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Proceedings from the 2018 International Consensus Meeting on Orthopedic Infections: management of periprosthetic shoulder infection

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The Second International Consensus Meeting on Orthopedic Infections was held in Philadelphia, Pennsylvania, in July 2018. A multidisciplinary team of international experts from all 9 subspecialties of orthopedic surgery and allied fields of infectious disease, microbiology, and epidemiology was assembled to form the International Consensus Group. The following consensus proceedings from the

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International Consensus Meeting involve 30 questions pertaining to the management of periprosthetic shoulder infection.

Keywords: Shoulder arthroplasty; periprosthetic shoulder infection; unexpected positive cultures; MRSA; component retention; resection shoulder arthroplasty; two-stage exchange; irrigation and débridement

Treatment for unexpected positive cultures

Question 1: What is the treatment (if any) for unexpected positive cultures (UPCs) in revision shoulder arthroplasty without clinical or radiographic signs of infection?

Recommendation:

Unknown. Few publications offer protocols for addressing UPCs. Of these, the most common options include antibiotics, reoperation, and withholding of 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:

Of the 8 studies[38,45,57,62,80,108,118,149] returned from a comprehensive literature review (Supplementary data) that allude to treatment of UPCs, only 6 described the author's treatment protocol, but these do not allow definitive conclusions to be drawn about the effect of each treatment type on outcomes, if any were reported (Question 1: Table I).[38,45,57,62,80,149] Despite providing neither a methodology for treatment assignment nor results that were not in aggregate, Foruria et al[45] 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. In the study of Hsu et al,[62] 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 (receiving 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 3 patients in both the culture-positive cohort (defined as at least 2 UPCs; n = 27) and the control cohort (0 or 1 UPC; n = 28) required a subsequent procedure. None of these 3 culture-positive cohort patients who received the extended antibiotic regimen had subsequent positive cultures at revision, whereas 1 of 3 control cohort patients did.[62] Two studies do present these data, but they are not robust.[108,118] Few studies fully meet the defined inclusion and exclusion criteria, and many of these reported results in an aggregate. Only 2 studies compared different treatment options using nonaggregated outcomes.

Padegimas et al[108] compared individuals undergoing revision shoulder arthroplasty, 28 of whom had UPCs and 89 who did not. They noted that all patients received the authors' standard postoperative empirical oral antibiotics for 2 weeks and then continued to receive antibiotics for an additional 6 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, there were 3 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 UPCs (7.1%), but this difference did not reach statistical significance ($P = .109$).[108]

Piggott et al[118] reported on 8 of 24 cases with positive *Cutibacterium* (formerly *Propionibacterium*) *acnes* cultures that were ''unexpected'' as defined by their inclusion criteria. The primary outcome was termed a favorable clinical outcome, which was defined as a post-treatment improvement in pain and function and a lack of additional operations. Four of the 8 UPC patients met the favorable clinical outcome end point, 3 did not, and 1 was lost to follow-up. The antibiotics used varied by clinical judgment and susceptibility and were not well reported. The addition of rifampin and its duration were well documented. The 4 patients who had a favorable outcome received rifampin in addition to the antibiotic regimen with an average duration of 608.5 days (range, 126-1540 days). Of the 3 patients without a favorable clinical outcome, 1 received antibiotics plus rifampin for 196 days, 1 received antibiotics alone for 189 days, and 1 underwent surgery.[118]

Question 1: Table I Summary of studies offering limited data on treatment and outcomes

Author	No. of patients with UPC	Treatment protocols	Outcomes
Kelly and Hobgood[80]	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 et al[38]	6	IV cefazolin for 36 h postoperatively and clindamycin or penicillin on 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 receiving oral suppressive therapy had no signs of infection at time authors were writing; outcomes not otherwise reported.
Foruria et al[45]	107	Variable; 34 patients treated with antibiotic regimen (range, 8-700 d) postoperatively, 19 treated with chronic antibiotic suppression, 54 did not receive antibiotics other than preoperative prophylaxis	Variable results were mostly reported in aggregate. Authors noted that duration of antibiotic regimen had no effect on likelihood of a repeated positive culture during follow-up.
Grosso et al[57]	17	13 patients received tobramycin- or gentamicin-impregnated cement; all received IV antibiotics for 24 h postoperatively; no additional therapy after culture results	1 clinical infection at 6 weeks postoperatively, confirmed as superficial wound infection during irrigation and débridement
Hsu et al[62]	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 culture	Variable; high suspicion of infection patients received IV 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 >2 cultures became positive, the regimen was changed to IV 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 et al[149]	75	Variable; 54 patients received only the standard 2-3 doses of IV postoperative antibiotics and nothing further; 14 received additional, unspecified antibiotics (range, 1-6 weeks); 7 received only oral, unspecified antibiotics.	10 patients required re-revision, 7 of whom 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; *IV*, intravenous

There is a clear need for additional research into treatment options for UPCs. No conclusion can be made at this time as to what treatment option, if any, is appropriate for UPCs.

Question 2 : Is there a role for postoperative antibiotics after irrigation and débridement for hematoma complicating a primary or revision shoulder arthroplasty while awaiting culture results?

Recommendation:

Antibiotics should be given after irrigation and débridement for hematoma after shoulder (primary or revision) arthroplasty while awaiting culture results.

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 citations. After review of the abstracts, 11 articles[4,14,25,47,91,104,112,129,133,137,138] 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 irrigation and débridement of a hematoma after shoulder arthroplasty. However, given the concern for the presence of infection at the time of irrigation and débridement for hematoma after shoulder arthroplasty, as discussed in Evaluation Question 21 (Is there a role for obtaining tissue cultures in performing irrigation and débridement for hematoma after shoulder (primary or revision) arthroplasty?), we believe it is reasonable to initiate empirical antibiotic treatment while awaiting the culture results. Oral antibiotics (frequently doxycycline) are used pending final culture results, although there are no clinical outcomes data to justify a particular antibiotic selection or route or even the use of antibiotics at all in this setting.

Question 3: Is there a role for postoperative antibiotic treatment for revision arthroplasty with subsequent UPCs for a virulent organism (eg, methicillin-resistant *Staphylococcus aureus* [MRSA], methicillin-sensitive *S. aureus* [MSSA], or *Escherichia coli*)?

Recommendation:

In aggregate, published studies do not clearly show superiority of prolonged antibiotic use to 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 are limited as most UPCs are with less virulent organisms (eg, *C. acnes*, coagulase-negative *Staphylococcus* species).

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 and suppressive antibiotics after revision shoulder arthroplasty (Supplementary data). Among the published studies for outcomes after revision shoulder arthroplasty with subclinical presentations and UPCs, all were retrospective studies with differing methodologies.[45,57,62,80,108] All of the studies reported the majority of positive cultures (>80%) from indolent organisms (*C. acnes* or coagulase-negative *Staphylococcus*). None of the studies found a detrimental effect to not prescribing prolonged postoperative antibiotics, although 1 study with no comparison group reported a 25% recurrence rate after UPCs. For those studies that treated UPCs with prolonged antibiotics, recurrence rates were low (0%-3.5%). One systematic review confirmed a pooled ''true infection'' rate after UPCs of 10.2%, with antibiotic use not influencing the rate of occurrence of true infection after UPCs ($P = .498$). [82]

Grosso et al[57] used antibiotic cement and 24 hours of routine postoperative antibiotics with 1 superficial infection and no deep infections after revision shoulder arthroplasty. Foruria et al[45] 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 infections. Padegimas et al[108] reported a 23.9% UPC rate after revision shoulder arthroplasty with standardized UPC treatment with 6 weeks of antibiotics or 2 weeks of antibiotics at the surgeon's discretion. They found only 1 recurrent infection in the UPC group (3.5%) vs. 3.4% in the non-UPC group. Kelly and Hobgood[80] reported a UPC rate of 29% (8/28) after revision shoulder arthroplasty and treated only 1 with antibiotics postoperatively for 4 weeks (because of superficial wound infection); 2 of 8 (25%) developed late clinical infection with *C. acnes*. Last, Hsu et al[62] reported a 49% positive culture rate after revision shoulder arthroplasty and treated patients by a protocol of 6 weeks of intravenous (IV) antibiotics and 6 months of oral antibiotics if >2 cultures were positive; 0% of patients had recurrence of infection with this protocol for the positive culture group and negative culture groups. On the other hand, risks from prolonged antibiotic use are significant. Two studies reported a 19%-42% complication side effect rate from antibiotic use that was seen with both oral and IV medications.[57,62]

The majority (>80%) of UPCs reported in the shoulder literature are *C. acnes* or coagulase-negative *Staphylococcus* organisms. Because of small numbers, meaningful comparisons to more virulent organisms could not be performed. Other studies in the lower extremity literature suggest that periprosthetic joint infections (PJIs) from virulent organisms have higher reinfection rates despite surgery (45%-49%) for MRSA, enterococci, and streptococcus.[3,72,81] In the lower extremity arthroplasty literature, there is 1 randomized controlled study that reported a limited benefit to prolonged oral antibiotic therapy after 2-stage revision with negative cultures (5% vs. 19%), although culture profiles from the reinfection (mostly virulent) tended to differ from the original infection organism profile.[78]

In aggregate, these studies do not clearly show superiority of prolonged antibiotic use to no prolonged antibiotic treatment in the setting of revision shoulder arthroplasty with subsequent cultures positive for virulent organisms. The clinical implications may differ between occult PJI and unsuspected PJI 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 for those patients in whom suspicion of infection is low. In addition, there are well-reported risks of antibiotic-related side effects and resistance with widespread use.

Question 4: Is there a role for postoperative antibiotic treatment when a revision arthroplasty is performed with subsequent UPCs of the shoulder caused by an indolent organism (eg, *C. acnes* or coagulase-negative *Staphylococcus*)?

Recommendation:

Postoperative antibiotic treatment beyond 24 hours after revision arthroplasty with UPCs 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:

Refer to the rationale for Question 3.

The long-term consequences of an unexpected indolent positive culture after revision shoulder arthroplasty are unknown. Review of literature (Appendix: *Search Methodology*) 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.

Antibiotic treatment for PJI

Question 5: Is there a need for antibiotic therapy after irrigation and débridement of patients with acute shoulder PJI caused by a virulent organism (eg, MRSA, MSSA, or *E. coli*)?

Recommendation:

In the absence of high-level data, we propose that patients with acute PJI of the shoulder caused by virulent organisms such as MRSA, MSSA, and *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 of 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 PJI, 9 of which described treatment with irrigation and débridement with or without modular component exchange for acute (<3 months from surgery or acute hematogenous spread) infection.[2,29,33,36,68,71,107,140,162] These 9 studies included only small numbers of patients, with only 6 patients with acute PJI caused by a virulent organism.[36]

There were no studies that compared irrigation and débridement alone with irrigation and débridement with postoperative antibiotics for the treatment of acute PJI. The 9 studies had varied definitions of acute, with periods ranging from 4 weeks to 3 months.[2,29,33,36,68,71,107,140,162] Data regarding the pathogenic organism were not clearly reported, thus making it difficult to determine whether the virulence was a factor in treatment or outcome. The surgical management of the acute infections varied, including arthroscopic irrigation and débridement, open irrigation and débridement, and open irrigation and débridement 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, or *E. coli*) after irrigation and débridement.

