sensitivity and specificity of the laboratory assay to be 95 and 96% respectively, compared to the quick test lateral flow of 77 and 91%, respectively, but again, only a single elbow arthroplasty was included in the pooled group.

Finally, in a pilot study by Wouthuyzen-Bakker et al., synovial calprotectin was examined as a biomarker for PJI [5]. This test is attractive because of the low cost, the possibility to obtain a quantitative value, the use of a lateral flow assay with the possibility to use it as a point of care test and its availability, as it is already used in routine care for other indications in most hospitals. Unfortunately, while this study included TEA, no PJIs were included in the TEA group. The single elbow examined was in a control group without infection. This pilot study revealed that synovial calprotectin had an overall sensitivity, specificity, positive predictive value and negative predictive value of 89%, 90%, 81% and 95%, respectively.

Other biomarkers examined in a pooled meta-analysis by Lee et al. [6] included α-defensin, LE, interleukin (IL)-6 and IL-8. The overall sensitivity of these molecular tests was 85% compared to culture, which was 80%. Alpha-defensin in this study had the highest diagnostic odds ratio. Unfortunately, all studies included hip and knee arthroplasties and not a single study examined TEA.

Of significant note, despite their ability to identify PJIs with a high likelihood in most other joints, all biomarkers utilized in these studies require some element of polymorphonuclear cells to be present in the synovial fluid for detection. These tests do not discriminate between other inflammatory conditions and infection, which would be the most useful to surgeons. Specifically, as inflammatory conditions have historically been the primary indication for surgical intervention about the elbow, a test to discriminate between infection and other inflammatory conditions such as rheumatoid arthritis or gout does not yet exist.

Nevertheless, as these tests have shown promise in PJI in other joints, studies should be undertaken specific to the elbow. However, at this time conclusions are difficult to draw given the lack of clinical data specific to the elbow, which forms the basis of our recommendation.

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**Authors:** Jonathan Barlow, Joaquin Sanchez-Sotelo

# QUESTION 6: What are the diagnostic criteria for elbow periprosthetic joint infection (PJI)? (Clinical criteria, radiographic criteria, intraoperative findings, pathology, cultures and serum biomarkers.)

**RECOMMENDATION:** The following three parameters provide a definitive diagnosis of elbow PJI:

- A sinus tract that is communicating with the prosthesis (Strength: Strong)
- Isolation of identical pathogens from two or more separate cultures (tissue or articular fluid) obtained under sterile conditions (Strength: Strong)
- Presence of intra-articular pus (Strength: Consensus)

The following criteria are concerning for infection and should be considered in aggregate (Strength: Limited):

- Warmth, redness, swelling of the elbow
- Elevated serum inflammatory markers (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)) – except in cases of inflammatory arthropathies
- Elevated synovial white blood cell (WBC) count
- Elevated synovial polymorphonuclear percentage
- Isolation of organism from one sample (tissue or articular fluid)
- Histologic evidence of acute inflammation
- Early unexpected component loosening
- Endosteal scalloping, rapid progressive loosening on radiographs

**LEVEL OF EVIDENCE:** Consensus

**DELEGATE VOTE:** Agree: 92%, Disagree: 8%, Abstain: 0% (Super Majority, Strong Consensus)

## RATIONALE

The limited total number of total elbow arthroplasty (TEA) infections reported in the literature makes the assessment of preoperative factors consistent with infection challenging. In addition, limited early recognition of the role of low-grade, indolent infections (*Staph-*

*ylococcus epidermidis, Cutibacterium acnes)* may make interpretation of earlier studies challenging. Nonetheless, the literature provides valuable insights into the diagnosis of PJI in TEA.

Given the subcutaneous nature of the elbow, many infected TEAs do develop draining sinuses. This diagnostic criteria has been consistently used in the literature and was predictive of positive cultures in the vast majority of cases. In the review by Cheung et al. of 29 patients with PJI, 11 (38%) had draining sinuses [1]. Peach et al. showed a 38% rate of draining sinus, as well [2].

Culture growth was the most commonly-cited diagnostic criteria in the literature. Several studies considered a TEA to be infected in the presence of one positive culture [1,3–9]. Several other studies only made the diagnosis of PJI if two cultures were positive for the same pathogen [10–12]. The latter is consistent with the MusculoSkeletal Infection Society (MSIS) criteria [13]. In light of the publication by Wee et al. regarding "unexpected positive cultures," using the criteria of one positive culture for the diagnosis in the absence of other signs would likely over-diagnose PJI [14]. Therefore, one positive culture should be used in the constellation of other signs and symptoms of infection. If two cultures from two separate sources return the same pathogen, the diagnosis of PJI is supported strongly by the literature.

Numerous other criteria were used in the diagnosis of PJI. While these signs and symptoms were frequently seen, they were not seen with enough reproducibility to be diagnostic in isolation. Warmth, redness and swelling were consistently seen [15]. Elevated serum ESR and CRP, as well as aspirate WBC (and differential), and acute inflammation on intraoperative pathology were commonly seen in TEA PJI. However, many of the patients receiving a TEA have inflammatory arthropathy as their underlying diagnosis, leading to a substantial number of false positives. Furthermore, in the setting of low-grade infections, aspiration and serum laboratory studies are not accurate in isolation. These diagnostic criteria should be used in combination with clinical and radiographic assessments to assess likelihood of true PJI.

The radiographic appearance of the TEA and pace of loosening can provide insight into the likelihood of PJI. Early unexpected radiographic failures (< two years) are more likely to be consistent with PJI than late failures [14,16]. In addition, endosteal scalloping and rapidly progressive loosening were associated with PJI in TEA in most series in the literature [4,9,15].

Based on available literature, it is hard to make consensus quantitative assessments of number of criteria required from the "associated criteria" category. Certainly, based on the literature, an increase in the number of positive criteria increases the likelihood of true PJI.

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