prophylactic antibiotics. J Shoulder Elbow Surg. 2016;25:304–310. doi:10.1016/j.jse.2015.08.002.

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QUESTION 8: Does the sampling technique (e.g., number of samples, tissue versus fluid versus implant, anatomic locations) affect the results for culture of specimens obtained in the evaluation of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: We recommend five deep tissue specimens for culture be obtained from various surgical sites (e.g., capsule, humeral canal and periprosthetic membranes in the proximal humerus and glenoid). Use of swabs is discouraged. Fresh instruments should be used to obtain and place samples directly into sterile containers. Fluid sampling may be beneficial but has lower yield compared to tissue.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

The shoulder presents a unique challenge in evaluating and treating PJI. The diagnosis of PJI is currently heavily reliant on culture results around the time of revision surgery. These culture results are frequently positive—often unexpectedly [1–4]—and the implications have yet to be fully elucidated [5–8]. To understand the most effective methods for obtaining samples for culture, a systematic review of the existing literature was undertaken. A Scopus [9] search was performed with the query, "(shoulder OR "upper extremity") AND (arthroplasty OR replacement OR revision) AND (culture OR microbiologic OR microbiology)." The resulting titles and abstracts (n = 218) from this query were reviewed for any pertinence to the question of number of samples for culture, specimen type and anatomic locations. All pertinent articles (n = 28) were then fully reviewed, and any other pertinent citations in these gathered articles were obtained and reviewed.

In cases concerning for possible shoulder PJI an attempt to make a preoperative case for surgical planning is desirable. Historically, preoperative joint aspiration and fluid culture has served in this endeavor. However, recent evidence has demonstrated a poor sensitivity of fluid cultures [6,10–12]. Three separate analyses out of a single institution repeatedly demonstrated decreased rates of positive cultures (27-38%) from fluid specimens compared to solid tissue (34-66.5%) and explants (46-55.6%) [6,10,11]. In a separate analysis, Dilisio et al. compared arthroscopic biopsy results (a minimum of three samples) and preoperative fluroscopically-guided aspiration for culture in patients who went on to open revision arthroplasty [12]. They found that arthroscopic biopsy had 100% concordance with culture at the time of open surgery; however, aspirated fluid had a sensitivity 16.7% and specificity of 100%. However, while these data suggest that fluid aspiration is not the optimal specimen type for culture, it is less invasive compared to arthroscopic biopsy.

Another potential source for culture is sampling of the explanted components. In separate analyses, Lucas et al. and Ahsan et al.demonstrated similar positive culture results from explant vortex samples and solid tissue cultures [6,10]. Lucas et al. also found that 56% (24/43) of loose glenoid components were culture-positive after vortex sampling compared to 13% (1/8) of stable glenoid components [6]. However, in 53 patients undergoing revision shoulder arthroplasty (25 infections), Grosso et al. found that cultures of fluid from explant sonication had a sensitivity and specificity of 56% and 93%, respectively, when using a threshold of 20 colony-forming-units (CFU) per milliliter (mL) [13]. When removing this threshold, the sensitivity improved to 96% but the specificity decreased to 64%. This was compared to 96% and 75% sensitivity and specificity, respectively, for solid tissue cultures. Unfortunately, this analysis excluded those patients that received preoperative antibiotics—a population that has historically benefited the most from explant sonication cultures [14]. In a separate analysis of 136 revision or resection shoulder arthroplasties, Piper et al. was unable to find a statistically-significant improvement in sensitivity of explant sonication (66.7%) compared to solid tissue cultures (54.5%) [15]. Despite this, the authors advocated for explant sonication. However, taking into account all of the existing literature specific to shoulder PJI, there is little support for routine use of explant culturing in revision shoulder arthroplasty.

When collecting solid tissue for culture, a common question is the optimum location and number of samples. Specifically in the shoulder, Pottinger et al. and Frangiamore et al. demonstrated a positive correlation between the number of samples taken and the number of positive culture results [4,16]. Pottinger et al. found an odds ratio for positive culture results of 1.24-1.35 per sample obtained [4]. Frangiamore, however, found no association between the number of samples obtained and the proportion of samples that were positive [16]. In an analysis of *C. acnes* in revision shoulder arthroplasty, Matsen et al. determined that, given their proportion of positive cultures, four specimens would provide a 95% chance of detecting the organism [11]. With the goal of increasing the sensitivity of tissue culture without additional costs of unnecessary cultures and sacrificing specificity, the appropriate number of samples can be a difficult target, aggravated by the current lack of a uniform definition of PJI specific to shoulder arthroplasty [17]. From the general arthroplasty literature, Atkins et al. reviewed 297 revision hip and knee arthroplasty cases with modeling to determine that five to six specimens provided the best sensitivity and specificity of PJI diagnosis with a target of two positive cultures [18]. In a more recent analysis, Peel et al. reviewed 499 patients undergoing arthroplasty (60 shoulders) using the Musculoskeletal Infection Society (MSIS) definition of PJI [19,20]. Using the results of their review, they performed mathematical modeling to determine that the optimal number of samples for standard tissue culture was four. Unfortunately, the use of the modified MSIS definition of PJI may confound the results of their analysis as applied to shoulder arthroplasty—known to be a more indolent presentation of infection. Given this current evidence, it is recommended that four to five samples be obtained during revision shoulder arthroplasty to minimize cost and likelihood of false-positive results while increasing culture sensitivity in revision shoulder arthroplasty.

In determining the best locations for specimen selection, it is first imperative to sample from any sites consistent with active infection through signs of inflammation, acute purulence or necrosis. In their analysis of the origin of *C. acnes* positive cultures in revision shoulder arthroplasty, Matsen et al. found that periprosthetic

membranes, especially the humeral membrane, had the highest rate of positive cultures for *C. acnes* [11]. For arthroscopic evaluation of PJI, Dilisio et al. biopsied at least three different sites with evidence of synovitis and prosthetic contact [12].

REFERENCES

[1] Falconer TM, Baba M, Kruse LM, Dorrestijn O, Donaldson MJ, Smith MM, et al. Contamination of the surgical field with Propionibacterium acnes in primary shoulder arthroplasty. J Bone Joint Surg Am. 2016;98:1722–1728. doi:10.2106/JBJS.15.01133.

[2] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:620–627. doi:10.1016/j.jse.2012.07.017.

[3] Koh CK, Marsh JP, Drinković D, Walker CG, Poon PC. Propionibacterium acnes in primary shoulder arthroplasty: rates of colonization, patient risk factors, and efficacy of perioperative prophylaxis. J Shoulder Elbow Surg. 2016;25:846–852. doi:10.1016/j.jse.2015.09.033.

[4] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[5] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.

[6] Lucas RM, Hsu JE, Whitney IJ, Wasserburger J, Matsen FA. Loose glenoid components in revision shoulder arthroplasty: is there an association with positive cultures? J Shoulder Elbow Surg. 2016;25:1371–1375. doi:10.1016/j.jse.2015.12.026.

[7] Padegimas EM, Lawrence C, Narzikul AC, Zmistowski BM, Abboud JA, Williams GR, et al. Future surgery after revision shoulder arthroplasty: the impact of unexpected positive cultures. J Shoulder Elbow Surg. 2017;26:975–981. doi:10.1016/j.jse.2016.10.023.

[8] Topolski MS, Chin PYK, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: the value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006;15:402–406. doi:10.1016/j.jse.2005.10.001.

[9] Scopus. Document details n.d. https://www-scopus-com.proxy1.lib.tju.edu/record/display.uri?eid=2-s2.0-00273003555&origin=inward&txGid=A7C2209533A7FC3E01AB869C3A68C558.wsnAw8kcdt7IPYLOoV48gA%3a1 (accessed June 21, 2017).

[10] Ahsan ZS, Somerson JS, Matsen FA. Characterizing the Propionibacterium load in revision shoulder arthroplasty: a study of 137 culture-positive cases. J Bone Joint Surg Am. 2017;99:150–154. doi:10.2106/JBJS.16.00422.

[11] 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 Joint Surg Am. 2013;95:e1811–e1817. doi:10.2106/JBJS.L.01733.

[12] Dilisio MF, Miller LR, Warner JJP, Higgins LD. Arthroscopic tissue culture for the evaluation of periprosthetic shoulder infection. J Bone Joint Surg Am. 2014;96:1952–1958. doi:10.2106/JBJS.M.01512.

[13] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.

[14] Trampuz A, Piper KE, Hanssen AD, Osmon DR, Cockerill FR, Steckelberg JM, et al. Sonication of explanted prosthetic components in bags for diagnosis of prosthetic joint infection is associated with risk of contamination. J Clin Microbiol. 2006;44:628–631. doi:10.1128/JCM.44.2.628-631.2006.

[15] Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR, et al. Microbiologic diagnosis of prosthetic shoulder infection by use of implant sonication. J Clin Microbiol. 2009;47:1878–1884. doi:10.1128/JCM.01686-08.

[16] Frangiamore SJ, Saleh A, Grosso MJ, Alolabi B, Bauer TW, Iannotti JP, et al. Early versus late culture growth of Propionibacterium acnes in revision shoulder arthroplasty. J Bone Joint Surg Am. 2015;97:1149–1158. doi:10.2106/JBJS.N.00881.

[17] Hsu JE, Somerson JS, Vo KV, Matsen FA. What is a "periprosthetic shoulder infection"? A systematic review of two decades of publications. Int Orthop. 2017;41:813–822. doi:10.1007/s00264-017-3421-6.

[18] Atkins BL, Athanasou N, Deeks JJ, Crook DW, Simpson H, Peto TE, et al. Prospective evaluation of criteria for microbiological diagnosis of prosthetic-joint infection at revision arthroplasty. The OSIRIS Collaborative Study Group. J Clin Microbiol. 1998;36:2932–2939.

[19] Peel TN, Spelman T, Dylla BL, Hughes JG, Greenwood-Quaintance KE, Cheng AC, et al. Optimal periprosthetic tissue specimen number for diagnosis of prosthetic joint infection. J Clin Microbiol. 2017;55:234–243. doi:10.1128/JCM.01914-16.

[20] Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Orthop Res. 2014;32 Suppl 1:S98–S107. doi:10.1002/jor.22553.

Treatment

3.1. TREATMENT: ANTIBIOTICS FOR UNEXPECTED POSITIVE CULTURES

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QUESTION 1: Is there a role for postoperative antibiotics after performing an irrigation and debridement (I&D) for hematoma complicating a primary or revision shoulder arthroplasty while awaiting culture results?

RECOMMENDATION: Antibiotics should be given after performing an I&D for hematoma after shoulder (primary or revision) arthroplasty while awaiting cultures.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 91%, Disagree: 9%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

A literature search using the terms "shoulder" and "hematoma" resulted in 337 in citations. After review of the abstracts, 11 articles [1–11] that pertained to the topic of hematoma after shoulder arthroplasty were identified for full text review. Review of these 11 articles did not identify any specific studies addressing the use of antibiotics after performing I&D of a hematoma after shoulder arthroplasty. However, given the concern for the presence of infection at the time of I&D for hematoma following shoulder arthroplasty, as discussed in Section 2:5, Question 2 ("Is there a role for obtaining wound cultures when performing an I&D for hematoma after shoulder (primary or revision) arthroplasty?"), we believe it is reasonable to initiate empiric antibiotic treatment while awaiting the culture results. In our clinical practice, oral antibiotics (frequently doxycycline) are used pending final culture results, though there is no clinical outcomes data to justify a particular antibiotic selection, route or even the use of antibiotics at all in this setting.

REFERENCES

[1] Parvizi J, Ghanem E, Joshi A, Sharkey PF, Hozack WJ, Rothman RH. Does "excessive" anticoagulation predispose to periprosthetic infection? J Arthroplasty. 2007;22:24–28. doi:10.1016/j.arth.2007.03.007.

[2] Galat DD, McGovern SC, Hanssen AD, Larson DR, Harrington JR, Clarke HD. Early return to surgery for evacuation of a postoperative hematoma after primary total knee arthroplasty. J Bone Joint Surg Am. 2008;90:2331–2336. doi:10.2106/JBJS.G.01370.

[3] Saltzman MD, Marecek GS, Edwards SL, Kalainov DM. Infection after shoulder surgery. J Am Acad Orthop Surg. 2011;19:208–218.

[4] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.

[5] Cheung EV, Sperling JW, Cofield RH. Infection associated with hematoma formation after shoulder arthroplasty. Clin Orthop Relat Res. 2008;466:1363–1367. doi:10.1007/s11999-008-0226-3.

[6] Richards J, Inacio MCS, Beckett M, Navarro RA, Singh A, Dillon MT, et al. Patient and procedure-specific risk factors for deep infection after primary shoulder arthroplasty. Clin Orthop Relat Res. 2014;472:2809–2815. doi:10.1007/s11999-014-3696-5.

[7] Lovy AJ, Keswani A, Beck C, Dowdell JE, Parsons BO. Risk factors for and timing of adverse events after total shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:1003–1010. doi:10.1016/j.jse.2016.10.019.

[8] Alentorn-Geli E, Samitier G, Torrens C, Wright TW. Reverse shoulder arthroplasty. Part 2: systematic review of reoperations, revisions, problems, and complications. Int J Shoulder Surg. 2015;9:60–67. doi:10.4103/0973-6042.154771.

[9] Singh JA, Sperling JW, Schleck C, Harmsen WS, Cofield RH. Periprosthetic infections after total shoulder arthroplasty: a 33-year perspective. J Shoulder Elbow Surg. 2012;21:1534–1541.

[10] Morris BJ, O'Connor DP, Torres D, Elkousy HA, Gartsman GM, Edwards TB. Risk factors for periprosthetic infection after reverse shoulder arthroplasty. J Shoulder Elbow Surg. 2015;24:161–166. doi:10.1016/j.jse.2014.05.020.

[11] Bohsali KI, Bois AJ, Wirth MA. Complications of shoulder arthroplasty. J Bone Joint Surg Am. 2017;99:256–269. doi:10.2106/JBJS.16.00935.

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QUESTION 2: Is there a role for postoperative antibiotic treatment for revision arthroplasty with subsequent unexpected positive cultures for a virulent organism (e.g., methicillin-resistant *S. aureus* (MRSA), methicillin-sensitive *Staphylococcus aureus* (MSSA) or E. coli)?

RECOMMENDATION: In aggregate, published studies do not clearly show superiority for prolonged antibiotic use over no prolonged antibiotic treatment in the setting of revision shoulder arthroplasty with subsequent cultures positive for virulent organisms. However, the data on this specific clinical scenario is limited as the vast majority of unexpected positive cultures are with less virulent organisms (e.g., *C. acnes*, Coagulase-negative *Staphylococcus* (CNS)).

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 4%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

A comprehensive literature review was performed to identify all studies on prophylactic/suppressive antibiotics after revision shoulder arthroplasty. Searches for the terms "shoulder replacement," "infection," "antibiotics," "postoperative" and "joint replacement" were performed using the search engines PubMed, Google Scholar and Cochrane review, which were searched through February 2018. Inclusion criteria for our systematic review were all English studies (Level I-IV evidence) that reported on antibiotic prophylaxis, or lack thereof, in cases of revision shoulder arthroplasty. Exclusion criteria were non-English language articles, nonhuman studies, retracted papers, incomplete antibiotic records, case reports, review papers, studies without clinical follow-up/infection rates, and technique papers without patient data. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed.

The prevalence of subclinical infections (unexpected positive culture (UPC)) is common with shoulder arthroplasty due to anatomic and demographic factors. The rate of positive cultures in primary and revision arthroplasty settings have been reported as high as 56 % [1–3], although much lower for virulent organisms. However, the significance and optimal treatment for UPCs caused by virulent organisms remains unknown. There is limited data in the shoulder literature for or against any role for postoperative prophylactic/suppressive antibiotics after revision shoulder arthroplasty without clinical or radiographic signs of infection. While several studies described the use of prophylactic or suppressive antibiotics after revision shoulder arthroplasty, there were no prospective randomized studies and none of the studies specifically evaluated efficacy by antibiotic or organism type.

Among the published studies for outcomes after revision shoulder arthroplasty with subclinical presentations and unexpected positive cultures, all were retrospective studies with differing methodologies [4–8]. All of the studies reported the majority of positive cultures (> 80%) from indolent organisms (*C. acnes* and/or CNS). None of the studies found a detrimental effect to NOT prescribing prolonged antibiotics postoperative, although one study with no comparison group reported a 25% recurrence rate after UPC. In studies that treated UPC with prolonged antibiotics, recurrence rates were low (0-3.5%). One systematic review confirmed a pooled "true infection" rate after UPC of 10.2%, with antibiotic use not influencing the rate of occurrence of "true infection" after UPCs (P = 0.498) [9].

Grosso et al. used antibiotic cement and 24 hours routine postoperative antibiotics with 1 superficial infection and no deep infections after revision shoulder arthroplasty [4]. Foruria et al. reported at least a 10% persistent infection rate after single stage shoulder arthroplasty revision, although antibiotic use and positive cultures did not influence the rate of true infection. [5]. Padegimas et al. reported a 23.9% UPC rate after revision shoulder arthroplasty with standardized UPC treatment of 6 weeks antibiotics or 2 weeks antibiotics at surgeon discretion . They found only 1 recurrent infection in the UPC group, 3.5% versus 3.4% in the non-UPC group [6]. Kelly et al. reported 8/28 (29%) UPC rate after revision shoulder arthroplasty, and only treated one with antibiotics postoperatively for 4 weeks (due to superficial wound infection). Of 8 patients, 2 (25%) developed late clinical infection with *C. acnes* [8]. Lastly, Hsu et al. reported a 49% positive culture rate after revision shoulder arthroplasty, and treated patients based on a protocol of 6 weeks IV and 6 months of oral antibiotics if > 2 cultures positive. Zero percent of patients had recurrence of infection with this protocol in the positive culture group and negative culture groups [7]. On the other hand, risks from prolonged antibiotic use are significant. Two studies reported a 19-42% complication side-effect rate from its use, which was seen in both oral and intravenous medication use [4,7].

The vast majority (> 80%) of UPC's reported in the shoulder literature were *P. acnes* or CNS organisms. Due to small numbers, meaningful comparisons to more virulent organisms could not be performed. Other studies in the lower extremity literature suggest that periprosthetic joint infections from virulent organisms have higher reinfection rates despite surgery (45-49%) for MRSA, Enterococcus and Streptococcus [10–12]. In the lower extremity arthroplasty literature, there was one randomized controlled study which found a limited benefit associated with prolonged oral antibiotic therapy after two-stage revision with negative cultures (5% versus 19%), although culture profiles from the reinfections (mostly virulent) tended to differ from the original infection organism profile [13].

In aggregate, these studies do not clearly show superiority for prolonged antibiotic use over no prolonged antibiotic treatment in the setting of revision shoulder arthroplasty with subsequent cultures returning for virulent organisms. The clinical implications may differ between occult PJIs and unsuspected PJIs in that preoperative diagnostic tests may be performed in the occult PJI setting, which may guide future treatment pathways. Prolonged antibiotic therapy may not be necessary in those patients with low suspicion of infection. In addition, there are well-reported risks of antibiotic related side-effects and resistance with widespread use.

REFERENCES

[1] 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. doi:10.1016/j.jse.2014.09.042.

[2] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.
[3] Brolin TJ, Hackett DJ, Abboud JA, Hsu JE, Namdari S. Routine cultures for seemingly aseptic revision shoulder arthroplasty: are they necessary? J Shoulder Elbow Surg. 2017;26:2060–2066. doi:10.1016/j.jse.2017.07.006.
[4] Grosso MJ, Sabesan VJ, Ho JC, Ricchetti ET, Iannotti JP. Reinfection rates after 1-stage revision shoulder arthroplasty for patients with unexpected positive intraoperative cultures. J Shoulder Elbow Surg. 2012;21:754–758. doi:10.1016/j.jse.2011.08.052.
[5] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:620–627. doi:10.1016/j.jse.2012.07.017.
[6] Padegimas EM, Lawrence C, Narzikul AC, Zmistowski BM, Abboud JA, Williams GR, et al. Future surgery after revision shoulder arthroplasty: the impact of unexpected positive cultures. J Shoulder Elbow Surg. 2017;26:975–981. doi:10.1016/j.jse.2016.10.023.
[7] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.
[8] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.
[9] Kim SJ, Kim JH. Unexpected positive cultures including isolation of Propionibacterium acnes in revision shoulder arthroplasty. Chin Med J (Engl). 2014;127:3975–3979.
[10] Johnson AJ, Zywiel MG, Jones LC, Delanois RE, Stroh DA, Mont MA. Reduced re-infection rates with postoperative oral antibiotics after two-stage revision hip arthroplasty. BMC Musculoskelet Disord. 2013;14:123. doi:10.1186/1471-2474-14-123.
[11] Akgün D, Trampuz A, Perka C, Renz N. High failure rates in treatment of streptococcal periprosthetic joint infection: results from a seven-year retrospective cohort study. Bone Joint J. 2017;99-B:653–659. doi:10.1302/0301-620X.99B5.BJJ-2016-0851.R1.
[12] Kheir MM, Tan TL, Higuera C, George J, Della Valle CJ, Shen M, et al. Periprosthetic joint infections caused by Enterococci have poor outcomes. J Arthroplasty. 2017;32:933–947. doi:10.1016/j.arth.2016.09.017.
[13] Kayupov E, Fillingham YA, Okroj K, Plummer DR, Moric M, Gerlinger TL, et al. Oral and intravenous tranexamic acid are equivalent at reducing blood loss following total hip arthroplasty: a randomized controlled trial. J Bone Joint Surg Am. 2017;99:373–378. doi:10.2106/JBJS.16.00188.

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QUESTION 3: Is there a role for postoperative antibiotic treatment when a revision arthroplasty is performed with subsequent unexpected positive cultures of the shoulder caused by an indolent organism (e.g., *C. acnes* or coagulase-negative *Staphylococcus*(CNS))?

RECOMMENDATION: Postoperative antibiotic treatment beyond 24 hours after revision arthroplasty with unexpected positive cultures for an indolent organism does not appear to reduce the risk of subsequent infection.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 84%, Disagree: 4%, Abstain: 12% (Super Majority, Strong Consensus)

RATIONALE

A comprehensive literature review was performed to identify all studies on prophylactic/suppressive antibiotics after revision shoulder arthroplasty. Searches for the terms "shoulder replacement," "indolent," "infection," "antibiotics," "postoperative" and/or "joint replacement" were performed using the search engines PubMed, Google Scholar and Cochrane review, which were searched through February 2018. Inclusion criteria for our systematic review were all English studies (Level I-IV evidence) that reported on antibiotic prophylaxis, or lack thereof, in cases of revision shoulder arthroplasty. Exclusion criteria were non-English language articles, nonhuman studies, retracted papers, incomplete antibiotic records, case reports, review papers, studies without clinical follow-up/infection rates and technique papers without patient data. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed.

The prevalence of subclinical infections (unexpected positive culture (UPC)) is common after shoulder arthroplasty due to anatomic and demographic factors. In fact, the rate of positive cultures in primary and revision arthroplasty settings have been reported as high as 56% [1–3]. The significance of such cultures remains unknown. There is limited data in the shoulder literature for or against the role for postoperative antibiotics after revision shoulder arthroplasty without clinical or radiographic signs of infection. While several studies described the use of prophylactic or suppressive antibiotics after revision shoulder arthroplasty, there were no prospective randomized studies and none of the studies specifically evaluated efficacy by antibiotic or organism.

Among the published studies for outcomes after revision shoulder arthroplasty with subclinical presentations and unexpected positive cultures, all were retrospective studies with differing methodologies [4–8]. All of the studies reported the majority of positive cultures (> 80%) from indolent organisms (*C. acnes* and/or CNS). None of the studies found a detrimental effect to not prescribing prolonged antibiotics postoperatively, although one study with no comparison group reported a 25% recurrence rate after UPC. One systematic review confirmed a pooled true infection rate after UPC of 10.2%, with antibiotic use not influencing the rate of occurrence of true infection after UPCs (P = 0.498) [9].

Grosso et al. used antibiotic-implegnated cement and 24 hours of routine postoperative antibiotics after revision shoulder arthroplasty and reported 1 superficial infection and no deep infections (91% of organisms cultured were indolent) [4]. Foruria et al. reported 10% persistent infection rate after single stage revision shoulder arthroplasty, although postoperative antibiotic use and positive cultures did not influence the rate of true infections (83% of cultures were positive for indolent organisms) [5]. Padegimas et al. reported a 23.9% UPC rate after revision shoulder arthroplasty with standardized UPC treatment of 6 weeks antibiotics or 2 weeks antibiotics at surgeon discretion. They found only 1 recurrent infection in the UPC group, 3.5% versus 3.4% in the non-UPC group [6]. Kelly et al. reported 8/28 (29%) UPC rate after revision shoulder arthroplasty and only treated one with antibiotics postoperatively for 4 weeks (due to superficial wound infection). Of 8 patients, 2 (25%) developed late clinical infection with *C. acnes* [7]. Lastly, Hsu et al. reported a 49% positive culture rate after revision shoulder arthroplasty and treated patients

based with a protocol of 6 weeks intravenous and 6 months of oral antibiotics if > 2 cultures were positive. Zero percent of patients had recurrence of infection with this protocol in both the positive culture and negative culture groups [8]. On the other hand, the risks of prolonged antibiotic use are significant. Two studies reported a 19-42% complication side-effect rate associated with prolonged antibiotic administration, which was seen in both oral and intravenous medication use [4,8].