Nevertheless, postoperative antibiotics were always part of the treatment of acute PJI in the published literature. Treatment types and length varied; both IV and oral regimens were employed, and treatment lengths ranged from 13 days to chronic lifetime suppression.[2,36] Most studies used a 4- to 6-week protocol of postoperative antibiotic therapy.[29,33,36,71,107,140,162] It appears to be the consensus opinion that acute shoulder PJI treated with irrigation and débridement 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.

Question 6: Is there a role for antibiotic therapy in the management of acute shoulder PJI with an indolent organism (eg, *C. acnes* or coagulase-negative *Staphylococcus*) after irrigation and débridement?

Recommendation:

Antibiotic therapy after irrigation and débridement for management of acute shoulder PJI with an indolent organism has not been well studied in the literature. The limited data available suggest that 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:

Strategies for treatment of PJI include chronic antibiotic suppression, irrigation and débridement with or without component retention, 1- or 2-stage revision, placement of antibiotic spacer, resection arthroplasty, and arthrodesis. These strategies have been adopted from the hip and knee arthroplasty experience and literature. Most of the data published specifically addressing acute PJI commingle shoulder

PJI with hip and knee PJI, with few data specific to treatment of acute shoulder PJI. The role of antibiotic therapy is not well described, nor is the ideal duration or specific antibiotic. PubMed, Google Scholar, Ovid-Medline, Cochrane, and Web of Science were searched for the keywords ''shoulder,'' ''infection,'' ''periprosthetic,'' ''arthroplasty,'' and ''antibiotic'' to identify relevant articles through a title screen, abstract review, and finally a full-text review.

Dennison et al[36] in 2017 published a retrospective case series of acute PJI treated at the Mayo Clinic that included 10 shoulders in 9 patients treated with irrigation and débridement and antibiotics. They defined acute PJI as any infection requiring irrigation and débridement within 6 weeks of the index arthroplasty or within 3 weeks of symptoms from a delayed-onset acute hematogenous infection. There were 4 acute postoperative and 6 delayed-onset, acute hematogenous infections. Five of the shoulders had a positive culture for indolent bacteria; the other 5 had more virulent bacteria. No patient underwent component exchange. The postoperative antibiotic treatment ranged from 3 to 6 weeks (mean, 5.2 weeks). Antibiotics were determined by an orthopedic infectious disease specialist on the basis of organism susceptibility and host factors. For 9 of the 10 shoulders, additional oral antibiotic therapy included trimethoprim-sulfamethoxazole with or without rifampin, penicillin, or a combination of trimethoprim-sulfamethoxazole with penicillin. Chronic suppression was maintained in 6 shoulders, whereas 3 others had failure requiring resection arthroplasty. The authors concluded that irrigation and débridement 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 described 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 about the importance of combining therapy with rifampin.

Given the limited nature of the data available, the exact role and protocol for antibiotic treatment after irrigation and débridement for the treatment of acute shoulder PJI infection caused by indolent organisms remain 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 IV and oral regimens were employed, and treatment lengths ranged from 13 days to chronic lifetime suppression.[36,134] Most studies used a 4- to 6-week protocol of postoperative antibiotic therapy.[29,36,106] By consensus, we believe that cases of acute shoulder PJI treated with irrigation and débridement should be followed by a course of antibiotic therapy.

Question 7: Is there a role for nonoperative suppressive antibiotic therapy (SAT) in the management of subacute or chronic shoulder PJI?

Recommendation:

There is a role for SAT of selected cases of periprosthetic infection of the shoulder.

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,'' and ''ICOAS'' to identify studies on suppressive treatment of PJI of the shoulder. The majority of published studies were retrospective. A total of 8 shoulder cases were identified (5 successful, 3 failures). Most studies reported on SAT after an initial surgical procedure like débridement or emptying of abscesses.

Five studies evaluating SAT included cases of infected shoulder arthroplasty (8 shoulders). Prendki et al[124] reported on 38 patients with a minimum suppressive treatment of 6 months for a periprosthetic infection (24 hips, 13 knees, 1 shoulder); 60% of the patients were taking antibiotics and without relapse of infection (including the shoulder) at 24 months. There were 6 failures and 9 deaths. Some of these patients had a surgical procedure before initiation of suppressive treatment. It is unclear how many patients were treated without initial surgery.

Wouthuyzen-Bakker et al[160] reported on a retrospective study of 21 patients (2 shoulders) with median follow-up of 21 months. 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 1 was a failure. Only 6 patients were treated without initial débridement and 4 had a successful outcome.

Pradier et al[121] 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 débridement; 22 patients failed to respond to treatment. Both shoulders were failures. Three cases had acquisition of tetracycline resistance of the initial pathogen.

Prendki et al[123] reported on a larger series of joint infections (136 patients); 79 (58%) had some type of initial surgical procedure. There were 2 shoulders, and both were successfully treated with SAT. It is unclear whether these 2 patients had initial surgery. Prendki et al[123] also reported on 21 patients in another study including 1 shoulder (successful). Of these 21 patients, 5 had fistulas before starting chronic SAT; 40% of the patients were free of clinical signs of infection after 2 years.

Multiple other studies have included PJI of other joints, primarily hip and knee arthroplasty.

Segreti et al[135] reported on prolonged suppressive treatment in 18 patients (12 knees and 6 total hip

arthroplasties); 8 had acute infection and 10 had chronic infection. All had surgical débridement before antibiotic treatment. Duration of oral antibiotic suppressive treatment varied from 4 to 103 months. Overall, 14 patients remained asymptomatic; 22% 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[127] reported on 36 patients (15 hips, 19 knees, and 2 elbows); 47% had acute onset (<4 weeks), and 53% were chronic infection. All patients had open débridement. 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; 8% had complications related to antibiotic treatment.

Pavoni et al[115] reported on 34 patients (no shoulders included) with infection. Fourteen had surgical débridement. Seventeen patients had no relapse of infection during the time of this study (11 of these patients had no initial surgical débridement).

Siqueira et al[139] reported on 92 patients (no shoulders). They compared patients undergoing surgical débridement followed by a short period of antibiotics with patients receiving prolonged SAT. The 5-year infection-free prosthetic survival rate was 68.5% for the antibiotic suppression group compared with 41.1% in the nonsuppression group. Hip infections had a lower rate of failures, and results were better in the suppression group if there was a *Staphylococcus aureus* infection.

Shelton et al[136] reported cure of a draining sinus track in a case of 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 a role for suppressive treatment of PJI in the hip and knee in patients with stable implants who cannot or do not want to undergo major revision surgery. However, the studies included patients with acute, subacute, and chronic infections, and the duration and type of treatment varied. Most of the published case series included patients who had long-term SAT after initial surgical irrigation and débridement. It is difficult to identify and to evaluate the outcome for patients who had only chronic suppressive treatment. Furthermore, only a few shoulders are included, and therefore no recommendations can be given for type and duration of SAT for PJI in the shoulder. It is difficult to extrapolate from hip and knee infection data because the clinical manifestation and type of pathogen are different in the shoulder compared with the hip and knee. Last, profound concerns about antibiotic stewardship and antibiotic-related complications must be carefully weighed against any perceived potential modest success of this strategy.

Question 8: Is there a role for oral SAT in the setting of retained prostheses after IV therapy in subacute or chronic PJI?

Recommendation:

The administration of oral SAT 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 time. For patients with a PJI for whom the medical-surgical treatment is suboptimal or clearly insufficient to achieve control (because of surgical contraindications, technical difficulties, severe medical comorbidities, or multidrug-resistant bacteria), chronic oral SAT is considered an alternative strategy. SAT refers to the use of antibiotics administered indefinitely, with a "noncurative" intent, with the objective of avoiding or reducing symptoms and delaying or preventing progression that may lead to the patient's dysfunction and loss of the implant.

A search of MEDLINE and Embase from 1980 to January 2018 was conducted. The terms used were PJI or infected arthroplasty and suppressive therapy or suppressive antibiotics. Case reports, reviews, and guidelines were excluded. Thirteen articles were 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 the medical literature (MEDLINE and Embase) about PJI or arthroplasty and suppressive therapy or suppressive antibiotics yielded 13 references.[23,54,96,115,121-123,125,127,135,139,151,160] Twelve are retrospective descriptive series and 1 is a propensity score controlled cohort study.[139] Most of the cases included in these series were hip and knee infections, and only 9 of the 680 were PJIs. Therefore, this review is primarily based on the results obtained from research of prosthetic hip and knee infections.

The efficacy of SAT varied from 23% at 3.5 years[151] to 86.2% at 5 years.[127] 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 ranging from acute PJI cases that could probably be cured by débridement and several weeks of antibiotic therapy to patients with evident chronic infections showing active fistula and no surgery performed.

In summary, analysis of the literature on SAT faces the following major problems: different classifications of PJIs and the terms that are used to describe them (early, acute, delayed, chronic, subacute, and so on); differences in the medical-surgical strategies as standard of care of the PJI according to the types of infection; differences in the criteria used to select patients for SAT; differences in the criteria used to evaluate the efficacy of SAT; and absence of control groups to compare the efficacy of SAT. As well, other "minor" problems include insufficient follow-up, variety of antibiotics used, and 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 hips, 51 knees, 4 elbows, 3 ankles, and 2 shoulders—most of them diagnosed with early PJI but including also late infections) managed with débridement and prosthesis retention and prolonged antimicrobial therapy for more than a year, the rate of failure among patients who discontinued antibiotic treatment was 4-fold higher than in those who continued.[23] Although 82% of the patients who stopped antibiotics did not have failure (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 4 months of antibiotic withdrawal.

Another more recent study is the only one that included controls.[139] Ninety-two patients receiving SAT (71 hip PJIs and 21 knee PJIs) 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 to whom 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 previous 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 2-stage revision (38) or by débridement and exchange of polyethylene (54) followed by IV antibiotics before SAT was started. A better result was observed in SAT-treated patients than in controls (68.5% vs. 41.1%; $P = .08$) at 5 years. Analyzed by type of surgery, differences were noted in patients with prosthesis retention (64.7% vs. 30.4%; $P < .001$), but they were not observed in those managed by 2-stage exchange ($P = .13$). The proportion of success among patients with late infections was 64.3%. One of the drawbacks of the study is 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.[96,121–123,127] Those who did not tolerate the first selected agent usually tolerated a new one.[160]

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 identify 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 in considering SAT: identification of the microorganism that is causing the infection; availability of oral antibiotics that are not toxic when administered for long periods; and practicality of 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, SAT is indicated only 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.

Question 9: Is there a role for oral SAT in acute PJI in the setting of retained prostheses after initial IV therapy? Is the duration the same as for lower extremity arthroplasty? Should it differ by pathogen (eg, MSSA vs. MRSA)?

Recommendation:

Whereas the role of débridement, antibiotics, and implant retention (DAIR) in the treatment of acute prosthetic shoulder infection has not been well studied, there is likely to be a role for oral SAT in the setting of retained infected shoulder prostheses after DAIR. There is no evidence to guide the optimal duration of treatment or whether treatment should vary by organism.

Level of evidence: Limited

Delegate vote: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

Rationale:

The treatment of an acute hip or knee PJI after irrigation and débridement with implant retention includes a course of oral antibiotics that follows the IV antibiotic therapy.[35,146,164] Although the efficacy of this approach is debated, with reported success rates ranging from 0% to 89%,[77] 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.[97] An analogous algorithm of treatment has been advocated in the setting of acute shoulder PJI when it is treated with irrigation and débridement with implant retention,[16,42,119] although specific recommendations for route and duration of antibiotic therapy are not clear.[95,101]

There is very little published literature evaluating the efficacy of this course of treatment in shoulder PJI (Supplementary data). Most studies addressing the treatment of acute shoulder PJIs are retrospective case series without control cohorts.[2,5,17,23,29,36,52,68,71,79,102,107,122,131,140,159,162,163] As many of these studies were composed of

patients undergoing heterogeneous treatment protocols, the subset of patients undergoing DAIR is often small, further limiting the ability of these studies to provide useful data. The overall number of patients presented in these articles is also small; no study exceeded 50 shoulders, and the majority reported on the outcomes of fewer than 10 patients with acute shoulder PJIs treated with irrigation and débridement and implant retention followed by IV and then oral antibiotics. Details about 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 about the efficacy of this treatment as stratified by organism, including MRSA vs. MSSA. Complicating any synthesis of the data further is heterogeneous mix type of infected arthroplasty (anatomic total shoulder arthroplasty [TSA], reverse TSA [RTSA], or hemiarthroplasty). Extrapolating these results to assess the actual utility of oral SAT in acute PJI in the setting of retained prosthesis after initial IV therapy, much less recommending an optimal duration of therapy, is not feasible.

Whether DAIR is even a viable treatment approach for shoulder PJIs in any setting has been challenged.[101] A systematic review of the literature found that the failure rate of implant retention in the setting of prosthetic shoulder infection was 31.4% vs. 6.3% after a 2-stage exchange, 9.7% after explantation with placement of a permanent spacer, and 9.9% after a 1-stage exchange.[106]

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 after débridement as well as the current understanding of the role that biofilm plays in treatment failure,[74,90,102,103] is likely to be a reasonable approach to the treatment of acute prosthetic shoulder infections in treating patients with implant retention, at least until more rigorous outcomes data that support the contrary are available.

Question 10: Should the duration of oral SAT differ by pathogen (eg, MSSA vs. MRSA) in the treatment of subacute or chronic shoulder PJI?

Recommendation:

There is insufficient evidence to determine whether the duration of oral SAT should differ by pathogen in the treatment of subacute or chronic shoulder PJI.

Level of evidence: Limited

Delegate vote: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

Rationale:

There is currently no widely accepted definition of SAT in reference to shoulder PJI. A thorough search of PubMed, Embase, and Google Scholar databases was performed in February 2018 to identify articles related to the use of SAT for the treatment of shoulder PJI using the search terms "prosthetic joint infection," "suppressive therapy," "antibiotic suppressive therapy," and "suppression." From this search, it is clear that the term SAT is variably used. In some cases, it is used to mean prolonged antibiotic therapy after surgery (irrigation and débridement and implant revision) with the intention of effecting a cure and discontinuation of antibiotics; in others, it means treatment of active PJI in patients unable to undergo additional surgical intervention. In the latter case, it is palliative 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. SAT is also used to refer to indefinite or lifelong use of antibiotic therapy in patients without clinical evidence of active infection but thought to be at high risk for relapse.

With use of an inclusive definition of SAT, 8 relevant studies were identified.[54,122-124,135,139,151,160] In these studies, 34 patients with shoulder PJI had SAT. Failure was defined as a relapse of infection based on the criteria described in each manuscript. These criteria were inconsistent. The relapse rate was 29% (10/34 cases). There was insufficient detail to comment on treatment duration, dose of antibiotics, or type of antibiotics.

There is limited evidence for success after discontinuation of SAT. Reports of hip and knee PJI demonstrate that there is a relapse rate of around 30% within 4 months after SAT is discontinued, even after long periods of treatment.[122] A study of 24 patients with PJI (2 shoulder patients) did observe that treatment succeeded in almost all patients with a PJI caused by a *Staphylococcus epidermidis*.[160] This may be due to the fact that *S. epidermidis* is low virulence, and the natural course of infection is often dormant and low grade in nature.

Safety issues related to prolonged use of antibiotics are an important consideration. Although information is scarce, the safety data published for case series indicate a low rate of antibiotic withdrawal due to adverse events.[21,122,135]

It is important that clinicians and researchers more precisely define SAT. It appears reasonable for SAT to refer to chronic use of low-dose antibiotic therapy in patients with persistent PJI in which the aim is to prevent acute exacerbation or recurrence of local symptoms or greater systemic involvement rather than to effect cure and eradication of infection. SAT is differentiated from antibiotic treatment that is longer than usual protocols but eventually stopped, which is meant to eradicate infection. Differentiation of these terms may allow future investigators to make more concrete recommendations for the use of SAT in shoulder PJI.

Question 11: What are the recommendations for the route (IV vs. oral) and duration of postoperative antibiotic treatment when a 1-stage revision arthroplasty is performed for subacute or chronic shoulder PJI of the shoulder caused by an indolent organism (eg, *C. acnes* or coagulase-negative *Staphylococcus*)?

Recommendation:

Before identification of pathogenic organisms, a course of oral antibiotics may be initiated that covers the potential organism until intraoperative cultures are finalized. If the cultures are positive and PJI is diagnosed, a continued course of antibiotics (up to 6 weeks) should be pursued. There is no evidence to support a preferred route (oral vs. IV), type, and duration of antibiotic treatment.

Level of evidence: Consensus

Delegate vote: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

Rationale:

Shoulder PJI negatively affects the outcome of shoulder arthroplasty and is often treated with revision surgery.[29] 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).[10,14,15] Shoulder PJI is commonly manifested as painful arthroplasty and often lacks typical clinical findings of acute infection. Results of laboratory workup, such as inflammatory markers, white blood cell (WBC) count, and shoulder aspiration, are often normal, leaving clinicians with limited tools to confirm infection before revision surgery. This is mostly due to predominance of indolent organisms such as *Cutibacterium* (formerly *Propionibacterium*) *acnes* (39%-66%) and coagulase-negative *Staphylococcus* (24%-28%) in periprosthetic shoulder infection.[80,120]

Two-stage revision including aggressive débridement and 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 in eradicating infection in short-term to midterm follow-up.[43,131,145] This approach has many shortcomings, including subjecting patients to 2 operations, spacer complications such as fracture or dislocation, and loss of rotator cuff and bone stock leading to poor joint function.

Recently, 1-stage revision has been advocated for low-virulence indolent infections. Nelson et al[106] and Cuff et al[32] showed similar rates of eradication with 1-stage compared with 2-stage treatment. Beekman et al[10] reported results of single-stage revision for infected reverse shoulder arthroplasty and showed that at 2-year follow-up, 90% of patients were infection free with a Constant score of 55.6%. George et al[51] conducted a systematic review and found that the average Constant score was 51% after 1-stage revision compared with 41% for 2-stage revision. These studies make a reasonable case for 1-stage revision arthroplasty to eradicate indolent infections while preserving function, but they have highly variable protocols for type and duration of postoperative antibiotics.

To address the question of antibiotic therapy after 1-stage revision arthroplasty for shoulder PJI 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 1-stage revision for indolent shoulder PJI, which resulted in 8 relevant articles included in this review.

Most reports do not clearly describe antibiotic therapy after revision surgery. This section reviews and summarizes 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. oral), type, and duration.

Grosso et al[57] retrospectively reviewed patients with no perioperative sign of infection who underwent single-stage revision shoulder arthroplasty and had at least 1 positive intraoperative culture and were not treated with an extended course of antibiotics. The majority of the cultures (56%) were *C. acnes*, followed by coagulase-negative *Staphylococcus* (35%). The rate of recurrence was low (5.9%), and the authors suggested that cultures in cases of seemingly uninfected single-stage revision do not require extended antibiotic therapy.

Padegimas et al[108] reported on a series of 117 cases with no preoperative concern for infection treated with single-stage revision arthroplasty and followed up for >4 years; 28 (23.9%) had an intraoperative UPC, of which 15 (57.1%) were *C. acnes* and the majority in male patients. They did not identify any predictor for reoperation, but they observed a higher rate of reoperation in patients without UPCs (20.2% vs. 7.1%); however, this did not reach clinical significance. In their cohort, 18 (64.3%) patients were treated with IV antibiotics for 6 weeks and 10 (35.7%) patients received only 2 weeks of oral antibiotics. Among culture-positive patients, there was only 1 reoperation in a patient who did not receive prolonged antibiotics.

Coste et al[29] reported on the outcome of treatment in 42 patients with shoulder PJI with a mean 34 months of follow-up. They defined infection on the basis of 7 criteria, including presence of sinus track, elevated serum WBC count, elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) level, positive culture including preoperative aspiration, radiographic evidence of implant loosening, and abnormality detected on bone scan, but no details were given on how these criteria were weighted in their definition; 20 cases followed primary arthroplasty and 22 occurred after revision. Thirty patients (71.4%) had subacute or chronic infection. At final follow-up, 22 (73.3%) were infection free, but there was wide variation in how patients were treated. They were able to obtain antibiotic information of 30 patients, and they judged treatment to be inadequate in 15 patients with regard to duration and type of antibiotics. Five patients were treated with

antibiotic only, and only 2 remained infection free at final follow up (60% failure rate).

Cuff et al[32] reported their results of 22 patients with infection after hemiarthroplasty (n = 17) and open cuff repair (n = 5) treated with 1-stage vs. 2-stage revision. In their series, *S. aureus* was the most common organism. Coagulase-negative *Staphylococcus* species (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 1-stage and 2-stage revision. The majority of the patients had 6 weeks of IV antibiotics; patients with no clinical sign of infection and with normal findings on intraoperative histologic evaluation were treated with 2 weeks of IV antibiotics. It is not clear what type of IV antibiotics were given.

Keller et al[79] performed a retrospective study of orthopedic hardware infection that was treated with débridement and retention of hardware, with single-stage revision, or without surgery to determine whether treatment with 6 weeks of oral antibiotics changes the rate of success at 1 year. They included only patients who had 2 separate positive cultures taken with a sterile technique from the same site that grew the same organism. Of the 89 patients in their study, 42 (47.2%) were infection free at 1 year. Patients with MRSA or gram-negative organisms, prior infection at the same site, or higher Charlson comorbidity score were less likely to achieve treatment success. Patients who were receiving oral suppression for 3-6 months had a significantly lower recurrence rate, but continuation of 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 1 year (odds ratio, 5.1; 95% confidence interval, 1.32-19.75).

Piggott et al[118] reported a retrospective study of surgical and nonsurgical management of 24 patients with *C. acnes* shoulder PJI from 1 center with median follow-up of 2 years. They defined definite PJI as 2 positive *C. acnes* cultures or 1 positive *C. acnes* culture plus sinus track, clinical purulence, or positive results of histopathologic examination. Probable PJI was defined as 1 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 incision and débridement with retention in 1 case, 1-stage revision in 4 cases, 2-stage revision in 7 cases, and spacer placement with no reimplantation in 3 cases. The median duration of antibiotic treatment was 6.3 months (range, 1.3-50.7 months). They found similar success rate with antibiotic only (67%) vs. surgery plus antibiotic treatment (71%; $P = 1.0$). Fifteen patients (71%) had rifampin as part of their antibiotic treatment, but taking rifampin did not significantly change their outcome (73% vs. 60%; $P = .61$), and 40% of patients who received rifampin had to stop it because of side effects.

Hsu et al[62] reported a retrospective study of 55 failed shoulder arthroplasty cases without clinical evidence of infection that underwent 1-stage revision and compared the outcome at an average of 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 prescribed oral amoxicillin and clavulanic acid for 3 weeks. If cultures were negative or only 1 culture was positive, the antibiotic was stopped at 3 weeks. If ≥2 cultures became positive at any point, IV ceftriaxone with or without vancomycin was started or continued for 6 weeks. They reported 42% antibiotic side effects in this cohort, more commonly among patients treated with IV antibiotics.

Klatte et al[85] retrospectively reviewed their experience of 26 patients with infected shoulder arthroplasty treated by 1-stage revision at mean follow-up of 4.7 years (range, 1.1-13.3 years). The most common organisms were *S. 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). Oral antibiotics were given to 4 patients for 5 days, 8 patients for 14 days, and 2 patients for 24 days and stopped when the CRP level was normalized and the wound was healed.

The literature on antibiotic treatment after 1-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 coagulase-negative staphylococci often have minimal clinical signs of infection. Thus, the diagnosis of infection is frequently made up to 2 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.[61]

There is no consensus on duration and type of antibiotics for this period. Antibiotic treatment after cultures are finalized should be dictated by clinical index of suspicion for infection, culture results, and risk-benefit analysis of antibiotic side effects. There is no high-level evidence to guide this decision.

Question 12: What are the recommendations regarding the route (IV vs. oral) and length of postoperative antibiotic treatment when a 1-stage revision arthroplasty is performed for subacute or chronic shoulder PJI caused by a virulent organism (eg, MRSA, MSSA, or *E. coli*)?

Recommendation:

IV antibiotics and IV followed by oral antibiotics are both reasonable options for 1-stage revision shoulder arthroplasty for subacute or 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 a treatment option for shoulder PJI.[50,62,68,95] However, the outcomes depend on the virulence of the organism, and the ideal duration and mode of antibiotic (IV or oral) treatment associated with single-stage revision are not known.

A literature search of PubMed and Embase databases of all English literature until March 2018 was conducted to query keywords "(shoulder OR 'upper extremity') AND (arthroplasty OR replacement) AND (infection OR infected)." A total of 1434 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 application of final exclusion criteria ("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 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 for PJI. These studies did not stratify results by the virulence of the organism. Thus, no firm conclusions about treatment according to the virulence of the organism can be made.

Beekman et al[10] retrospectively reviewed 11 patients with an infected reverse shoulder arthroplasty who underwent single-stage revision arthroplasty. Two of these patients had monobacterial infection with a virulent organism (*S. aureus* and *E. coli*). Both of these patients received at least 3 days of IV antibiotic and were discharged on oral antibiotics, which were continued for at least 3 months. Ince et al[66] retrospectively reviewed 16 patients with shoulder PJI (3 with identified virulent organisms) who underwent single-stage revision shoulder arthroplasty. Three patients (~19%) required revision. All patients received IV antibiotics for a mean of 8.6 days (range, 5-14 days), and antibiotics were stopped when the surgical incision had healed or laboratory values (ESR, CRP level, and WBC count) were trending down. No recurrence of infection was reported in 9 patients who were reviewed. Klatte et al[85] reported on the results of single-stage revision shoulder arthroplasty for PJI in 35 patients, of whom 26 were available for review. Patients received IV antibiotics for a mean of 10.6 days (range, 5-29 days), and 11 patients received oral antibiotics for a mean duration of 12.8 days (range, 5-24 days). There were 2 recurrences. Cuff et al[32] retrospectively reviewed 22 infected shoulder arthroplasties, of which 11 were treated with single-stage revision to reverse shoulder arthroplasty and IV antibiotics. Five of the 10 patients had virulent pathogens, and patients received antibiotics for 2 weeks (1 patient) or 6 weeks (4 patients), depending on cultures and intraoperative histology results. There was 1 recurrence of infection.

There is little evidence regarding the subsequent antibiotic management of subacute and chronic shoulder PJI due to highly virulent organisms treated with 1-stage revision. IV antibiotics and IV followed by oral antibiotics are both reasonable options. However, there is no consensus on the antibiotic type and duration of antibiotic treatment. In current practice, clinical judgement and trending of laboratory values (ESR and CRP) may help guide duration of antibiotic treatment.

Question 13: What is the optimal antibiotic treatment for culture-negative cases with positive clinical, radiographic, or intraoperative findings for acute shoulder PJI?

Recommendation:

The limited data suggest that treatment should consist of an empirical 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:

Five percent to 34% of periprosthetic shoulder infections are culture negative.[146] A MEDLINE database search was performed with the following terms: ("culture negative") AND ((prosthetic joint infection OR periprosthetic joint infection) OR (arthroplasty AND infection)). Ten original articles[12,26,64,75,83,84,94,111,126,158] and one systematic review[161] have been published on the topic of culture-negative PJI, none addressing shoulder PJI, and they focused on outcomes of culture-negative vs. culture-positive PJI (not on the best treatment). The existing publications indicate that the outcome of treatment of culture-negative PJI is similar to that of culture-positive PJI. 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.[7]

In a large multicenter study of the microbial etiology of PJI that included >2500 PJI cases in Spain, Benito et al[11] analyzed the microbiology of 42 cases of shoulder PJI (data not published). Twenty-eight (66.7%) PJIs were

caused by aerobic gram-positive cocci, mainly coagulase-negative staphylococci and *S. aureus*; 9 (21.4%) were due to *Cutibacterium* spp, and 9 (21.4%) were due to *Enterobacteriaceae*; 2 cases were due to *Pseudomonas aeruginosa*, and 5 (11.9%) 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. Consultation with an infectious disease specialist is recommended to arrive at a treatment strategy that includes empirical coverage against the most common pathogens of acute PJI. A broad-spectrum antibiotic regimen that covers aerobic gram-positive cocci (including MRSA 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 epidemiologic background.

- Treatment with vancomycin, teicoplanin, or daptomycin would cover aerobic gram-positive cocci (mainly staphylococci), 67% of infections according to the mentioned data; these antibiotics are also active against *Cutibacterium* spp. However, a β-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.[30] *C. acnes* is highly susceptible to a wide range of antibiotics, including β-lactams, quinolones, clindamycin, and rifampin.[1] However, resistance is beginning to emerge. Reports note an increasing emergence of resistance to macrolides, clindamycin, tetracycline, and trimethoprim-sulfamethoxazole.[1]
- Aerobic gram-negative bacilli mainly include *Enterobacteriaceae* and *P. aeruginosa*. Besides coverage of aerobic gram-positive cocci (with vancomycin, teicoplanin, or daptomycin), the addition of ceftriaxone is a good option to cover *Enterobacteriaceae* (if there is no suspicion of mechanisms of *Enterobacteriaceae* acquired resistance, such as extended-spectrum β-lactamase producing *Enterobacteriaceae*); ceftriaxone is also 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 extended-spectrum β-lactamase producing *Enterobacteriaceae* are suspected; it also has activity against *P. aeruginosa*.

Clearly knowing the organism and antibiotic susceptibility allows the selection of an antibiotic that is maximally bactericidal to the specific pathogen and minimally toxic to the patient. However, in lieu of these data, the empirical treatment should be administered intravenously with the decision for a second phase with oral antimicrobial treatment evaluated on a case by case basis. The role of rifampin is not clear in the scenario of a culture-negative PJI as it has demonstrated efficacy only in the staphylococcal infections. Moreover, the emergence of resistance to rifampin is high if it is used without a concurrent antibiotic to which the pathogen is susceptible, which cannot be clearly determined in a culture-negative PJI.

Question 14: What is the optimal antibiotic treatment of culture-negative cases with positive clinical, radiographic, or intraoperative findings for subacute or chronic shoulder PJI?

Recommendation:

The limited data suggest that treatment should consist of an empirical 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, 14 studies were considered for inclusion, and 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 used. There are limited observational data on empirical antimicrobial treatment options for patients with nonshoulder PJIs. 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 about 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.[56,129,137] There is limited evidence in nonshoulder arthroplasty settings of good outcomes with vancomycin[64,161] and cephalosporins.[75,161] Most studies in the nonshoulder literature did not find culture negativity to be a poor prognostic factor,[26,65,75,83,84,89,161] although 1 study[155] did find worse outcomes in culture-negative knee PJI treated with irrigation and débridement.

The addition of rifampin may be considered if there is strong suspicion for gram-positive infection, particularly staphylococcal, and in the setting of maintained hardware.[165] Synergy in the laboratory has been shown with

rifampin for *Cutibacterium*[46]; however, there is insufficient clinical experience of rifampin in the treatment of *Cutibacterium* infection to endorse its use.[67] Rifampin should never be used in monotherapy as resistance rapidly emerges. Rifampin should be used with careful monitoring for drug toxicity and drug interactions.

Prior antimicrobial exposure is a strong risk factor for culture negativity.[65,94,161] When infection is suspected, antibiotics should be withheld before 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 of hip and knee PJI suggest that a single dose of perioperative antibiotic therapy does not reduce operative culture yield.[117,147] 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 might be a contaminant.[9,49] Aseptic inflammation and unusual organisms should also be considered in the differential diagnosis of the culture-negative infection. In these cases, with concern for infection, pathologic examination may help identify granulomas or other signs of atypical infection; thus, sending tissue samples for pathologic examination 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.

Bone graft

Question 15: Should bone graft or cement be removed during treatment of acute shoulder PJI?

Recommendation:

Unknown. There are no reported investigations to guide the decision-making process regarding how to manage cement or autograft bone 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 (Supplementary data). In addition, it is unknown whether complete removal of this material is necessary to eradicate shoulder PJI. The goal of surgical intervention in the setting of PJI is to débride 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 may require 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 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 complications that come with complete removal of these materials. In addition, it is unknown whether retention of this material requires a change in the postoperative antibiotic management. Finally, it is also unknown how different bacterial species and antibiotic sensitivity profiles may influence the successful treatment of PJI. Future investigation is required to answer this question in an evidence-based fashion to develop a treatment algorithm for which cases can predictably be successful with retention of cement or graft and which settings require complete removal of all graft and cement materials.

Question 16: Should bone graft or cement be removed in treatment of subacute or chronic shoulder PJI?

Recommendation:

Unknown. There are no reported investigations to guide the decision-making process regarding how to manage cement or autograft bone 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:

Refer to the rationale for Question 15.

Component retention

Question 17: Is there a role for irrigation and débridement with implant retention in treatment of acute shoulder PJI?

Recommendation:

There is insufficient high-quality evidence to support or to discourage the use of irrigation and débridement with implant retention in treatment of acute shoulder PJI.

Level of evidence: Limited

Delegate vote: Agree: 96%, Disagree: 4%, Abstain: 0% (Unanimous, Strongest Consensus)

Rationale:

There are few data provided by systematic search (Supplementary data) demonstrating the outcome or infection-free implant survivorship for the treatment of

acute shoulder PJI with irrigation and débridement and implant retention. To date, there are only 37 patients (38 shoulders) with outcomes after this procedure described in the literature.[29,36,107,114] These studies, all level IV retrospective case series, demonstrated a 50% failure rate (defined as continued infection) and the requirement for additional treatment. Three of 4 studies treated acute, subacute, and chronic infections with this technique, but the sample size was too small to analyze how timing of infection influences outcomes.[29,107,114]

Jacquot et al[68] found that 1 of 2 shoulders classified as chronic PJI, 2 of 4 shoulders classified as subacute PJI, and 2 of 7 shoulders classified as acute PJI had recurrent infection requiring additional treatment. The study of Dennison et al[36] was the only study that specifically compared the outcome of acute (surgery within 6 weeks after index arthroplasty and <3 weeks of symptoms) and delayed onset/delayed acute cases (>6 weeks after index arthroplasty with <3 weeks of symptoms). This retrospective level IV case series examined 9 patients (10 shoulders) and found that 3 of 10 had recurrent infection requiring resection arthroplasty (mean follow-up, 4.1 years; range, 0.58-12.8 years). The method of irrigation and débridement varied in this study, with 3 performed arthroscopically and 7 open. All of the patients requiring resection had irrigation and débridement performed open; the numbers were too small to perform any meaningful analysis of how this may influence outcomes or infection-free survivorship. In addition, 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 débridement with implant retention plays a role in the treatment of shoulder PJI. Specific attention to answer 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 antibiotic use (type, duration, and method of delivery) will be critical to guide these treatment decisions.

Question 18: What are the indications for irrigation and débridement with component retention in subacute or chronic shoulder PJI?

Recommendation:

Irrigation and débridement with component retention alone for subacute or chronic shoulder PJI in the literature is less successful than component explantation 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 of 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 débridement and implant retention for subacute or chronic infection.

Irrigation and débridement with component retention for shoulder PJI in the subacute and chronic setting is associated with low rates of eradication of infection.[2,17,29,41,68,107,140,144,159,162] Of the 51 surgical cases identified in studies with a reported eradication rate, approximately half (n = 24 [47%]) were successfully cured with débridement alone. The majority of these successful treatments were from 2 recent studies that integrated modular component exchange with partial component retention.[68,144]

Stone et al[144] described patients with shoulder PJI treated with 1-stage partial component exchange compared with patients with 1-stage complete hardware removal and 2-stage revisions. The greatest success rate was with complete 1-stage revisions (96% eradication of infection) compared with only 63% eradication for partial 1-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 persistent infection.

A French multicenter study described 32 patients who underwent revision for infection after reverse shoulder arthroplasty. Of these, 13 patients underwent débridement, modular component exchange, and partial component retention.[68] Only 7 patients (54%) were successfully cleared of infection with débridement alone. However, the 15% complication rate reported with débridement was lower than that reported for resection (33%), 1-stage revision (20%), or 2-stage revision (36%). The authors proposed that initial débridement be considered for primary treatment of infected reverse shoulder arthroplasty, given that more than half of patients were successfully treated with relatively few complications.

Primary treatment of subacute or chronic shoulder PJI with débridement, irrigation, and component retention is an option, particularly in patients in whom 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 with 1- or 2-stage revision.

Question 19: Should modular components be exchanged during irrigation and débridement of acute shoulder PJI?

Recommendation:

Whereas there is logic in exchanging nonfixed modular components, such as the bearing surfaces, to allow thorough irrigation and débridement 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 irrigation and débridement for acute PJI was undertaken. Five papers were found that recorded whether modular components were exchanged,[36,68,107,144,162] totaling 53 patients. The pooled infection-free survivorship was 65% in the modular exchange group (19/29) vs. 58% (14/24) in the no-exchange group ($P = .77$, Fisher exact test).

Three of these papers[36,107,162] specified the outcome for patients with acute débridement and retention with and without modular exchange. In total, 10 patients underwent acute débridement and retention of prosthesis without modular exchange with an infection-free survivorship of 70% (7/10). Eight patients are recorded as having undergone polyethylene exchange during débridement of an acute infection, with an infection-free survivorship of 62.5% (5/8; $P > .05$).

Question 20: Should modular components be exchanged during irrigation and débridement of subacute or chronic shoulder PJI?

Recommendation:

We defer to the response for Question 21: Should well-fixed glenoid components be removed during surgical treatment of 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 or chronic shoulder PJI. Therefore, it can be extrapolated that modular components, which can be exchanged to remove biofilm with far less morbidity than for 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)

Question 21: Should well-fixed glenoid components be removed during surgical treatment of subacute or chronic shoulder 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 or chronic PJI. Certainly, there may be cases (ie, high-risk surgical patients) in which the patient and surgeon may choose to accept the higher failure rate with component retention to avoid surgical morbidity introduced by removal of 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 (Supplementary data). In this updated systematic review, 3 additional studies were identified that met inclusion and exclusion criteria and added to the data from the prior systematic review by Nelson et al,[106] which involved a search until April 2014 (Question 21: Table I). Only the study by Jacquot et al[68] defined a subset of patients treated for subacute or chronic PJI; 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 by a 1-stage or 2-stage procedure (<10%).[106] Because of this, one must recommend for treatment of subacute or chronic shoulder PJI with removal of all, even well-fixed, components. However, these studies were based on retrospective review of patients treated according to the surgeon's preference, and the features of the particular infections are not well documented (bacteria, antibiotic sensitivity). It is possible, perhaps even probable, that patients treated with implant retention vs. removal may

Question 21: Table I Studies on surgical treatment of subacute and chronic shoulder PJIs

Study	Date	Study design	I&D and component retention		1-stage revision		2-stage revision	
			No. treated	Failed treatment (%)	No. treated	Failed treatment (%)	No. treated	Failed treatment (%)
Nelson et al[106]	2016	Systematic review	35	11	282	28	97	6
Stone et al[144]	2017	Retrospective case series	15	4	45	2	19	4
Marcheggiani Muccioli[95]	2017	Systematic review	27	8	77	3	98	14
Jacquot et al[68]	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%)

PJIs, Periprosthetic joint infections; *I&D*, irrigation and débridement; *N/A*, not applicable.

have had different infectious presentations that led the treating surgeon to the chosen approach. Further comparative research is needed on this topic. In addition, there may be cases (ie, high-risk surgical patients) in which the patient and surgeon may choose to accept the higher failure rate with component retention to minimize surgical morbidity.

Question 22: 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 UPCs, 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:

PJI is one of the most challenging complications of shoulder arthroplasty.[45,128] The difficulty of diagnosis and treatment is attributed to *Cutibacterium acnes*, which is a bacterial microorganism with low virulence.[39] Unlike in knee and hip PJI, laboratory tests may be inadequate for diagnosis of indolent shoulder PJI caused by this organism.[128] The prevalence of *C. acnes* has been reported to be as high as 50% in intraoperative cultures obtained during revision surgery for a painful and stiff shoulder arthroplasty.[45] This determination led to the definition of a new clinical entity, unexpected positive intraoperative cultures (UPCs). Because 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.[86,113] Because of the inadequacy of Gram stain and frozen section and the long incubation time, it is difficult to make a decision about implant removal during revision surgery.[128] Moreover, in the case of the well-fixed implant, the explantation procedure can be difficult and have associated morbidity.[57,62,86]

There is limited evidence for removal of well-fixed implants in revision shoulder arthroplasty without clinical or radiographic signs of infection.[120,128] Pottinger et al[120] reported that implants may need to be removed in patients who have risk factors for positive culture as these cases are more likely to be PJI. Although McGoldrick et al[99] recommended single-stage reimplantation in the presence of loose implants, they did not comment on management of well-fixed implants. Similarly, Grosso et al[57] reported low infection recurrence rates with the removal of all components and single-stage reimplantation in patients with UPCs. On the other hand, Topolski et al[149] and Kelly and Hobgood[80] reported high recurrence rates with the retention of implants. Lutz et al[92] evaluated infection with *C. acnes* in patients who underwent shoulder, knee, or hip osteosynthesis or arthroplasty and reported that the absence of septic findings could not exclude the presence of infection. They emphasized that implant removal is important for the successful treatment of *C. acnes* infection.

Implant

Question 23: What is the optimal implant for treatment of acute shoulder PJI: RTSA, anatomic TSA, or hemiarthroplasty?

Recommendation:

The optimal implant for treatment of acute shoulder 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.[140] There are a number of options for the treatment of acute PJI, including antibiotic treatment alone, débridement with or without exchange of modular components, single-stage complete exchange, 2-stage exchange with antibiotic spacer, definitive permanent implantation of an antibiotic spacer, and resection arthroplasty.

Results of systematic review (Supplementary data) are summarized in Question 23: Table I. Of 42 studies, 19 differentiated acute shoulder PJI from subacute or chronic PJI, with 20% of cases (93/459) in the acute category. Although there are a fair number of studies that describe patients with acute PJI, the types of implants explanted and implanted were not consistently reported or stratified, and therefore the ability to draw conclusions about reinfection rates and clinical outcomes is limited. Also, a clear obstacle in synthesizing the literature is that a consensus definition for shoulder PJI is not used by these studies,[63] and defining reinfection is highly variable in the literature. Thus, the choice of optimal implant is difficult to determine. 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 débridement

Irrigation and débridement with component retention or exchange of modular components is often considered a reasonable option in acute PJI. The reported outcomes are variable with regard to reinfection rates and clinical outcomes (Question 23: Table II).[2,10,25,29,69,71,107,131,140,159,162] In aggregate, these 11 studies reported a 42% recurrence rate for acute PJI treated with irrigation and débridement (19 of 45 patients). Given these data, the surgeon must weigh the risks of recurrent infection with the morbidity of implant removal. The decision of whether to perform irrigation

