Diagnosis

2.1. DIAGNOSIS: CULTURE SIGNIFICANCE

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

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

LEVEL OF EVIDENCE: Moderate

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

RATIONALE

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

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

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

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

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

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

RECOMMENDATION: The relevance of unexpected positive cultures is unknown.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

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

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

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

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

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