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QUESTION 6: Should the duration of oral suppressive antimicrobial therapy differ by pathogen (e.g., methicillin-sensitive *Staphylococcus aureus* (MSSA) vs. methicillin-resistant *S. aureus* (MRSA)) in the treatment of subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There is insufficient evidence to determine whether the duration of oral suppressive antimicrobial therapy should differ by pathogen in the treatment of subacute/chronic shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

There is currently no widely shared and commonly used definition of the term "suppressive antimicrobial therapy" (SAT) in reference to antimicrobial therapy for shoulder PJI. A thorough search of PubMed, Embase and Google Scholar databases was undertaken in February, 2018 to identify articles related to the use of suppressive antibiotic therapy for the treatment of shoulder PJI using search terms: "prosthetic joint infection," "suppressive therapy," "antibiotic suppressive therapy," "suppression."

From the results of this search, it is clear that the term SAT is used in various ways. It is often used to mean prolonged antibiotic therapy following surgery (irrigation and debridement and implant revision) with the intention of effecting a cure and discontinuation of antibiotics. In other cases, SAT is described for the treatment of active PJI in patients unable to undergo additional surgical intervention. Treatment in this scenario is palliative; it is based on the principle that organisms within a biofilm cannot be fully eradicated and that the antimicrobial inhibits the organisms in the biofilm from spreading. This may halt dissemination of the infection and prevent sepsis but is highly unlikely to eradicate the underlying infection. Suppressive antibiotic therapy is also used to define indefinite or life-long use of antibiotic therapy in patients without clinical evidence of active infection but thought to be at high-risk for relapse.

Using an inclusive definition of "suppressive antimicrobial therapy," twelve relevant studies were identified [1–8]. From these studies, 34 patients were noted to have had shoulder PJI and received SAT. Failure was defined as a relapse of infection based on the criteria described in each manuscript. These criteria were not consistent. Collectively, patients prescribed SAT had a PJI relapse rate of 29% (10/34 cases). There was not sufficient level of detail to comment on treatment duration, dose of antibiotics or type of antibiotics.

There is some support for success after discontinuation of SAT. Antimicrobial-free periods are not reported in any of the reported series. Reports of hip and knee PJI demonstrate that there is a relapse rate of around 30% within 4 months when suppressive antibiotic treatment is discontinued, even after a long period of suppressive therapy [7]. A study 24 patients with PJI (2 shoulder patients) did observe that treatment succeeded in almost all patients with a PJI caused by a *S. epidermidis* [1]. This finding may not be surprising since *S. epidermidis* has low virulence and the natural course of infection is often dormant and low-grade in nature.

Safety issues in the setting of SAT are an important consideration. Although information is very scarce, the safety data in the published case series indicate a low rate of antibiotic withdrawal due to adverse events [4,7,9].

Moving forward, it may be useful for clinicians and researchers to more precisely define "suppressive antibiotic therapy." The authors would suggest that SAT refer to "the chronic use of low-dose antibiotic therapy in patients with persistent PJI in which the aim is no longer to cure, but to prevent acute exacerbation or recurrence of local symptoms and/or greater systemic involvement." The key to this definition is the recognition that antibiotic therapy is not curative anymore in its intent. Suppressive antibiotic therapy is thereby differentiated from longer-than-standard "prolonged" administration of antibiotics meant to eradicate infection and cease after the infection is deemed to be cleared. Differentiation of these terms may allow future investigators to make more concrete recommendations regarding the use of SAT in shoulder PJI.

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QUESTION 7: What are the recommendations for the route (intravenous (IV) vs. oral (PO)) and duration of postoperative antibiotic treatment when a one-stage revision arthroplasty is performed for subacute or chronic shoulder periprosthetic joint infection (PJI) of the shoulder caused by an indolent organism (e.g., *C. acnes* or coagulase-negative Staphylococcus)?

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

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

Periprosthetic shoulder infection negatively impacts the outcome of shoulder arthroplasty and is often treated with revision surgery [1]. The overall rate of infection after shoulder replacement is reported as 1.2-3.0% (0.5-3.9% for anatomic and up to 10.0% for reverse shoulder arthroplasty) [2–4]. Prosthetic shoulder infection commonly presents as painful arthroplasty and often lacks typical clinical findings of acute infection. Laboratory workup, such as inflammatory markers, white blood cell count and shoulder aspiration are usually negative, leaving clinicians with limited tools to confirm infection prior to revision surgery. This is mostly due to predominance of indolent organisms, such as *Cutibacterium acnes* (formerly known as *Propionibacterium acnes)* (39-66%) and *Coagulase negative staphylococcus* (24-28%) in periprosthetic shoulder infection [5,6]. Two-stage revision including aggressive debridement, antibiotic spacer placement followed by prolonged IV antibiotics was adopted by shoulder surgeons from treatment of PJI of other joints and showed 63-100% success rate in eradicating infection in short to mid-term follow up [7–9]. This approach has many short-comings, including subjecting patients to two operations and spacer complications, such as fracture, dislocation and loss of rotator cuff and bone stock, leading to poor joint function. Recently, one-stage revision has been advocated for low virulence indolent infections. Nelson et al. [10] and Cuff et al. [11] showed similar rates of eradication after one-stage versus two-stage revision arthroplasty. Beekman et al. reported results of single stage revision for infected reverse shoulder arthroplasty and showed at two year follow-up 90% of patients were infection free with a Constant score of 55.6% [4]. George et al. did a systematic review and found that the average Constant score was 51% after one-stage revision which was better than 41% two-stage revision [12]. These studies make a reasonable case for one-stage revision arthroplasty to eradicate indolent infections while preserving the function of the patient's joint, but they have highly variable protocols for type and duration of postoperative antibiotics. To answer the question above we review and summarize the limited evidence around antibiotic therapy following one-stage revision arthroplasty for periprosthetic shoulder infection with indolent organisms.

A PubMed search was conducted with terms arthroplasty, replacement, shoulder (Mesh) and revision which resulted in 120 papers. Abstracts of the papers were reviewed to identify papers reporting one-stage revision for indolent periprosthetic shoulder infection which resulted in 8 relevant articles that are included in this review.

Most authors retrospectively reporting their experience with treatment of shoulder arthroplasty infection incompletely report the antibiotic therapy following revision surgery. This section will review and summarize the current literature on treatment outcome of infected shoulder arthroplasty with specific focus on antibiotic regimen, as incomplete as it may be, including route (IV vs. PO), type and duration.

Grosso et al. [13] retrospectively reviewed patients with no perioperative sign of infection who underwent single stage revision shoulder arthroplasty and postoperatively had at least 1 positive culture and were not treated with an extended course of antibiotics. The majority of the cultures (56%) were *C. acnes* followed by coagulase negative staphylococci (CoNS) (35%). The rate of recurrence was very low (5.9%). Authors suggested unexpected cultures after a seemingly uninfected one-stage revision did not require extended antibiotic therapy.

Padegimas et al. [14] reviewed 117 one-stage revision shoulder arthroplasty with no preoperative concern for infection who were followed for more than 4 years and found that 28 (23.9%) had an unexpected positive culture postoperatively of which 15 (57.1%) were *C. acnes,* and majority were in male patients. They did not identify any predictor for reoperation, but they observed a higher rate of reoperation in patients without unexpected cultures (20.2% vs. 7.1%) but this did not reach clinical significance. In their cohort, 18 (64.3%) patients were treated with IV antibiotics for 6 weeks, and 10 (35.75) patients only received 2 weeks of PO antibiotics. There was only one reoperation among culture positive patients and that was in a patient who did not receive prolonged antibiotics.

Coste et al. [1] reported on the outcome of treatment in 42 patients with infected shoulder arthroplasty with a mean 34 months follow up. They defined infection based on seven criteria including