Question 23: Table I Studies stratified by infection acuity and implant type

Author	Journal	Year	Acuity			Procedure(s)	Final implant					Re-infection by implant type	Functional by implant type
			Acute	*Subacute*	*Chronic*		*Hemi*	*TSA*	*Reverse*	*Spacer*	*Resection*		
Acherman[2]	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[5]	Eur J Orthop Surg Traum	2012	8	22	14	I&D/partial Single-stage Two-stage Resection	2	1	23			unclear re-infection rate, 12 of 44 needed revision	No comparison of implant types
Assenmacher[8]	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[10]	JBJS Br	2010	3	7	1	Single-stage			10	1		3 of 3 recurrence with I&D	Median CM 55
Boileau[17]	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[20]	JSES	2006	1	2	4	Resection					7	Resection only	Resection only
Buchalter[22]	JSES	2017	NOT STRATIFIED			Two-stage	4	5	10			5 of 19 recurrence, not stratified by acuity/implant	No comparison of implant types
Cheung[25]	Clin Orthop Relat Res	2008	6	0	0	I&D/partial	8	4				2 of 6 recurrence	I&D 'unsatisfactory' in 5 of 12 postoperative hematomas; no implant types
Coste[29]	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[32]	JBJS Br	2008	NOT STRATIFIED			Single-stage Two-stage			17			No recurrence	Mean ASES, 57.0; pain, 3.5; SST, 4.0
Debeer[34]	Acta Orthop Belg	2006	NOT STRATIFIED			Resection					7	Resection only	Resection only
Foruria[45]	JSES	2013	NOT STRATIFIED			I&D/partial	45	61	1			10% recurrence but no stratification	No comparison of implant types
Ghijselings[52]	Acta Orthop Belg	2013	5	7	5	Two-stage Antibiotic spacer Resection			3	6	8	No differentiation between 'early' and 'acute hematogenous'	Patients more satisfied with resection than with antibiotic spacer
Grosso[57]	JSES	2012	NOT STRATIFIED			Single-stage	2	7	8			No comparison of implant types	No comparison of implant types
Hsu[62]	JBJS Am	2016	NOT STRATIFIED			Single-stage	33	14	1			No recurrence in hemi, TSA, or reverse	No comparison of implant types

(*continued on next page*)

Question 23: Table I Studies stratified by infection acuity and implant type (*continued*)

Ince[66]	JBJS Br	2005	NOT STRATIFIED			Single-stage	15		1			No recurrence in hemi or reverse	Mean CM, 33.6; UCLA, 18.3
Jahoda[69]	Acta Chir Orthop Traumatol Cech	2008	1	3	7	I&D/partial Two-stage	NOT STRATIFIED					2 of 6 recurrent with I&D (mixed acute and subacute)	n/a
Jawa[70]	JBJS Am	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[71]	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[80]	Clin Orthop Relat Res	2009	NOT STRATIFIED			Single-stage	1	3	24			No comparison of implant types	No comparison of implant types
Klatte[85]	Bone Joint J	2013	4	15	16	Single-stage	19		7			2 of 35 recurrence, acuity unknown	Hemi: CM 43.3 Hemi with bipolar head: CM 56 Reverse: CM 61
Lee[87]	Int Orthop	2018	8	4	0	Two-stage	2		10			No recurrence in hemi or reverse	Pain 2.3, ASES 64.2, CM 66.1
Levy[88]	Orthopedics	2015	NOT STRATIFIED			Spacer				9		No recurrence with antibiotic spacer	Pain 2.0, SST 6.3, ASES 65.8, SANE 54.6
Mahure[93]	Orthopedics	2016	NOT STRATIFIED			Spacer				9		No recurrence with antibiotic spacer	ASES 57
Muh[105]	JSES	2013	NOT STRATIFIED			Resection					22	n/a	n/a
Ortmaier[107]	Eur J Orthop Surg Traumatol	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[116]	Arch Orthop Trauma Surg	2018	NOT STRATIFIED			I&D Antibiotic spacer				19		no recurrence	CM, 38.3; pain, 1.5; FE, 59.2°, Abd, 52.5°
Rispoli[130]	JBJS Br	2007	NOT STRATIFIED			Resection					18	no report of recurrence	ASES, 36; SST, 3.1
Romanò[131]	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[132]	Clin Orthop Relat Res	2011	8	7		Two-stage			17			1 of 17 recurrence with reverse	Penn, 66.4; FE, 123°; ER, 26°
Sperling[139]	Clin Orthop Relat Res	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[141]	JSES	2015	NOT STRATIFIED			Resection					7	1 of 7 recurrence	n/a
Stine[142]	JSES	2010	0	0	30	Spacer Two-stage	10	1	4	15		0 of 30 recurrence	Inadequate stratification to compare implant types

(*continued on next page*)

Question 23: Table I Studies stratified by infection acuity and implant type (*continued*)

Stone[143]	JSES	2017	NOT STRATIFIED			I&D/partial One-stage Two-stage	STRATIFICATOIN UNCLEAR				4 of 15 recurrence with I&D, uncertain acuity	
Strickland[144]	JBJS Br	2008	3	7	9	Two-stage	13	5	1			7 of 19 recurrence with two-stage	No comparison of implant types
Themistocleous[147]	JSES	2007	NOT STRATIFIED			Spacer				4		no stratification	n/a
Topolski[148]	JSES	2006	NOT STRATIFIED			Single-stage	NOT STRATIFIED					n/a	n/a
Twiss[152]	Semin Arthroplasty	2010	NOT STRATIFIED			Spacer Two-stage	Stratification UNCLEAR					0 of 30 recurrence	n/a
Verhelst[154]	JSES	2011	0	4	17	Spacer Resection				10	11	2 of 21 recurrence	Inadequate stratification to compare implant types
Weber[157]	Int Ortho	2011	NOT STRATIFIED			I&D/partial Two-stage Resection	NOT STRATIFIED					0 of 1 recurrent for I&D	
Zavala[160]	JSES	2012	5	2	0	I&D/partial Resection			5		2	1 of 4 recurrence with I&D	
Zhang[161]	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%**

Hemi, hemiarthroplasty; *TSA*, total shoulder arthroplasty; *I&D*, irrigation and débridement; *FE*, forward elevation; *ER*, external rotation; *CM*, Constant-Murley score; *ASES*, American Shoulder and Elbow Surgeons score; *SST*, Simple Shoulder Test score; *UCLA*, University of California–Los Angeles score; *N/A*, not applicable; *SANE*, Single Assessment Numeric Evaluation; *Abd*, abduction.

Question 23: Table II Success of I&D with component retention or exchange of modular components

Author	Journal	Year	No. undergoing I&D	No. recurrent infection
Achermann[2]	Infection	2013	4	1
Beekman[10]	JBJS Br	2010	3	3
Cheung[25]	Clin Orthop Relat Res	2008	6	2
Coste[29]	JBJS Br	2004	8	6
Jahoda[69]	Acta Chir Orthop Traumatol Cech	2008	6	2
Jerosch[71]	Arch Orthop Trauma Surg	2003	2	0
Ortmaier[107]	Eur J Orthop Surg Traumatol	2014	4	2
Romanò[131]	Int Orthop	2012	5	1
Sperling[140]	Clin Orthop Relat Res	2001	2	1
Weber[159]	Int Orthop	2011	1	0
Zavala[162]	JSES	2012	4	1
Total			45	19

I&D, irrigation and débridement

and débridement may also depend on the acuity of symptoms, with some studies suggesting low recurrence when it is performed within 2 weeks of symptom onset, even when the time between index surgery and symptom onset is prolonged [29,162] (ie, secondary hematogenous infection[36]).

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 or glenoid bone loss.[29,59,60] In the setting of a shoulder PJI, a thorough

débridement is required, and this 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 the functional outcome after implantation with an anatomic implant may be compromised by rotator cuff loss or instability.[37,60,76] Some studies report that the reverse implant appears to better compensate for soft tissue loss or bone deficiency[31,60] and can improve pain control and functional recovery without a high recurrent infection rate.[10,32,85,87,132]

Nevertheless, some reports of treatment with a reverse shoulder arthroplasty for failed arthroplasty note suboptimal functional results and a high rate of complication.[13,44,55,68,73,100,141,157] Therefore, hemiarthroplasty should be a consideration in cases in which minimizing complications and further surgery is a priority.[48,53]

Indications for hemiarthroplasty

In cases of acute shoulder PJI 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.[8,62,85] In addition, in some cases of substantial glenoid bone loss, recurrent instability of a reverse, and patient factors such as noncompliance precluding implantation of a reverse, conversion to a hemiarthroplasty[48] may be the preferred choice to minimize intraoperative and postoperative complications.[40]

Indications for TSA

Whereas better pain relief and functional scores can be obtained with primary TSA compared with hemiarthroplasty,[6] the rate of polyethylene glenoid component loosening in the setting of revision is high.[19] In the setting of acute PJI, conversion to TSA 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[20,34,105,130,142] and indefinite placement of an antibiotic spacer[88,93,116] can be considered for acute PJI.

Resection

Question 24: What are the indications for resection shoulder arthroplasty in acute 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:

In a systematic search (Supplementary data), no manuscripts that reported on resection shoulder arthroplasty for acute PJI were identified. The available literature has no evidence pertaining to resection arthroplasty in *acute* shoulder PJI to provide guidance on this question.

Question 25: Is there a role for resection shoulder arthroplasty in the management of subacute or chronic PJI?

Recommendation:

The available literature does not support specific indications for resection arthroplasty for subacute or chronic shoulder PJI with information of sufficient quality to provide guidance. Resection arthroplasty is

Question 25: Table I Articles specifically concerning resection arthroplasty in shoulder PJI, with details as noted

Author	Year	No.	Failed	CMS	SST	Surgery before resection (No.)	VAS	ASES	FE	Abd	ER
Verhelst[156]	2011	11 E	2/11	40.4			2.6		85.5°	78.1°	21°
		10 EAS									
Rispoli[130]	2017	18 E			3.1		4.5	36	70°		31°
Stevens[142]	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°
Maynou[98]	2006	10 E	0	28							
Braman[20]	2006	7 E	0			2.2			28°		8°
Ghijselings[52]	2013	8 E		27.8	2.4		3.6				
		5 EAS		20.6	1		6				

CMS, Constant-Murley score; *SST*, Simple Shoulder Test; *VAS*, visual analog scale; *ASES*, American Shoulder and Elbow Surgeons score; *FE*, forward elevation; *Abd*, abduction; *ER*, external rotation; *E*, explantation alone; *EAS*, explantation and antibiotic spacer.

Many data are incomplete because not all ideal data were recorded by the authors (see George et al[51]). In 3 studies,[52,142,156] there are comparison cases of explantation and antibiotic spacer with explantation alone.

an acceptable salvage treatment to eradicate shoulder PJI when revision to a definitive implant is considered too risky because of the patient's medical comorbidities 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 (Appendix: *Search strategy and Table*). In addition, many of these case series include no other cohort against which to compare any other form of treatment strategy for shoulder PJI. The available literature is further limited by the fact that published series evaluate outcomes with a variety of methods: pain relief, recorded either as a subset of a score (eg, the Constant-Murley or American Shoulder and Elbow Surgeons score) or as a visual analog scale score; function, recorded either as a subset of a score or by direct description; and management of infection, recorded as eradicated, recurrent, or persistent, without clear definition of diagnostic criteria.

