SH54. What is the relevance of positive cultures in the evaluation for shoulder PJI? What defines a clinically relevant positive culture result(s) versus a culture contaminant? How should positive cultures be considered in the diagnostic criteria?

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Methodology:
A comprehensive literature review was performed to identify all studies related to positive cultures in the setting of shoulder arthroplasty. A Pubmed search using the MESH terms "Arthroplasty, replacement, shoulder AND cultures", "Arthroplasty, replacement, shoulder AND infection/diagnosis AND cultures", "Shoulder prosthesis AND adverse effects", and "Prosthesis related infections/microbiology" was performed. A Google Scholar search using "Shoulder arthroplasty and infection", "Shoulder arthroplasty and cultures", and "Shoulder Periprosthetic joint infection and cultures" was also performed. Articles were searched through 2024. Inclusion criteria for our systematic review were all English primary research articles (Level I-IV evidence) that reported on shoulder arthroplasty and specimen cultures. Exclusion criteria were non-English language articles, case reports, review papers, studies with less than 10 patients in the sample size and technique papers without patient data. Prior systematic reviews, meta-analysis or review articles were cross-referenced to ensure no relevant studies were missed. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria were followed. 27 articles met inclusion and exclusion criteria and were reviewed.

Recommendation: In the absence of obvious signs of infection such as sinus tract formation or intra-articular purulence, multiple factors must be taken into consideration when determining if culture positivity reflects true infection warranting treatment. The literature supports a prolonged culture hold of 13 days. Multiple positive cultures returning within the first 7 days has a higher likelihood of representing true infection, although true positives may still result within the first 11 to 13 days. Contamination typically results in light growth whereas stronger positivity (growth in multiple quadrants) is more likely to reflect clinical significance. Ultimately, these factors should be considered and treated in the context of the patient's clinical presentation and remain in the minor criteria.

Level of Evidence: Moderate

Rationale:

Diagnosis of shoulder periprosthetic infections represents a challenging clinical problem. Several studies have examined the rate of culture positivity at the time of shoulder arthroplasty and have found the presence of Cutibacterium (formerly Propionibacterium) in the deep tissues of 3.1-56% of patients (2,3,4,5,7,10,13,14,17,21,27). However high false positive rates ranging from 2.8-15% have also been reported (7,8,11,21,24) and multiple studies have demonstrated that positive cultures do not necessarily correlate with clinical infection, worse outcomes or early component failure (6,10,12,14,21). Additionally, there is no standard of practice regarding specimen handling,

processing, culturing, and reporting of cultures, further complicating interpretation and application of the currently available evidence (23).

Considering that the most common pathogens, *Cutibacterium* and Coagulase Negative Staphylococcus (CNS), may not always present with clinical signs such as purulence or sinus tract formation, multiple factors must be taken into consideration when differentiating true positive culture results from contaminants including the duration that cultures are held, the length of time before they turn positive and the strength of positivity.

Time to Positivity:

- Due to the fastidious nature of the Cutibacterium, prolonged culture holds up to 13 days have previously been recommended. Earlier return of positive cultures can help differentiate true infections from contamination resulting from specimen processing during this extended period. Butler-Wu et al. retrospectively compared culture characteristics among revision arthroplasty patients with Cutibacterium infections to cases in which positive cultures were thought to represent contaminants. They observed a trend toward reduced time to positivity for Cutibacterium (Propionibacterium) infections with an average of 7.3 days compared to 10.7 days in cases with suspected contamination (15). 70% of cultures in this series became positive after 7 days and all relevant results were positive by 13 days. Frangiamore et al. also reviewed the relationship between the time to Cutibacterium growth and the likelihood of a culture representing true infection. 46 revision arthroplasties were included and categorized as "probable true infection" vs "probable contaminant" based on culture results and intraoperative findings. They found that the time to positivity was shorter in the probable true positive group with a median time of 5 days versus 9 days for probable contaminants (16). They did note a 14% rate of "true positive" growth after 7 days however no probable infection patient had a culture change to positive after 11 days. In the contaminate group, 56% of the cases did not turn positive until 7 days and 44% changed after 11 days. They also observed that significantly fewer days to bacterial growth were observed in cases with a higher number of total positive cultures or a higher proportion of positive cultures. Similarly, Bokshan et al. performed a retrospective review evaluating time to positivity for C. acnes before and after implementation of a regulated "automated" anaerobic chamber system. They also noted that true infections had a significantly shorter time to positivity, but like Frangiamore noted a significant negative correlation between the proportion of positive samples for C. acnes and the time until positivity (18). Fernandez-Rodriquez et al. assessed time to culture positivity in Cutibacterium inoculations with varying bacterial loads and noted that higher concentrations were detected as early as 3 days (19). By day 7, even the most dilute samples were detected on anaerobic media and they concluded that any cultures that turn positive beyond day 7 likely represent contamination or very low loads of C. acnes with no clinical relevance. Hsu et al. performed a multicenter study evaluating the relationship between time to positivity and strength of culture positivity in various dilutions of a C. acnes positive specimen compared to negative control samples (22). Similar to the study by Fernandez-Rodriquez, they observed a mean time to positivity of 3.6 days in samples with the highest bacterial concentrations. The mean time to positivity in all positive control samples was 4.0 days ±1.3 days whereas negative control samples showed growth at a

mean of 8.1± 5.1 days. On the other hand, Mook et al. prospectively evaluated the rate of positive culture growth from the deep tissues of patients undergoing open approaches to the shoulder. A sterile gauze was cultured and used as a negative control in this study, and they noted a 13% false positive rate occurring at an average of 14 days (7).

Bacterial Load and Semiquantitative Analysis:

- Efforts to interpret the results of cultures are typically based on the number of cultures that are "positive" or "negative". It is suspected that a greater number of specimens producing the same bacteria is more likely to reflect clinical significance. However, there is not an obvious threshold for culture results that allow distinction between a true positive and false positive infection. Semi-quantitative assessment of whether the growth occurs in broth only or produces 1 colony on a standard streaked plate versus growth in multiple quadrants can help distinguish clinically significant results from very low bacterial loads that may not be relevant or reflect contamination (1,9). The concepts of the Specimen Propi Value (SPV) and the Specimen Propi Score (SPS) have been introduced to quantify the amount of bacteria in each specimen and total of culture positive specimens in the shoulder (1,9,13,25). These authors suggest that higher SPV and SPS reflect higher overall bacterial burden and clinical relevance. Macniven et al. observed that although 4% negative control air swabs were considered culture positive with growth in broth or 1 colony (SPV > 0), none were found to have an SPV ≥ 1 (26). In their series examining the rate of culture positivity in negative control air swabs that found a 15% false positive culture rate, Namdari et al. noted that all false positive samples were rated as very light growth for C. acnes and moderate growth for CNS species (11). No specimens were quantified as heavy growth using semi-quantitative evaluation. In the multicenter study by Hsu et al. noted earlier, it was observed that strength of positivity was significantly lower in negative control samples compared to samples with true Cutibacterium growth (22). A false positive rate of 14% was noted in the negative controls but none of these samples showed growth beyond 1 quadrant. Similarly, very low bacterial concentrations in positive control groups were associated with growth in only an average of 0.3±0.3 quadrants. Samples with the highest concentrations on the other hand were noted to growth in an average of 2.4± 1.3 quadrants.

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