MINI-SYMPOSIUM: REVISION HIP ARTHROPLASTY

(v) Post-operative infection in total hip arthroplasty

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Summary
The diagnosis of infection starts with a comprehensive history and thorough physical examination. First line investigations should include C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Elevation of one or both of these tests suggests infection and hip aspiration should be undertaken to confirm the diagnosis. Hip aspiration also allows identification of the infecting microorganism. Radionucleotide tests presently have a limited role but may be useful as first line investigations in patients with active inflammatory conditions. If there is still doubt regarding the diagnosis following these investigations then one should use clinical judgment and possibly proceed to intraoperative frozen section. Acute infections can sometimes be successfully treated with retention of the prosthesis but the gold standard treatment for chronic infections is two-stage reimplantation.

Introduction
Total hip arthroplasty is one of the most successful surgical interventions with very high patient satisfaction rates. Deep infection is a catastrophic complication to what should otherwise be a predictably good outcome. The treatment of deep infection is associated with high patient morbidity and inordinately high hospital and physician resource utilisation. Making the diagnosis is often not straightforward and consequences of missed infection are dire to both the patient and physician. Indiscriminate use of the battery of tests available to help make the diagnosis can easily confuse the issue. Possible treatment options range from conservative measures in the form of antibiotic therapy alone to staged procedures and in the extreme case, disarticulation (Table 1). Fortunately, evolution of practice has helped address some past management controversies but decision-making remains a challenge when one is dealing with an infected hip arthroplasty.

Pathogenesis
Both aerobic and anaerobic bacteria have been implicated in hip arthroplasty infections. Rarely, fungi, mycobacterium and brucella may be the source of infection. \textit{Staphylococcus epidermidis} which is part of normal skin flora and
Staphylococcus aureus are the most common infecting organisms.1 Streptococcus species, Coliforms, Pseudomonas, Anaerobes and other bacteria may be infective bacteria, their relative importance varying from hospital to hospital. The microorganisms are introduced onto the surface of the hip prosthesis either intraoperatively, secondary to superficial surgical site hemotoma or infection or from hematogenous spread.

Aside from existing in free-floating forms (planktonic bacteria) Staphylococcus aureus, Staphylococcus epidermidis and Pseudomonas aeruginosa have the ability to produce a hydrated matrix of extracellular polysaccharides (glycocalyx) and protein, forming a biofilm once adherent to the implant surface. The biofilm acts as a protective barrier against antimicrobial agents and host defences. Within the biofilm complex communities composed of one or more species of microorganisms can exist. From time to time bacteria resident within the biofilm may be shed into the bloodstream resulting in systemic upset.

Biofilm bacteria that are firmly established onto the prosthesis surface can in most instances only be eradicated by removing the colonised implant. Nishimura et al. have demonstrated that biofilm can form within 24 h of bacterial adherence to the surface of the prosthesis.2 Certain strains of S. aureus use a different mechanism to adhere onto the prosthesis surface. These strains elaborate binding factors known as adhesins which bind to host proteins, particularly collagen, that cover the implant surface.3

Infection by virulent strains of bacteria and polymicrobial infections have become more commonplace. Methicillin resistant S. aureus (MRSA) is increasingly being isolated from infected arthroplasties and is currently the commonest multiple drug resistant infective organism.4 S. aureus strains with reduced susceptibility to vancomycin have been isolated and will probably become increasingly important in the future.5 S. epidermidis and certain gram-negative bacilli infections are also showing multiple-drug-resistance.

### Diagnosis

History taking in the patient with a total hip arthroplasty that may be infected should be comprehensive. Systemic risk factors for infection should be elicited. Conditions resulting in immunocompromise including diabetes mellitus, rheumatoid arthritis, steroid therapy, psoriasis, renal failure, organ transplantation and advanced age should be noted. Multiple previous operations on the same hip are associated with increased infection risk. A history of concurrent infection such as urinary tract infection, infection of another implanted device, dental abscess or recent oral surgery is important.

Hip pain is a consistent symptom in the infected arthroplasty. The duration of symptoms, presence of fever, rigors and the interval between previous surgery and symptom onset should be established. General examination should determine whether the patient is obese or has signs of malnutrition, as both factors are associated with increased risk of infection. Local examination of the wound will establish tenderness, presence of local inflammation, abscess, wound discharge, sinus and placement and relationship of surgical scars.

Review of charts may reveal pre-morbid functional status in the form of hip scores, which can be compared to the patient’s present status. Any breach in operating room protocol may have been noted, including unusually high traffic, presence of a large number of non-essential personnel, or problems with airflow systems on the day. Other factors like poor choice or non-use of prophylactic antibiotics may have been recorded. The surgery may have been of particularly long duration, which is a factor that independently increases the risk of post-operative infection.

Specimens sent for microbiological analysis may indicate the offending organisms and antibiotic sensitivities. Any antibiotics that the patient has had should be noted. Special investigations are indicated where the diagnosis of deep infection is in doubt following history taking and examination and in instances where the infecting organism has not been identified and antibiotic sensitivities are unknown.

### Radiological investigations

Radiographs are neither sensitive nor specific for diagnosing deep periprosthetic infection. Subtle radiographic signs such as localised osteopenia, periostitis and endosteal scalloping may suggest the presence of active infection. Significant osteolysis early on in the post-operative period also favors a diagnosis of infection provided the implanted materials were not sub-standard or defective. A review of serial radiographs will yield more useful information than a single radiograph. However, in the vast majority of patients, radiographic findings are not helpful in differentiating between aseptic and septic loosening.

Ultrasonography has been used to locate abscesses and facilitate fluid aspiration for culture. The use of magnetic resonance imaging is presently limited to identifying sinus tracts and pockets of pus and fluid collection. Scatter artifact in the immediate area around implanted prostheses distorts the image quality and limits the usefulness of this imaging modality.

### Radionucleotide scans

Radionucleotide scans, in the form of technetium scans, came into widespread use in the diagnosis of periprosthetic infections in the 1980s, following early favourable reports. 99mTc MDP uptake is dependant on blood flow and reflects metabolic activity and bone turnover in skeletal tissue.
Uptake is increased in instances of septic and mechanical loosening of implants, rendering the test of little use in distinguishing the two modes of loosening. Subsequent reports demonstrating the non-specific nature of this investigation in diagnosing periprosthetic infection have resulted in diminished enthusiasm for its routine use. Levitsky et al. reported a sensitivity of 33%, specificity of 86%, a positive predictive value of 30%, and a negative predictive value of 88%.6

Gallium (67Ga) scanning has been in use over the past four decades. The 67Ga tracer is produced by a cyclotron and following injection into the body it is initially bound to transferrin. The Gallium bound to transferrin accumulates at inflammatory foci and also binds to lactoferrin, which is present in high concentrations in these foci. Some of the circulating gallium is thought to be taken up directly by bacteria at the sight of infection. The distribution of the tracer within the body is picked up by a γ-camera. Results have been disappointing with the use of this test in diagnosing periprosthetic infections due to low sensitivity and accuracy.7

In theory, the area surrounding an infected prosthesis should be teeming with inflammatory cells, including recruited white blood cells and immunoglobulins. This is the basis for use of radioactive labelled scans. In 111In-labelled white blood cell scans, whole blood is harvested from the patient and erythrocytes are allowed to separate by a process of sedimentation. The remaining white blood cell-platelet mixture is centrifuged to separate the white blood cells and these are then labelled with radioactive Indium. Once reintroduced into the body, the white cells should preferentially cluster around the infected implant and be picked up by a γ-camera as an area of increased activity. Neutrophils are the predominant type of white blood cell that take up the tracer and a minimum number of 2000 white cells/mm³ is required for satisfactory images. Despite the labor and expense entailed in this procedure, the test cannot be reliably used to diagnose the infected hip prosthesis. Reported sensitivities are variable ranging from 38% to 100%, with specificities of 15–100% and accuracy of 60–96%. In a bid to improve on the diagnostic accuracy of labelled white blood cell scans, 111In-labelled immunoglobulin G (IgG) scans have been developed. When used in the diagnosis of infected hip prostheses the test has a reported sensitivity of 77.8% and specificity of 95.5%.8

Because of the questionable value of radionuclide scans as first line diagnostic tests in infected total hip arthroplasties, combinations of tests were investigated to improve diagnostic accuracy. Kraemer et al.9 investigated technetium/gallium scanning in diagnosing infection in total hip arthroplasty. They reported a sensitivity of 38%, specificity of 100% and positive predictive value of 100%, negative predictive value of 79% and accuracy of 81%. In the same study, the accuracy of the combined test was compared to that of hip aspiration alone and combined technetium/gallium/aspiration. The combined accuracy of all three tests of 85% was just marginally higher than that of hip aspiration alone, at 84%. The authors concluded that technetium/gallium imaging is not an effective method for investigating painful hip protheses for sepsis and offered no additional advantage over hip aspiration. Joseph et al.10 looked at combined 111In-labelled WBC/99mTc sulfur and found 100% specificity, 46% sensitivity, 100% positive predictive value, 84% negative predictive value and 88% accuracy. Inclusion of blood pooling and flow phase data increased the sensitivity to 66%, negative predictive value to 89% and accuracy to 90%. However, the specificity dropped to 98% and the positive predictive value dropped to 91%. They stated that routine use of these combined radionuclide tests could not be supported.

One new tracer that has been investigated in this field includes 18F-FDG. Activated inflammatory cells express increased numbers of inward glucose transporters. These same transporters carry 18F-FDG, which accumulates inside the cells. A high resolution imaging technique, positron emission tomography (PET), is used to determine the distribution of the tracer. Early reports suggested that this investigation might be useful in diagnosing infection but presently its use in differentiating septic from aseptic loosening in periprosthetic infections is limited as interpretation of results and diagnostic criteria are yet to be established.11

Quoted figures for the diagnostic accuracy of radionuclide scans in the diagnosis of hip arthroplasty infections are variable, but on the whole there is little evidence to support their routine use as first line tests. The sensitivity and specificity of these tests are at best comparable to that of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). However, they may have a role in diagnosing infection in patients with active inflammatory conditions e.g. rheumatoid arthritis, accounting in part for raised ESR and CRP.

Blood investigations

Useful blood investigations include inflammatory markers, such as the ESR and CRP. The white cell count is rarely elevated in chronic hip arthroplasty infections12 and is in general not useful in guiding treatment. Both ESR and CRP are non-specific markers that are influenced by a host of inflammatory conditions. When these conditions are excluded, the sensitivity, specificity, positive predictive value and negative predictive value of ESR in diagnosing total hip arthroplasty infection has been reported as 82%, 85%, 58% and 95%, respectively. The corresponding values for CRP are 96%, 92%, 74% and 99%, respectively.13 As these markers are not always elevated together, Spangehl et al.11 suggested that the combination should be used and they found it reliable in predicting periprosthetic infections. They defined elevated ESR as a level greater than 30 mm/h and elevated CRP as greater than 10 mg/L. Elevated levels of the cytokine Interleukin-6, a factor that is produced by monocytes and macrophages, have recently been shown to be correlated positively with the presence of chronic periprosthetic infection. With a normal serum IL-6, defined as <10 pg/ml, the test has a sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 100%, 95%, 89%, 100% and 97%.14 Unfortunately, the levels of IL-6 may be elevated in patients with chronic inflammatory disease such as rheumatoid arthritis. Other conditions associated with elevated IL-6 levels include previous antibiotic treatment, acquired
immunodeficiency syndrome, multiple sclerosis, and Paget’s disease of bone.

**Aspiration**

Hip aspiration is a minimally invasive procedure with low morbidity. It can be undertaken in the operating room with the help of image guidance or in the radiology suite under local anaesthetic. The procedure should be done under sterile conditions and care should be taken not to introduce microorganisms into the hip. The aspirate is sent for microscopic analysis, cell count, gram staining and culture and antibiotic sensitivities. A synovial fluid cell count of more than 50,000 leukocytes per ml with predominantly polymorphonuclear cells (80%) is suggestive of bacterial infection.\(^1^3\) The glucose level in the fluid should also be compared to circulating blood glucose, with a lower level in the aspirate suggesting the presence of bacterial infection. Positive cultures other than contaminants indicate the presence of infection and allow antibiotic sensitivities to be determined.

There is no clear definition of what should be considered contamination, with authors applying different criteria in published series. Williams et al.\(^1^5\) reported the sensitivity and specificity of aspiration to be 80% and 94%, respectively. Lachiewicz et al.\(^1^6\) reported a sensitivity of 92%, specificity of 97% and accuracy of 96% in a study performed on 193 revision hip arthroplasties. A review of the literature involving 1915 aspirates in 18 studies showed preoperative aspiration was generally deemed to be a useful test.\(^1^7\) The sensitivity of hip aspiration is affected by prior antibiotic administration. If the patient is already on antibiotic therapy these should be stopped for at least 2 weeks prior to aspiration. Other limitations of the procedure include the inability to sample biofilm microorganisms as the organisms within the aspirate consist of planktonic bacteria. The technique of lavaging the joint with normal saline and aspirating the fluid in the event of a dry aspirate remains controversial. More invasive preoperative tissue drill biopsies have no advantage over aspiration in terms of bacterial accuracy and result in more false positives.\(^1^5\)

Based on a prospective analysis of 202 revision hip arthroplasties with 17% confirmed infection rate, Spagehl et al.\(^1^5\) concluded that a combination of normal ESR and CRP level is reliable for predicting the absence of infection. They suggest aspiration is indicated when the ESR or CRP is elevated or when a clinical suspicion of infection remains. Lachiewicz et al.\(^1^6\) recommended aspiration if the prosthesis had been in place for less than five years and the ESR was abnormal.

**Intraoperative investigations**

**Frozen section**

Biopsy specimens for frozen section analysis can be taken at the time of open procedure to the hip. Once a decision is made to go ahead with re-implantation on the basis of normal inflammatory markers and sterile aspirate, frozen section analysis can be used to help confirm absence of infection. Tissue specimens are taken from the most inflamed tissue in the acetabulum, femur and surrounding areas. They are immediately sent for analysis by the pathologist. Not all hospitals are geared towards frozen section analysis and preoperative discussion with a pathologist with an interest in periprosthetic infections is often helpful.

Lonner et al.,\(^1^8\) in a prospective study on 175 revision total joint arthroplasties (142 hip and 33 knee), reported a sensitivity of 84%, specificity of 96%, positive predictive value of 70% and negative predictive value of 98% in identifying infections when a positive result was defined as at least five polymorphonuclear cells per high power-field at microscopy. When an index of at least 10 polymorphonuclear cells per high-power field was used the sensitivity and negative predictive value remained the same but the specificity increased to 99% and the positive predictive value increased significantly to 89%. On the basis of the results of the study, a positive frozen section is generally considered to be more than 10 polymorphonuclear cells per high-power field. Spagehl et al.\(^1^3\) resort to intraoperative frozen section when the diagnosis of infection remains in doubt following ESR, CRP and hip aspirate or when inflammatory marker levels remain elevated on the basis of some other inflammatory condition.

The value of intraoperative frozen section has been questioned of late. In a prospective study on 121 revision arthroplasties Banit et al.\(^1^9\) found that it lacked the positive predictive value and sensitivity for accurate determination of infection of hip arthroplasties (45% sensitivity, 92% specificity, 55% positive predictive value, and 88% negative predictive value).