The long-term consequences for an unexpected indolent positive culture after revision shoulder arthroplasty are unknown. However, despite lacking randomized comparative methodologies, the literature shows limited evidence that prolonged antibiotic use is not necessary in this scenario. Furthermore, there are well-reported risks of antibiotic-related side-effects and resistance with widespread use.

REFERENCES

[1] 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. doi:10.1016/j.jse.2014.09.042.

[2] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[3] Brolin TJ, Hackett DJ, Abboud JA, Hsu JE, Namdari S. Routine cultures for seemingly aseptic revision shoulder arthroplasty: are they necessary? J Shoulder Elbow Surg. 2017;26:2060–2066. doi:10.1016/j.jse.2017.07.006.

[4] Grosso MJ, Sabesan VJ, Ho JC, Ricchetti ET, Iannotti JP. Reinfection rates after 1-stage revision shoulder arthroplasty for patients with unexpected positive intraoperative cultures. J Shoulder Elbow Surg. 2012;21:754–758. doi:10.1016/j.jse.2011.08.052.

[5] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:620–627. doi:10.1016/j.jse.2012.07.017.

[6] Padegimas EM, Lawrence C, Narzikul AC, Zmistowski BM, Abboud JA, Williams GR, et al. Future surgery after revision shoulder arthroplasty: the impact of unexpected positive cultures. J Shoulder Elbow Surg. 2017;26:975–981. doi:10.1016/j.jse.2016.10.023.

[7] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.

[8] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.

3.2. TREATMENT: ANTIBIOTIC FOR PERIPROSTHETIC JOINT INFECTION

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QUESTION 1: Is there a need for antibiotic therapy following irrigation and debridement of patients with acute shoulder periprosthetic joint infection (PJI) caused by a virulent organism (e.g., methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-sensitive *Staphylococcus aureus* (MSSA) or *E. coli*)?

RECOMMENDATION: In the absence of high level data, we propose that patients with acute PJI of shoulder caused by virulent organisms, such as MRSA, MSSA or E. coli, receive postoperative antibiotics. The optimal antibiotic, route of administration and duration of treatment are unknown and should be individualized after consultation with infectious disease specialists.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

A systematic review was performed using PubMed and Google Scholar databases in February, 2018 to identify studies regarding the treatment outcomes after shoulder arthroplasty. The keywords included "shoulder AND (replacement OR arthroplasty) AND infection." This search identified 46 articles with relevance to surgical treatment of shoulder prosthetic joint infection, 9 of which described treatment with irrigation and debridement with or without modular component exchange for acute infection (< 3 months from surgery or acute hematogenous spread) [1–9]. These nine studies only included small numbers of patients with only 6 patients with acute PJI caused by a virulent organism [1].

There were no studies identified that directly compared irrigation and debridement versus irrigation and debridement with postoperative antibiotics for the treatment of acute PJI. The nine studies had varied definitions of "acute," with periods ranging from four weeks to three months [1–9]. Data regarding the pathogenic organism was not clearly reported, thus making it difficult to determine whether the virulence was a factor in the treatment or outcome. The surgical management of the acute infections varied, including arthroscopic irrigation and debridement, open irrigation and debridement, and open irrigation and debridement with modular component exchange. Given the limitations of the data, it is not possible to answer the narrow question of whether there is a role for antibiotic therapy in the management of acute shoulder PJI caused by a virulent organism (MRSA, MSSA, *E. coli*) after irrigation and debridement.

Nevertheless, postoperative antibiotics were always part of the treatment of acute PJI in the published literature. Treatment types and length varied; both intravenous and oral regimens were employed, and treatment lengths ranged from 13 days to chronic lifetime suppression [1,2]. Most studies used a four to six-week protocol of postoperative antibiotic therapy [1,3–8]. It appears to be the consensus opinion that acute shoulder PJI treated with irrigation and debridement should be followed by a course of antibiotic therapy. The type, dose and route of administration of the antibiotic should be individualized and determined after consultation with an infectious disease specialist.

REFERENCES

[1] Dennison T, Alentorn-Geli E, Assenmacher AT, Sperling JW, Sánchez-Sotelo J, Cofield RH. Management of acute or late hematogenous infection after shoulder arthroplasty with irrigation, débridement, and component retention. J Shoulder Elbow Surg. 2017;26:73–78. doi:10.1016/j.jse.2016.05.018.

[2] Achermann Y, Sahin F, Schwyzer HK, Kolling C, Wüst J, Vogt M. Characteristics and outcome of 16 periprosthetic shoulder joint infections. Infection. 2013;41:613–620. doi:10.1007/s15010-012-0360-4.

[3] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.

[4] Jerosch J, Schneppenheim M. Management of infected shoulder replacement. Arch Orthop Trauma Surg. 2003;123:209–214. doi:10.1007/s00402-003-0497-9.

[5] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.

[6] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.

[7] Stone GP, Clark RE, O'Brien KC, Vaccaro L, Simon P, Lorenzetti AJ, et al. Surgical management of periprosthetic shoulder infections. J Shoulder Elbow Surg. 2017;26:1222–1229. doi:10.1016/j.jse.2016.11.054.

[8] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. J Shoulder Elbow Surg. 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.

[9] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.

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QUESTION 2: Is there a role for antibiotic therapy in the management of acute shoulder periprosthetic joint infection (PJI) with an indolent organism (e.g., *C. acnes* or Coagulase Negative *Staphylococcus*) after irrigation and debridement (I&D)?

RECOMMENDATION: Antibiotic therapy following I&D for management of acute shoulder PJI with an indolent organism has not been well-studied in the literature. The limited data available suggests treatment should consist of antibiotic therapy; however, the optimal antibiotic, route of administration and duration of treatment are unknown.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

Treatment strategies for PJI include chronic antibiotic suppression, irrigation and debridement with or without component retention, one or two-stage revision, placement of antibiotic spacer, resection arthroplasty, or arthrodesis. These strategies have been adopted from the hip and knee arthroplasty experience and literature. Most of the data published specifically addressing acute PJI commingles shoulder PJIs with hip and knee PJIs with very little data specific to treatment of acute shoulder PJI alone. The role of antibiotic, the ideal duration or specific antibiotic are not well described. PubMed, Google Scholar, Ovid-Medline, Cochrane and Web of Science were all searched for the following keywords: "shoulder," "infection," "periprosthetic," "arthroplasty," "antibiotic" to identify relevant articles through a title screen, abstract review and, finally, a full text review to identify the relevant manuscripts.

After an extensive review of the literature, we identified a case series of 10 shoulders in 9 patients treated with I&D and antibiotics for acute PJI.

In 2017, Dennison et al. [1] published a retrospective case series of acute PJI treated at the Mayo clinic. They defined acute PJI as any infection requiring I&D within 6 weeks of the index arthroplasty or within 3 weeks of symptoms from a delayed-onset acute hematogenous infection. Anything outside of this time frame was excluded.

They found 10 shoulders in 9 patients with 4 acute postoperative and 6 delayed-onset acute hematogenous infections. Five of the shoulders had a positive culture for indolent bacteria, the other 5 cultured more virulent bacteria. No patient underwent component exchange. The postoperative antibiotic treatment ranged from 3 to 6 weeks with a mean of 5.2 weeks. Antibiotics were determined by an orthopaedic infectious disease specialist based on organism susceptibility and host factors. Nine of the 10 shoulders underwent additional oral antibiotic therapy, which included trimethoprim-sulfamethoxazole with or without rifampin, penicillin or a combination of trimethoprim-sulfamethoxazole with penicillin. Chronic suppression was maintained in 6 shoulders. Of the 10 shoulders, 3 had failure requiring resection arthroplasty. The authors concluded that I&D with antibiotics allowed component retention in 70% of patients treated for acute PJI, although nearly all were prescribed chronic antibiotic suppression.

No studies reported on duration of therapy specific to acute shoulder PJI caused by indolent organisms. Publications reporting on acute shoulder PJI caused by both virulent and indolent organisms describe a wide duration of therapy from 2 weeks to 3 months with poorly described "additional" periods of antibiotics or indefinite therapy. There is conflicting literature regarding the importance of combining therapy with rifampin.

Given the limited nature of the data available, the exact role and protocol for antibiotic treatment after I&D for the treatment of acute shoulder periprosthetic joint infection caused by indolent organism remains unclear. Further studies are required to determine the optimal treatment. Nevertheless, postoperative antibiotics are traditionally prescribed as part of the treatment of acute PJI. Treatment types and length varied; both intravenous and oral regimens were employed, and treatment lengths ranged from 13 days to chronic lifetime suppression [1,2]. Most studies used a four to six-week protocol of postoperative antibiotic therapy [1,3,4]. By consensus we believe that cases of acute shoulder PJI treated with irrigation and debridement should followed by a course of antibiotic therapy.

REFERENCES

[1] Dennison T, Alentorn-Geli E, Assenmacher AT, Sperling JW, Sánchez-Sotelo J, Cofield RH. Management of acute or late hematogenous infection after shoulder arthroplasty with irrigation, débridement, and component retention. J Shoulder Elbow Surg. 2017;26:73–78. doi:10.1016/j.jse.2016.05.018.

[2] Saper M, Stephenson K, Heisey M. Arthroscopic irrigation and debridement in the treatment of septic arthritis after anterior cruciate ligament reconstruction. Arthrosc J Arthrosc Relat Surg. 2014;30:747–754. doi:10.1016/j.arthro.2014.02.015.
[3] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.
[4] Nelson GN, Davis DE, Namdari S. Outcomes in the treatment of periprosthetic joint infection after shoulder arthroplasty: a systematic review. J Shoulder Elbow Surg. 2016;25:1337–1345. doi:10.1016/j.jse.2015.11.064.

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QUESTION 3: Is there a role for nonoperative suppressive treatment in the management of subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Although there is a role for suppressive antibiotic treatment of selected cases of periprosthetic infection of the shoulder, there are only a few shoulders included in the published literature. The vast majority of published cases describe initial irrigation and debridement, and these are not well separated in the literature from the small number of cases of patients treated with antibiotics alone. No patient treated with antibiotics alone for shoulder PJI has had antibiotics stopped and remained infection-free, thus concerns related to efficacy, long-term toxicity and development of resistant strains are paramount with this strategy. No recommendations can be given on indication, type and duration of suppressive antibiotic treatment.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

A literature search (Medline, PubMed) was performed including terms "periprosthetic infection," "PJI," "shoulder arthroplasty," "suppressive treatment," "chronic antibiotic treatment," "ICOAS" to identify studies on suppressive treatment of periprosthetic joint infection of the shoulder. The vast majority of published studies are retrospective, and in total eight shoulder cases were identified (five successful, three failures). Most studies reported on suppressive antibiotic treatment after initial surgical procedure like debridement or emptying abscesses.

Five studies, evaluating suppressive antibiotic treatment included cases of infected shoulder arthroplasty (eight shoulders). Prendki et al. [1] reported on 38 patients with a minimum suppressive treatment of 6 months for a periprosthetic infection (24 hips, 13 knees, **1 shoulder**). Sixty percent of the patients were on antibiotics and without relapse of infection (including the shoulder) at 24 months. There were six failures and nine deaths. Some of these patients had a surgical procedure before initiating suppressive treatment. It is unclear how many patients that were treated without initial surgery.

Wouthuyzen-Bakker et al. reported on a retrospective study of 21 patients (**2 shoulders**) with median follow up of 21 months [2]. They reported 90% success if the patients had a standard prosthesis but only 50% success in patients with a tumor prosthesis. One shoulder case was successful and one was a failure. Only six patients were treated without initial debridement and four had a successful outcome.

Pradier et al. [3] reported on 78 patients (**2 shoulders**) treated with oral tetracyclines as suppressive treatment with a minimum follow up of 2 years. All patients had surgical debridement. Twenty-two patients failed to respond to treatment. Both shoulders were failures. Three cases had acquisition of tetracycline resistance of the initial pathogen.

Prendki et al. [4] reported on a larger series of joint infections, 136 patients. Seventy-nine (58%) had some type of initial surgical procedure. There were **2 shoulders** and both were successfully treated with suppressive antibiotic treatment. It is unclear whether these 2 patients had initial surgery. Prendki et al. also reported on 21 patients (2017) in another study including **1 shoulder** (successful). Of these 21 patients, 5 had fistulas before starting chronic suppressive antibiotic treatment. Forty percent of the patients were free of clinical signs of infection after 2 years [4].

Multiple other studies have included PJI of other joints, primarily hip and knee arthroplasty.

Segreti et al. [5] reported on prolonged suppressive treatment in 18 patients (12 knees and 6 total hip arthroplasties). Eight had acute infection and 10 had chronic infection. All had surgical debridement before antibiotic treatment. Duration of oral antibiotic suppressive treatment varied from 4-103 months. Overall 14 patients remained asymptomatic. Twenty-two percent of the patients had complications related to antibiotic treatment. The authors concluded that suppressive treatment can be an alternative for patients who cannot or will not undergo major surgical revision.

Rao et al. [6] reported on 36 patients (15 hips, 19 knees and 2 elbows). Fouty-seven percent had acute onset (less than 4 weeks) and 53% were chronic infection. All patients had open debridement. Mean duration of treatment was 52.6 months (range 6-128 months). They reported favorable results (retention of a functioning prosthesis) in 86% with a mean follow up of 5 years. Eight percent had complications related to antibiotic treatment.

In 2004, Pavoni et al. reported on 34 patients (again, no shoulders included) with infection. Fourteen had surgical debridement [7]. Seventeen patients had no relapse of infection during the time of this study (11 of these patients had no initial surgical debridement).

Siqueira et al. [8] reported on 92 patients (no shoulders). They compared patients undergoing surgical debridement followed by a short period of antibiotics to prolonged suppressive antibiotic treatment. The five-year infection-free prosthetic survival rate was 68.5% for the antibiotic suppression group compared to 41.1% in the non-suppression group. Hip infections had lower rate of failures, and the suppression group results were better, if there was a *Staphylococcus aureus* infection.

Shelton et al. [9] reported a case of curing of a draining sinus tract in a hip infection. After suppressive treatment the patient discontinued antibiotic treatment and had no relapse of infection or fistula for a period of 8 years.

In summary, a review of the literature demonstrates that there is role for suppressive treatment in periprosthetic joint infection in the hip and knee in patients with stable implants and that cannot,

or do not want, major revision surgery. However, the studies include heterogeneous cohorts of patients with acute, subacute and chronic infections, and the duration and type of treatment varies. Most of the published case series include patients that had long term suppressive antibiotic treatment after an initial surgical irrigation and debridement. It is difficult to identify and evaluate outcome for the patients that only had chronic suppressive treatment. Furthermore, only a few shoulders are included, and, therefore, no recommendations can be given regarding type and duration of suppressive antibiotic treatment for periprosthetic infection in the shoulder. It is difficult to extrapolate from hip and knee infection data, since the clinical manifestation and type of pathogen are different in the shoulder compared to hip and knee. Lastly, profound concerns regarding antibiotic stewardship and antibiotic-related complications must be carefully weighed against any perceived potential modest success of this strategy.

REFERENCES

[1] Prendki V, Sergent P, Barrelet A, Oziol E, Beretti E, Berlioz-Thibal M, et al. Efficacy of indefinite chronic oral antimicrobial suppression for prosthetic joint infection in the elderly: a comparative study. Int J Infect Dis IJID. 2017;60:57–60. doi:10.1016/j.ijid.2017.05.008.

[2] Wouthuyzen-Bakker M, Nijman JM, Kampinga GA, van Assen S, Jutte PC. Efficacy of antibiotic suppressive therapy in patients with a prosthetic joint infection. J Bone Joint Infect. 2017;2:77–83. doi:10.7150/jbji.17353.

[3] Pradier M, Nguyen S, Robineau O, Titecat M, Blondiaux N, Valette M, et al. Suppressive antibiotic therapy with oral doxycycline for Staphylococcus aureus prosthetic joint infection: a retrospective study of 39 patients. Int J Antimicrob Agents. 2017;50:447–452. doi:10.1016/j.ijantimicag.2017.04.019.

[4] Prendki V, Ferry T, Sergent P, Oziol E, Forestier E, Fraisse T, et al. Prolonged suppressive antibiotic therapy for prosthetic joint infection in the elderly: a national multicentre cohort study. Eur J Clin Microbiol Infect Dis. 2017;36:1577–1585. doi:10.1007/s10096-017-2971-2.

[5] Segreti J, Nelson JA, Trenholme GM. Prolonged suppressive antibiotic therapy for infected orthopedic prostheses. Clin Infect Dis. 1998;27:711–713.

[6] Rao N, Crossett LS, Sinha RK, Le Frock JL. Long-term suppression of infection in total joint arthroplasty. Clin Orthop Relat Res. 2003:55–60. doi:10.1097/01.blo.0000087321.60612.cf.

[7] Pavoni GL, Giannella M, Falcone M, Scorzolini L, Liberatore M, Carlesimo B, et al. Conservative medical therapy of prosthetic joint infections: retrospective analysis of an 8-year experience. Clin Microbiol Infect. 2004;10:831–837. doi:10.1111/j.1469-0691.2004.00928.x.

[8] Siqueira MBP, Saleh A, Klika AK, O'Rourke C, Schmitt S, Higuera CA, et al. Chronic suppression of periprosthetic joint infections with oral antibiotics increases infection-free survivorship. J Bone Joint Surg Am. 2015;97:1220–1232. doi:10.2106/JBJS.N.00999.

[9] Shelton TJ, Skaggs AW, Pereira GC. Self-resolution of a draining sinus tract in a patient with chronic periprosthetic hip infection. Case Rep Orthop. 2018;2018.

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QUESTION 4: Is there a role for oral suppressive antimicrobial therapy in the setting of retained prostheses after intravenous therapy in subacute or chronic periprosthetic joint infection (PJI)?

RECOMMENDATION: The administration of oral suppressive antimicrobial therapy may have a role in management of patients with chronic or subacute PJI who cannot undergo further surgical intervention.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Many cases of PJI can be managed by means of an adequate medical-surgical strategy with antibiotic treatment administered for a finite period of time. For patients with a PJI, where the medical-surgical treatment is suboptimal or clearly insufficient to achieve control (because of surgical contraindications, technical difficulties, severe medical comorbidities or multi-drug resistant bacteria), chronic oral SAT is considered an alternative strategy.

SAT refers to the use of antibiotics administered indefinitely with a "non-curative" intention and the objective of avoiding or reducing the symptoms and delaying or preventing the progression that may lead to patient dysfunction and the loss of the implant.

A search of Medline and Embase from 1980 to January 2018 was conducted. The terms used were: prosthetic joint infection or infected arthroplasty and suppressive therapy or suppressive antibiotics. Case reports, reviews and guidelines were excluded. Thirteen articles were finally reviewed. When the search was performed including the term "shoulder arthroplasty" or "prosthetic shoulder" and "suppressive antibiotic therapy" or "suppressive antibiotics" no articles specifically on this topic were found. However, a search in medical literature (Medline and Embase) about prosthetic joint infection or arthroplasty and suppressive therapy or suppressive antibiotics yielded 13 references [1–13]. Twelve are retrospective descriptive series, and one is a propensity score controlled cohort study [9]. The vast majority of the cases contained in these series were hip and knee infections, and only 9 of the 680 were prosthetic infections. Therefore, the present review is based on the results obtained with prosthetic hip and knee infections for shoulder prostheses.

Efficacy of SAT varied from 23% at 3.5 years [2] to 86.2% at 5 years [4]. Nonetheless, these wide discrepancies are explained by the use of different criteria in selecting patients for SAT and in defining the response to treatment. The case mix of patients in whom SAT has been prescribed includes a wide spectrum of situations: from acute PJI cases that could probably be cured by debridement and several weeks of antibiotic therapy, to patients with evident chronic infections showing active fistula and no surgery performed.

In summary, the analysis of the literature on SAT faces the following major problems:

1. Different classifications of the PJIs and the terms that are used to describe them (early, acute, delayed, chronic, subacute and so on).
2. Differences in the used medical-surgical strategies as standard of care of the PJI according to the types of infection.
3. Differences in the criteria used to select patients for SAT.
4. Differences in the criteria used to evaluate the efficacy of SAT.
5. Absence of control groups to compare the efficacy of SAT.

As well as other "minor" problems:

1. Insufficient follow up.

2. Variety of antibiotics used.
3. Small sample sizes, in general.

Thus, it is difficult to determine the effectiveness of SAT, although some evidence can be obtained by indirect means. In a cohort of 112 cases with PJI (52 hip, 51 knee, 4 elbow, 3 ankle, 2 shoulder—most of them diagnosed with early PJI, but also including late infections) managed with debridement, prosthesis retention and prolonged antimicrobial therapy for more than a year, the rate of failure among patients that discontinued antibiotic treatment was 4-fold higher than those who continued [7]. Although 82% of the patients who stopped antibiotics did not fail (probably the infection was actually eradicated), the occurrence of failure in some of them indicates that a proportion of those who were not cured by this strategy benefitted from SAT. Failures mainly occurred within the first four months of antibiotic withdrawal.

Another more recent study is the only one that included controls [9]. Ninety-two patients receiving SAT (71 hip PJI and 51 knee PJI) were compared by a propensity score (based on age, sex, type of prosthesis, type of surgery, Charlson index, number of previous revisions and microorganisms) with 276 controls in which clinicians did not administer SAT. The decision to use SAT was individualized, but it is presumed that it was due to "high risk of failure." In fact, 67% of the patients had undergone prior revision surgery. Thirty-six of the cases were "early" PJI and 56 were "late" PJI (no definition of "early" was provided). Cases were managed either by a two-stage revision (38) or by debridement and exchange of polyethylene (54) followed by intravenous antibiotics before SAT was started. A significantly better result was observed in SAT treated patients than in controls (68.5% vs. 41.1%; $p = 0.08$) at 5 years. When analyzed by type of surgery the differences were clear among those managed by prosthesis retention (64.7% vs. 30.4%; $p < 0.001$) but they were not observed in those managed by two-stage exchange ($p = 0.13$). The proportion of success among patients with "late" infections was 64.3%. One of the drawbacks of the study was the fact that the authors included as failures any death during the first year, and the occurrence of severe pain during the follow-up, making it difficult to assess the proportion of true failures because of a lack of infection control.

Interestingly, most series show reassuring data about the safety of long-term antibiotic administration [4,6,10,11,13]. Those who did not tolerate the first selected agent usually tolerated an alternative [12].

In summary, there seems to be some evidence that SAT benefits patients at high risk of failure of prosthesis retention. The main problem is to select in which patients the risk is high enough to compensate for the inconvenience of long-term antibiotic use.

The following conditions also need to be met when considering SAT:

1. Identification of the microorganism that is causing the infection.
2. Availability of oral antibiotics that are not toxic when administered over long periods of time.
3. Practicality of a close follow-up of the patient.

Bearing all these considerations in mind and also the antibiotic stewardship and resistance implications of long-term antimicrobial therapy, the SAT is only indicated after a careful risk-benefit analysis. The temptation to use this strategy to avoid the need for complex but potentially eradicative surgery should be resisted.

REFERENCES

[1] Goulet JA, Pellicci PM, Brause BD, Salvati EM. Prolonged suppression of infection in total hip arthroplasty. J Arthroplasty. 1988;3:109–116.
[2] Tsukayama DT, Wicklund B, Gustilo RB. Suppressive antibiotic therapy in chronic prosthetic joint infections. Orthopedics. 1991;14:841–844.
[3] Segreti J, Nelson JA, Trenholme GM. Prolonged suppressive antibiotic therapy for infected orthopedic prostheses. Clin Infect Dis. 1998;27:711–713.
[4] Rao N, Crossett LS, Sinha RK, Le Frock JL. Long-term suppression of infection in total joint arthroplasty. Clin Orthop Relat Res. 2003:55–60. doi:10.1097/01.blo.0000087321.60612.cf.
[5] Pavoni GL, Giannella M, Falcone M, Scorzolini L, Liberatore M, Carlesimo B, et al. Conservative medical therapy of prosthetic joint infections: retrospective analysis of an 8-year experience. Clin Microbiol Infect. 2004;10:831–837. doi:10.1111/j.1469-0691.2004.00928.x.
[6] Marculescu CE, Berbari EF, Hanssen AD, Steckelberg JM, Harmsen SW, Mandrekar JN, et al. Outcome of prosthetic joint infections treated with debridement and retention of components. Clin Infect Dis. 2006;42:471–478. doi:10.1086/499234.
[7] Byren I, Bejon P, Atkins BL, Angus B, Masters S, McLardy-Smith P, et al. One hundred and twelve infected arthroplasties treated with "DAIR" (debridement, antibiotics and implant retention): antibiotic duration and outcome. J Antimicrob Chemother. 2009;63:1264–1271. doi:10.1093/jac/dkp107.
[8] Prendki V, Zeller V, Passeron D, Desplaces N, Mamoudy P, Stirnemann J, et al. Outcome of patients over 80 years of age on prolonged suppressive antibiotic therapy for at least 6 months for prosthetic joint infection. Int J Infect Dis. 2014;29:184–189. doi:10.1016/j.ijid.2014.09.012.
[9] Siqueira MBP, Saleh A, Klika AK, O'Rourke C, Schmitt S, Higuera CA, et al. Chronic suppression of periprosthetic joint infections with oral antibiotics increases infection-free survivorship. J Bone Joint Surg Am. 2015;97:1220–1232. doi:10.2106/JBJS.N.00999.
[10] Prendki V, Ferry T, Sergent P, Oziol E, Forestier E, Fraisse T, et al. Prolonged suppressive antibiotic therapy for prosthetic joint infection in the elderly: a national multicentre cohort study. Eur J Clin Microbiol Infect Dis. 2017;36:1577–1585. doi:10.1007/s10096-017-2971-2.
[11] Pradier M, Nguyen S, Robineau O, Titecat M, Blondiaux N, Valette M, et al. Suppressive antibiotic therapy with oral doxycycline for Staphylococcus aureus prosthetic joint infection: a retrospective study of 39 patients. Int J Antimicrob Agents. 2017;50:447–452. doi:10.1016/j.ijantimicag.2017.04.019.
[12] Wouthuyzen-Bakker M, Nijman JM, Kampinga GA, van Assen S, Jutte PC. Efficacy of antibiotic suppressive therapy in patients with a prosthetic joint infection. J Bone Jt Infect 2017;2:77–83. doi:10.7150/jbji.17353.
[13] Pradier M, Robineau O, Boucher A, Titecat M, Blondiaux N, Valette M, et al. Suppressive antibiotic therapy with oral tetracyclines for prosthetic joint infections: a retrospective study of 78 patients. Infection. 2018;46:39–47. doi:10.1007/s15010-017-1077-1.

