The infected joint arthroplasty continues to be a very challenging problem. No test has 100% diagnostic accuracy for PPI and the treating surgeon must correlate the clinical and radiographic presentation with a combination of blood tests, synovial fluid analysis, microbiological and histopathological evaluation of periprosthetic tissue and intra-operative inspection to reach a definitive diagnosis.

Diagnosis should begin with a high index of suspicion for new onset of pain or symptoms in well-functioning joints. Plain radiographs may identify osteolysis or early signs of implant failure and should be promptly investigated further for PPI.

Serum blood tests: Peripheral blood ESR and CRP remain the most widely used next step for the diagnosis of PPI. Both of these tests are widely available, inexpensive, and have a rapid turnaround time in laboratories. The results should be interpreted with caution due to their relative lack of specificity. The sensitivity and specificity values for CRP is approximately 88% and 74%, respectively; while that of ESR is slightly lower at 75% and 70%, respectively. The combined ESR and CRP tests are 96% sensitive for ruling out PPI but the specificity of this combination is as low as 56%. The role of Interleukin-6 and Procalcitonin in routine clinical practice for diagnosing infection remains to be established.

Advanced imaging modalities such as three-phase bone scintigraphy, radioactive 111In labeled autologous leukocytes scan, [18F]Fluoro-2-deoxyglucose positron emission tomography (FDG-PET) may be used as a part of the diagnostic algorithm at this point. However, they require expert interpretation and are limited by availability and high costs. When available they have high sensitivity and specificity but their routine use is not recommended and indications have to be individualized in the light of clinical presentation.

In the presence of high clinical suspicion, the clinician should plan synovial fluid analysis. This provides a synovial fluid white cell count with differential cell count, specimen for culture and possibility of analyzing other synovial fluid markers. It is important to note that failed metal-on-metal hip arthroplasties can give a falsely elevated synovial fluid cell count when using automated cell counters. This can be overcome by manually counting cell numbers.

Synovial fluid culture: Synovial fluid should be directly into blood culture bottles, and antibiotics should be withheld at least 2 weeks prior to aspiration, whenever possible. Cultures also help establish the organism, virulence and sensitivities that help plan subsequent treatment algorithm.

Novel synovial fluid markers: The role of synovial fluid ESR, CRP, leukocyte esterase and antimicrobial peptides such as alpha defensin and d-dimers continue to be researched.

Periprosthetic tissue biopsy provides valuable information in microbiological diagnosis and workup of PPI. Routine use of gram staining is not recommended due to poor sensitivity. However, frozen section may have some role especially when performed by skilled pathologist; 5 to 10 neutrophils per high power field is considered consistent with PPI.
Tissue culture remains the gold standard for diagnosis despite false-positive and false-negative results. Whenever possible multiple samples should be obtained (3 to 5) to aid interpretation. A threshold of 2 to 3 positive specimens yielding indistinguishable microorganisms has been recommended to improve sensitivity.

Histological analysis of peri-prosthetic tissue: Acute inflammation, evidenced by neutrophilic infiltrate on fixed or frozen tissue, is suggestive of PPI. Acute inflammation is defined as the presence of at least 5 neutrophils per high-powered field, in at least 5 separate microscopic fields. Sonication of removed prosthetic components is used to dislodge the biofilm and the associated bacteria from the surface of the implant. With this approach, low-frequency ultrasound waves pass through liquid surrounding the prosthesis, creating areas of high and low pressure. Microscopic bubbles are formed during the low-pressure stage and collapse during the high-pressure stage, releasing energy and liberating bacteria from the surface of the implant. The fluid surrounding the implant can be used for culture or analysis.

PCR testing: Synovial fluid aspirate, periprosthetic tissue or sonicate fluid may be subject to molecular diagnosis to amplify genetic material and improve microbiological diagnosis of PPI. This technique has shown increased sensitivity in patients who had received antibiotics within 14 days before implant removal. Results have to be carefully interpreted with due consideration for possibility of false positive results.

The Future: The move from culture-based to genetic sequencing type strategies has started. Our increased capacity to rapidly sequence and to recognize patterns, allied to powerful computer analytics, holds great promise.

References: