THE PATHCARE NEWS

DIAGNOSIS OF PROSTHETIC JOINT INFECTIONS (PJI)

Serum-biomarkers of infection such as CRP and ESR and synovial fluid leucocyte count and neutrophil percentage are useful tests to support the diagnosis of PJI. However, it is important to define the infecting micro-organism to direct antimicrobial therapy. Preoperative synovial fluid culture may establish the diagnosis, but if these cultures are negative, then multiple peri-prosthetic tissue samples should be cultured to identify the pathogen (s).

Synovial fluid analysis:

- Diagnostic joint aspiration should be performed prior to antibiotic therapy
- A synovial fluid leucocyte count and differential count may be useful to assess prosthetic joint infection. An EDTA tube is recommended for collection to prevent clotting of the fluid (>1ml).
- European Bone and Joint Infection Society (EBJIS) definition (hip and knee PJI)[1] and supported by the Musculoskeletal Infection Society (MSIS):
  - Infection likely: total leukocyte count > 1,500 cells/µL or proportion of polymorphonuclear neutrophils (PMN) > 65%.
  - Infection confirmed: total leukocyte count > 3,000 cells/µL or proportion of polymorphonuclear neutrophils (PMN) > 80%.
- These cell counts should be interpreted with caution when other possible causes of inflammation are present: gout or other crystal arthropathy, metallosis, active inflammatory joint disease (e.g. rheumatoid arthritis), periprosthetic fracture, or the early postoperative period.
- The synovial C-reactive protein (CRP) may be a useful biomarker of chronic prosthetic joint infection. Studies have shown that the synovial CRP levels are significantly higher in chronic PJI than in aseptic causes of arthroplasty failure. However, the cut-off values vary widely between studies and are influenced by the testing methods. The synovial CRP cut-off values with the turbidimetric method varied between 2.8-10 mg/l.[2] Recent studies have found that the synovial CRP provides no additional benefit when compared to the serum-CRP in the diagnosis of PJI.[3]
- Microscopy: The Gram stain has low sensitivity.
- Culture yield may be increased by inoculating the fluid (1-4ml fluid) into a pediatric blood culture bottle using aseptic technique.[4] Other types of blood culture bottles require higher volumes that may be difficult to obtain.

Intra-operative tissue samples:

- Sample each tissue biopsy using a separate sterile instrument to minimize contamination and place into a sterile container (sterile tissue packs: 6 sterile bottles containing liquid broth culture medium).
- Multiple tissue samples are required to increase the yield and to facilitate the interpretation of these results. At least 5 tissue samples, particularly from the bone-implant interface membrane, should be submitted for culture[1].
- In clinically stable patients, antibiotic prophylaxis should not be given until tissue samples have been collected to prevent false negative cultures. Optimally the patient should not have been exposed to any antimicrobial therapy two weeks prior to the surgery.
- Prolonged/extended culture up to 14 days may facilitate the isolation of slow-growing organisms such as coagulase-negative staphylococci and *Cutibacterium spp.*, a common pathogen in shoulder arthroplasty infection.
- Culture methods also has the advantage of providing antimicrobial susceptibility results to direct antimicrobial therapy.
- In some cases, particularly where antibiotic treatment has been given and culture method may be compromised, molecular-based tests, such as the panbacterial PCR test which targets a conserved bacterial gene, the 16S ribosomal RNA gene, may be useful to identify the infecting organism based on the unique nucleic acid sequence. The sensitivity of this test has been found to be higher on peri-prosthetic tissue than synovial fluid, but may also be influenced by sample selection.[5]

Sterile tissue packs:

- To facilitate the aseptic collection of tissue biopsy samples for culture, we provide autoclaved tissue packs that include 6 sterile containers with nutrient broth.
- Arrange with your local PathCare laboratory/depot prior to the planned surgery to order and have these tissue packs available at the operating theatre.
- The nutrient broth bottles will be incubated for an extended period of up to 14 days to increase the yield for slow-growing pathogens such as coagulase-negative staphylococci and Cutibacterium spp. Cultures are evaluated daily for positive growth and subcultured when turbid or if still clear, on set days for further evaluation. If not reported already, a report will usually follow after 7 days' and after 14 days' of incubation.

Interpretation of culture results:

- All major PJI definitions classify two identical cultures as evidence of infection. This means that for common contaminants such as the coagulase-negative staphylococci, an identical species with the same antibiotic susceptibility pattern should be isolated to consider it as clinically significant.
- A single positive culture must be interpreted with caution and evaluated together with other evidence of infection. Virulent organisms (e.g. *Staphylococcus aureus* or Gram negative organisms) are more likely to represent infection than common contaminants such as coagulase-negative staphylococci.

References:

1. M. McNally, et al. The EBJIS definition of periprosthetic joint infection. Bone Joint J 2021;103-B(1):18–25.
2. Praz et al. Value of the synovial C-reactive protein test in the diagnosis of total hip and knee periprosthetic joint infections: A case-control study. Orthopaedics & Traumatology: Surgery & Research 107 (2021) 102903.
3. Yilmaz et al. Diagnosis of Periprosthetic Joint Infection: The Utility of Biomarkers in 2023. Antibiotics 2023, 12, 1054. https://doi.org/10.3390/antibiotics12061054.
4. Lluı´s Font-Vizcarra, et al. Blood Culture Flasks for Culturing Synovial Fluid in Prosthetic Joint Infections. Clin Orthop Relat Res (2010) 468:2238–2243. DOI 10.1007/s11999-010-1254-3.
5. Zhang et al. Advantages of 16S rRNA PCR for the diagnosis of prosthetic joint infection. Experimental and Therapeutic Medicine 20: 3104-3113, 2020.

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