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QUESTION 5: Is there a role for oral suppressive antimicrobial therapy in acute periprosthetic joint infection (PJI) in the setting of retained prostheses after initial intravenous (IV) therapy? Same duration as for lower extremity arthroplasty? Should it differ by pathogen (e.g., methicillin-sensitive *Staphylococcus aureus* (MSSA) vs. methicillin-resistant *S. aureus* (MRSA))?

RECOMMENDATION: While the role of debridement, antibiotics and implant retention (DAIR) in the treatment of acute prosthetic shoulder infection has not been well-studied, there is likely a role for oral suppressive antimicrobial therapy in the setting of retained infected shoulder prostheses after DAIR. There is no evidence to guide the optimal duration of treatment or if treatment should vary by organism.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

A comprehensive systematic review was performed using MeSH terms: "(Arthroplasty, Replacement, Shoulder OR Shoulder joint) AND (Infection OR Debridement OR Anti-Bacterial Agents OR keyword "acute," OR "infection," OR "antibiotics") using Ovid-Medline. The inclusion criteria for this systematic review were English language, shoulder arthroplasty studies that included patients who underwent treatment for periprosthetic shoulder joint infection using irrigation and debridement with component. Exclusion criteria were non-English language articles, technique papers, non-human studies, studies that only presented data on one-stage or two-stage revision, hip or knee arthroplasty articles. Our initial search produced 288 abstracts; 260 were excluded, because they did not fit inclusion criteria, and the remaining 18 manuscripts were obtained and reviewed to assure inclusion criteria. Additionally, the references of these manuscripts were reviewed to ensure no additional relevant material would be missed.

The treatment of an acute hip or knee PJI following irrigation and debridement with implant retention includes a course of oral antibiotics that follows the IV antibiotic therapy [1–3]. Although the efficacy of this approach is debated, with reported success rates ranging from 0% to 89% [4], the use of oral antibiotics (for varying durations) in patients with retained hardware has been reported to be nearly universal, especially in the United States [5]. An analogous algorithm of treatment has been advocated in the setting of acute shoulder PJI when treated with irrigation and debridement with implant retention [6–8], although specific recommendations regarding route and duration of antibiotic therapy are not clear [9,10].

There is very little published literature evaluating the efficacy of this course of treatment in shoulder PJI. Most studies addressing the treatment of acute shoulder PJIs are retrospective case series without control cohorts [11–28]. As many of these studies were comprised of patients undergoing heterogeneous treatment protocols, the subset of patients undergoing DAIR is often only a small subset further limiting the ability of these studies to provide useful data. The overall number of patients presented in these articles is also very small; no study exceeded 50 shoulders and the majority reported on the outcomes of less than 10 patients with acute shoulder PJIs treated with irrigation and debridement and implant retention followed by IV and then oral antibiotics. Details regarding antibiotic use and duration are not always presented or correlated with clinical outcomes. Given the small number of overall cases to draw from, it is difficult to make any inferences regarding the efficacy of this treatment as stratified by organism, including MRSA versus MSSA. Complicating any synthesis of the data further is that patients reported in these studies also varied as to the type of infected arthroplasty (anatomic total shoulder, reverse total shoulder or hemiarthroplasty). Extrapolating these results to assess the actual utility of oral suppressive antimicrobial therapy in acute PJI in the setting of retained prosthesis after initial IV therapy is not feasible nor is it possible to establish a recommended optimal duration of therapy.

Whether DAIR is even a viable treatment approach for shoulder PJIs in any setting has been challenged [10]. A systematic review of the literature published in 2016 found that the failure rate of implant retention in the setting of prosthetic shoulder infection was 31.4% versus a 6.3% failure rate following a two-stage exchange, a 9.7% failure rate following explantation with placement of permanent spacer, and 9.9% following a one-stage exchange [29].

However, despite the lack of supporting medical literature, the use of oral antibiotics, based on the more extensive experience with the treatment of hip and knee infections following debridement as well as the current understanding of the role biofilm plays in treatment failure [25,30–32], is likely a reasonable approach for the treatment of acute prosthetic shoulder infections when treating with implant retention, at least until more rigorous outcomes data that supports the contrary is available.

REFERENCES

[1] Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. N Engl J Med. 2004;351:1645–1654. doi:10.1056/NEJMra040181.

[2] Del Pozo JL, Patel R. Infection associated with prosthetic joints. N Engl J Med. 2009;361:787–794. doi:10.1056/NEJMcp0905029.

[3] Tande AJ, Patel R. Prosthetic joint infection. Clin Microbiol Rev. 2014;27:302–345. doi:10.1128/CMR.00111-13.

[4] Kapadia BH, Berg RA, Daley JA, Fritz J, Bhave A, Mont MA. Periprosthetic joint infection. Lancet. 2016;387:386–394. doi:10.1016/S0140-6736(14)61798-0.

[5] Marschall J, Lane MA, Beekmann SE, Polgreen PM, Babcock HM. Current management of prosthetic joint infections in adults: results of an Emerging Infections Network survey. Int J Antimicrob Agents. 2013;41:272–277. doi:10.1016/j.ijantimicag.2012.10.023.

[6] Favard L. Revision of total shoulder arthroplasty. Orthop Traumatol Surg Res. 2013;99:S12–S21. doi:10.1016/j.otsr.2012.11.010.

[7] Boileau P. Complications and revision of reverse total shoulder arthroplasty. Orthop Traumatol Surg Res. 2016;102:S33–S43. doi:10.1016/j.otsr.2015.06.031.

[8] Pinder EM, Ong JC, Bale RS, Trail IA. Ten questions on prosthetic shoulder infection. Shoulder Elbow. 2016;8:151–157. doi:10.1177/1758573216632464.

[9] Marcheggiani Muccioli GM, Huri G, Grassi A, Roberti di Sarsina T, Carbone G, Guerra E, et al. Surgical treatment of infected shoulder arthroplasty. A systematic review. Int Orthop. 2017;41:823–830. doi:10.1007/s00264-017-3399-0.

[10] Mook WR, Garrigues GE. Diagnosis and management of periprosthetic shoulder infections. J Bone Joint Surg Am. 2014;96:956–965. doi:10.2106/JBJS.M.00402.

[11] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.

[12] Jerosch J, Schneppenheim M. Management of infected shoulder replacement. Arch Orthop Trauma Surg. 2003;123:209–214. doi:10.1007/s00402-003-0497-9.

[13] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.

[14] Weber P, Utzschneider S, Sadoghi P, Andress H-J, Jansson V, Müller PE. Management of the infected shoulder prosthesis: a retrospective analysis and review of the literature. Int Orthop. 2011;35:365–373. doi:10.1007/s00264-010-1019-3.

[15] Amaravathi RS, Kany J, Melet M, Katz D, Sauzieres P, Valenti P, et al. Analysis of infection in shoulder arthroplasty: a multicentre study. Eur J Orthop Surg Traumatol. 2012;22:145–150. doi:10.1007/s00590-011-0806-x.

[16] Romanò CL, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. Int Orthop. 2012;36:1011–1017. doi:10.1007/s00264-012-1492-y.

[17] Achermann Y, Sahin F, Schwyzer HK, Kolling C, Wüst J, Vogt M. Characteristics and outcome of 16 periprosthetic shoulder joint infections. Infection. 2013;41:613–620. doi:10.1007/s15010-012-0360-4.

[18] Ghijselings S, Stuyck J, Debeer P. Surgical treatment algorithm for infected shoulder arthroplasty: a retrospective analysis of 17 cases. Acta Orthop Belg. 2013;79:626–635.

[19] 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:e15–e20. doi:10.1016/j.jse.2014.04.007.

[20] Dennison T, Alentorn-Geli E, Assenmacher AT, Sperling JW, Sánchez-Sotelo J, Cofield RH. Management of acute or late hematogenous infection after shoulder arthroplasty with irrigation, débridement, and component retention. J Shoulder Elbow Surg. 2017;26:73–78. doi:10.1016/j.jse.2016.05.018.

[21] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. J Shoulder Elbow Surg. 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.

[22] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.

[23] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.

[24] Pradier M, Robineau O, Boucher A, Titecat M, Blondiaux N, Valette M, et al. Suppressive antibiotic therapy with oral tetracyclines for prosthetic joint infections: a retrospective study of 78 patients. Infection. 2018;46:39–47. doi:10.1007/s15010-017-1077-1.

[25] Moran E, Masters S, Berendt AR, McLardy-Smith P, Byren I, Atkins BL. Guiding empirical antibiotic therapy in orthopaedics: the microbiology of prosthetic joint infection managed by debridement, irrigation and prosthesis retention. J Infect. 2007;55:1–7. doi:10.1016/j.jinf.2007.01.007.

[26] Byren I, Bejon P, Atkins BL, Angus B, Masters S, McLardy-Smith P, et al. One hundred and twelve infected arthroplasties treated with "DAIR" (debridement, antibiotics and implant retention): antibiotic duration and outcome. J Antimicrob Chemother. 2009;63:1264–1271. doi:10.1093/jac/dkp107.

[27] Keller SC, Cosgrove SE, Higgins Y, Piggott DA, Osgood G, Auwaerter PG. Role of suppressive oral antibiotics in orthopedic hardware infections for those

not undergoing two-stage replacement surgery. Open Forum Infect Dis. 2016;3:ofw176. doi:10.1093/ofid/ofw176.
[28] Boileau P, Melis B, Duperron D, Moineau G, Rumian AP, Han Y. Revision surgery of reverse shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:1359–1370. doi:10.1016/j.jse.2013.02.004.
[29] Nelson GN, Davis DE, Namdari S. Outcomes in the treatment of periprosthetic joint infection after shoulder arthroplasty: a systematic review. J Shoulder Elbow Surg. 2016;25:1337–1345. doi:10.1016/j.jse.2015.11.064.
[30] Lister JL, Horswill AR. Staphylococcus aureus biofilms: recent developments in biofilm dispersal. Front Cell Infect Microbiol. 2014;4:178. doi:10.3389/fcimb.2014.00178.
[31] Kaldalu N, Hauryliuk V, Tenson T. Persisters-as elusive as ever. Appl Microbiol Biotechnol. 2016;100:6545–6553. doi:10.1007/s00253-016-7648-8.
[32] Morgenstern M, Post V, Erichsen C, Hungerer S, Bühren V, Militz M, et al. Biofilm formation increases treatment failure in Staphylococcus epidermidis device-related osteomyelitis of the lower extremity in human patients. J Orthop Res. 2016;34:1905–1913. doi:10.1002/jor.23218.

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QUESTION 6: Should the duration of oral suppressive antimicrobial therapy differ by pathogen (e.g., methicillin-sensitive *Staphylococcus aureus* (MSSA) vs. methicillin-resistant *S. aureus* (MRSA)) in the treatment of subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There is insufficient evidence to determine whether the duration of oral suppressive antimicrobial therapy should differ by pathogen in the treatment of subacute/chronic shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

There is currently no widely shared and commonly used definition of the term "suppressive antimicrobial therapy" (SAT) in reference to antimicrobial therapy for shoulder PJI. A thorough search of PubMed, Embase and Google Scholar databases was undertaken in February, 2018 to identify articles related to the use of suppressive antibiotic therapy for the treatment of shoulder PJI using search terms: "prosthetic joint infection," "suppressive therapy," "antibiotic suppressive therapy," "suppression."

From the results of this search, it is clear that the term SAT is used in various ways. It is often used to mean prolonged antibiotic therapy following surgery (irrigation and debridement and implant revision) with the intention of effecting a cure and discontinuation of antibiotics. In other cases, SAT is described for the treatment of active PJI in patients unable to undergo additional surgical intervention. Treatment in this scenario is palliative; it is based on the principle that organisms within a biofilm cannot be fully eradicated and that the antimicrobial inhibits the organisms in the biofilm from spreading. This may halt dissemination of the infection and prevent sepsis but is highly unlikely to eradicate the underlying infection. Suppressive antibiotic therapy is also used to define indefinite or life-long use of antibiotic therapy in patients without clinical evidence of active infection but thought to be at high-risk for relapse.

Using an inclusive definition of "suppressive antimicrobial therapy," twelve relevant studies were identified [1–8]. From these studies, 34 patients were noted to have had shoulder PJI and received SAT. Failure was defined as a relapse of infection based on the criteria described in each manuscript. These criteria were not consistent. Collectively, patients prescribed SAT had a PJI relapse rate of 29% (10/34 cases). There was not sufficient level of detail to comment on treatment duration, dose of antibiotics or type of antibiotics.

There is some support for success after discontinuation of SAT. Antimicrobial-free periods are not reported in any of the reported series. Reports of hip and knee PJI demonstrate that there is a relapse rate of around 30% within 4 months when suppressive antibiotic treatment is discontinued, even after a long period of suppressive therapy [7]. A study 24 patients with PJI (2 shoulder patients) did observe that treatment succeeded in almost all patients with a PJI caused by a *S. epidermidis* [1]. This finding may not be surprising since *S. epidermidis* has low virulence and the natural course of infection is often dormant and low-grade in nature.

Safety issues in the setting of SAT are an important consideration. Although information is very scarce, the safety data in the published case series indicate a low rate of antibiotic withdrawal due to adverse events [4,7,9].

Moving forward, it may be useful for clinicians and researchers to more precisely define "suppressive antibiotic therapy." The authors would suggest that SAT refer to "the chronic use of low-dose antibiotic therapy in patients with persistent PJI in which the aim is no longer to cure, but to prevent acute exacerbation or recurrence of local symptoms and/or greater systemic involvement." The key to this definition is the recognition that antibiotic therapy is not curative anymore in its intent. Suppressive antibiotic therapy is thereby differentiated from longer-than-standard "prolonged" administration of antibiotics meant to eradicate infection and cease after the infection is deemed to be cleared. Differentiation of these terms may allow future investigators to make more concrete recommendations regarding the use of SAT in shoulder PJI.

REFERENCES

[1] Wouthuyzen-Bakker M, Nijman JM, Kampinga GA, van Assen S, Jutte PC. Efficacy of antibiotic suppressive therapy in patients with a prosthetic joint infection. J Bone Joint Infect. 2017;2:77–83. doi:10.7150/jbji.17353.
[2] Tsukayama DT, Wicklund B, Gustilo RB. Suppressive antibiotic therapy in chronic prosthetic joint infections. Orthopedics. 1991;14:841–844.
[3] Siqueira MBP, Saleh A, Klika AK, O'Rourke C, Schmitt S, Higuera CA, et al. Chronic suppression of periprosthetic joint infections with oral antibiotics increases infection free survivorship. J Bone Joint Surg Am. 2015;97:1220–1232. doi:10.2106/JBJS.N.00999.
[4] Segreti J, Nelson JA, Trenholme GM. Prolonged suppressive antibiotic therapy for infected orthopedic prostheses. Clin Infect Dis. 1998;27:711–713.
[5] Prendki V, Sergent P, Barrelet A, Oziol E, Beretti E, Berlioz-Thibal M, et al. Efficacy of indefinite chronic oral antimicrobial suppression for prosthetic joint infection in the elderly: a comparative study. Int J Infect Dis. 2017;60:57–60. doi:10.1016/j.ijid.2017.05.008.
[6] Prendki V, Ferry T, Sergent P, Oziol E, Forestier E, Fraisse T, et al. Prolonged suppressive antibiotic therapy for prosthetic joint infection in the elderly: a national multicentre cohort study. Eur J Clin Microbiol Infect Dis. 2017;36:1577–1585. doi:10.1007/s10096-017-2971-2.

[7] Pradier M, Robineau O, Boucher A, Titecat M, Blondiaux N, Valette M, et al. Suppressive antibiotic therapy with oral tetracyclines for prosthetic joint infections: a retrospective study of 78 patients. Infection. 2018;46:39–47. doi:10.1007/s15010-017-1077-1.
[8] Goulet JA, Pellicci PM, Brause BD, Salvati EM. Prolonged suppression of infection in total hip arthroplasty. J Arthroplasty. 1988;3:109–116.
[9] Brown SR, Davies WA, DeHeer DH, Swanson AB. Long-term survival of McKee-Farrar total hip prostheses. Clin Orthop Relat Res. 2002:157–163.

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QUESTION 7: What are the recommendations for the route (intravenous (IV) vs. oral (PO)) and duration of postoperative antibiotic treatment when a one-stage revision arthroplasty is performed for subacute or chronic shoulder periprosthetic joint infection (PJI) of the shoulder caused by an indolent organism (e.g., *C. acnes* or coagulase-negative Staphylococcus)?

RECOMMENDATION: Prior to identification of pathogenic organisms from intraoperative cultures, a course of oral antibiotics may be initiated that covers the potential organism until intraoperative cultures are finalized. If the cultures are positive and periprosthetic infection is diagnosed, then a continued course of antibiotics (up to six weeks) should be pursued. There is no evidence to support a preferred route (PO vs. IV), type and duration of antibiotic treatment.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

Periprosthetic shoulder infection negatively impacts the outcome of shoulder arthroplasty and is often treated with revision surgery [1]. The overall rate of infection after shoulder replacement is reported as 1.2-3.0% (0.5-3.9% for anatomic and up to 10.0% for reverse shoulder arthroplasty) [2–4]. Prosthetic shoulder infection commonly presents as painful arthroplasty and often lacks typical clinical findings of acute infection. Laboratory workup, such as inflammatory markers, white blood cell count and shoulder aspiration are usually negative, leaving clinicians with limited tools to confirm infection prior to revision surgery. This is mostly due to predominance of indolent organisms, such as *Cutibacterium acnes* (formerly known as *Propionibacterium acnes)* (39-66%) and *Coagulase negative staphylococcus* (24-28%) in periprosthetic shoulder infection [5,6]. Two-stage revision including aggressive debridement, antibiotic spacer placement followed by prolonged IV antibiotics was adopted by shoulder surgeons from treatment of PJI of other joints and showed 63-100% success rate in eradicating infection in short to mid-term follow up [7–9]. This approach has many short-comings, including subjecting patients to two operations and spacer complications, such as fracture, dislocation and loss of rotator cuff and bone stock, leading to poor joint function. Recently, one-stage revision has been advocated for low virulence indolent infections. Nelson et al. [10] and Cuff et al. [11] showed similar rates of eradication after one-stage versus two-stage revision arthroplasty. Beekman et al. reported results of single stage revision for infected reverse shoulder arthroplasty and showed at two year follow-up 90% of patients were infection free with a Constant score of 55.6% [4]. George et al. did a systematic review and found that the average Constant score was 51% after one-stage revision which was better than 41% two-stage revision [12]. These studies make a reasonable case for one-stage revision arthroplasty to eradicate indolent infections while preserving the function of the patient's joint, but they have highly variable protocols for type and duration of postoperative antibiotics. To answer the question above we review and summarize the limited evidence around antibiotic therapy following one-stage revision arthroplasty for periprosthetic shoulder infection with indolent organisms.

A PubMed search was conducted with terms arthroplasty, replacement, shoulder (Mesh) and revision which resulted in 120 papers. Abstracts of the papers were reviewed to identify papers reporting one-stage revision for indolent periprosthetic shoulder infection which resulted in 8 relevant articles that are included in this review.

Most authors retrospectively reporting their experience with treatment of shoulder arthroplasty infection incompletely report the antibiotic therapy following revision surgery. This section will review and summarize the current literature on treatment outcome of infected shoulder arthroplasty with specific focus on antibiotic regimen, as incomplete as it may be, including route (IV vs. PO), type and duration.

Grosso et al. [13] retrospectively reviewed patients with no perioperative sign of infection who underwent single stage revision shoulder arthroplasty and postoperatively had at least 1 positive culture and were not treated with an extended course of antibiotics. The majority of the cultures (56%) were *C. acnes* followed by coagulase negative staphylococci (CoNS) (35%). The rate of recurrence was very low (5.9%). Authors suggested unexpected cultures after a seemingly uninfected one-stage revision did not require extended antibiotic therapy.

Padegimas et al. [14] reviewed 117 one-stage revision shoulder arthroplasty with no preoperative concern for infection who were followed for more than 4 years and found that 28 (23.9%) had an unexpected positive culture postoperatively of which 15 (57.1%) were *C. acnes,* and majority were in male patients. They did not identify any predictor for reoperation, but they observed a higher rate of reoperation in patients without unexpected cultures (20.2% vs. 7.1%) but this did not reach clinical significance. In their cohort, 18 (64.3%) patients were treated with IV antibiotics for 6 weeks, and 10 (35.75) patients only received 2 weeks of PO antibiotics. There was only one reoperation among culture positive patients and that was in a patient who did not receive prolonged antibiotics.

Coste et al. [1] reported on the outcome of treatment in 42 patients with infected shoulder arthroplasty with a mean 34 months follow up. They defined infection based on seven criteria including

presence of a sinus tract, elevated serum white blood cell (WBC) count, elevated erythrocyte sedimentation rate, or C-reactive protein (CRP), positive culture including preoperative aspiration, X-ray evidence of implant loosening and positive bone scan, with no further details on how these criteria were weighted in their definition. There were 20 infections following primary arthroplasty and 22 after revision surgery. Thirty patients (71.4%) had subacute or chronic infection. At final follow up, 22 (73.3%) were infection-free, but there was a wide variation in how patients were treated. They were able to obtain antibiotic information in 30 patients and they judged treatment to be inadequate in 15 patients with regards to duration and type of antibiotics. Five patients were treated with antibiotics only, and only two remained infection-free at final follow up (60% failure rate).

Cuff et al. [11] reported their results of 22 patients with infection following hemiarthroplasty (n = 17) and open cuff repair (n = 5) treated with one versus two-stage revision. In their series, *S. aureus* was the most common organism. CoNS (n = 3) and *C. acnes* (n = 1) were also identified. None of their patients had recurrent infection at mean follow up of 43 months and there was no difference in any of the outcome measures between one versus two-stage revision. The majority of the patients were given six weeks of IV antibiotics, while patients with no clinical signs of infection and with negative intraoperative histology were treated with two weeks of IV antibiotics. It is not clear what type of IV antibiotics were perscribed.

Keller et al. [15] performed a retrospective study of orthopaedic hardware infection that was treated with debridement and retention of hardware, single-stage revision or without surgery to determine if treatment with six weeks of oral antibiotics alters the rate of success at one year. They only included patients who had two separate positive cultures of the same organism from samples taken with a sterile technique from the same site. Of the 89 patients in their study, 42 (47.2%) were infection-free at one year. Patients with methicillin-resistant *S. aureus* (MRSA) or gram-negative organisms, prior infection at the same site, and higher Charlson comorbidity score were less likely to achieve treatment success. They concluded that patients who were on oral suppression for 3-6 months had a significantly lower recurrence rate but continuing antibiotics beyond 6 months did not have the same benefit. Specifically, *C. acnes* infection (n = 32) was associated with a higher likelihood of treatment success at one year (odds ratio: 5.1, 95% confidence interval: 1.32-19.75).

Piggott et al. [16] reported a retrospective study of surgical and nonsurgical management of 24 patients with *C. acnes* PJI from one center with median follow up of 2 years. They defined definite PJI as two positive *C. acnes* cultures or one positive *C. acnes* culture plus sinus tract, clinical purulence or positive histopathology. Probable PJI was defined as one positive *C. acnes* infection and any suspicious clinical sign of infection. There were 11 (46%) definite and 13 (54%) probable PJI cases. The surgery group included 1 incision and debridement with retention, 4 one-stage revisions, 7 two-stage revisions and 3 spacer placements with no re-implantation. The median duration of antibiotic treatment was 6.3 months (range 1.3-50.7). They showed similar success rates with antibiotics only (67%) versus surgery plus antibiotic treatment (71%) (p = 1.0). Fifteen patients (71%) had rifampin as part of their antibiotic treatment but being on rifampin did not significantly change their outcome (73% vs. 60%; p = 0.61) and 40% of patients who received rifampin had to stop it due to side effects.

Hsu et al. [17] reported a retrospective study of 55 failed shoulder arthroplasty cases without clinical evidence of infection who underwent one-stage revision and compared their outcome at average 4 years between patients with ≥ 2 positive cultures (n = 27) and those with 1 or no positive cultures (n = 28). They reported comparable Simple Shoulder Test scores and reoperation rates. All patients received IV vancomycin and ceftriaxone as prophylaxis. If the index of suspicion for infection was high, the IV antibiotics were continued for 3 weeks until the cultures were finalized. If suspicion was low, the patients were started on oral amoxicillin and clavulanic acid for 3 weeks. If cultures were negative or only one culture was positive, antibiotic was stopped at 3 weeks. If ≥ 2 positive cultures became positive at any point, IV ceftriaxone +/- vancomycin was started and/or continued for 6 weeks. They reported 42% antibiotic side effects in this cohort which was higher than the IV antibiotics group.

Klatte et al. [18] retrospectively reviewed their experience with 26 infected shoulder arthroplasty patients treated with one-stage revision at mean follow-up of 4.7 years (range 1.1-13.3 years). The most common organisms were *Staphylococcus epidermis* and *C. acnes*. The majority of patients (94%) were infection-free at final follow up. Antibiotic therapy was tailored to clinical signs, serial CRP levels and serum WBC count. IV antibiotics were given for a mean of 10.6 days (range: 5-29 days). PO antibiotics were given to 4 patients for 5 days, 8 patients for 14 days and 2 patients for 24 days and stopped when CRP normalized and the wound had healed.

The literature on antibiotic treatment following one-stage revision shoulder arthroplasty for subacute and chronic infection is primarily based on heterogeneous case series with inconsistent definitions for infection, and variable treatment protocols. Shoulder PJI with indolent slow growing organisms, such as *C. acnes* and CNS, often have minimal clinical signs of infection. Thus, the diagnosis of infection is frequently made up to two weeks after the revision has been completed. As a practical approach to management, many clinicians recommend using antibiotics for all revision shoulder arthroplasty surgery pending the final cultures results [19].

There is no consensus on duration and type of antibiotics for this period. Antibiotic treatment after cultures are finalized should be dictated by the clinical index of suspicion for infection, culture results, and risk-benefit analysis of antibiotic side effects. There is no high-level evidence currently available to guide this decision.

REFERENCES

[1] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.

[2] Bohsali KI, Bois AJ, Wirth MA. Complications of Shoulder Arthroplasty. J Bone Joint Surg Am. 2017;99:256–269. doi:10.2106/JBJS.16.00935.

[3] Bohsali KI, Wirth MA, Rockwood CA. Complications of total shoulder arthroplasty. J Bone Joint Surg Am. 2006;88:2279–2292. doi:10.2106/JBJS.F.00125.

[4] Beekman PDA, Katusic D, Berghs BM, Karelse A, De Wilde L. One-stage revision for patients with a chronically infected reverse total shoulder replacement. J Bone Joint Surg Br. 2010;92:817–822. doi:10.1302/0301-620X.92B6.23045.

[5] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.

[6] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.

[7] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. J Bone Joint Surg Br. 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.

[8] Romanò CL, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. Int Orthop. 2012;36:1011–1017. doi:10.1007/s00264-012-1492-y.

[9] Fink B, Sevelda F. Periprosthetic joint infection ofsShoulder arthroplasties: diagnostic and treatment options. Biomed Res Int. 2017;2017:4582756. doi:10.1155/2017/4582756.

[10] Nelson GN, Davis DE, Namdari S. Outcomes in the treatment of periprosthetic joint infection after shoulder arthroplasty: a systematic review. J Shoulder Elbow Surg. 2016;25:1337–1345. doi:10.1016/j.jse.2015.11.064.

[11] Cuff DJ, Virani NA, Levy J, Frankle MA, Derasari A, Hines B, et al. The treatment of deep shoulder infection and glenohumeral instability with debridement, reverse shoulder arthroplasty and postoperative antibiotics. J Bone Joint Surg Br. 2008;90:336–342. doi:10.1302/0301-620X.90B3.19408.

[12] George DA, Volpin A, Scarponi S, Haddad FS, Romanò CL. Does exchange arthroplasty of an infected shoulder prosthesis provide better eradication rate and better functional outcome, compared to a permanent spacer or resection arthroplasty? a systematic review. BMC Musculoskelet Disord. 2016;17:52. doi:10.1186/s12891-016-0901-6.
[13] Grosso MJ, Sabesan VJ, Ho JC, Ricchetti ET, Iannotti JP. Reinfection rates after 1-stage revision shoulder arthroplasty for patients with unexpected positive intraoperative cultures. J Shoulder Elbow Surg. 2012;21:754–758.
[14] Padegimas EM, Lawrence C, Narzikul AC, Zmistowski BM, Abboud JA, Williams GR, et al. Future surgery after revision shoulder arthroplasty: the impact of unexpected positive cultures. J Shoulder Elbow Surg. 2017;26:975–981. doi:10.1016/j.jse.2016.10.023.
[15] Keller SC, Cosgrove SE, Higgins Y, Piggott DA, Osgood G, Auwaerter PG. Role of suppressive oral antibiotics in orthopedic hardware infections for those not undergoing two-stage replacement surgery. Open Forum Infect Dis. 2016;3:ofw176. doi:10.1093/ofid/ofw176.
[16] Piggott DA, Higgins YM, Melia MT, Ellis B, Carroll KC, McFarland EG, et al. Characteristics and treatment outcomes of Propionibacterium acnes prosthetic shoulder infections in adults. Open Forum Infect Dis. 2016;3. doi:10.1093/ofid/ofv191.
[17] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.
[18] Klatte TO, Junghans K, Al-Khateeb H, Rueger JM, Gehrke T, Kendoff D, et al. Single-stage revision for peri-prosthetic shoulder infection: outcomes and results. Bone Joint J. 2013;95-B:391–395. doi:10.1302/0301-620X.95B3.30134.
[19] Hsu JE, Bumgarner RE, Matsen FA. Propionibacterium in shoulder arthroplasty: what we think we Know today. J Bone Joint Surg Am. 2016;98:597–606. doi:10.2106/JBJS.15.00568.

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QUESTION 8: What are the recommendations regarding the route (intravenous (IV) vs. oral (PO)) and length of postoperative antibiotic treatment when a one-stage revision arthroplasty is performed for subacute/chronic shoulder periprosthetic joint infection (PJI) caused by a virulent organism (e.g., methicillin-sensitive *Staphylococcus aureus* (*S. aureus*), or MSSA, vs. methicillin-resistant *S. aureus* (MRSA), E. coli)?

RECOMMENDATION: Intravenous antibiotics or intravenous followed by oral antibiotics are both reasonable options for one-stage revision shoulder arthroplasty for subacute/chronic shoulder PJI caused by a virulent organism. As there is no consensus on the route or duration, these treatment parameters should be selected in consultation with an infectious disease specialist.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Single-stage revision shoulder arthroplasty is an option for infected shoulder arthroplasty [1–4]. However, the outcomes depending on the virulence of the organism and the ideal duration and mode of antibiotic (IV or oral) treatment associated with single stage revision for PJI is not known.

For this purpose, a comprehensive search on PubMed and Embase database of all English literature till March 2018 was conducted to query keywords: (shoulder OR 'upper extremity') AND (arthroplasty OR replacement) AND (infection OR infected). A total of 1,434 articles were retrieved by the initial search. After review of the title and abstract of all studies, articles focusing on "management of infection" were extracted for further review (n = 31). After applying final exclusion ("two stage revision," "antibiotic spacer" or "antibiotic suppression") and inclusion criteria ("single stage revision," "antibiotic"), a full text review of the articles was conducted, and 6 articles were selected for final analysis. Articles reporting single stage revision but without any information on antibiotic type and or duration were further excluded (n = 2).

The selected studies for analysis (n = 4) evaluated the role of postoperative antibiotic therapy for single stage revision shoulder arthroplasty for PJI. However, it must be emphasized that these studies did not stratify results by the virulence of the organism. Thus, no firm conclusions regarding treatment according to the virulence of the organism can be made.

Beekman et al. retrospectively reviewed 11 consecutive patients with an infected reverse shoulder arthroplasty who underwent single stage revision arthroplasty [5]. Two of these patients had monobacterial infection with a virulent organism (*Staphylococcus aureus* and *Escherichia coli*). Both of these patients received at least three days of IV antibiotic and were discharged on oral antibiotics, which were continued for at least three months. Ince et al. retrospectively reviewed 16 patients with an infected shoulder arthroplasty (three with identified virulent organisms) that underwent single stage revision shoulder arthroplasty [6]. Three patients (~19%) had undergone revision surgery prior to review. All patients received intravenous antibiotics for mean of 8.6 days (range: 5-14 days) and antibiotics were stopped when the surgical incision had healed and/or infection labs (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cell (WBC) count) were down trending. No recurrence of infection was reported in 9 patients that were reviewed. Klatte et al. reported their results of single stage revision shoulder arthroplasty for PJI in 35 patients, of which 26 were available for review [7]. Patients received IV antibiotics for a mean of 10.6 days (range: 5-29 days), and 11 patients received PO antibiotics for a mean duration of 12.8 days (range: 5-24 days). There were two recurrences. Cuff et al. retrospectively reviewed 22 infected shoulder arthroplasties of which 11 were treated with single stage revision to reverse shoulder arthroplasty and intravenous antibiotics [8]. Five of the 10 patients had virulent pathogens. Patients received antibiotics for 2 (1 patient) or 6 (4 patients) weeks depending on cultures and intraoperative histology results. There was one recurrence of infection.

There is little evidence regarding the subsequent antibiotic management of subacute and chronic shoulder PJI due to high viru-

lence organisms treated with one-stage revision. IV antibiotics or IV followed by PO antibiotics are both reasonable options. However, there is no consensus on the antibiotic type and duration of antibiotic treatment. Presently, clinical judgement and normalization of infection labs (ESR and CRP) for six weeks, if elevated preoperatively, are helpful in determining the duration of antibiotic treatment.

REFERENCES

[1] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.

[2] Marcheggiani Muccioli GM, Huri G, Grassi A, Roberti di Sarsina T, Carbone G, Guerra E, et al. Surgical treatment of infected shoulder arthroplasty. A systematic review. Int Orthop. 2017;41:823–830. doi:10.1007/s00264-017-3399-0.

[3] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.

[4] George DA, Logoluso N, Castellini G, Gianola S, Scarponi S, Haddad FS, et al. Does cemented or cementless single-stage exchange arthroplasty of chronic periprosthetic hip infections provide similar infection rates to a two-stage? A systematic review. BMC Infect Dis. 2016;16:553. doi:10.1186/s12879-016-1869-4.

[5] Beekman PDA, Katusic D, Berghs BM, Karelse A, De Wilde L. One-stage revision for patients with a chronically infected reverse total shoulder replacement. J Bone Joint Surg Br. 2010;92:817–822. doi:10.1302/0301-620X.92B6.23045.

[6] Ince A, Seemann K, Frommelt L, Katzer A, Loehr JF. One-stage exchange shoulder arthroplasty for peri-prosthetic infection. J Bone Joint Surg Br. 2005;87:814–818. doi:10.1302/0301-620X.87B6.15920.

[7] Klatte TO, Junghans K, Al-Khateeb H, Rueger JM, Gehrke T, Kendoff D, et al. Single-stage revision for peri-prosthetic shoulder infection: outcomes and results. Bone Joint J. 2013;95-B:391–395. doi:10.1302/0301-620X.95B3.30134.

[8] Cuff DJ, Virani NA, Levy J, Frankle MA, Derasari A, Hines B, et al. The treatment of deep shoulder infection and glenohumeral instability with debridement, reverse shoulder arthroplasty and postoperative antibiotics. J Bone Joint Surg Br. 2008;90:336–342. doi:10.1302/0301-620X.90B3.19408.

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QUESTION 9: What is the optimal antibiotic treatment for culture-negative cases with positive clinical, radiographic or intraoperative findings for acute shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: The limited data suggests treatment should consist of an empiric antibiotic regimen recommended by an infectious disease specialist considering the local organism profile.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

The incidence of culture-negative PJI ranges from 5 to 34% [1]. The following predefined keywords were used during the search using Medline database: ("culture negative") AND ((prosthetic joint infection OR periprosthetic joint infection) OR (arthroplasty AND infection)). Nine original articles [2–11] and a single systematic review [12] have been published on the topic of culture-negative PJI. However, these studies have addressed culture-negative PJI of knee and hip arthroplasty, but not prosthetic shoulder or elbow infections, and have focused on outcomes of culture-negative versus culture-positive PJI (not on the best treatment). The existing publications indicate that the outcome of a patient with culture-negative PJI is similar to that of PJI with a pathogen identified. In these studies, most of these patients with culture-negative PJI have been treated with glycopeptides, mainly vancomycin. Previous antibiotic use was common in these patients, potentially confounding the ability to culture an organism [13].

In a large multicenter study of the microbial etiology of PJI that included more than 2500 PJI cases in Spain [14], Benito et al. analyzed the microbiology of 42 infections of shoulder arthroplasty (data not published); twenty-eight (66.7%) PJIs were caused by aerobic gram-positive cocci, mainly coagulase-negative Staphylococci, followed by *S. aureus*; nine (21.4%) were due to *Cutibacterium* spp. and another nine (21.4%) to *Enterobacteriaceae*; two cases were caused by *Pseudomonas* aeruginosa; five (11.9%) of the PJI cases were polymicrobial infections.

Given the limited nature of the available data, the antibiotic treatment recommended for culture-negative cases of acute shoulder PJI with positive clinical, radiographic or intraoperative findings remains unclear. It is recommended to work with an infectious disease consultant to arrive at a treatment strategy which includes, in addition to surgical irrigation and debridement with exchange of modular elements, empiric coverage against the most common pathogens of acute PJI. A broad-spectrum antibiotic regimen that covers aerobic gram-positive cocci (including methicillin-resistant *Staphylococcus aureus* and coagulase-negative staphylococci) and gram-negative bacilli, as well as *Cutibacterium* species, could be recommended. The need for antibiotic activity against specific multidrug-resistant microorganisms should be considered according to the patient's clinical and epidemiological background.

Treatment with vancomycin or teicoplanin or daptomycin would cover aerobic gram-positive cocci (mainly Staphylococci), in other words, 67% of infections according to the mentioned data. These antibiotics are also active against *Cutibacterium* spp.; however, a beta-lactam (penicillin or cephalosporins) would probably be more active than vancomycin according to a study of 28 strains of *C. acnes* isolated from shoulder surgery [15]. *C. acnes* is highly susceptible to a wide range of antibiotics, including beta-lactams, quinolones, clindamycin and rifampin [16]. However, resistance is beginning to emerge. Recent reports note an increasing emergence of resistance to macrolides, clindamycin, tetracycline and trimethoprim-sulfamethoxazole [16].

- Aerobic gram-negative bacilli would mainly include *Enterobacteriaceae* and *P. aeruginosa*. Besides of the coverture of aerobic gram-positive cocci (with vancomicin, teicoplanin or daptomicin), adding ceftriaxone would be a good option in order to additionally cover *Enterobacteriaceae*, (if there are no suspicion of mechanisms of *Enterobacteriaceae* acquired

resistance such as extended-spectrum beta-lactamases producing (ESBL) *Enterobacteriaceae*). Ceftriaxone is also very active against *Cutibacterium* spp. If *P. aeruginosa* is a concern, cefepime or ceftazidime (instead of ceftriaxone) should be considered. Meropenem (instead of a cephalosporin) would be an option if ESBL-*Enterobacteriaceae* are suspected; it also has activity against *P. aeruginosa*.

- Clearly knowing the organism and antibiotic susceptibility allows for the selection of an antibiotic which is maximally bactericidal to the specific pathogen and minimally toxic to the patient. However, in lieu of this data, the empirical treatment should be typically administered intravenously; the possibility of a second phase with oral antimicrobial treatment should be evaluated on a case by case basis. Consideration of antimicrobial coverage provided before the culture was taken could help to choose the antibiotic regimen, as the clinician may presume the preoperative antibiotic is effective and, theoretically, is the reason the bacteria did not grow in culture. The role of rifampin is not clear in the scenario of a culture-negative PJI, as it has demonstrated its efficacy only in the staphylococcal infections. Moreover, the emergence of resistance with rifampin is high if it is used without another simultaneous antibiotic to which the pathogen is susceptible, and this cannot be guaranteed in a culture-negative PJI.

Long courses of antimicrobial treatment are recommended for infections of hip (3 months) and knee (6 months) prostheses managed with debridement, antibiotics and implant retention (DAIR) [17]. Based on many observational studies and one clinical trial [18] most patients with acute PJI managed with DAIR may be safely treated for 8 weeks [13]. Available information on this topic refers to prosthetic knee and hip infections, and it remains unclear how this data applies to shoulder PJI, where the microbiology of infection varies compared with hip and knee.

REFERENCES

[1] Tande AJ, Patel R. Prosthetic Joint Infection. Clin Microbiol Rev. 2014;27:302–345. doi:10.1128/CMR.00111-13.

[2] Kim YH, Park JW, Kim JS, Kim DJ. The outcome of infected total knee arthroplasty: culture-positive versus culture-negative. Arch Orthop Trauma Surg. 2015;135:1459–67. doi:10.1007/s00402-015-2286-7.

[3] Kim YH, Kulkarni SS, Park JW, Kim JS, Oh HK, Rastogi D. Comparison of infection control rates and clinical outcomes in culture-positive and culture-negative infected total-knee arthroplasty. J Orthopaedics. 2015;12:S37–S43. doi:10.1016/j.jor.2015.01.020.

[4] Parvizi J, Erkocak OF, Della Valle CJ. Culture-negative periprosthetic joint infection. J Bone Joint Surg Am. 2014;96:430–436. doi:10.2106/JBJS.L.01793.

[5] Puhto AP, Puhto TM, Niinimäki TT, Leppilahti JI, Syrjälä HPT. Two-stage revision for prosthetic joint infection: Outcome and role of reimplantation microbiology in 107 cases. J Arthroplasty. 2014;29:1101–1104. doi:10.1016/j.arth.2013.12.027.

[6] Choi HR, Kwon YM, Freiberg AA, Nelson SB, Malchau H. Periprosthetic joint infection with negative culture results: Clinical characteristics and treatment outcome. J Arthroplasty. 2013;28:899–903. doi:10.1016/j.arth.2012.10.022.

[7] Huang R, Hu CC, Adeli B, Mortazavi J, Parvizi J. Culture-negative periprosthetic joint infection does not preclude infection control hip. Clin Orthop Relat Res. 2012;470:2717–2723. doi:10.1007/s11999-012-2434-0.

[8] Malekzadeh D, Osmon DR, Lahr BD, Hanssen AD, Berbari EF. Prior use of antimicrobial therapy is a risk factor for culture-negative prosthetic joint infection. Clin Orthop Relat Res 2010;468:2039–2045. doi:10.1007/s11999-010-1338-0.

[9] Berbari EF, Marculescu C, Sia I, Lahr BD, Hanssen AD, Steckelberg JM, et al. Culture-negative prosthetic joint infection. Clin Infect Dis. 2007;45:1113–1119. doi:10.1086/522184.

[10] Kang J-S, Shin E-H, Roh T-H, Na Y, Moon KH, Park J-H. Long-term clinical outcome of two-stage revision surgery for infected hip arthroplasty using cement spacer: culture negative versus culture positive. J Orthop Surg (Hong Kong). 2018;26:2309499017754095. doi:10.1177/2309499017754095.

[11] Wang J, Wang Q., Shen H, Zhang X. Comparable outcome of culture-negative and culture-positive periprosthetic hip joint infection for patients undergoing two-stage revision. Int Orthop. 2018;42:469–477. doi:10.1007/s00264-018-3783-4.

[12] Yoon H-K, Cho S-H, Lee D-Y, Kang B-H, Lee S-H, Moon D-G, et al. A review of the literature on culture-negative periprosthetic joint infection: epidemiology, diagnosis and treatment. Knee Surg Relat Res. 2017;29:155–164. doi:10.5792/ksrr.16.034.

[13] Ariza J, Cobo J, Baraia-Etxaburu J, Benito N, Bori G, Cabo J, et al. Executive summary of management of prosthetic joint infections. Clinical practice guidelines by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC). Enferm Infecc Microbiol Clin. 2017;35:189–195. doi:10.1016/j.eimc.2016.08.012.

[14] Benito N, Franco M, Ribera A, Soriano A, Rodriguez-Pardo D, Sorlí L, et al. Time trends in the aetiology of prosthetic joint infections: a multicentre cohort study. Clin Microbiol Infect. 2016;22:732.e1-732.e8. doi:10.1016/j.cmi.2016.05.004.

[15] Crane JK, Hohman DW, Nodzo SR, Duquin TR. Antimicrobial susceptibility of Propionibacterium acnes isolates from shoulder surgery. Antimicrob Agents Chemother. 2013;57:3424–3426. doi:10.1128/AAC.00463-13.

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

[17] Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013;56:e1–e25. doi:10.1093/cid/cis803.

[18] Sayeed Y, Quien M, Anoushiravani A, Kim K, Camus T, Schwarzkopf R, et al. Irrigation and debridement for periprosthetic hip infection: does timing play a role? J Hip Surg. 2017. doi:10.1055/s-0037-1603627.

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QUESTION 10: What is the optimal antibiotic treatment for culture-negative cases with positive clinical, radiographic or intraoperative findings for subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: The limited data suggests treatment should consist of an empiric antibiotic regimen recommended by an infectious disease specialist considering the local organism profile.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

A systematic review was conducted in March 2018 using PubMed and Google Scholar databases. Keywords included "shoulder" AND ("prosthetic joint infection" OR "arthroplasty infection") AND ("culture" or "culture-negative"). After title and abstract review, fourteen studies were considered for inclusion; additional references were identified from review of reference lists.

There are no studies that have reported clinical outcomes for culture-negative shoulder arthroplasty infections stratified by antimicrobials utilized. There are limited observational data on empiric antimicrobial treatment options for patients with non-shoulder arthroplasty infections. Antimicrobials for culture-negative infections should be selected in light of suspected organisms and their typical antimicrobial resistance profiles, drug tissue penetration (including bone penetration), bioavailability (if oral antimicrobials are selected), host factors (including comorbidities and allergies) and safety considerations. Prior antimicrobial exposure may inform organisms suppressed from culture growth. Additional considerations include the type of surgical procedure, such as whether hardware is retained or exchanged and the use of antimicrobial-laden cement. In the shoulder, most culture-positive subacute and chronic infections are due to coagulase-negative Staphylococci and *Cutibacterium* species [1–3]. Limited evidence in non-shoulder arthroplasty settings have reported good outcomes with vancomycin [4,5] and cephalosporins [5,6]. Most studies in the non-shoulder literature did not find culture negativity to be a poor prognostic factor [5–11], although one study [12] did find worse outcomes in culture-negative knees treated with irrigation and debridement.

The addition of rifampin may be considered if there is strong suspicion for gram-positive infection, particularly staphylococcal, in the setting of maintained hardware [13]. Synergy in the laboratory has been shown with rifampin for *Cutibacterium* [14]; however, there is insufficient clinical experience on the role of rifampin for the treatment of *Cutibacterium* infection to endorse its use [15]. Rifampin should never be used in monotherapy as resistance rapidly emerges; when employed rifampin should be used with careful monitoring and with full consideration of drug toxicities and drug interactions.

Prior antimicrobial exposure is a strong risk factor for culture-negativity [5,7,16]. When infection is suspected, antibiotics should be withheld prior to surgery whenever possible to reduce the likelihood of culture-negative infection. Whether a single dose of perioperative antimicrobial prophylaxis reduces the yield of organisms in low-burden infection is uncertain; two small randomized studies on hip and knee PJI suggest that a single dose of perioperative antibiotic therapy does not reduce operative culture yield [17,18]. Multiple operative samples should also be collected to increase the overall culture yield and to guard against placing too much emphasis on a single positive culture that, in some cases, may be a contaminant [19,20]. Aseptic inflammation and unusual organisms should also be considered in the differential of the culture-negative infection. In these cases, with concern for infection, pathology may be helpful to identify granulomas or other signs of atypical infection; thus, sending tissue samples for pathology is recommended to assist in properly interpreting any culture results. In the appropriate clinical and epidemiologic context, for example in immunocompromised hosts, and, in the setting of penetrating trauma, fungal and mycobacterial cultures should also be considered.

REFERENCES

[1] Grosso MJ, Frangiamore SJ, Yakubek G, Bauer TW, Iannotti JP, Ricchetti ET. Performance of implant sonication culture for the diagnosis of periprosthetic shoulder infection. J Shoulder Elbow Surg. 2018;27:211–216. doi:10.1016/j.jse.2017.08.008.

[2] Richards J, Inacio MCS, Beckett M, Navarro RA, Singh A, Dillon MT, et al. Patient and procedure-specific risk factors for deep infection after primary shoulder arthroplasty. Clin Orthop Relat Res. 2014;472:2809–2815. doi:10.1007/s11999-014-3696-5.

[3] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.

[4] Huang R, Hu CC, Adeli B, Mortazavi J, Parvizi J. Culture-negative periprosthetic joint infection does not preclude infection control. Clin Orthop Relat Res. 2012;470:2717–2723. doi:10.1007/s11999-012-2434-0.

[5] Yoon HK, Cho SH, Lee DY, Kang BH, Lee SH, Moon D-G, et al. A review of the literature on culture-negative periprosthetic joint infection: epidemiology, diagnosis and treatment. Knee Surg Relat Res. 2017;29:155–164. doi:10.5792/ksrr.16.034.

[6] Kang JS, Shin EH, Roh TH, Na Y, Moon KH, Park JH. Long-term clinical outcome of two-stage revision surgery for infected hip arthroplasty using cement spacer: Culture negative versus culture positive. J Orthop Surg. (Hong Kong) 2018;26:2309499017754095. doi:10.1177/2309499017754095.

[7] Ibrahim MS, Twaij H, Haddad FS. Two-stage revision for the culture-negative infected total hip arthroplasty: a comparative study. Bone Joint J. 2018;100-B:3–8. doi:10.1302/0301-620X.100B1.BJJ-2017-0626.R1.

[8] Li H, Ni M, Li X, Zhang Q, Li X, Chen J. Two-stage revisions for culture-negative infected total knee arthroplasties: A five-year outcome in comparison with one-stage and two-stage revisions for culture-positive cases. J Orthop Sci. 2017;22:306–312. doi:10.1016/j.jos.2016.11.008.

[9] Kim YH, Kulkarni SS, Park JW, Kim JS, Oh HK, Rastogi D. Comparison of infection control rates and clinical outcomes in culture-positive and culture-negative infected total-knee arthroplasty. J Orthop. 2015;12:S37–S43. doi:10.1016/j.jor.2015.01.020.

[10] Kim YH, Park JW, Kim JS, Kim DJ. The outcome of infected total knee arthroplasty: culture-positive versus culture-negative. Arch Orthop Trauma Surg. 2015;135:1459–1467. doi:10.1007/s00402-015-2286-7.

[11] Choi HR, Kwon YM, Freiberg AA, Nelson SB, Malchau H. Periprosthetic joint infection with negative culture results: clinical characteristics and treatment outcome. J Arthroplasty. 2013. doi:10.1016/j.arth.2012.10.022.

[12] Urish KL, Bullock AG, Kreger AM, Shah NB, Jeong K, Rothenberger SD, et al. A multicenter study of irrigation and debridement in total knee arthroplasty periprosthetic joint infection: treatment failure is high. J Arthroplasty. 2018;33:1154–1159. doi:10.1016/j.arth.2017.11.029.

[13] Zimmerli W, Widmer AF, Blatter M, Frei R, Ochsner PE. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. Foreign-Body Infection (FBI) Study Group. JAMA. 1998;279:1537–1541.

[14] Furustrand Tafin U, Corvec S, Betrisey B, Zimmerli W, Trampuz A. Role of rifampin against Propionibacterium acnes biofilm in vitro and in an experimental foreign-body infection model. Antimicrob Agents Chemother. 2012;56:1885–1891. doi:10.1128/AAC.05552-11.

[15] Jacobs AME, Van Hooff ML, Meis JF, Vos F, Goosen JHM. Treatment of prosthetic joint infections due to Propionibacterium. Similar results in 60 patients treated with and without rifampicin. Acta Orthop. 2016;87:60–66. doi:10.3109/17453674.2015.1094613.

[16] Malekzadeh D, Osmon DR, Lahr BD, Hanssen AD, Berbari EF. Prior use of antimicrobial therapy is a risk factor for culture-negative prosthetic joint infection. Clin Orthop Relat Res. 2010;468:2039–2045. doi:10.1007/s11999-010-1338-0.

[17] Tetreault MW, Wetters NG, Aggarwal V, Mont M, Parvizi J, Della Valle CJ. The Chitranjan Ranawat Award: should prophylactic antibiotics be withheld before revision surgery to obtain appropriate cultures? Clin Orthop Relat Res. 2013. doi:10.1007/s11999-013-3016-5.

[18] Pérez-Prieto D, Portillo ME, Puig-Verdié L, Alier A, Gamba C, Guirro P, et al. Preoperative antibiotic prophylaxis in prosthetic joint infections: not a concern for intraoperative cultures. Diagn Microbiol Infect Dis. 2016;86:442–445. doi:10.1016/j.diagmicrobio.2016.09.014.

[19] Atkins BL, Athanasou N, Deeks JJ, Crook DW, Simpson H, Peto TE, et al. Prospective evaluation of criteria for microbiological diagnosis of prosthetic-joint infection at revision arthroplasty. The OSIRIS Collaborative Study Group. J Clin Microbiol. 1998;36:2932–2939.

[20] Gandhi R, Silverman E, Courtney PM, Lee G-C. How many cultures are necessary to identify pathogens in the management of total hip and knee arthroplasty infections? J Arthroplasty. 2017;32:2825–2828. doi:10.1016/j.arth.2017.04.009.

3.3. TREATMENT: BONE GRAFT

Author: Michael Khazzam

QUESTION 1: Should bone graft or cement be removed during treatment of acute shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Unknown. There are no reported investigations to guide the decision-making process regarding how to manage cement and/or autograft bone graft in the setting of shoulder PJI.

LEVEL OF EVIDENCE: No Evidence

DELEGATE VOTE: Agree: 90%, Disagree: 5%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

There is no current literature to guide evidence-based recommendations regarding how to manage autograft bone or cement in the setting of acute infection after primary shoulder arthroplasty. Additionally, it is unknown how or if complete removal of this material is necessary to eradicate shoulder PJI. The goal of surgical intervention in the setting of PJI is to debride any material that may result in persistent infection including surfaces with biofilm. Complete removal of autograft bone or cement at times can be extremely difficult and can result in significant bone loss especially if bone graft was used to reconstruct glenoid bone deficiency. A long stem, cemented, well-fixed humeral stem requires a humeral osteotomy or cortical window for complete cement removal which adds significant additional morbidity to the revision procedure. The significance of retaining these materials is unclear and, in order to avoid the complications that come with complete removal of these materials, investigation is needed to understand the risks associated with incomplete removal of cement or bone graft and the risks of recurrent PJI that are associated with this practice. Additionally, it is unknown whether retention of this material requires a change in the postoperative antibiotic management. Finally, it is also unknown how the species of bacterial pathogen and antibiotic sensitivity profile may influence the successful treatment of PJI. Future investigation is required to answer this question in an evidence-based fashion.

Methods

Systematic review of the literature was performed using MeSH terms: cement and infection and shoulder arthroplasty/ replacement, cement and retention and infection, bone graft and infection and shoulder arthroplasty/replacement using search engines PubMed, Web of Science, and CINAHL. Inclusion criteria for this systematic review were Level of Evidence I-IV, English language, shoulder arthroplasty studies which included patient who underwent treatment for PJI and evaluation of the impact of cement removal and/or autograft bone removal classified as either acute, subacute, or chronic infection. Exclusion criteria were non-English language articles, review papers, technique papers, non-human studies, biomechanics or basic science papers, and articles that discussed only hip and or knee arthroplasty PJI. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were used manage the data of this review. The initial search produced 213 abstracts; all of these were excluded as they did not contain any details or evaluation of the question under investigation. Therefore, there are no current studies to reference the impact or effects of cement removal or autograft bone removal in the setting of shoulder arthroplasty PJI for acute, subacute or chronic infection.

Author: Michael Khazzam

QUESTION 2: Should bone graft or cement be removed in treatment for subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Unknown. There are no reported investigations to guide the decision-making process regarding how to manage cement and/or autograft bone graft in the setting of shoulder PJI. An attempt should be made to remove all loose, necrotic and foreign material.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

A systematic review of the literature was performed using "MeSH terms:" cement and infection and shoulder arthroplasty/ replacement, cement and retention and infection, bone graft and infection and shoulder arthroplasty/replacement using search engines PubMed, Web of Science, and CINAHL. Inclusion criteria for this systematic review were Level of Evidence I-IV, English Language, shoulder arthroplasty studies which included patient who underwent treatment for PJI and evaluated the impact of cement removal and or autograft bone removal classified as either acute, subacute, or chronic infection. Exclusion criteria were non-English language arti-

cles, review papers, technique papers, non-human studies, biomechanics or basic science papers, articles that discussed only hip and or knee arthroplasty PJI. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were used manage the data of this review. The initial search produced 213 abstracts, all of these were excluded as they did not contain any details or evaluation of the question under investigation. Therefore, there are no current studies to reference the impact or effects of cement removal or autograft bone removal in the setting of shoulder arthroplasty PJI for acute, subacute or chronic infection.

There is no current literature to guide an evidence-based recommendation regarding how to manage autograft bone or cement that was placed at the time of primary shoulder arthroplasty and has become infected. Additionally, what is unknown is how or if complete removal of this material is necessary to eradicate shoulder PJI. The goal of surgical intervention in the setting of PJI to debride any material that may result in retained biofilm that, if not removed, may result in a recurrent infection. Complete removal of autograft bone or cement at times can be extremely difficult and can result in significant bone loss especially if bone graft was used to reconstruct bone deficiency of the glenoid. A long stem cemented well-fixed humeral stem can at times require a long humeral osteotomy or cortical windows for complete cement removal which adds significant additional morbidity to the revision procedure.

The significance of retaining these materials is unclear and investigation is needed to understand the risks associated with incomplete removal of cement or bone graft, and what risks of recurrent PJI are associated with this practice to avoid the morbidity that may come with complete removal of these materials. Additionally, it is unknown how retention of this material requires a change in the postoperative antibiotic recommendations for the type, method of delivery or duration of treatment. Finally, it is also unknown how the species of the bacterial pathogen may influence the successful treatment and risk of recurrent PJI, where some less virulent pathogens (such as *C. acnes*) may be more difficult to eradicate with retention of cement or bone graft because of the slow growing nature. Future investigation related to the impact of type of bacteria can provide data to develop a treatment algorithm for which cases can predictably be successful with retention of cement or graft and for which settings require complete removal of all graft and cement materials.

3.4. TREATMENT: COMPONENT RETENTION

Author: Michael Khazzam

QUESTION 1: Is there a role for irrigation and debridement (I&D) with implant retention when treating acute shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There is insufficient high-quality evidence to support or discourage the use of I&D with implant retention to treat acute shoulder PJI.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 4%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

There is little data demonstrating the outcome or infection-free implant survivorship for the treatment of acute shoulder PJI with I&D and implant retention. To date, there are only 37 patients (38 shoulders) with outcomes following this procedure reported in the literature [1–4]. These studies were all grade IV level of evidence (LOE) retrospective case series and demonstrated a 50% failure rate (defined as continued infection) and requiring additional treatment. Three of four studies treated acute, subacute and chronic infections using this technique, but the sample size was too small to analyze how time of infection influences outcomes [1,3,4]. For example, Jacquot et al. found that 1 of the 2 shoulders classified as chronic PJI, 2 of 4 subacute, and 2 of 7 acute had recurrent infection requiring additional treatment [3].

Dennison et al. was the only study found specifically investigating the efficiency of acute (surgery within 6 weeks following index arthroplasty and less than 3 weeks of symptoms) and "delayed onset/delayed acute" (more than 6 weeks following index arthroplasty with symptoms less than 3 weeks) [2]. This retrospective LOE IV case series examined 9 patients (10 shoulders) and found 3 of 10 had recurrent infection requiring resection arthroplasty (mean follow up 4.1 years range 0.58-12.8 years). The method of I&D varied in this study with 3 performed arthroscopically and 7 open. All of the subjects requiring resection had their I&D performed open; the numbers were too small to perform any meaningful analysis of how this may influence outcomes or infection free survivorship. Additionally, 6 of 10 shoulders were maintained on chronic suppressive antibiotics indefinitely without explanation of why the authors selected this treatment.

Further research will be needed to determine how irrigation and debridement with implant retention plays a role in the treatment algorithm of PJI. Specific attention towards answering the questions regarding the effect of the pathogen and the antibiotic sensitivity profile; surgical approach (open or arthroscopic); timing from presentation and index arthroplasty; need for exchange of modular component parts; and type, duration, and method of delivery of antibiotics will be critical to guide these treatment decisions.

Methods

A systematic review was performed using MeSH terms: "I&D shoulder arthroplasty/shoulder replacement, single staged shoulder arthroplasty/shoulder replacement, implant retention revision shoulder arthroplasty/shoulder replacement, acute infection shoulder arthroplasty/ shoulder replacement" using search engines PubMed, Web of Science, and CINAHL. The inclusion criteria for

this systematic review were LOE I-IV, English language, shoulder arthroplasty studies that included patients who underwent treatment for PJI using I&D with component retention (polyethylene and or glenosphere exchange without stem or baseplate removal was included). Exclusion criteria were non-English language articles, review papers, technique papers, non-human studies, and studies that only presented data on one-stage or two-stage revision, hip or knee arthroplasty articles. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were used manage the data of this review. Our initial search produced 66 abstracts; 61 were excluded, because they did not fulfill the inclusion criteria, and the remaining 4 manuscripts were obtained and reviewed to assure inclusion criteria. Additionally, the references of these manuscripts were reviewed to ensure no additional material would be missed. This left four studies for analysis, only one of which evaluated the role for I&D with implant retention for the treatment of acute shoulder PJI.

REFERENCES

[1] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.
[2] Dennison T, Alentorn-Geli E, Assenmacher AT, Sperling JW, Sánchez-Sotelo J, Cofield RH. Management of acute or late hematogenous infection after shoulder arthroplasty with irrigation, débridement, and component retention. J Shoulder Elbow Surg. 2017;26:73–78. doi:10.1016/j.jse.2016.05.018.
[3] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.
[4] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.

Authors: Jeremy Somerson, William Levine

QUESTION 2: What are the indications for irrigation and debridement (I&D) with component retention in subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: I&D with component retention alone for subacute/chronic shoulder PJI in the literature is less successful than component explant, but may play a role in select patients.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

A systematic review was performed using PubMed and Google Scholar databases in February 2018 to identify studies regarding the treatment outcomes after shoulder arthroplasty. The keywords included "shoulder AND (replacement OR arthroplasty) AND infection." This identified 46 articles with relevance to surgical treatment of shoulder PJI; 10 of which described treatment with debridement and implant retention for subacute/chronic infection.

I&D with component retention for shoulder PJI in the subacute and chronic setting has shown low rates of eradication of infection [1–10]. Of the 51 surgical cases identified in studies with a reported eradication rate, approximately half (n = 24, 47%) were successfully cured with debridement alone. The majority of these successful treatments were from two recent studies that integrated modular component exchange with partial component retention [1,2].

Stone et al. [1] reported on patients with shoulder PJI treated with one-stage partial component exchange compared to patients with one-stage complete hardware removal and two-stage revisions. The greatest success rate was with complete one-stage revisions (96% eradication of infection) compared to only 63% eradication for partial one-stage revisions. The authors concluded that there are some circumstances in which retaining a prosthesis may be preferred (such as well-fixed components), but that the surgeon must be aware of a higher risk of recurrent infection.

A French multicenter study reported on 32 patients who underwent revision for infection after reverse shoulder arthroplasty (RSA); of these, 13 patients underwent debridement, modular component exchange and partial component retention [2]. Only 7 patients (54%) were successfully cleared of infection with debridement alone. However, the 15% complication rate reported with debridement was lower than that reported for resection (33%), one-stage revision (20%) or two-stage revision (36%). The authors propose that initial debridement be considered for primary treatment of infected RSA given that more than half of patients were successfully treated with relatively few complications.

Primary treatment of subacute/chronic shoulder PJI with debridement, irrigation and component retention is an option, particularly in patients in which the risks of more aggressive surgery outweigh the potential benefits. However, patients and surgeons should be aware that the published rate of recurrence is substantially greater with this strategy compared to one- or two-stage revision.

REFERENCES

[1] Stone GP, Clark RE, O'Brien KC, Vaccaro L, Simon P, Lorenzetti AJ, et al. Surgical management of periprosthetic shoulder infections. J Shoulder Elbow Surg. 2017;26:1222–1229. doi:10.1016/j.jse.2016.11.054.
[2] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.
[3] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.
[4] Boileau P, Melis B, Duperron D, Moineau G, Rumian AP, Han Y. Revision surgery of reverse shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:1359–1370. doi:10.1016/j.jse.2013.02.004.
[5] Farshad M, Grögli M, Catanzaro S, Gerber C. Revision of reversed total shoulder arthroplasty. Indications and outcome. BMC Musculoskelet Disord. 2012;13:160. doi:10.1186/1471-2474-13-160.
[6] Achermann Y, Sahin F, Schwyzer HK, Kolling C, Wüst J, Vogt M. Characteristics and outcome of 16 periprosthetic shoulder joint infections. Infection. 2013;41:613–620. doi:10.1007/s15010-012-0360-4.
[7] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. J Shoulder Elbow Surg. 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.
[8] Weber P, Utzschneider S, Sadoghi P, Andress H-J, Jansson V, Müller PE. Management of the infected shoulder prosthesis: a retrospective analysis and review of the literature. Int Orthop. 2011;35:365–373. doi:10.1007/s00264-010-1019-3.

[9] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.

[10] Sperling JW, Kozak TKW, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001;382:206.

Author: Richard Page, James Beazley, Nicola Luppino

QUESTION 3: Should modular components be exchanged during irrigation and debridement (I&D) of acute shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Whilst there is logic in exchanging non-fixed modular components, such as the bearing surfaces, to allow thorough I&D of the entire effective joint space and removal of as much biofilm as possible, there is insufficient literature to provide clear guidance.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

A thorough search of the PubMed database for manuscripts addressing the exchange of modular parts during shoulder I&D for acute PJI was undertaken. Five papers were found that recorded if modular components were exchanged [1–5], totalling 53 patients. The pooled infection-free survivorship was 65% in the "modular exchange group" (19/29) versus 58% (14/24) in the "no exchange group" ($p = 0.77$ Fisher's exact test).

Of these papers, three [1,3,5] specified the outcome for patients with acute debridement and retention with and without modular exchange. In total, 10 patients underwent acute debridement and retention of prosthesis without modular exchange with an infection free survivorship of 70% (7/10). Eight patients are recorded as having undergone poly exchange during debridement of an acute infection, with an infection free survivorship of 62.5% (5/8; $p > 0.05$).

REFERENCES

[1] Dennison T, Alentorn-Geli E, Assenmacher AT, Sperling JW, Sánchez-Sotelo J, Cofield RH. Management of acute or late hematogenous infection after shoulder arthroplasty with irrigation, débridement, and component retention. J Shoulder Elbow Surg. 2017;26:73–78. doi:10.1016/j.jse.2016.05.018.

[2] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.

[3] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.

[4] Stone GP, Clark RE, O'Brien KC, Vaccaro L, Simon P, Lorenzetti AJ, et al. Surgical management of periprosthetic shoulder infections. J Shoulder Elbow Surg. 2017;26:1222–1229. doi:10.1016/j.jse.2016.11.054.

[5] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. J Shoulder Elbow Surg. 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.

Authors: Richard Page, Scott E. Paxton, Ben Clark, Surena Namdari

QUESTION 4: Should modular components be exchanged during irrigation and debridement (I&D) of subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: We defer to the response for the Question 5: "Should well-fixed glenoid components be removed during surgical treatment for subacute or chronic shoulder PJI?"

It would seem that the recommendation, although of limited strength, would be for well-fixed components to be removed during surgical intervention for subacute/chronic shoulder PJI. Therefore, it can be extrapolated that modular components, which can be exchanged to remove biofilm with far less morbidity than well-fixed components, should likewise be either exchanged or removed and replaced with an antibiotic spacer.

LEVEL OF EVIDENCE: No Evidence

DELEGATE VOTE: Agree: 95%, Disagree: 5%, Abstain: 0% (Unanimous, Strongest Consensus)

Author: Surena Namdari

QUESTION 5: Should well-fixed glenoid components be removed during surgical treatment for subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Based on the higher rate of reinfection with component retention, we recommend removal of even well-fixed glenoid components in cases of single-stage revision for suspected subacute/chronic PJI. Certainly, there may be cases (i.e., high-risk surgical patients) where the patient and surgeon may choose to accept the higher failure rate with component retention in order to avoid surgical morbidity introduced by removing well-fixed components.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

A comprehensive literature review was performed to identify all studies on surgical treatment of subacute and chronic shoulder PJI. Previously, we have performed a systematic review on shoulder PJI treatment. In that study, we searched for the terms "shoulder arthroplasty infection" and "shoulder replacement infection" using the search engines PubMed and Embase through April 2014. Inclusion criteria were titles that specified periprosthetic infection of the shoulder (if "Periprosthetic infection" was mentioned, but no joint was specified, the article was included for further review) and articles pertaining to revision shoulder arthroplasty. Exclusion criteria were duplicate titles, review articles, editorials, technique articles without reported patient outcomes and instructional course lecture articles. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed. For this question, the same search terms were used and the dates between May 2014 and February 2018 were searched in order to update the previous systematic review. The prior systematic review identified 663 titles, and an additional 243 were evaluated for the updated review.

In this updated systematic review, three additional studies were identified that met inclusion and exclusion criteria and added to the data from the prior systematic review by Nelson et al. [1] that involved a search until April 2014. Only the study by Jacquot et al. [2] defined a subset of patients treated for subacute or chronic PJI, and the other studies grouped both acute and chronic cases. Based on the available data (all retrospective), there is clearly a higher failure rate of treatment when components are retained (31.3%) as opposed to exchanged via a one-stage or two-stage procedure (< 10%) [1]. Because of this, one must recommend for treatment of subacute/chronic shoulder PJI with removal of all, even well-fixed, components. However, it should be noted that these studies were all based on retrospective review of patients treated according to surgeon preference, and the features of the particular infections are not well documented (bacteria, antibiotic sensitivity, etc.). It is possible, perhaps even probable, that patients treated with implant retention versus removal may have had different infectious presentations that led the treating surgeon to their chosen approach. Further comparative research is needed on this topic. In addition, there may be cases (i.e., high-risk surgical patients) where the patient and surgeon may choose to accept the higher failure rate with component retention in order to minimize surgical morbidity.

REFERENCES

[1] Nelson GN, Davis DE, Namdari S. Outcomes in the treatment of periprosthetic joint infection after shoulder arthroplasty: a systematic review. J Shoulder Elbow Surg. 2016;25:1337–1345. doi:10.1016/j.jse.2015.11.064.

TABLE 1. Updated systematic literature review

Study	Date	Study Design	# Treated w/ I&D and Component Retention	# Failed Treatment (%)	# Treated w/ One-stage Revision	# Failed Treatment (%)	# Treated w/ Two-stage Revision	# Failed Treatment (%)
Nelson [1]	2016	Systematic Review	35	11	282	28	97	6
Stone [3]	2017	Retrospective Case Series	15	4	45	2	19	4
Marcheggiani Muccioli [4]	2017	Systematic Review	27	8	77	3	98	14
Jacquot [2]	2015	Retrospective Case Series	6	3	n/a	n/a	n/a	n/a
Total			**83**	**26 (31.3%)**	**404**	**33 (8.2%)**	**214**	**24 (11.2%)**

I&D, irrigation and debridement

[2] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.
[3] Stone GP, Clark RE, O'Brien KC, Vaccaro L, Simon P, Lorenzetti AJ, et al. Surgical management of periprosthetic shoulder infections. J Shoulder Elbow Surg. 2017;26:1222–1229. doi:10.1016/j.jse.2016.11.054.
[4] Marcheggiani Muccioli GM, Huri G, Grassi A, Roberti di Sarsina T, Carbone G, Guerra E, et al. Surgical treatment of infected shoulder arthroplasty. A systematic review. Int Orthop. 2017;41:823–830. doi:10.1007/s00264-017-3399-0.

Authors: Richard Page, Akin Cil, Gokhan Karademir

QUESTION 6: Is there a role for routine exchange of all well-fixed implants in revision shoulder arthroplasty without clinical or radiographic signs of infection?

RECOMMENDATION: Unknown. Even in the setting of possible subsequent unexpected positive cultures, there is sparse literature on the routine exchange of well-fixed implants in revision shoulder arthroplasty.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

Periprosthetic shoulder infection is one of the most challenging complications of shoulder arthroplasty [1,2]. The difficulty of diagnosis and treatment is attributed to *Cutibacterium acnes* which is a microorganism with low antigenicity [3]. Unlike knee and hip PJI, laboratory tests may be inadequate for diagnosing indolent infection caused by this agent [2]. The prevalence of *Cutibacterium acnes* has been reported to be as high as 50% of intraoperative cultures obtained at the time of revision surgery for a painful and stiff total shoulder arthroplasty [1]. This determination led to the definition of a new clinical entity: "Unexpected positive intraoperative cultures." Due to the fact that this bacterium is a member of the normal skin flora of the shoulder region, it is unknown whether a positive culture should be interpreted as a contamination or a definitive infection [4,5]. Due to the inadequacy of gram stain and frozen-section, and long incubation time; it is difficult to make a decision regarding implant removal during revision surgery [2]. Moreover, in the case of the well-fixed implants, the explant procedure can be difficult and have associated morbidity [5–7].

There is lack of evidence regarding the role for revision of well-fixed implants in revision shoulder arthroplasty without clinical or radiographic signs of infection [2,8]. In a study by Pottinger et al., [8] it has been reported that implants may need to be removed in patients who have risk factors for positive culture. McGoldrick et al. [9] have suggested single-stage reimplantation in the presence of loose implants. However, the authors have not commented on well-fixed implants. Similarly, Grosso et al. [6] have reported low recurrence with the removal of all components and single-stage reimplantation in the patients with unexpected positive intraoperative cultures. On the other hand, Topolski et al. [10] and Kelly et al. [11] reported high recurrence with the retention of implants. Lutz et al. [12] have evaluated infection with *Cutibacterium acnes* in the patients who underwent osteosynthesis or arthroplasty in the shoulder, knee or hip regions and reported that the absence of sepsis findings could not exclude the infection. The authors emphasized that the removal of the implants was important in the success of the treatment of *Cutibacterium acnes* infection of prosthetic material.