**Gram stain**

Intraoperative gram stain is not a reliable investigation for determining the presence of infection in revision hip arthroplasty. It is insensitive, has a poor positive predictive value and is of little use in determining suitability for re-implantation.\(^2^0\)

**Microbiologic tissue and/or fluid culture**

The gold standard for determining the presence or absence of periprosthetic infection remains the results of microbiologic culture of tissue and/or fluid obtained during revision arthroplasty. However, tissue and fluid cultures can still yield false-negative and false-positive results. For example, some authors have described cases in which, despite the presence of acute inflammation in the periprosthetic membrane and a clinical postoperative course consistent with infection, the intraoperative cultures remained negative.\(^2^1\) On the other hand, Padgett et al.\(^2^2\) reported that 30% of 142 hips treated with revision arthroplasty had at least one positive intraoperative culture. A clinically important infection later developed in only one case in their series, however, suggesting a high frequency of false-positive cultures probably caused by contamination of the tissue sample. In a prospective study involving revision arthroplasty in 297 patients with a total of 41 infections, Atkins et al.\(^2^3\) noted that only 65% of all samples obtained from the infected joints were culture-positive. They recommended obtaining five or six culture
specimens from each patient and suggested that the cut-off for a definite diagnosis of infection be growth of the identical organism on culture of three or more specimens.

In general, it is recommended that surgeons take special precautions to minimise tissue contamination, such as obtaining multiple samples from deep tissues, using clean instruments for tissue retrieval, transferring tissue to the culture bottle without allowing contact with the operative field or gloves, and transferring of the culture samples to the laboratory for processing as quickly as possible. False-negative cultures are likely when the patient received preoperative or intraoperative antibiotics, when the offending organism cannot be isolated by the routine laboratory protocols, or when the submitted tissue samples were extensively cauterised. To minimise the incidence of false-negative cultures, representative samples should be obtained with sharp dissection, administration of antibiotics should be discontinued at least 2 weeks prior to the surgery, and intraoperative antibiotics should be withheld until the tissue samples are retrieved.24

**Polymerase chain reaction**

Polymerase chain reaction (PCR) techniques have been investigated in the quest to detect subclinical joint infections. The ability to amplify minute levels of bacterial DNA to detectable levels should in theory improve our diagnostic accuracy of periprosthetic infections. However, present techniques are insensitive due to problems of contamination and result in a high rate of false positives.25 With further refinement these techniques may be applicable in the future.

**Classification**

Early classification systems of periprosthetic hip infection did little to guide treatment. Fitzgerald et al.26 classified infection following total hip arthroplasty into three distinct groups:

- **Stage I**: Acute postoperative infections that included the classic fulminant postoperative infection, the infected hematoma and surgical site infection that progresses to deep infection.
- **Stage II**: Infections that become apparent 6–24 months postoperatively due to indolent infection.
- **Stage III**: Infections that develop two or more years postoperatively in a previously asymptomatic arthroplasty.

These were presumed to be due to hematogenous spread of infection.

In a landmark study, Tsukuyama et al.27 divided hip arthroplasty infections into different types based on the above classification but with addition of a fourth type for positive intraoperative cultures taken at the time of direct exchange arthroplasty of presumed non-infected joints. Based on their experience of 106 patients treated according to a defined protocol, they were able to show success rates for eradication of infection in each of the types (Table 2).

Although the strategies employed yielded modest success rates, the guidelines suggested formed a basis for a classification system that was useful in guiding treatment. The drawbacks of the classification were lack of consideration of the general health of the patient and of any operative factors at a local level.

McPherson et al.28 have attempted to address this in a staging system that they proposed. They found significant positive correlation of systemic host grade and local extremity grade to a number of parameters in a sample of 50 patients with chronic infection. Further studies are required to validate the usefulness of this grading system for early infections and positive intraoperative cultures. For the purposes of this discussion acute infections are defined as postoperative infections within 2 weeks of surgery and hematogenous infections with symptoms for less than 2 weeks. Chronic infections include all infections recognised 2 weeks or later after surgery and hematogenous infections symptomatic for a period longer than 2 weeks.