The systematic review by George et al[51] of management strategies for shoulder PJI found 8 papers (83 cases) relating to resection arthroplasty. The number of cases reported ranged from 5 to 21, with a mean duration of follow-up of 39.8 months (standard deviation: 20.8; range: 19.2-102.6). Infection was eradicated in 72 of 83 (86.7%), with no difference (statistical or clinically meaningful) in infection eradication observed between resection, single-stage exchange, two-stage exchange, 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. Patients reported worse functional scores (Constant-Murley score) 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 means that it is not possible to provide a conclusion concerning the indication for one modality over another if the aim of intervention is to eradicate infection while optimizing the functional outcome for patients.

In review of the available literature, the majority of PJIs for which resection is reported as an outcome are RTSAs.[68,105,131] It is not clear whether this relates to the more challenging reconstructions often encountered after revision RTSA or perhaps the nature of the population of RTSA patients, who tend to have more medical comorbidities and lower functional demands.

The concept that resection arthroplasty carries the advantage of being one final surgery should be tempered by the results showing that 2 débridements were required on average for infection to be clinically eradicated (mean follow-up, 20 months).[20] Braman et al[20] showed that in their series of 7 patients, whereas 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[130] 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. If preoperative impairment was not substantial (defined as a Constant-Murley score of >30), there was no significant improvement after surgery.[68] The same authors considered that reimplantation (whether single- or 2-stage revision) delivered better functional outcomes than resection arthroplasty.[68] Zavala et al[162] concluded that resection is inferior to a DAIR strategy in providing for function without increasing the risk of persistent or recurrent infection at a minimum of 12 months of follow-up while also commenting that implant removal led to potentially revision-limiting bifocal bone loss. Debeer et al[34] recommended resection for the elderly with PJI and with lower functional expectations. A single comparative study (unpublished) comparing resection with staged reimplantation demonstrated that there is benefit for range of motion if a staged reimplantation could be safely undertaken with no increased risk of persistent or recurrent infection.[27] Resection arthroplasty for subacute or chronic PJI may provide some pain relief in approximately one-third to one-half of cases.[24,98,105,130,140,162]

There are some technical and prognostic factors that may affect the patient's functional outcome and satisfaction. Retention of the tuberosities appears useful for function, possibly by reducing the tendency for proximal humeral migration.[156] In addition, there is some debate about how an antibiotic spacer may compare with resection alone with respect to eradication of infection and function. Verhelst et al[156] reported that use of a spacer (permanent or temporary) did not appear to compromise eradication of infection but also did not necessarily confer benefit for function or pain relief postoperatively. In contrast, Ghijselings et al,[52] in a comparative series evaluating resection vs. 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. In the setting of bilateral disease, Ueda et al[153] concluded that there is improved function for domestic activities with bilateral retained antibiotic spacers compared with historical reports of resection arthroplasties for PJI.

In summary, the functional result is relatively poor, but the eradication of infection is good (86.7%), especially considering that patients with resection arthroplasty are likely to be frail or to have difficult-to-treat pathogens.[51] It remains unclear whether a resection arthroplasty is preferred to a retained antibiotic-impregnated cement spacer; some studies suggested 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 because of the patient's medical comorbidities or technical complexity of revision surgery.

Articles specifically concerning resection arthroplasty in shoulder PJI, with details, are noted in Question 25: Table I.[51,52,142,156]

Revision

Question 26: Is there a role for an antibiotic spacer for the treatment of shoulder PJI?

Recommendation:

An antibiotic-loaded cement spacer may be used as part of a shoulder 2-stage exchange arthroplasty for local delivery of high concentration of antibiotics. An antibiotic-loaded cement spacer may be used as a definitive and 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 shoulder periprosthetic infection.[28,58,70,101] The antibiotic-loaded cement spacer delivers antibiotics to the local tissues, eliminates dead space, and maintains soft tissue tension and shoulder function; for these reasons, it is used as a temporary spacer in 2-stage reimplantation.[58,70] Less commonly, it can be considered a permanent and definitive spacer if the patient declines further surgery or if the patient is not a good surgical candidate for the second stage of 2-stage reimplantation (eg, sick patient, significant bone loss).[88,93,116,148]

The role of antibiotic-loaded cement spacer in shoulder PJI has been studied previously in retrospective cohort studies (Appendix: *Search Strategy* and Question 26: Table I). An antibiotic-loaded cement spacer is indicated as a temporary spacer in the 2-stage treatment of shoulder PJI in conjunction with IV antibiotics.[58,70] However, use as a definitive and permanent spacer has also been described for treatment of patients who are at high surgical risk or refuse the second stage of 2-stage treatment.[88,93,116] Jawa et al[70] reported a retrospective review of 28 patients with infected shoulder arthroplasty who were managed with antibiotic-loaded cement spacer; 16 patients underwent a 2-stage operation and 12 patients declined the second stage

Question 26: Table I Studies examining the role of antibiotic-loaded cement spacer in treatment of infected shoulder arthroplasty

Study	No. of patients or shoulders	Follow-up	Antibiotics used in the cement spacer	Spacer role	Recurrence of infection and complications associated with spacer
Jerosch and Schneppenheim[71]	10	6-30 mo (range)	No information	Temporary: 8 Permanent: 2	Recurrence: 0%
Themistocleous[148]	4	22 mo	Tobramycin Vancomycin	Temporary: 2 Permanent: 2	Recurrence: 0%
Coffey et al[28]	16	20.5 mo	Gentamicin	Temporary: 12 Permanent: 4	Recurrence: 0%
Jawa et al[70]	28	27.6 mo	Tobramycin Vancomycin	Temporary: 16 Permanent: 12	Recurrence: 5 (18%) Dislocation: 1 (3.5%) Fracture of spacer: 3 (11%)
Stine et al[143]	30	2.4 yr	Tobramycin Vancomycin	Temporary: 18 Permanent: 15	Recurrence: 0%
Romanò et al[131]	32	2.4 yr	No information	Temporary: 17 Permanent: 15	Recurrence: 3% (one in permanent group)
Levy et al[88]	9	25 mo	Tobramycin Vancomycin	Permanent	Recurrence: 0%
Mahure et al[93]	9	4 yr	Tobramycin Vancomycin Gentamicin	Permanent	Recurrence: 0% Glenoid erosion: 2 (22%) Periprosthetic fracture: 1 (11%)
Pellegrini et al[116]	19	8 yr	Gentamicin Clindamycin Vancomycin	Permanent	Recurrence: 0% Glenoid osteolysis: 1 (5.3%)
Padegimas et al[110]	37	4 yr	Tobramycin Vancomycin	Temporary	Spacer revision: 1 (2.7%) 6 positive cultures at second stage but no clinical signs of infection
Lee et al[87]	12	40.8 mo	Vancomycin	Temporary: 9	Recurrence: 0%
Torrens et al[150]	21		Tobramycin	Temporary	Revision of spacer: 1 Positive cultures at second stage: 3 (13.6%)

of the procedure. At final follow-up, 5 patients had recurrence of infection (18%) and 5 patients had severe pain (18%). Complications with use of cement spacer included dislocation (1 patient) and fracture (3 patients). Torrens et al[150] reported a culture-positive rate of 13.6% (3 shoulders) from 22 antibiotic-loaded cement spacers retrieved during second-stage reimplantation. In contrast to the studies by Jawa et al and Torrens et al, other investigators have reported a lower rate of recurrence of infection with antibiotic-loaded cement spacer. Pellegrini et al[116] reported no recurrence of infection with a definitive antibiotic spacer in a cohort of 19 low-demand, elderly patients who had infected shoulder arthroplasties. 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[88] retrospectively reviewed outcomes in 9 patients with infected shoulder arthroplasty who elected not to have the second-stage reimplantation. These patients had acceptable function with the antibiotic spacer at a mean follow-up of 25 months. There was no recurrence of infection (0%), and only 1 patient (11%) was unsatisfied with the results. Mahure et al[93] reported no recurrence of infection (0%) in a retrospective case series of patients with shoulder PJI who elected antibiotic-loaded cement spacer as a definitive treatment after the first stage of the two-stage treatment. In a retrospective study, Romanò et al[131] reviewed 44 patients with shoulder PJI; 32 patients had treatment with a temporary or permanent antibiotic-loaded spacer. There was 1 recurrence of infection in the definitive spacer group. Lee et al[87] used antibiotic-loaded cement spacer for the first-stage implantation in 12 patients. All patients received IV antibiotics followed by the second-stage treatment. There was no recurrence of infection (0%) at mean follow-up of 41 months. Improved functional outcome with the use of antibiotic-loaded cement spacer was reported by Jerosch and Schneppenheim[71] in a retrospective review of 10 patients with shoulder PJI. Patients were able to perform physical therapy with the antibiotic spacer in situ, and 8 patients underwent the 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, gentamicin, and tobramycin) have been used alone or in combination. Spacer design and patient-specific anatomic features have also been studied with regard to infection clearance and patient satisfaction. Padegimas et al[110] retrospectively compared stemless and stemmed antibiotic spacers in a cohort of 37 patients with shoulder PJI. They found no difference between the 2 types of spacers with respect to their ability to control infection and the percentage transition (70% in both groups) to second-stage reimplantation. There are insufficient data to compare handmade vs. commercial premade antibiotic-loaded cement spacers.

Question 27: What are the indications for 1-stage vs. 2-stage exchange arthroplasty in the management of acute shoulder PJI?

Recommendation:

Unknown. Single-stage exchange for shoulder PJI has a statistically significant lower reinfection rate and lower complication rate than 2-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:

Shoulder PJI is a devastating complication with significant morbidity. The incidence of PJI after primary shoulder arthroplasty has a reported range of 1%-4% and up to 4%-15% after revision arthroplasty.[29,109] Historically, treatment of shoulder PJI has been influenced by evidence from hip and knee arthroplasty infection management experience.[51,106] Two-stage exchange arthroplasty with implant removal, irrigation and débridement, and insertion of antibiotic spacer followed by delayed reimplantation has been suggested as the ''gold standard'' for shoulder PJI.[51] However, single-stage exchange has also been advocated

Question 27: Table I Reinfection and complication

	Patients	Reinfection	Pathogens	Constant score	Complications
1-Stage					
12 papers	161 patients	5.6% reinfection	72 *C. acnes*	49.1	12.70%
	6 acute	$P < .05$	29 CoNS	44 patients	79 patients
	13 subacute		20 MSSA	$P < .11$	$P < .05$
	8 chronic		3 MRSA		
2-Stage					
27 papers	325 patients	11.4% reinfection	68 *C. acnes*	51.1	21.90%
	47 acute	$P < .05$	64 CoNS	102 patients	205 patients
	46 subacute		33 MRSA	$P < .05$	$P < .05$
	74 chronic		56 MSSA		

CoNS, coagulase-negative staphylococci; *MSSA*, methicillin-sensitive *Staphylococcus aureus*; *MRSA*, methicillin-resistant *Staphylococcus aureus*.

Question 27: Table II Functional outcome

	Neer (total)	ASES score (mean)	SST (mean)	DASH	FF (mean)	Abd (mean)	ER (mean)
1-Stage							
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
2-Stage							
27 papers	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

ASES, American Shoulder and Elbow Surgeons; *SST*, Simple Shoulder Test; *DASH*, Disabilities of the Arm, Shoulder, and Hand; *FF*, forward flexion; *Abd*, abduction; *ER*, external rotation; *N/A*, not applicable.

to achieve similar infection control with a single operation.[10,66,85] The purpose for this review was to understand the roles of single-stage and 2-stage exchange revision in the setting of acute shoulder PJI and to 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 2-year follow-up minimum. In a literature review (Supplementary data), we identified 12 articles that evaluated 1-stage exchange and 27 articles that evaluated 2-stage exchange.