REFERENCES

[1] Foruria AM, Fox TJ, Sperling JW, Cofield RH. Clinical meaning of unexpected positive cultures (UPC) in revision shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:620–627. doi:10.1016/j.jse.2012.07.017.
[2] Ricchetti ET, Frangiamore SJ, Grosso MJ, Alolabi B, Saleh A, Bauer TW, et al. Diagnosis of periprosthetic infection after shoulder arthroplasty: a critical analysis review. JBJS Rev. 2013;1. doi:10.2106/JBJS.RVW.M.00055.
[3] 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;33:829–833. doi:10.1007/s00264-008-0534-y.
[4] 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. doi:10.1016/j.jse.2009.01.023.
[5] Lavergne V, Malo M, Gaudelli C, Laprade M, Leduc S, Laflamme P, et al. Clinical impact of positive Propionibacterium acnes cultures in orthopedic surgery. Orthop Traumatol. Surg Res 2017;103:307–314. doi:10.1016/j.otsr.2016.12.005.
[6] Grosso MJ, Sabesan VJ, Ho JC, Ricchetti ET, Iannotti JP. Reinfection rates after 1-stage revision shoulder arthroplasty for patients with unexpected positive intraoperative cultures. J Shoulder Elbow Surg. 2012;21:754–758. doi:10.1016/j.jse.2011.08.052.
[7] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.
[8] 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;94:2075–2083. doi:10.2106/JBJS.K.00861.
[9] McGoldrick E, McElvany MD, Butler-Wu S, Pottinger PS, Matsen FA. Substantial cultures of Propionibacterium can be found in apparently aseptic shoulders revised three years or more after the index arthroplasty. J Shoulder Elbow Surg. 2015;24:31–35. doi:10.1016/j.jse.2014.05.008.
[10] Topolski MS, Chin PYK, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: the value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006;15:402–406. doi:10.1016/j.jse.2005.10.001.
[11] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. Clin Orthop Relat Res. 2009;467:2343–2348. doi:10.1007/s11999-009-0875-x.
[12] Lutz M-F, Berthelot P, Fresard A, Cazorla C, Carricajo A, Vautrin A-C, et al. Arthroplastic and osteosynthetic infections due to Propionibacterium acnes: a retrospective study of 52 cases, 1995-2002. Eur J Clin Microbiol Infect Dis. 2005;24:739–744. doi:10.1007/s10096-005-0040-8.

3.5. TREATMENT: IMPLANT

Authors: Mark Frankle, Jason Hsu

QUESTION 1: What is the optimal implant for treatment of acute periprosthetic joint infection (PJI): reverse total shoulder arthroplasty (TSA), anatomic total shoulder arthroplasty (aTSA) versus hemiarthroplasty?

RECOMMENDATION: The optimal implant for treatment of acute PJI is dependent on the status of the rotator cuff, humeral and glenoid bone stock, and patient factors.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

Acute shoulder PJI is most commonly considered to be an infection presenting within 3 months after index arthroplasty as described by Sperling et al. [1]. In this scenario, the surgeon has a number of options in the treatment of acute PJI including antibiotic treatment alone, debridement with or without exchange of modular components, single stage complete exchange, two-stage exchange with antibiotic spacer, indefinite implantation of an antibiotic spacer and resection arthroplasty.

Methodology

Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we conducted a systematic review to identify all studies concerning diagnosis and treatment of "infection" at the time of revision shoulder arthroplasty. We searched for all studies published in English using the terms (("revision" OR "failed") AND "shoulder" AND ("arthroplasty" OR "replacement")) limited to dates between January 1, 1996 and February 3, 2018. A total of 2,354 studies were identified. We reviewed the titles and abstracts of all studies and excluded studies that included patients with shoulder infection without arthroplasty or included patients with arthroplasty of joints other than the shoulder. The reference lists for all included studies were searched for any additional references and three references were added to our list. A total of 42 studies met inclusion criteria and were included in the final analysis. Relevant data were extracted from the selected publications, including stratification of acute/subacute/chronic classification, procedures performed, final implants, reinfection rates and functional/clinical results.

Results are summarized in Table 1. Of 42 studies, 19 stratified acute PJI from subacute/chronic PJI with 20% of included patients (93/459) in the acute category. While there were a fair number of studies that described patients with acute PJI, the types of implants explanted and implanted were not regularly reported or stratified; and, therefore, drawing conclusions regarding reinfection rates and clinical outcomes was limited. Also, a clear obstacle in synthesizing the literature was that no consensus definition for shoulder PJI was utilized by these studies [2], and defining reinfection is highly variable in the literature, making the optimal implant of choice for treatment difficult to determine. It should be noted that this review does not include data based on duration of symptoms which may play an important role in choice of intervention.

Indications for Irrigation and Debridement

Irrigation and debridement (I&D) with component retention or exchange of modular components is often considered a reasonable option in acute PJI. This has variable outcomes in the literature with regards to reinfection rates and clinical outcomes (Table 2) [1,3–12]. When aggregated, these 11 studies report a **42% recurrence rate for acute PJI treated with I&D** (19 of 45 patients). Given this data, the surgeon must weigh the risks of recurrent infection with and morbidity of implant removal. The decision on whether to perform an I&D may also depend on the acuity of symptoms with some studies suggesting low recurrence when performed within 2 weeks of symptom onset, even when the time between index surgery and symptom onset is prolonged [6,12] (i.e., secondary hematogenous infection [13]).

Indications for Reverse Shoulder Arthroplasty

Conversion to reverse shoulder arthroplasty may be preferred to an anatomic implant in cases of rotator cuff deficiency and proximal humeral and or glenoid bone loss [6,14,15]. In the setting of a prosthetic shoulder infection, a thorough debridement is required and often necessitates resection of necrotic and infected tissue for adequate infection control. Both infection and soft tissue loss are associated with poor functional outcomes after revision arthroplasty, and implantation of an anatomic implant may not be able to sufficiently compensate for rotator cuff loss and/or instability [15–17]. A reverse implant may better compensate for soft tissue loss or bony deficiency [15,18] and can improve pain control and functional recovery without a high recurrent infection rate in some studies [4,19–22].

In some reports, treatment with a reverse shoulder arthroplasty as a treatment for failed arthroplasty is associated with sub-optimal functional results and a high rate of complication [23–30]. Therefore, hemiarthroplasty should be a consideration in cases in which minimizing complications and further surgery is a priority [31,32].

Indications for Hemiarthroplasty

In cases of acute PJI in a shoulder with an intact rotator cuff, revision to hemiarthroplasty is also a reasonable option with potentially similar results to reverse arthroplasty in the setting of infection [19,33,34]. In addition, in some cases of substantial glenoid bone loss, recurrent instability of a reverse and patient factors, such as

TABLE 1. Studies stratified by infection, acuity and implant type

Author	Journal	Year	Acuity			Procedure(s)	Final Implant					Reinfection By Implant Type	Functional By Implant Type
			Acute	*Subacute*	*Chronic*		*Hemi*	*TSA*	*Reverse*	*Spacer*	*Resection*		
Achermann	Infection	2013	4	5	7	I&D/partial Single-stage Two-stage	NOT DESCRIBED					1 of 4 recurrence with I&D for acute	No comparison of implant types
Amaravathi	Eur J Orthop Surg Traum	2012	8	22	14	I&D/partial Single-stage Two-stage Resection	2	1	23			unclear reinfection rate, 12 of 44 needed revision	No comparison of implant types
Assenmacher	JSES	2017	1	6	28	Two-stage	19	7	9			5 of 35 recurrence, not stratified by acuity/implant	Pain, FE, and ER similar hemi vs TSA vs reverse ($p = 0.76$)
Beekman	JBJS Br	2010	3	7	1	Single-stage			10	1		3 of 3 recurrence with I&D	Median CM 55
Boileau	JSES	2013	1	2	4	I&D/partial Single-stage Two-stage Resection			8		3	2 of 2 recurrence with I&D, uncertain acuity	Likely reverse only
Braman	JSES	2006	1	2	4	Resection					7	Resection only	Resection only
Buchalter	JSES	2017	NOT STRATIFIED			Two-stage	4	5	10			5 of 19 recurrence, not stratified by acuity/implant	No comparison of implant types
Cheung	CORR	2011	6	0	0	I&D/partial	8	4				2 of 6 recurrence	I&D 'unsatisfactory' in 5 or 12 post op hematoma; no implant types
Coste	JBJS Br	2004	12	6	24	Antibiotics only I&D/partial Single-stage Two-stage Resection	NOT STRATIFIED					2 of 2 recurrence with arthroscopic I&D 4 of 6 recurrence with open I&D - those that were undertaken earlier were successful	No comparison of implant types
Cuff	JBJS Br	2008	NOT STRATIFIED			Single-stage Two-stage			17			No recurrence	Mean ASES 57.0, pain 3.5, SST 4.0

TABLE 1. Studies stratified by infection, acuity and implant type (*Cont.*)

Author	Journal	Year	Acuity			Procedure(s)	Final Implant					Reinfection By Implant Type	Functional By Implant Type
DeBeer	Acta Orthop Belg	2006	NOT STRATIFIED			Resection					7	Resection only	Resection only
Foruria	JSES	2013	NOT STRATIFIED			I&D/partial	45	61	1			10% reucrrence but no stratification	No comparison of implant types
Ghijselings	Acta Orthop Belg	2013	5	7	5	Two-stage Abx spacer Resection			3	6	8	No differentiation between 'early' and 'acute hematog-enous'	Resection patients more satisfied than abx spacer
Grosso	JSES	2012	NOT STRATIFIED			Single-stage	2	7	8			No comparison of implant types	No comparison of implant types
Hsu	JBJS	2016	NOT STRATIFIED			Single-stage	33	14	1			No recurrence in hemi, TSA, or reverse	No comparison of implant types
Ince	JBJS Br	2005	NOT STRATIFIED			Single-stage	15		1			No recurrent in hemi or reverse	Mean CM 33.6, UCLA 18.3
Jahoda	Acta Chir Orthop	2008	1	3	7	I&D/partial Two-stage	NOT STRATIFIED					2 of 6 recur-rent with I&D (mixed acute and subacute)	n/a
Jawa	JBJS	2011	6	14	8	Abx spacer Two-stage	3	2	10	12	1	recurrence in 5 of 28 patients	Reverse: Flexion 74, 5 moderate pain, 5 severe pain TSA/hemi: Flexion 61, 4 mild pain, 1 moderate pain
Jerosch	Arch Orthop Trauma Surg	2003	UNCLEAR STRATIFICATION			I&D/partial Two-stage	NOT STRATIFIED					0 of 2 recurrence with early I&D	n/a
Kelly	CORR	2009	NOT STRATIFIED			Single-stage	1	3	24			No comparison of implant types	No comparison of implant types
Klatte	JBJS Br	2013	4	15	16	Single-stage	19		7			2 of 35 recurrence, acuity unknown	Hemi: CM 43.3 Hemi w bipolar head: CM 56 Reverse: CM 61

TABLE 1. Studies stratified by infection, acuity and implant type (*Cont.*)

Author	Journal	Year	Acuity			Procedure(s)	Final Implant					Reinfection By Implant Type	Functional By Implant Type
Lee	Int Ortho	2017	8	4	0	Two-stage	2		10			No recurrence in hemi or reverse	Pain 2.3, ASES 64.2, CM 66.1
Levy	Orthopedics	2015	NOT STRATIFIED			Spacer				9		No recurrence with abx spacer	Pain 2.0, SST 6.3, ASES 65.8, SANE 54.6
Mahure	Orthopedics	2016	NOT STRATIFIED			Spacer				9		No recurrence with abx spacer	ASES 57
Muh	JSES	2013	NOT STRATIFIED			Resection					22	n/a	n/a
Ortmaier	Eur J Orthop Surg Traum	2014	4	9	7	I&D/partial Two-stage Resection	1		14	1	4	2 of 4 recurrence with I&D in acute 3 of 3 recurrence with I&D in subacute	
Pellegrini	Arch Orthop Trauma Surg	2018	NOT STRATIFIED			I&D Abx spacer				19		no recurrence	CM 38.3, pain 1.5, FE 59.2, Abd 52.5
Rispoli	JBJS Br	2007	NOT STRATIFIED			Resection					18	no report of recurrence	ASES 36, SST 3.1
Romano	Int Ortho	2012	9	21	14	Two-stage Spacer Resection	NOT STRATIFIED					1 of 5 recurrence with I&D	Not stratified "Resection with poorest outcomes"
Sabesan	CORR	2011	8	7		Two-stage			17			1 of 17 recurrence with reverse	Penn 66.4, FE 123, ER 26
Sperling	CORR	2001	4	5	23	I&D/partial Two-stage Resection	NOT STRATIFIED					1 of 2 recurrence with I&D for acute 2 of 4 recurrence with I&D for subacute/chronic	n/a
Stevens	JSES	2015	NOT STRATIFIED			Resection					7	1 of 7 recurrence	n/a
Stine	JSES	2010	0	0	30	Spacer Two-stage	10	1	4	15		0 of 30 recurrence	Inadequate stratification to compare implant types

TABLE 1. Studies stratified by infection, acuity and implant type (*Cont.*)

Author	Journal	Year	Acuity			Procedure(s)	Final Implant					Reinfection By Implant Type	Functional By Implant Type
Stone	JSES	2017	NOT STRATIFIED			I&D/partial One-stage Two-stage	STRATIFICATOIN UNCLEAR					4 of 15 recurrence with I&D, uncertain acuity	
Strickland	JBJS Br	2008	3	7	9	Two-stage	13	5	1			7 of 19 recurrence with two-stage	No comparison of implant types
Themistocleous	JSES	2007	NOT STRATIFIED			Spacer				4		no stratification	n/a
Topolski	JSES	2006	NOT STRATIFIED			Single-stage	NOT STRATIFIED					n/a	n/a
Twiss	Seminars in Arthroplasty	2010	NOT STRATIFIED			Spacer Two-stage	STRATIFICATOIN UNCLEAR					0 of 30 recurrence	n/a
Verhelst	JSES	2011	0	4	17	Spacer Resection				10	11	2 of 21 reucrrence	Inadequate stratification to compare implant types
Weber	Int Ortho	2011	NOT STRATIFIED			I&D/partial Two-stage Resection	NOT STRATIFIED					0 of 1 recurrent for I&D	
Zavala	JSES	2012	5	2	0	I&D/partial Resection			5		2	1 of 4 recurrence with I&D	
Zhang	JSES	2015	NOT STRATIFIED			Two-stage	2	1	15				No comparison of implant types
			Acute	*Subacute*	*Chronic*		*Hemi*	*TSA*	*Reverse*	*Spacer*	*Resection*		
		TOTAL	**93**	**148**	**218**	**TOTAL**	**179**	**111**	**198**	**86**	**90**		
			20%	**32%**	**47%**		**27%**	**17%**	**30%**	**13%**	**14%**		

I&D; irrigation and debridement; TSA, total shoulder arthroplasty

TABLE 2. Success of I&D with component retention or exchange of modular components

Author	Journal	Year	No. Undergoing I&D	No. Recurrent Infection
Achermann	Infection	2013	4	1
Beekman	JBJS Br	2010	3	3
Cheung	CORR	2011	6	2
Coste	JBJS Br	2004	8	6
Jahoda	Acta Chir Orthop	2008	6	2
Jerosch	Arch Orthop Trauma Surg	2003	2	0
Ortmaier	Eur J Orthop Surg Traum	2014	4	2
Romano	Int Ortho	2012	5	1
Sperling	CORR	2001	2	1
Weber	Int Ortho	2011	1	0
Zavala	JSES	2012	4	1
TOTAL			**45**	**19**

noncompliance precluding implantation of a reverse, conversion to a hemiarthroplasty [32] may be the preferred choice to minimize intraoperative and postoperative complications [35].

Indications for Total Shoulder Arthroplasty

While better pain relief and functional scores can be obtained with total shoulder arthroplasty than hemiarthroplasty [36], the rate of polyethylene glenoid component loosening in the setting of revision is high [37]. In the setting of acute PJI, conversion to total shoulder should be strictly limited to cases in which the rotator cuff is fully intact, glenoid bone stock is sufficient, and bacterial burden is minimal.

In select cases, resection arthroplasty [38–42] and indefinite placement of an antibiotic spacer [43–45] can be considered for acute PJI.

REFERENCES

[1] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.

[2] Hsu JE, Somerson JS, Vo KV, Matsen FA. What is a "periprosthetic shoulder infection"? A systematic review of two decades of publications. Int Orthop. 2017;41:813–822. doi:10.1007/s00264-017-3421-6.

[3] Achermann Y, Sahin F, Schwyzer HK, Kolling C, Wüst J, Vogt M. Characteristics and outcome of 16 periprosthetic shoulder joint infections. Infection. 2013;41:613–620. doi:10.1007/s15010-012-0360-4.

[4] Beekman PDA, Katusic D, Berghs BM, Karelse A, De Wilde L. One-stage revision for patients with a chronically infected reverse total shoulder replacement. J Bone Joint Surg Br. 2010;92:817–822. doi:10.1302/0301-620X.92B6.23045.

[5] Cheung EV, Sperling JW, Cofield RH. Infection associated with hematoma formation after shoulder arthroplasty. Clin Orthop Relat Res. 2008;466:1363–1367. doi:10.1007/s11999-008-0226-3.

[6] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.

[7] Jahoda D, Pokorný D, Nyc O, Barták V, Hromádka R, Landor I, et al. [Infectious complications of total shoulder arthroplasty]. Acta Chir Orthop Traumatol Cech. 2008;75:422–428.

[8] Jerosch J, Schneppenheim M. Management of infected shoulder replacement. Arch Orthop Trauma Surg. 2003;123:209–214. doi:10.1007/s00402-003-0497-9.

[9] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.

[10] Romanò CL, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. Int Orthop. 2012;36:1011–1017. doi:10.1007/s00264-012-1492-y.

[11] Weber P, Utzschneider S, Sadoghi P, Andress H-J, Jansson V, Müller PE. Management of the infected shoulder prosthesis: a retrospective analysis and review of the literature. Int Orthop. 2011;35:365–373. doi:10.1007/s00264-010-1019-3.

[12] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. J Shoulder Elbow Surg. 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.

[13] Dennison T, Alentorn-Geli E, Assenmacher AT, Sperling JW, Sánchez-Sotelo J, Cofield RH. Management of acute or late hematogenous infection after shoulder arthroplasty with irrigation, débridement, and component retention. J Shoulder Elbow Surg. 2017;26:73–78. doi:10.1016/j.jse.2016.05.018.

[14] Hackett DJ, Hsu JE, Matsen FA. Primary shoulder hemiarthroplasty: what can be learned From 359 cases that were surgically revised? Clin Orthop Relat Res. 2018;476:1031–1040. doi:10.1007/s11999.0000000000000167.

[15] Hernandez NM, Chalmers BP, Wagner ER, Sperling JW, Cofield RH, Sanchez-Sotelo J. Revision to reverse total shoulder arthroplasty restores stability for patients with unstable shoulder prostheses. Clin Orthop Relat Res. 2017;475:2716–2722. doi:10.1007/s11999-017-5429-z.

[16] Kany J, Jose J, Katz D, Werthel J-D, Sekaran P, Amaravathi RS, et al. The main cause of instability after unconstrained shoulder prosthesis is soft tissue deficiency. J Shoulder Elbow Surg. 2017;26:e243–e251. doi:10.1016/j.jse.2017.01.019.

[17] Dines JS, Fealy S, Strauss EJ, Allen A, Craig EV, Warren RF, et al. Outcomes analysis of revision total shoulder replacement. J Bone Joint Surg Am. 2006;88:1494–1500. doi:10.2106/JBJS.D.02946.

[18] Cuff DJ, Pupello DR, Santoni BG, Clark RE, Frankle MA. Reverse shoulder arthroplasty for the treatment of rotator cuff deficiency: a concise follow-up, at a minimum of 10 years, of previous reports. J Bone Joint Surg Am. 2017;99:1895–1899. doi:10.2106/JBJS.17.00175.

[19] Klatte TO, Junghans K, Al-Khateeb H, Rueger JM, Gehrke T, Kendoff D, et al. Single-stage revision for peri-prosthetic shoulder infection: outcomes and results. Bone Joint J. 2013;95-B:391–395. doi:10.1302/0301-620X.95B3.30134.

[20] Cuff DJ, Virani NA, Levy J, Frankle MA, Derasari A, Hines B, et al. The treatment of deep shoulder infection and glenohumeral instability with debridement, reverse shoulder arthroplasty and postoperative antibiotics. J Bone Joint Surg Br. 2008;90:336–342. doi:10.1302/0301-620X.90B3.19408.

[21] Lee SH, Kim SJ, Kook SH, Kim JW. Two-stage revision of infected shoulder arthroplasty using prosthesis of antibiotic-loaded acrylic cement: minimum three-year follow-up. Int Orthop. 2018;42:867–874. doi:10.1007/s00264-017-3699-4.

[22] Sabesan VJ, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. Clin Orthop Relat Res. 2011;469:2538–2543. doi:10.1007/s11999-011-1774-5.

[23] Black EM, Roberts SM, Siegel E, Yannopoulos P, Higgins LD, Warner JJP. Reverse shoulder arthroplasty as salvage for failed prior arthroplasty in patients 65 years of age or younger. J Shoulder Elbow Surg. 2014;23:1036–1042. doi:10.1016/j.jse.2014.02.019.

[24] Flury MP, Frey P, Goldhahn J, Schwyzer H-K, Simmen BR. Reverse shoulder arthroplasty as a salvage procedure for failed conventional shoulder replacement due to cuff failure--midterm results. Int Orthop. 2011;35:53–60. doi:10.1007/s00264-010-0990-z.
[25] Groh GI, Groh GM. Complications rates, reoperation rates, and the learning curve in reverse shoulder arthroplasty. J Shoulder Elbow Surg. 2014;23:388–394. doi:10.1016/j.jse.2013.06.002.
[26] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.
[27] Jo SH, Kim JY, Cho NS, Rhee YG. Reverse total shoulder arthroplasty: salvage procedure for failed prior arthroplasty. Clin Orthop Surg. 2017;9:200–206. doi:10.4055/cios.2017.9.2.200.
[28] Melis B, Bonnevialle N, Neyton L, Lévigne C, Favard L, Walch G, et al. Glenoid loosening and failure in anatomical total shoulder arthroplasty: is revision with a reverse shoulder arthroplasty a reliable option? J Shoulder Elbow Surg. 2012;21:342–349. doi:10.1016/j.jse.2011.05.021.
[29] Stephens BC, Simon P, Clark RE, Christmas KN, Stone GP, Lorenzetti AJ, et al. Revision for a failed reverse: a 12-year review of a lateralized implant. J Shoulder Elbow Surg. 2016;25:e115–e124. doi:10.1016/j.jse.2015.09.027.
[30] Walker M, Willis MP, Brooks JP, Pupello D, Mulieri PJ, Frankle MA. The use of the reverse shoulder arthroplasty for treatment of failed total shoulder arthroplasty. J Shoulder Elbow Surg. 2012;21:514–522. doi:10.1016/j.jse.2011.03.006.
[31] Glanzmann MC, Kolling C, Schwyzer H-K, Audigé L. Conversion to hemiarthroplasty as a salvage procedure for failed reverse shoulder arthroplasty. J Shoulder Elbow Surg. 2016;25:1795–1802. doi:10.1016/j.jse.2016.03.011.
[32] Gamradt SC, Gelber J, Zhang AL. Shoulder function and pain level after revision of failed reverse shoulder replacement to hemiarthroplasty. Int J Shoulder Surg. 2012;6:29–35. doi:10.4103/0973-6042.96991.
[33] Assenmacher AT, Alentorn-Geli E, Dennison T, Baghdadi YMK, Cofield RH, Sánchez-Sotelo J, et al. Two-stage reimplantation for the treatment of deep infection after shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:1978–1983. doi:10.1016/j.jse.2017.05.005.
[34] Hsu JE, Gorbaty JD, Whitney IJ, Matsen FA. Single-stage revision is effective for failed shoulder arthroplasty with positive cultures for Propionibacterium. J Bone Joint Surg Am. 2016;98:2047–2051. doi:10.2106/JBJS.16.00149.
[35] Farshad M, Gerber C. Reverse total shoulder arthroplasty-from the most to the least common complication. Int Orthop. 2010;34:1075–1082. doi:10.1007/s00264-010-1125-2.
[36] Antuna SA, Sperling JW, Cofield RH, Rowland CM. Glenoid revision surgery after total shoulder arthroplasty. J Shoulder Elbow Surg. 2001;10:217–224. doi:10.1067/mse.2001.113961.
[37] Bonnevialle N, Melis B, Neyton L, Favard L, Molé D, Walch G, et al. Aseptic glenoid loosening or failure in total shoulder arthroplasty: revision with glenoid reimplantation. J Shoulder Elbow Surg. 2013;22:745–751. doi:10.1016/j.jse.2012.08.009.
[38] Muh SJ, Streit JJ, Lenarz CJ, McCrum C, Wanner JP, Shishani Y, et al. Resection arthroplasty for failed shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:247–252. doi:10.1016/j.jse.2012.05.025.
[39] Rispoli DM, Sperling JW, Athwal GS, Schleck CD, Cofield RH. Pain relief and functional results after resection arthroplasty of the shoulder. J Bone Joint Surg Br. 2007;89:1184–1187. doi:10.1302/0301-620X.89B9.19464.
[40] Stevens NM, Kim HM, Armstrong AD. Functional outcomes after shoulder resection: the patient's perspective. J Shoulder Elbow Surg. 2015;24:e247–e254. doi:10.1016/j.jse.2015.03.027.
[41] Debeer P, Plasschaert H, Stuyck J. Resection arthroplasty of the infected shoulder: a salvage procedure for the elderly patient. Acta Orthop Belg. 2006;72:126–130.
[42] Braman JP, Sprague M, Bishop J, Lo IK, Lee EW, Flatow EL. The outcome of resection shoulder arthroplasty for recalcitrant shoulder infections. J Shoulder Elbow Surg. 2006;15:549–553. doi:10.1016/j.jse.2005.11.001.
[43] Levy JC, Triplet J, Everding N. Use of a functional antibiotic spacer in treating infected shoulder arthroplasty. Orthopedics. 2015;38:e512–e519. doi:10.3928/01477447-20150603-60.
[44] Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Definitive treatment of infected shoulder arthroplasty with a cement spacer. Orthopedics. 2016;39:e924–e930. doi:10.3928/01477447-20160623-07.
[45] Pellegrini A, Legnani C, Macchi V, Meani E. Management of periprosthetic shoulder infections with the use of a permanent articulating antibiotic spacer. Arch Orthop Trauma Surg. 2018;138:605–609. doi:10.1007/s00402-018-2870-8.

3.6. TREATMENT: RESECTION

Authors: José M. Mora, Simon Lambert

QUESTION 1: What are the indications for resection shoulder arthroplasty in acute periprosthetic joint infection (PJI)?

RECOMMENDATION: There are no available reports on resection shoulder arthroplasty for acute PJI. At this time there is no evidence to routinely recommend this treatment for this indication.

LEVEL OF EVIDENCE: No Evidence

DELEGATE VOTE: Agree: 88%, Disagree: 8%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

Search Strategy

A request via the Royal Society of Medicine Library utilizing ProQuest Dialog, searching Embase and Medline archives. Search terms: (excision arthroplasty) OR (resection arthroplasty) AND (acute periprosthetic infection) OR (chronic periprosthetic infection) OR (subacute periprosthetic infection). Yielded 1,649 references. After limiting these to shoulder-specific references and eliminating duplicates 100 references were further searched for exact matching to the question of the role of resection arthroplasty in the management of acute PJI (subacute or chronic PJI). All full papers, reviews and abstracts in English between 1990 and 2018 were examined, and those reporting the indications and outcomes of resection (excision) arthroplasty of the shoulder were examined further. Personal searches of PubMed archives were performed by both authors using the same criteria, and their searches were compared. The bibliographies of two recent reviews (one specifically examining the question of resection, the value of spacers and one-and two-stage revision arthroplasty in subacute or chronic PJI [1], the other a more general review [2]) were examined for further references and cross-checked with the first enquiry and the personal searches.

No manuscripts were identified which reported on resection shoulder arthroplasty for acute PJI.

Conclusion

The available literature has no evidence pertaining to resection arthroplasty in acute shoulder PJI to provide guidance on this question.

REFERENCES

[1] George DA, Volpin A, Scarponi S, Haddad FS, Romanò CL. Does exchange arthroplasty of an infected shoulder prosthesis provide better eradication rate and better functional outcome, compared to a permanent spacer or resection arthroplasty? a systematic review. BMC Musculoskelet Disord. 2016;17:52. doi:10.1186/s12891-016-0901-6.

[2] Bonnevialle N, Dauzères F, Toulemonde J, Elia F, Laffosse J-M, Mansat P. Periprosthetic shoulder infection: an overview. EFORT Open Rev. 2017;2:104–109. doi:10.1302/2058-5241.2.160023.

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QUESTION 2: Is there a role for resection shoulder arthroplasty in the management of subacute or chronic periprosthetic joint infection (PJI)?

RECOMMENDATION: The available literature does not support specific indications for resection arthroplasty for subacute or chronic shoulder PJI with sufficient quality information to provide guidance. Resection arthroplasty is an acceptable salvage treatment to eradicate shoulder PJI when revision to a definitive implant is considered too risky due to patient medical co-morbidities or technical complexity.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 95%, Disagree: 0%, Abstain: 5% (Unanimous, Strongest Consensus)

RATIONALE

There are no prospective studies or randomized trials on this topic, and all published reports are retrospective case series. In addition, many of these case series include no other cohort to directly compare against any other form of treatment strategy for infected shoulder arthroplasty. The available literature is further limited by the fact that all published series examine outcomes using a variety of methods: (a) pain relief, recorded either as a subset of a score, e.g., the Constant-Murley (CMS) or American Shoulder and Elbow Surgeons (ASES) scores, or as a visual analog scale (VAS); (b) function, recorded either as a subset of a score, or by direct description; (c) management of infection, recorded as either "eradicated," "recurrent" or "persistent" (with no clear definition on how these categories was diagnosed/confirmed).

The systematic review of management strategies for shoulder PJI by George et al. [1] found 8 papers (total number of cases, 83) relating to the use of resection arthroplasty. The number of cases reported per series varied between 5 and 21 with a mean duration of follow-up of post-resection 39.8 months (standard deviation 20.8), minimum 19.2 (9.4), maximum 102.6 (41.9). The number of infections considered eradicated was 72/83 (86.7%) with no difference (statistical or clinically meaningful) in infection eradication observed between resection, single-stage, two-stage and permanent spacer arthroplasty. Preoperative and postoperative functional scores were incompletely reported. Single-stage revision cases had better preoperative scores than other groups, and better outcomes. It should be noted that patients reported worse functional scores (CMS) after surgery than before surgery, particularly for resection arthroplasty. There was no consistency in the choice or duration of antibiotic administration after surgery. Importantly, the authors pointed out that the limited quality of the available literature meant that it was not possible to provide a conclusion concerning the indication for one modality over another if the aim of intervention was to eradicate infection while optimizing the functional outcome for patients.

When reviewing the available literature, it should be noted that the majority of PJI for which resection is reported as an outcome are reverse total shoulder arthroplasties [2–4]. It is not clear whether this relates to the more challenging reconstructions often encountered after revision reverse total shoulder arthroplasty (TSA) or perhaps the nature of the reverse TSA patient population who tend to have more medical comorbidities and lower functional demands.

Patient outcomes including eradication of infection, pain relief and function were reported using variable standards. The concept that resection arthroplasty carries the advantage of being "one final surgery" should be tempered by the results showing that, on average, two debridements were required for infection to be clinically eradicated (mean follow-up 20 months) [5]. Braman et al. [5] showed that in their series of seven patients, while the functional scores were generally poor, all patients were able to perform activities between the mouth, opposite axilla and perineum and were satisfied with the outcome. Other authors, however, have shown that patient satisfaction is poor overall. Rispoli et al. reported one-third of cases falling into the lower third of categories for satisfaction, and 16 of 18 cases having an unsatisfactory outcome by Neer criteria [6]. If preoperative impairment was not substantial (defined as a CMS of greater than 30) then there was no significant improvement after surgery [2]. The same authors considered that reimplantation (whether one- or two-stage) delivered better functional outcomes than resection arthroplasty [2]. Zavala et al. (2012) concluded that resection was inferior to a debridement, antibiotics, irrigation and implant retention (DAIR) strategy in providing for function without increasing the risk of persistent or recurrent infection at a minimum of 12 months follow-up, while also commenting that implant retrieval lead to (potentially) revision-limiting bifocal bone loss [7]. DeBeer et al. recommended resection be indicated for the elderly with PJI and with lower functional expectations [8]. A single comparative study comparing resection with staged reimplantaion demonstrated that there was benefit for range of motion if a staged reimplantation could be safely undertaken with no increased risk of persistent or recurrence of infection [9]. This study was presented at the American Academy of Orthopaedic Surgeons (AAOS) and does not appear to have been published elsewhere. Resection arthroplasty for subacute or chronic PJI may some provide pain relief in approximately one-third to one-half of cases [3,6,7,10–12].

There are some technical and prognostic factors which may effect patient functional outcome and satisfaction. Retention of the tuberosities appears useful for function, possibly by reducing the tendency for proximal humeral migration [12]. In addition, there is some debate regarding how an antibiotic spacer may compare with resection alone with respect to eradication of infection and function. Verhelst et al. reported that use of a spacer (permanent

TABLE 1. Articles specifically concerning resection arthroplasty in shoulder PJI, with details as noted

Author	Year	n	Failed	CMS	SST	Surgery Prior to Resection (N)	VAS	ASES	FE	Abd	ER
Verhelst	2011	11E	2/11	40.4			2.6		85.5°	78.1°	21°
		10 EAS									
Rispoli	2017	18 E			3.1		4.5	36	70°		31°
Stevens	2015	4 E	1/4		3.3	2 cases = 3 2 cases > 5	8.8	20.8	63°		25°
		4 EAS	0		6	1.5	0.4	69	85°		30°
Maynoud	2006	10 E	0	28							
Braman	2006	7 E	0			2.2			28°		8°
Ghijselings	2013	8 E		27.8	2.4		3.6				
		5 EAS		20.6	1		6				

NB: many data are incomplete since not all ideal data were recorded by the authors (see [6]). In three studies there are comparison cases of explantation and antibiotic spacer (EAS) and explantation alone (E) [1,13,14,16].

or temporary) did not appear to compromise eradication of infection but also did not necessarily confer benefit for function or pain relief postoperatively [13]. In contrast, Ghijselings in a comparative series evaluating resection with resection plus antibiotic-impregnated spacer reported a differential benefit for spacer with regard to domestic activities, but overall functional scores and pain relief were no different [14]. In the setting of bilateral pathology, Ueda et al. concluded there is improved function for domestic activities with bilateral retained antibiotic spacers when compared with historical reports of resection arthroplasties for PJI [15].

In summary, the functional result is relatively poor, but the eradication of infection is quite good (86.7%), especially considering that in these non-randomized studies patients with resection arthroplasty are likely frail and/or have difficult to treat pathogens [1]. It remains unclear whether a resection arthroplasty is preferred versus a retained antibiotic-impregnated cement spacer, with some studies suggesting a modestly better functional result with the spacer. Resection arthroplasty is an acceptable salvage treatment when revision to a definitive implant is considered too risky due to patient medical co-morbidities or technical complexity of revision surgery.

Search Strategy

A request via the Royal Society of Medicine Library utilising ProQuest Dialog, searching Embase and Medline archives with search terms (excision arthroplasty) OR (resection arthroplasty) AND (acute periprosthetic infection) OR (chronic periprosthetic infection) OR (subacute periprosthetic infection) yielded 1649 references. After limiting these to shoulder-specific references and eliminating duplicates, 100 references were further searched for exact matching to the question of the role of resection arthroplasty in the management of subacute/chronic PJI (SA/C PJI). All full papers, reviews and abstracts in English between 1990 and 2018 were examined, and those reporting the indications and outcomes of resection (excision) arthroplasty of the shoulder were examined further.

Personal searches of PubMed archives were performed by both authors using the same criteria, and their searches were compared. The bibliographies of two recent reviews (one specifically examining the question of resection, the value of spacers and one-and two-stage revision arthroplasty in subacute/chronic PJI [1], the other a more general review [17]) were examined for further references and cross-checked with the first enquiry and the personal searches. This strategy was compared with that of the most useful review [1] for completeness.

In Stevens et al. [16], there were seven patients available – eight cases (four explantation and four explantation and antibiotic spacer). In mobility there were three cases with data not available. In relation to "failed," there was only one case following explantation alone, which equates to 25% as a proportion of the group, or 12.5% as a proportion of all cases in this series.

REFERENCES

[1] George DA, Volpin A, Scarponi S, Haddad FS, Romanò CL. Does exchange arthroplasty of an infected shoulder prosthesis provide better eradication rate and better functional outcome, compared to a permanent spacer or resection arthroplasty? a systematic review. BMC Musculoskelet Disord. 2016;17:52. doi:10.1186/s12891-016-0901-6.

[2] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.

[3] Muh SJ, Streit JJ, Lenarz CJ, McCrum C, Wanner JP, Shishani Y, et al. Resection arthroplasty for failed shoulder arthroplasty. J Shoulder Elbow Surg. 2013;22:247–252. doi:10.1016/j.jse.2012.05.025.

[4] Romanò CL, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. Int Orthop. 2012;36:1011–1017. doi:10.1007/s00264-012-1492-y.

[5] Braman JP, Sprague M, Bishop J, Lo IK, Lee EW, Flatow EL. The outcome of resection shoulder arthroplasty for recalcitrant shoulder infections. J Shoulder Elbow Surg. 2006;15:549–553. doi:10.1016/j.jse.2005.11.001.

[6] Rispoli DM, Sperling JW, Athwal GS, Schleck CD, Cofield RH. Pain relief and functional results after resection arthroplasty of the shoulder. J Bone Joint Surg Br. 2007;89:1184–1187. doi:10.1302/0301-620X.89B9.19464.

[7] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. J Shoulder Elbow Surg. 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.

[8] Debeer P, Plasschaert H, Stuyck J. Resection arthroplasty of the infected shoulder: a salvage procedure for the elderly patient. Acta Orthop Belg. 2006;72:126–130.

[9] Codd T, Yamaguchi K, Pollock R, Flatow EL, Bigliani LU. Infected shoulder arthroplasties: treatment with staged reimplantation vs resection arthroplasty. Orthop Trans. 1996:20:59.
[10] Charalambous CP, Saidapur S, Alvi F, Haines J, Trail I. Excision arthroplasty following shoulder replacement. Acta Orthop Belg. 2011;77:448–452.
[11] Maynou C, Ménager S, Senneville E, Bocquet D, Mestdagh H. [Clinical results of resection arthroplasty for infected shoulder arthroplasty]. Rev Chir Orthop Reparatrice Appar Mot. 2006;92:567–574.
[12] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.
[13] Verhelst L, Stuyck J, Bellemans J, Debeer P. Resection arthroplasty of the shoulder as a salvage procedure for deep shoulder infection: does the use of a cement spacer improve outcome? J Shoulder Elbow Surg. 2011;20:1224–1233. doi:10.1016/j.jse.2011.02.003.
[14] Ghijselings S, Stuyck J, Debeer P. Surgical treatment algorithm for infected shoulder arthroplasty: a retrospective analysis of 17 cases. Acta Orthop Belg. 2013;79:626–635.
[15] Ueda Y, Comer GC, Saleh JR, Costouros JG. Simultaneous bilateral resection total shoulder arthroplasty with anatomic antibiotic cement spacer retention. JSES Open Access. 2017;1:129–132. doi:10.1016/j.jses.2017.07.003.
[16] Stevens NM, Kim HM, Armstrong AD. Functional outcomes after shoulder resection: the patient's perspective. J Shoulder Elbow Surg. 2015;24:e247–e254. doi:10.1016/j.jse.2015.03.027.
[17] Bonnevialle N, Dauzères F, Toulemonde J, Elia F, Laffosse J-M, Mansat P. Periprosthetic shoulder infection: an overview. EFORT Open Rev. 2017;2:104–109. doi:10.1302/2058-5241.2.160023.

3.7. TREATMENT: REVISION

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QUESTION 1: Is there a role for an antibiotic spacer for the treatment of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: An antibiotic loaded cement spacer may be used as part of a shoulder two-stage exchange arthroplasty for local delivery of high concentration of antibiotics. An antibiotic loaded cement spacer may be used as a definitive/permanent treatment option in select cases.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Antibiotic loaded cement spacers can be used in the management of infected shoulder arthroplasty [1–4]. The antibiotic loaded cement spacer delivers antibiotics to the local tissues, eliminates dead space, maintains soft tissue tension and shoulder function and is used for these reasons as a temporary spacer in two-stage reimplantation for infected shoulder arthroplasty [2,3]. Less commonly, it can be considered as a permanent/definitive spacer if the patient declines further surgery or if the patient is not a good surgical candidate for the second stage of two-stage reimplantation (e.g., sick patient, significant bone loss) [5–8].

The role of antibiotic loaded cement spacer in shoulder PJI has been studied previously in retrospective cohort studies (Table 1). An antibiotic loaded cement spacer is indicated as a temporary spacer in the two-stage treatment of shoulder PJI in conjunction with intravenous antibiotics [2,3]. However, use as a definite/permanent spacer has also been described as a treatment for patients who are a high surgical risk or refuse second stage of two-stage treatment [5–7]. Jawa et al. reported a retrospective review of 28 patients with infected shoulder arthroplasty who were managed with antibiotic loaded cement spacer [2]. Sixteen patients underwent a two-stage operation, and twelve patients declined second stage procedure. Five patients had recurrence of infection (18%), and 5 patients had severe pain (18%) at final follow up. Complications with the use of cement spacer included dislocation (1 patient) and fracture (3 patients). Torrens et al. reported a culture positive rate of 13.6% (3 shoulders) from 22 antibiotic loaded cement spacers retrieved during second stage reimplantation [9]. In contrast to studies by Jawa et al. and Torrens et al., other investigators have reported lower rates of recurrence of infection with antibiotic loaded cement spacer use. Pellegrini et al. reported no recurrence of infection with a definitive antibiotic spacer in a cohort of 19 low demand, elderly subjects who had infected shoulder arthroplasties [6]. At a mean follow up of 8 years, all patients reported satisfactory subjective and objective outcomes. One patient had glenoid osteolysis with no adverse effect on functional outcome. Levy et al. retrospectively reviewed outcomes in 9 patients with infected shoulder arthroplasty who elected to not have the second stage reimplantation [7]. These patients had acceptable function with their antibiotic spacers at a mean follow up of 25 months. There was no recurrence of infection (0%) and only one patient (11%) was unsatisfied with the results. Mahure et al. reported no recurrence of infection (0%) in a retrospective case series of patients with shoulder PJI who received an antibiotic loaded cement spacer as definitive treatment after first stage of the two-stage treatment [5,10]. In a retrospective study, Romano et al. reviewed 44 patients with infected shoulder arthroplasty of which 32 patients had treatment with a temporary or permanent antibiotic loaded spacer [11]. There was one recurrence of infection in the definitive spacer group. Lee et al. used an antibiotic loaded cement spacer for the first stage implantation in 12 patients with infected shoulder arthroplasty. All patients received intravenous antibiotics followed by the second stage treatment [12]. There was no recurrence of infection (0%) at mean follow up of 41 months. Improved functional outcomes with the use of antibiotic loaded cement spacer was reported by Jerosch et al. in a retrospective review of 10 patients with shoulder PJI [13]. Patients were able to perform physical therapy with the antibiotic spacer in situ, and 8 patients underwent second stage with no reported recurrence of infection.

There is no consensus on the optimal class of antibiotics to be used in spacer preparation. Heat stable antibiotics (vancomycin, gentamycin and tobramycin) have been used alone or in combination. Spacer design and patient-specific anatomic features have also been studied with regards to infection clearance and patient satis-

TABLE 1. Studies examining the role of antibiotic loaded cement spacer in treatment of infected shoulder arthroplasty

Study	Number of Patients / Shoulders (n) and Follow-up (FU)	Antibiotics Used in the Cement Spacer	Spacer Role	Recurrence of Infection and Complications Associated with Spacer
Jerosch and Schneppenheim, 2003	n = 10 FU:6-30 mos (range)	No information	Temporary: 8 Permanent: 2	Recurrence: 0%
Themistocleous et al., 2007	n = 4 FU:22 mos	Tobramycin Vancomycin	Temporary: 2 Permanent: 2	Recurrence: 0%
Coffey et al., 2010	n = 16 FU:20.5 mos	Gentamicin	Temporary: 12 Permanent: 4	Recurrence: 0%
Jawa et al., 2010	n = 28 FU= 27.6 mos	Tobramycin Vancomycin	Temporary: 16 Permanent: 12	Recurrence: 5 (18%) Dislocation: 1 (3.5%) Fracture of spacer: 3 (11%)
Stine et al., 2010	n = 30 FU: 2.4 yrs	Tobramycin Vancomycin	Temporary: 18 Permanent: 15	Recurrence: 0%
Romano et al., 2012	n = 32 FU:2.4 yrs	No information	Temporary: 17 Permanent: 15	Recurrence: 3% (one in permanent group)
Levy et al., 2014	n = 9 FU:25 mos	Tobramycin Vancomycin	Permanent	Recurrence: 0%
Mahure et al., 2016	n = 9 FU:4 yrs	Tobramycin Vancomycin Gentamycin	Permanent	Recurrence: 0% Glenoid erosion: 2 (22%) Periprosthetic fracture: 1 (11%)
Pellegrini et al., 2017	n = 19 FU:8 yrs	Gentamycin, Clindamycin, Vancomycin	Permanent	Recurrence: 0% Glenoid osteolysis (1; 5.3%)
Padegimas et al., 2018	n = 37 FU:4 yrs	Tobramycin Vancomycin	Temporary	Spacer revision: 1 (2.7%) 6 positive cultures at second stage but no clinical signs of infection
Lee et al., 2018	n = 12 FU:40.8 mos	Vancomycin	Temporary: 9	Recurrence: 0%
Torrens et al., 2018	n = 21	Tobramycin	Temporary	Revision of spacer: 1 3 Positive cultures at second stage (13.6%)

faction. Padegimas et al. retrospectively compared stemless and stemmed antibiotic spacers in a cohort of 37 patients with shoulder PJI [14]. They found no difference between the two types of spacers with respect to their ability to control infection and the percentage transition (70% in both groups) to the second stage of a two-stage procedure for infected shoulder arthroplasty. There is insufficient date to compare handmade versus commercial premade antibiotic loaded cement spacers.

An antibiotic loaded cement spacer is a reasonable treatment option as a temporary antibiotic spacer in conjunction with intravenous antibiotics for the two-stage treatment of shoulder PJI. The majority of studies report no recurrence of infection after revision to second stage. Use of an antibiotic loaded cement spacer as a definitive/permanent treatment can be considered for a low demand, debilitated patient who is a poor surgical candidate for second stage reimplantation or in cases where patient refuses second stage surgery. There is low rate of infection (5%) with acceptable functional outcome, but glenoid osteolysis is a concern with the use of cement spacer as a definitive treatment. There is no consensus on the ideal class of antibiotic (vancomycin versus aminoglycosides) to be used in cement spacers. There is insufficient data to compare hand-made versus commercial premade antibiotic spacers.

Search Methods

In order to establish guidelines for the use of an antibiotic loaded cement spacer in infected shoulder arthroplasty, a systematic review of literature on PubMed and Embase was performed of all English

literature till January 2018 to query, "(shoulder OR 'upper extremity') AND (arthroplasty OR replacement) AND (infection OR infected) AND (PROSTALAC OR ANTIBIOTIC SPACER). After excluding duplicates, a total of 34 articles were screened, and 16 studies focusing on use of an antibiotic loaded cement spacer as a temporary or permanent spacer were extracted for further review. After applying final exclusion ("one-stage revision," "antibiotic suppression") and inclusion criteria, a full text review of the articles was conducted, and 12 articles were selected for final analysis. All the articles evaluated the role of antibiotic loaded cement spacer for the treatment of shoulder PJI [2–14].

REFERENCES

[1] Mook WR, Garrigues GE. Diagnosis and management of periprosthetic shoulder infections. J Bone Joint Surg Am. 2014;96:956–965. doi:10.2106/JBJS.M.00402.

[2] Jawa A, Shi L, O'Brien T, Wells J, Higgins L, Macy J, et al. Prosthesis of antibiotic-loaded acrylic cement (PROSTALAC) use for the treatment of infection after shoulder arthroplasty. J Bone Joint Surg Am. 2011;93:2001–2009. doi:10.2106/JBJS.J.00833.

[3] Grubhofer F, ImamMD MA, Wieser K, Achermann Y, Meyer DC, Gerber C. Staged revision with antibiotic spacers for shoulder prosthetic joint infections yields high infection control. Clin Orthop Relat Res. 2018;476:146–152. doi:10.1007/s11999.0000000000000049.

[4] Coffey MJ, Ely EE, Crosby LA. Treatment of glenohumeral sepsis with a commercially produced antibiotic-impregnated cement spacer. J Shoulder Elbow Surg. 2010;19:868–873. doi:10.1016/j.jse.2010.01.012.

[5] Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Definitive treatment of infected shoulder arthroplasty with a cement spacer. Orthopedics. 2016;39:e924–e930. doi:10.3928/01477447-20160623-07.

[6] Pellegrini A, Legnani C, Macchi V, Meani E. Management of periprosthetic shoulder infections with the use of a permanent articulating antibiotic spacer. Arch Orthop Trauma Surg. 2018;138:605–609. doi:10.1007/s00402-018-2870-8.

[7] Levy JC, Triplet J, Everding N. Use of a functional antibiotic spacer in treating infected shoulder arthroplasty. Orthopedics. 2015;38:e512–e519. doi:10.3928/01477447-20150603-60.

[8] Themistocleous G, Zalavras C, Stine I, Zachos V, Itamura J. Prolonged implantation of an antibiotic cement spacer for management of shoulder sepsis in compromised patients. J Shoulder Elbow Surg. 2007;16:701–705. doi:10.1016/j.jse.2007.02.118.

[9] Torrens C, Santana F, Puig L, Sorli L, Alier A. Results of cement spacer sonication in the second stage of two-stage treatment of shoulder arthroplasty infection. J Orthop Surg Res. 2018;13:58. doi:10.1186/s13018-018-0763-8.

[10] Stine IA, Lee B, Zalavras CG, Hatch G, Itamura JM. Management of chronic shoulder infections utilizing a fixed articulating antibiotic-loaded spacer. J Shoulder Elbow Surg. 2010;19:739–748. doi:10.1016/j.jse.2009.10.002.

[11] Romanò CL, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. Int Orthop. 2012;36:1011–1017. doi:10.1007/s00264-012-1492-y.

[12] Lee SH, Kim SJ, Kook SH, Kim JW. Two-stage revision of infected shoulder arthroplasty using prosthesis of antibiotic-loaded acrylic cement: minimum three-year follow-up. Int Orthop. 2018;42:867–874. doi:10.1007/s00264-017-3699-4.

[13] Jerosch J, Schneppenheim M. Management of infected shoulder replacement. Arch Orthop Trauma Surg. 2003;123:209–214. doi:10.1007/s00402-003-0497-9.

[14] Padegimas EM, Narzikul A, Lawrence C, Hendy BA, Abboud JA, Ramsey ML, et al. Antibiotic spacers in shoulder arthroplasty: comparison of stemmed and stemless implants. Clin Orthop Surg. 2017;9:489–496. doi:10.4055/cios.2017.9.4.489.

