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## QUESTION 2: Are there significant differences in the yield of culture between preoperative aspiration and intraoperative culture samples? If so, which result should be utilized?

**RECOMMENDATION:** There may be differences in the yield of culture between preoperative aspiration and intraoperative culture samples, particularly in the case of polymicrobial infections or low-virulence organisms. The collection of multiple intraoperative tissue samples is considered by many experts to provide the highest yield in isolating organisms from a joint.

**LEVEL OF EVIDENCE:** Limited

**DELEGATE VOTE:** Agree: 98%, Disagree: 1%, Abstain: 1% (Unanimous, Strongest Consensus)

### RATIONALE

When interpreting culture results in general, one should be aware that the literature demonstrates a lack of reproducibility, whether from the synovial fluid or from the tissue.

Due to inherent methodologic difficulties and limitations in the existing literature and variation in culture techniques between institutions, it is not possible to make a general statement regarding the relative yields of synovial fluid and tissue culture. In general, we recommend that synovial fluid and tissue samples both be sent for culture, as the growth of an organism from either source is highly informative. However, clinicians should be aware that in general, culture techniques have a relatively poor sensitivity for periprosthetic joint infections (PJIs) (40 to 85%), and that negative culture results do not rule out PJI. The current literature does not provide evidence-based guidance on how to interpret contradictory synovial fluid versus tissue culture results. Considerable research is needed to optimize and standardize culture techniques to provide improved yield for isolation of infective organisms.

There are inherent methodologic difficulties in studying the comparative yield between synovial fluid and tissue culture results. First is the fact that while synovial fluid is usually sent to the lab for a single culture, intraoperative tissue samples are usually sent in multiples. Whenever a diagnostic test is completed multiple times and the results are interpreted in combination, the sensitivity increases and the specificity decreases by definition. Therefore, even if the sensitivity and specificity of synovial fluid and tissue culture were identical, the multiplicity of testing associated with tissue culture sampling would result in the observation that intraoperative culture has a higher yield. Tissue samples have a greater opportunity to yield a positive result, whether real or due to contamination.

Second, is the fact that there are no universal standards in arthroplasty culture technique. The collection, transport, sample preparation, culture media and culture times vary greatly between institutions [1-18]. The techniques may even vary based on whether the sample is a fluid or a tissue sample at the same institution. Therefore, the results published at one institution regarding the yield of synovial fluid culture or tissue culture cannot be assumed to apply to all institutions.

Third, is the fact that the definition of PJI has varied over time and had great variability before the MusculoSkeletal Infection Society (MSIS) definition. Many historical studies considered positive tissue cultures to be the gold standard for infection, eliminating the possibility of properly assessing the diagnostic characteristics of tissue culture. Furthermore, different centers have different definitions of what qualifies as a positive tissue culture, with variation in the number of positive samples requirements, the virulence of the organisms yielded and the assessment of broth-only results.

Microorganisms involved in infection of orthopaedic devices are highly adapted on the implant or in the bone-cement interphase, adhering to the environment within the in vivo biofilm, but are only to a minor part in a planktonic state in the synovial fluid [19]. This fact can explain the high rates of preoperative aspiration with false negative bacteriology [11]. Moreover, other factors such as bacterial load or the type of germ may affect synovial culture, which may explain the higher sensitivity of aspiration fluid culture observed in acute versus chronic infections [20, 21]. Although a recent study from Shanmugasundaram et al. could not show any influence of microbial virulence on organism isolation from preoperative aspiration versus intraoperative culture [14], some studies showed insufficient accuracy of synovial fluid culture in isolating low virulent pathogens in chronic PJI compared to intraoperative tissue culture [11, 21].

For the aforementioned reasons, a comparison of the yield of synovial fluid versus tissue cultures cannot be made with any confidence. There are exceedingly few studies comparing the culture sensitivity of synovial fluid versus tissue [1-18]. Of these reports in the literature, there are very significant limitations which prevent the appropriate comparison of synovial fluid versus tissue culture yield. Many of these studies have fewer than 10 patients with PJI. The diagnosis of PJI varies greatly in these studies. And many of these studies fail to provide the proper data in evaluating their analysis and conclusions. Studies seeking to compare synovial aspiration and intraoperative tissue culture results have shown a wide range of concordance (57-92%) [1-18] in the sense of false-negative, false-positive, true-negative and true-positive results. Among these 18 studies, nine were retrospective and nine collected their data prospectively.

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# QUESTION 3: Do bone cultures provide additional diagnostic accuracy in the diagnosis of periprosthetic joint infections (PJIs)?

**RECOMMENDATION:** Inconclusive. We cannot recommend for or against bone biopsy to provide additional diagnostic accuracy in the diagnosis of PJIs.

**LEVEL OF EVIDENCE:** Limited

**DELEGATE VOTE:** Agree: 90%, Disagree: 5%, Abstain: 5% (Super Majority, Strong Consensus)

## RATIONALE

Use of traditional culture remains the preferred method for isolation of the infecting organism(s) in PJIs. It is reasonable to assume that increasing the number of samples and taking culture from "representative areas of infection" enhances the yield of culture in isolating the infective organism. Current data supports obtaining synovial fluid and tissue samples for culture, with studies showing tissue to have a better yield than synovial fluid and is preferred over swabs [1,2]. Whether the tissue culture should include bone also has not been well studied. In general, multiple samples improve diagnostic accuracy [3]. Most data supports obtaining at least three distinct and as many as six intraoperative samples for culture [2,4]. The site of specimen retrieval includes the synovium, as well as tissue from the femur and tibia in the knee or the femur and the acetabulum in the hip. In addition to traditional cultures, sonication of implants has been shown to possibly increase chance of identifying the organism [5-7].

Only one study addresses the role of utilizing bone biopsy in the detection of infection in joint arthroplasty. In a prospective cohort study, Larsen et al. [8] assess the contribution of different specimen types in detecting PJI. It was found that bone biopsy did not provide any additional information and did not contribute independently to the diagnosis of infection. The bone biopsy was obtained from bone in contact with the prosthesis. Only 9 of 32 samples (28%) resulted in a positive culture after 6 days. This increased to 13 of 32 at 14 days. This was considerably less than soft tissue biopsies which resulted in 37 of 42 (88%) positive cultures. There were no cases where bone biopsy yielded a positive culture independent of soft tissue biopsy. This resulted in a negative likelihood ratio of 0.6 (95% confidence interval (CI), 0.5-0.8) which only slightly decreases the probability of infection with a negative result. This study found the optimal specimen set for diagnosis of periprosthetic joint infection included joint fluid, prosthetic component and five soft tissue biopsies [8].

Other studies have assessed the role of bone biopsy in detecting osteomyelitis and septic arthritis. Bone biopsy in osteomyelitis was found to have significantly improved sensitivity, specificity and predictive value in determining the etiological organism when compared to sinus tract biopsy [9] and soft-tissue and deep wound biopsy [10]. In the setting of septic arthritis, sampling of the ileum