To address the stated question, we reviewed data on acute shoulder PJI pertaining to infection eradication using single-stage or 2-stage exchange and additional functional outcomes, which are summarized in Question 27: Tables I and II. In total, 161 cases were identified with single-stage revision and 325 cases with 2-stage revision. The majority of studies reported timing of infection but few reported the success of treatment with either single-stage or 2-stage exchange based on timing of infection. Beekman et al[10] reported on 3 cases of acute PJI treated with single-stage exchange with no cases with reinfection. Two additional studies with a total of 3 cases of acute PJI found that no patients had reinfection.[66,68] Buchalter et al[22] reported 1 case of acute PJI treated with 2-stage reconstruction that had no reinfection. Acherman et al[2] reported 1 case of acute PJI that failed treatment with 2-stage exchange and had persistent infection.

This review highlights gaps in current literature. All studies identified were retrospective and thus have substantial selection bias. Whereas the findings in aggregate suggest that single-stage exchange is a viable option for acute PJI, the numbers were small, and there are no studies that control for various risk factors and selection biases, such as the particular pathogen, antibiotic resistance profile, timing of infection, or diagnostic features like obvious clinical findings of infection. Furthermore, there are insufficient numbers of studies that provide analysis for treatment of acute shoulder PJI using either single-stage or 2-stage exchange with regard to complications or functional outcomes.

Question 28: What are the indications for 1-stage vs. 2-stage revision in subacute or chronic shoulder PJI?

Recommendation:

The indications for single-stage vs. 2-stage exchange are unclear at this time. The pooled data demonstrate single-stage exchange to be superior to 2-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:

The purpose of this review was to understand and to compare the role of single-stage and 2-stage exchange for the treatment of shoulder PJI. Two-stage exchange arthroplasty with implant removal, irrigation and débridement, insertion of antibiotic spacer, and antibiotic treatment followed by reimplantation has been suggested as the gold standard for treatment of shoulder PJI.[51] In a comprehensive literature review (Supplementary data), we identified 12 articles that evaluated 1-stage exchange and 27 articles that evaluated 2-stage exchange. The majority of papers reported preoperative laboratory values for diagnosis of PJI based on elevated WBC count, CRP level, and ESR. Clinical findings, such as draining sinus, erythema, or swelling, were inconsistently reported. Most studies reported the number of joint aspirations performed with positive results for 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[140] and Strickland et al,[145] with acute meaning <3 months, subacute 3-12 months, and chronic >12 months. There was consistent reporting of the pathogens found either preoperatively or intraoperatively. *Cutibacterium acnes* was the most

Question 28: Table I Reinfection and complications for single-stage exchange

Cases	Reinfection rate	Pathogens	Constant score (mean)	Complication rate
161 total 13 subacute 8 chronic	5.6% ($P < .001$)	72 *C. acnes* 29 CoNS 20 MSSA 3 MRSA	49.1 ($P < .11$)	12.7% ($P < .001$)

CoNS, coagulase-negative staphylococci; *MSSA*, methicillin-sensitive *Staphylococcus aureus*; *MRSA*, methicillin-resistant *Staphylococcus aureus*.

Question 28: Table II Reinfection and complications for 2-stage exchange

Cases	Reinfection rate	Pathogens	Constant score (mean)	Complication rate
325 total 46 subacute 74 chronic	11.4% ($P < .001$)	88 *C. acnes* 64 CoNS 33 MSSA 56 MRSA	51.1 ($P < .05$)	21.9% ($P < .001$)

CoNS,coagulase-negative staphylococci; *MSSA*, methicillin-sensitive *Staphylococcus aureus*; *MRSA*, methicillin-resistant *Staphylococcus aureus*.

common organism identified in 160 cases, followed by coagulase-negative *Staphylococcus* species in 93 cases.[68,85,93,106,107,109,132,137,140,145,159] There were 57 reported cases of polymicrobial cultures and 27 cultures that resulted in no growth.[68,85,93,106,107]

To address the stated question, we reviewed studies in aggregate for subacute and chronic infection treated with either single-stage or 2-stage revision summarized in the Supplementary data (Question 28: Tables I and II). Four studies directly compared revision success rate for shoulder PJI with single-stage exchange in subacute or chronic presentation. The reinfection rate was 12.5% for chronic cases and 5.3% for subacute cases.[10,66,68] 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 subacute PJI treated with 2-stage exchange.[66,68,140] Several other studies reported the timing of infection but did not compare revision failure rates according to the subgroups of acute, subacute, and chronic PJI. In aggregate, using a frequency-weighted mean, the reinfection rate was 5.6% for single-stage exchange compared with 11.4% for 2-stage exchange, which was statistically significant ($P < .001$).

Analyses of complications related to single-stage or 2-stage exchange in acute, subacute, 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 with a 21.9% complication rate for 2-stage exchange, which was statistically significant (Question 28: Tables I and II). Although this finding suggests that patients undergoing 2-stage exchange have 1.72 times the risk of intraoperative or postoperative complication, the analysis was not able to account for treatment selection bias. The selection bias cannot be overemphasized as it very well may be that cases with more severe infections were preferentially treated with 2-stage revision, whereas less severe infections were treated with single-stage revision.

Frequency-weighted mean Constant-Murley score was 49.1 for single-stage patients and 51.1 for 2-stage exchange patients, which was similar to previous findings.[66,106] In the single-stage studies, a total of 57 patients had 78.2° of forward flexion, 42 patients had 52.4° of abduction, and 59 patients had 25.4° of external rotation. Two-stage exchange papers reported that 194 patients had 98.9° of forward flexion, 72 patients had 52.4° of abduction, and 144 patients had 29.2° of external rotation. No studies compared the timing of infection and treatment with single-stage or 2-stage revision.

All studies identified are retrospective and thus contain significant selection bias. Whereas our findings in aggregate suggest that 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, and diagnostic features like obvious clinical findings of infection. Thus, we cannot make a strong recommendation for use of single-stage exchange in place of 2-stage exchange for shoulder PJI without further investigation.

Question 29: Is there a role for preoperative joint aspiration before reimplantation during 2-stage exchange for shoulder PJI?

Recommendation:

There is a dearth of information on the role of preoperative joint aspiration before 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 before second-stage reimplantation.

Level of evidence: Limited

Delegate vote: Agree: 88%, Disagree: 4%, Abstain: 8% (Super Majority, Strong Consensus)

Rationale:

Controversy remains regarding the best surgical treatment of shoulder PJI. The literature documents interventions including open débridement with component retention or liner exchange, single-stage reimplantation comprising removal of all components and immediate reimplantation after thorough débridement and lavage, resection arthroplasty after removal of all components, and 2-stage reimplantation. The last involves a first stage that includes removal of all components followed by débridement and in many cases insertion of an antibiotic-impregnated polymethyl methacrylate cement spacer for local antibiotic delivery and preservation of soft tissue tension. The patient is then treated with IV (sometimes followed by oral) antibiotics and monitored, typically with serial serologic evaluation, before the second operation (second-stage revision), at which time the spacer is removed and new components are reimplanted.

In patients who undergo 2-stage reimplantation for shoulder PJI, shoulder joint aspiration or arthrocentesis before 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 culture, leukocyte cell count and differential, and 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.

However, there is little published information (search criteria are documented in the Supplementary data) on the use of shoulder aspiration before second-stage revision. In addition, there are no data documenting an advantage of shoulder aspiration over no aspiration or any alternative diagnostic tool for shoulder PJI. Sabesan et al[132] reported that 12 of 17 patients had aspiration before the first stage of reimplantation. Fluid was obtained for culture in 10, and 6 had positive cultures. Before the second stage, persistent infection was ruled out with preoperative ESR, CRP level, WBC count, and negative preoperative aspirate. One of the 17 patients had intraoperative frozen section that was positive for acute inflammation and had repeated treatment of infection. Two small case series studies recommended preoperative aspiration before consideration of second-stage revision, but only in cases with persistently elevated CRP level and WBC count.[52,159] Buchalter et al[22] have described their algorithm for 2-stage reimplantation for shoulder PJI but do not mention shoulder aspiration as a factor in their timing of second-stage revision. 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 before aspiration.[52,154,159] A negative culture of fluid aspirate or dry aspirate is not diagnostic of a resolved infection on the basis of studies that include preoperative shoulder aspirations.[57,154]

Question 30: Is there a role for pre-reimplantation open or arthroscopic tissue biopsy in the evaluation during 2-stage exchange of shoulder PJI?

Recommendation:

Unknown. There is one level IV study suggesting that open biopsy before second-stage revision for shoulder PJI can identify patients with persistent infection who may benefit from subsequent repeated irrigation and débridement before 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 before second-stage revision shoulder arthroplasty during 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[163] reported a level IV case series in which they performed open biopsy before second-stage revision for treatment of shoulder PJI or osteomyelitis after shoulder surgery. Eighteen patients (11 shoulder PJIs) were included. Patients were treated with a standard protocol including irrigation and débridement, removal of implants, antibiotic spacer placement, and antibiotic therapy for 6 weeks based on culture results and infectious disease service recommendations. At a minimum 4 weeks after completion of antibiotics, patients were re-evaluated to ensure that no clinical signs of infection were present and ESR and CRP level had normalized. The patients underwent open biopsy through a deltopectoral incision to obtain at least 3 soft tissue and bone cultures from tissue from the bone-antibiotic spacer interface. If cultures were negative for 7-14 days, patients underwent reimplantation. If cultures were positive, patients instead underwent repeated irrigation and débridement with antibiotic spacer exchange, and the protocol was repeated. Of the 18 patients, 4 (22%) had positive cultures indicative of persistent infection, with a 38% persistent infection rate for individuals infected with *C. acnes*. One patient had positive cultures on the second open biopsy and underwent a second spacer exchange before finally obtaining a negative result of the third biopsy and undergoing reimplantation. *C. acnes* was the most common pathogen, present in 44% of the index

shoulder PJIs. Among persistent infections, 3 of 4 patients (75%) had *C. acnes*, and the patient requiring 2 spacer exchanges had *C. acnes* on each occasion. At a mean of 24-month follow-up (range, 12-36 months), all 18 patients were reimplanted (2 hemiarthroplasties, 1 TSA, 15 RTSAs) and noted to be clinically infection free with average American Shoulder and Elbow Surgeons score of 71.

This study is limited in its level IV design and small sample size. Furthermore, patients undergoing 2-stage revision had variable index procedures from which they developed shoulder infection, including 1 open reduction–internal fixation proximal humerus fracture, 3 hemiarthroplasties, 6 rotator cuff repairs, 5 TSAs, and 3 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 biopsy prior to reimplantation during a two-stage exchange arthroplasty remains unclear.

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Supplementary data

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