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QUESTION 2: What are the indications for one- versus two-stage exchange arthroplasty in the management of acute shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Unknown. Single-stage exchange for shoulder PJI had a statistically significant lower reinfection rate and lower complication rate than two-stage exchange in aggregate; however, no studies exist directly comparing these treatments for acute shoulder PJI.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 4%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

A comprehensive literature review was performed to identify all studies on revision shoulder arthroplasty for PJI. Terms used for the search included "infection," "shoulder replacement," "arthroplasty," "1-stage," "2-stage," "reimplantation," "prosthetic-related infection" and included "resection," "spacer" or "exchange" among others using PubMed, Scopus and Embase through February 2018. Inclusion criteria for our systematic review were all English studies (Level I-IV evidence) that reported on single or two-stage revision, infection eradication for revision shoulder arthroplasty with a minimum follow up of twelve-months and minimum of five patients for analysis. Exclusion criteria for our review were all non-English studies, papers that exclude single or two-stage exchange, review papers, case reports or technique articles without outcome data. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were applied. Title and abstract screening was conducted through 248 results; full text review was conducted with 66 results and produced 31 articles that met inclusion and exclusion criteria for review.

Shoulder PJI is a devastating complication with significant morbidity. The incidence of PJI after primary shoulder arthroplasty has reported ranges of 1-4% and up to 4-15% after revision arthroplasty [1,2]. Historically, treatment for shoulder PJI has been influenced by evidence from hip and knee arthroplasty infection management experience [3,4]. Two-stage exchange arthroplasty with implant removal, irrigation and debridement (I&D), and insertion of antibiotic spacer, followed by delayed re-implantation has been suggested as gold standard for shoulder PJI [3]. However, single-stage exchange has also been advocated to achieve similar infection control with a single surgery [5–7]. The purpose for this review was to understand the roles of single-stage and two-stage exchange revision in the setting of acute shoulder PJI and compare the outcomes.

In this review, varying studies collected demographics, timing of infection, associated pathogens, surgical treatment, antibiotics, eradication rate for infection, surgical complications and functional outcomes with two-year follow-up minimum. We identified 12 articles that evaluated one-stage exchange and 27 articles that evaluated two-stage exchange.

While the definition and diagnosis of shoulder PJI is beyond the scope of this review, it should be noted that the majority of papers reported using preoperative laboratory values (including elevated white blood cell count, C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)), as well as joint aspiration and/or intra-

TABLE 1. Reinfection and complication

One-Stage	Patients	Reinfection %	Pathogens	Constant Score	Complications
12 Papers	161 Total	5.6% Reinfection	72 P. acnes	49.1	12.70%
	6 Acute	$p < 0.05$	29 CoNS	44 Patients	79 Patients
	13 Subacute		20 MSSA	$p < 0.11$	$p < 0.05$
	8 Chronic		3 MRSA		
Two-Stage	**Patients**	**Reinfection %**	**Pathogens**	**Constant Score**	**Complications**
27 Papers	325 Patients	11.4%	88 P. acnes	51.1	21.90%
	47 Acute	$p < 0.05$	64 CoNS	102 Patients	205 Patients
	46 Subacute		33 MRSA	$p < 0.05$	$p < 0.05$
	74 Chronic		56 MSSA		

operative cultures with bacterial growth to arrive at the diagnosis of shoulder PJI. Clinical findings, such as draining sinus, erythema or swelling, were inconsistently reported. There was inconsistent reporting and definition of the timing of infection as acute, sub-acute or chronic. The majority of studies report timing of infection using terms from Sperling et al. and Strickland et al. with acute meaning < 3 months, sub-acute meaning 3-12 months and chronic > 12 months [8, 9]. There was relatively consistent reporting of the pathogens found either pre- or intraoperatively. *Cutibacterium acnes* (*C. acnes*) was the most common organism identified with 160 cases or 32.9% of all cases followed by *Coagulase-negative Staphylococcus* (CoNS) with 93 cases or 19.1% [2,4,7–15]. There were 57 reported cases of poly-microbial infections and 27 cultures that resulted in no growth [4,7,10–12].

To address the stated question, we reviewed data on acute shoulder PJI pertaining to infection eradication using single or two-stage exchange and additional functional outcomes, which are summarized in Tables 1 and 2. In total, 161 cases were identified as treated with single-stage revision and 325 cases of two-stage revision. The majority of studies report timing of infection but few report the success of treatment with either single or two-stage exchange based on timing of infection. Beekman et al. performed analysis on three cases of acute PJI treated with single-stage exchange showing no cases with reinfection [5]. Two additional studies with a total of three cases of acute PJI found no patients had reinfection [6,10]. With two-stage exchange, Buchalter et al. [16] described 1 case of acute PJI that had no reinfection. Another study reported 1 case of acute PJI that failed treatment with two-stage exchange and had persistent infection. In total, four studies reported no cases of reinfection with two-stage exchange with specific analysis of an acute PJI subgroup.

This review has highlighted gaps that exist in current literature. All studies identified were retrospective and thus have substantial selection bias. While the findings in aggregate suggest single-stage exchange is a viable option for PJI, the numbers were small, and there are no studies that control for various risk factors and selection biases such as the particular pathogen, its antibiotic resistance profile, timing of infection or diagnostic features such as obvious clinical findings of infection. Furthermore, there are insufficient numbers of studies that provide analysis for treatment of acute

TABLE 2. Functional outcome

One-Stage	Neer (total)	ASES (mean)	SST (mean)	DASH	FF (mean)	ABD (mean)	ER (mean)
12 Papers	1,7,2	60.5	7.8	N/A	78.2	52.4	25.4
	10 Patients	50 Patients	27 Patients	None	57 Patients	42 Patients	59 Patients
Two-Stage	**Neer (total)**	**ASES (mean)**	**SST (mean)**	**DASH**	**FF (mean)**	**ABD (mean)**	**ER (mean)**
	22,33,32	67.6	4.1	57.7	98.9	52.4	29.2
	87 Patients	101 Patients	32 Patients	15 Patients	194 Patients	72 Patients	144 Patients

shoulder PJI using either single or two-stage exchange with regard to complications or functional outcomes.

REFERENCES

[1] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. J Bone Joint Surg Br. 2004;86:65–69.
[2] Padegimas EM, Maltenfort M, Ramsey ML, Williams GR, Parvizi J, Namdari S. Periprosthetic shoulder infection in the United States: incidence and economic burden. J Shoulder Elbow Surg. 2015;24:741–746. doi:10.1016/j.jse.2014.11.044.
[3] George DA, Volpin A, Scarponi S, Haddad FS, Romanò CL. Does exchange arthroplasty of an infected shoulder prosthesis provide better eradication rate and better functional outcome, compared to a permanent spacer or resection arthroplasty? a systematic review. BMC Musculoskelet Disord. 2016;17:52. doi:10.1186/s12891-016-0901-6.
[4] Nelson GN, Davis DE, Namdari S. Outcomes in the treatment of periprosthetic joint infection after shoulder arthroplasty: a systematic review. J Shoulder Elbow Surg. 2016;25:1337–1345. doi:10.1016/j.jse.2015.11.064.
[5] Beekman PDA, Katusic D, Berghs BM, Karelse A, De Wilde L. One-stage revision for patients with a chronically infected reverse total shoulder replacement. J Bone Joint Surg Br. 2010;92:817–822. doi:10.1302/0301-620X.92B6.23045.
[6] Ince A, Seemann K, Frommelt L, Katzer A, Loehr JF. One-stage exchange shoulder arthroplasty for peri-prosthetic infection. J Bone Joint Surg Br. 2005;87:814–818. doi:10.1302/0301-620X.87B6.15920.
[7] Klatte TO, Junghans K, Al-Khateeb H, Rueger JM, Gehrke T, Kendoff D, et al. Single-stage revision for peri-prosthetic shoulder infection: outcomes and results. Bone Joint J. 2013;95-B:391–395. doi:10.1302/0301-620X.95B3.30134.
[8] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.
[9] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. J Bone Joint Surg Br. 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.
[10] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.
[11] Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Definitive treatment of infected shoulder arthroplasty with a cement spacer. Orthopedics. 2016;39:e924–e930. doi:10.3928/01477447-20160623-07.
[12] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.
[13] Sabesan VJ, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. Clin Orthop Relat Res. 2011;469:2538–2543. doi:10.1007/s11999-011-1774-5.
[14] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.
[15] Weber P, Utzschneider S, Sadoghi P, Andress H-J, Jansson V, Müller PE. Management of the infected shoulder prosthesis: a retrospective analysis and review of the literature. Int Orthop. 2011;35:365–373. doi:10.1007/s00264-010-1019-3.
[16] Buchalter DB, Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Two-stage revision for infected shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:939–947. doi:10.1016/j.jse.2016.09.056.

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QUESTION 3: What are the indications for one- versus two-stage revision in subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: The indications for one-stage versus two-stage exchange are unclear at this time. The pooled data demonstrate one-stage exchange to be superior to two-stage exchange, but this may be a result of selection bias and other factors.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

A comprehensive literature review was performed to identify all studies on revision shoulder arthroplasty for periprosthetic joint infection (PJI). Terms used for the search included "infection," "shoulder replacement," "arthroplasty," "1-stage," "2-stage," "reimplantation," "prosthetic-related infection" and included "resection," "spacer" or "exchange" among others using PubMed, Scopus and Embase through February 2018. Inclusion criteria for our systematic review were all English language studies (Level I-IV evidence) that reported on single or two-stage revision, infection eradication for revision shoulder arthroplasty with a minimum follow up of twelve-months and minimum of five patients for analysis. Exclusion criteria for our review were all non-English language studies, papers that exclude single or two-stage exchange, review papers, case reports or technique articles without outcome data. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were applied. Title and abstract screen was conducted of 248 results and a full text review of 66, identified 31 articles that met inclusion and exclusion criteria for final review.

The purpose for this review was to understand and compare the role of single-stage and two-stage exchange for the treatment of shoulder PJI. Two-stage exchange arthroplasty with implant removal, irrigation and debridement (I&D), insertion of antibiotic spacer, antibiotic treatment, followed by re-implantation has been suggested as gold standard for treatment of shoulder PJI [1]. Varying studies collected demographics, timing of infection, associated pathogens, surgical treatment, antibiotics, eradication rate for infection, surgical complications and functional outcomes with two-year follow-up minimum. We identified 12 articles that evaluated one-stage exchange and 27 articles that evaluated two-stage exchange. The majority of papers reported preoperative laboratory values to diagnose PJI based on elevated white blood cell count, C-reactive protein and/or erythrocyte sedimentation rate. Clinical findings such as draining sinus, erythema or swelling were inconsistently reported. Most studies reported the number of joint aspirations performed and resulted positive with microbial growth. Although there was inconsistent reporting of timing of infection, the majority of studies that reported timing of infection used terms from Sperling et al. and Strickland et al. with acute meaning < 3 months, sub-acute meaning 3-12 months and chronic > 12 months [2,3]. There was consistent reporting of the pathogens found either pre- or intraoperatively. *Cutibacterium acnes* (*C. acnes*) was the most common organism identified with 160 cases followed by *Coagulase-negative Staphylococcus* (CoNS) with 93 cases [2,4–14]. There were 57 reported cases of polymicrobial cases and 27 cultures that resulted in no growth [4–8].

To address the stated question, we reviewed studies in aggregate for sub-acute and chronic infection when treated with either single

TABLE 1. Reinfection and complications for single stage exchange

Cases	Reinfection Rate	Pathogens	Constant Score (mean)	Complication Rate
161 Total 13 Subacute 8 Chronic	5.6 % ($p < 0.001$)	72 *C. acnes* 29 CoNS 20 MSSA 3 MRSA	49.1 ($p < 0.11$)	12.7 % ($p < 0.001$)

CoNS, Coagulase-negative *Staphylococcus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*

TABLE 2. Reinfection and complications for two-stage exchange

Cases	Reinfection Rate	Pathogens	Constant Score (mean)	Complication Rate
325 Total 46 Subacute 74 Chronic	11.4 % ($p < 0.001$)	88 *C. acnes* 64 CoNS 33 MSSA 56 MRSA	51.1 ($p < 0.05$)	21.9 % ($p < 0.001$)

CoNS, Coagulase-negative *Staphylococcus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*

or two-stage revision summarized in Tables 1 and 2. Four studies directly compared revision success rate for shoulder PJI with single-stage exchange in sub-acute or chronic presentation. The reinfection rate was 12.5% for chronic cases and 5.3% for sub-acute cases [4,14,15]. Regarding two-stage exchange, three studies specifically reported success rates for either sub-acute or chronic shoulder PJI. Reinfection rate was 6.3% for chronic PJI and 29.4% for sub-acute PJI treated with two-stage exchange [2,4,15]. Several other studies reported the timing of infection but did not compare revision failure rates according to the subgroups of acute, sub-acute or chronic PJI groups. In aggregate, using a frequency-weighted mean, the reinfection rate was 5.6% for one-stage exchange compared to 11.4% for two-stage exchange, which was statistically significant ($p < 0.001$).

Analyses of complications related to single or two-stage exchange in acute, sub-acute or chronic infection were limited. In aggregate, all surgical complications reported include aseptic loosening, fracture, nerve palsy, dislocation and hematoma. Our systematic review found a 12.7% complication rate for single-stage exchange compared to a 21.9% complication rate for two-stage exchange, which was statistically significant. Although this finding suggests that patients undergoing two-stage exchange have 1.72 times the risk of intra- or postoperative complication, the analysis was not able to account for likely bias in the selection of treatment. The selection bias cannot be over-emphasized—it very well may be that cases with more severe infections were preferentially treated with two stage while less severe infections were treated with single-stage revision.

Frequency-weighted mean Constant Murley Score (CMS) was 49.1 for single-stage patients and 51.1 for two-stage exchange, which was similar to prior findings [7,15]. In the single-stage studies, a total of 57 patients had 78.2 degrees of FF; 42 patients had 52.4 degrees of abduction and 59 patients had 25.4 degrees of external rotation. Two-stage exchange papers reported 194 patients had 98.9 degrees of FF, 72 patients with 52.4 degrees of abduction and 144 patients with 29.2 degrees of external rotation. No studies compare the timing of infection and treatment with single or two-stage revision.

All papers identified are retrospective thus contain significant selection bias. While our findings in aggregate suggest single-stage exchange is a viable option for PJI, there are few studies that address reinfection associated with various risk factors such as pathogens, timing of infection or diagnostic features such as obvious clinical findings of infection. Thus, we cannot recommend using single-stage exchange in place of two-stage exchange for shoulder PJI without further investigation.

REFERENCES

[1] George DA, Volpin A, Scarponi S, Haddad FS, Romanò CL. Does exchange arthroplasty of an infected shoulder prosthesis provide better eradication rate and better functional outcome, compared to a permanent spacer or resection arthroplasty? a systematic review. BMC Musculoskelet Disord. 2016;17:52. doi:10.1186/s12891-016-0901-6.

[2] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. Clin Orthop Relat Res. 2001:206–216.

[3] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. J Bone Joint Surg Br. 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.

[4] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. J Shoulder Elbow Surg. 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.

[5] Klatte TO, Junghans K, Al-Khateeb H, Rueger JM, Gehrke T, Kendoff D, et al. Single-stage revision for peri-prosthetic shoulder infection: outcomes and results. Bone Joint J. 2013;95-B:391–395. doi:10.1302/0301-620X.95B3.30134.

[6] Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Definitive treatment of infected shoulder arthroplasty with a cement spacer. Orthopedics. 2016;39:e924–e930. doi:10.3928/01477447-20160623-07.

[7] Nelson GN, Davis DE, Namdari S. Outcomes in the treatment of periprosthetic joint infection after shoulder arthroplasty: a systematic review. J Shoulder Elbow Surg. 2016;25:1337–1345. doi:10.1016/j.jse.2015.11.064.

[8] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. Eur J Orthop Surg Traumatol. 2014;24:723–731. doi:10.1007/s00590-013-1251-9.

[9] Padegimas EM, Maltenfort M, Ramsey ML, Williams GR, Parvizi J, Namdari S. Periprosthetic shoulder infection in the United States: incidence and economic burden. J Shoulder Elbow Surg. 2015;24:741–746. doi:10.1016/j.jse.2014.11.044.

[10] Sabesan VJ, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. Clin Orthop Relat Res. 2011;469:2538–2543. doi:10.1007/s11999-011-1774-5.
[11] Singh JA, Sperling JW, Schleck C, Harmsen W, Cofield RH. Periprosthetic infections after shoulder hemiarthroplasty. J Shoulder Elbow Surg. 2012;21:1304–1309. doi:10.1016/j.jse.2011.08.067.
[12] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. J Bone Joint Surg Br. 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.
[13] Weber P, Utzschneider S, Sadoghi P, Andress H-J, Jansson V, Müller PE. Management of the infected shoulder prosthesis: a retrospective analysis and review of the literature. Int Orthop. 2011;35:365–373. doi:10.1007/s00264-010-1019-3.
[14] Beekman PDA, Katusic D, Berghs BM, Karelse A, De Wilde L. One-stage revision for patients with a chronically infected reverse total shoulder replacement. J Bone Joint Surg Br. 2010;92:817–822. doi:10.1302/0301-620X.92B6.23045.
[15] Ince A, Seemann K, Frommelt L, Katzer A, Loehr JF. One-stage exchange shoulder arthroplasty for peri-prosthetic infection. J Bone Joint Surg Br. 2005;87:814–818. doi:10.1302/0301-620X.87B6.15920.

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QUESTION 4: Is there a role for preoperative joint aspiration prior to reimplantation during two-stage exchange for shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There is a dearth of information on the role of preoperative joint aspiration prior to second stage revision after treatment of shoulder PJI. Furthermore, several studies have pointed to the high incidence of "dry taps" and false negative cultures from joint aspirates. Thus, there is little evidence in support of routine preoperative aspiration prior to second stage reimplantation.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 88%, Disagree: 4%, Abstain: 8% (Super Majority, Strong Consensus)

RATIONALE

A systematic review of the published literature was performed on PubMed using the search terms Shoulder (Title) AND [Periprosthetic OR reverse shoulder OR total shoulder OR arthroplasty OR replacement OR prosthesis (Title/ Abstract)] AND [Infection OR infected OR septic OR sepsis OR PJI OR propionibacterium OR acnes OR staphylococcal OR staphylococcus OR second stage OR OR staged OR revision OR spacer OR two-stage OR two stage OR reimplantation OR purulent OR purulence OR sinus tract (Title)]. This search yielded 255 articles. All titles were reviewed and articles with potential relevance had their abstracts reviewed. In total, with full texts reviewed, 31 articles where considered relevant to this topic in some fashion. Articles were deemed relevant if they included any aspirate information on patients with shoulder arthroplasties. These articles were used to make the recommendation. The reference lists of the included articles were further searched to identify other references that may have been omitted.

Controversy remains regarding the best surgical treatment of shoulder PJI. The literature documents interventions including open debridement with component retention or liner exchange, single stage re-implantation comprising removal of all components and immediate re-implantation after thorough debridement and lavage, resection arthroplasty after removal of all components and two-stage re-implantation. The latter involves a first stage that includes removal of all components followed by debridement, and in many cases insertion of an antibiotic impregnated polymethylmethacrylate cement spacer for local antibiotic delivery and to preserve soft tissue tension. The patient is then treated with intravenous (sometimes followed by oral) antibiotics and monitored, typically with serial serologic evaluation, prior to the second surgery (second stage revision) at which time the spacer is removed and new components are re-implanted.

In patients who undergo two-stage re-implantation for shoulder PJI, shoulder joint aspiration or arthrocentesis prior to second stage revision is one method to evaluate for persistent infection after the first stage explantation and subsequent antibiotic treatment. The aspirate can be sent for cultures, leukocyte cell count and differential, and also for analysis of biomarkers such as alpha-defensin. Shoulder aspiration is an established diagnostic tool and is commonly used (although not routinely) as part of the workup of PJI, including shoulder PJI.

However, there is little published information on the use of shoulder aspiration prior to second stage revision. In addition, there is no data documenting an advantage of shoulder aspiration over no aspiration or over any alternative diagnostic tool for shoulder PJI. Sabesan et al. reported that 12 of 17 patients had preoperative aspiration prior to the first stage. re-implantation [1]. Fluid was obtained for culture in 10 and 6 had positive cultures. Prior to the second stage the patients were ruled out for persistent infection with preoperative erythrocyte sedimentation rate, C-reactive protein (CRP), white blood cell (WBC) count and a negative preoperative aspirate. One of the 17 patients had intraoperative frozen section that was positive for acute inflammation and had repeat treatment for infection. Two small case series studies recommend preoperative aspiration prior to considering second stage revision, but only in cases with persistently elevated CRP and WBC [2,3]. Buchalter et al. have described their algorithm for two-stage re-implantation for shoulder PJI but do not mention shoulder aspiration as a factor in their timing of second-stage revision [4]. Patients were offered a second stage reimplantation if they had no clinical signs of infection and their inflammatory markers normalized.

If shoulder joint aspiration is considered in the evaluation for PJI, it is typically recommended to hold antibiotics for at least 14 days prior to aspiration [2,3,5]. It is also important to note that a negative culture of fluid aspirate or dry aspirate is not diagnostic of a resolved infection based on studies that include preoperative shoulder aspirations [5,6].

REFERENCES

[1] Sabesan VJ, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. Clin Orthop Relat Res. 2011;469:2538–2543. doi:10.1007/s11999-011-1774-5.

[2] Weber P, Utzschneider S, Sadoghi P, Andress H-J, Jansson V, Müller PE. Management of the infected shoulder prosthesis: a retrospective analysis and review of the literature. Int Orthop. 2011;35:365–373. doi:10.1007/s00264-010-1019-3.

[3] Ghijselings S, Stuyck J, Debeer P. Surgical treatment algorithm for infected shoulder arthroplasty: a retrospective analysis of 17 cases. Acta Orthop Belg. 2013;79:626–635.

[4] Buchalter DB, Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Two-stage revision for infected shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26:939–947. doi:10.1016/j.jse.2016.09.056.

[5] Updegrove GF, Armstrong AD, Kim H-MM. Preoperative and intraoperative infection workup in apparently aseptic revision shoulder arthroplasty. J Shoulder Elbow Surg. 2015;24:491–500. doi:10.1016/j.jse.2014.10.005.

[6] Ricchetti ET, Frangiamore SJ, Grosso MJ, Alolabi B, Saleh A, Bauer TW, et al. Diagnosis of periprosthetic infection after shoulder arthroplasty: a critical analysis review. JBJS Rev. 2013;1. doi:10.2106/JBJS.RVW.M.00055.

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QUESTION 5: Is there a role for pre-reimplantation open or arthroscopic tissue biopsy in the evaluation during two-stage exchange of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Unknown. There is one level IV study suggesting that open biopsy prior to second-stage revision for shoulder PJI can identify patients with persistent infection who may benefit from subsequent repeat irrigation and debridement (I&D) prior to second stage reimplantation.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

PubMed and Embase were searched from 1980 to January 2018 to identify studies evaluating preoperative open or arthroscopic tissue biopsy prior to second stage revision shoulder arthroplasty after treatment of shoulder PJI. A secondary search of the references of included studies was also conducted. One article was selected for inclusion. Articles regarding hip and knee arthroplasty were excluded.

Zhang et al. reported a level IV case series in which they performed open biopsy prior to second stage revision for treatment of shoulder PJI [1]. Eighteen patients with shoulder PJI between 2005 and 2012 were included. Patients were treated with a standard protocol involving I&D, removal of implants, antibiotic spacer placement and antibiotic therapy based on culture results for six weeks based on infectious disease service recommendations. At a minimum four weeks after completion of antibiotics, patients were re-evaluated to ensure no clinical symptoms of infection were present and erythrocyte sedimentation rate/ C-reactive protein (ESR/CRP) had normalized. At this point, all patients underwent open biopsy via deltopectoral incision to obtain at least three soft tissue and bone cultures from tissue adjacent to the bone-antibiotic spacer interface. If cultures were negative for 7 to 14 days, patients underwent reimplantation. If cultures were positive, patients instead underwent repeat I&D with antibiotic spacer exchange and the protocol was repeated.

Zhang et al. found that 4 of 18 patients (22%) had positive cultures from the open biopsy indicative of persistent infection with a 38% persistent infection rate for individuals infected with *C. acnes*. One patient had positive cultures again on second open biopsy and underwent a second spacer exchange prior to finally obtaining a negative third biopsy and undergoing reimplantation. *C. acnes* was the most common pathogen, present in 44% of index shoulder PJIs. Among persistent infections, 3 of 4 patients (75%) had *C. acnes*, and the patient requiring two spacer exchanges had *C. acnes* on each occasion. At a mean of 24 month follow-up (range 12 to 36 months), all 18 patients were reimplanted (2 hemiarthroplasty, 1 total shoulder arthroplasty (TSA), 15 reverse total shoulder arthroplasty (RTSA)) and noted to be clinically infection-free with an average American Shoulder and Elbow Surgeons (ASES) score of 71.

This study is limited in its level IV design and small sample size. Furthermore, patients undergoing two-stage revision had variable index procedures from which they developed shoulder PJI, including one open reduction internal fixation (ORIF) proximal humerus fracture, three hemiarthroplasties, six rotator cuff repairs, five TSAs and three RTSAs. There is no comparison group of patients who did not undergo open biopsy, and no comparison to alternative methods such as shoulder aspiration or arthroscopic biopsy.

The role of open or arthroscopic biopsy prior to reimplantation during a two-stage exchange arthroplasty remains unclear.

REFERENCES

[1] 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:e15–e20. doi:10.1016/j.jse.2014.04.007.