**Treatment**

The main aims of treatment should be eradication of infection and to leave the patient with a functional prosthesis. Treatment approaches to these patients must be multi-disciplinary with continuous consultation with, amongst others, infectious disease experts, nutritionists, physiotherapists and occupational therapists.

**Antibiotic therapy alone**

This treatment strategy is indicated in patients with positive intraoperative cultures taken during revision for presumed aseptic loosening. Preoperatively, every effort should have been made to exclude infection. The distinction between mere contamination and potential and actual infection is not always clear-cut and this strategy may lead to

<table>
<thead>
<tr>
<th>Infection type</th>
<th>Treatment protocol</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Type 1 (n = 35)</td>
<td>Surgical debridement, exchange of polyethylene insert of acetabulum and intravenous antibiotics</td>
<td>71% cure</td>
</tr>
<tr>
<td>Type 2 (n = 34)</td>
<td>Removal of components, surgical debridement, antibiotic beads insertion and delayed reimplantation</td>
<td>85% cure</td>
</tr>
<tr>
<td>Type 3 (n = 6)</td>
<td>Surgical debridement, prosthesis retention and intravenous antibiotics</td>
<td>50% cure</td>
</tr>
<tr>
<td>Type 4 (n = 31)</td>
<td>Intravenous antibiotics</td>
<td>90% cure</td>
</tr>
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over-treatment. It is common practice to swab bone allografts before use in revision cases and these may on occasion present positive cultures. Antibiotic treatment may also be beneficial in these patients.

**Long-term antibiotic suppression**

This treatment option is reserved for patients who have a stable prosthesis, harbor a sensitive microorganism and are not candidates for two-stage re-implantation either because of poor general health contra-indicating further surgery or refusal to consent to surgery. The oral antibiotic chosen for this purpose should be well tolerated by a compliant patient with minimal toxicity, but resistance remains a concern. The addition of rifampicin to treatment regimens for implant related staphylococcal infections has been shown to result in improved rates of eradication of infection and reduced rates of antibiotic resistance.29 Rifampicin containing regimens have been demonstrated to have activity against staphylococcal biofilms.30

**Debridement and retention of prostheses**

Acute infections are often amenable to surgical debridement provided the prosthesis is stable. When dealing with modular implants, exchanging the bearings allows physical removal of microorganisms that may be interposed between the prosthesis and the bearing and removes biofilms that are resident in otherwise inaccessible areas. Copious amounts of saline lavage (at least 9L) should be used during the procedure. Addition of antibiotic to the lavage may be beneficial. Patients are maintained on parenteral antibiotics for a minimum of 6 weeks post-op. Antibiotic choices are based on pre-operative cultures and they are modified depending on results of intraoperative cultures. Crockarell et al.31 found that this treatment strategy was unsuccessful if undertaken more than 2 weeks after onset of symptoms in acute infections.

**Single stage exchange arthroplasty**

This treatment strategy is appropriate in a minority of cases of chronic infection. The prosthesis is removed, sinuses are excised, infected and devitalised tissue is debrided, and the wound is lavaged. Once a clean uninfected bed is achieved, then one proceeds to immediate re-implantation with a new prosthesis during the same procedure. The obvious advantages of this approach over delayed re-implantation are reduced patient morbidity of a single surgical procedure and attendant cost savings. Should there be any doubt regarding cleanliness of the wound following debridement then it is prudent to opt for staged surgery.

**Staged exchange arthroplasty**

In the first stage of surgery, the prosthesis and all foreign material are removed, together with infected and devitalised tissue. Copious saline lavage (9L) with one added antibiotic is used to irrigate tissues. The patient is then left with a resection arthroplasty and a device to deliver high concentrations of antibiotics locally. Local therapy is supplemented by parenteral antibiotics which may be converted to oral antibiotics depending on response to therapy. By convention the second stage is undertaken no earlier than 6 weeks following the first stage. A new prosthesis is re-implanted and antibiotic therapy is continued post-operatively for a minimum of 6 weeks.

**Local antibiotics**

Delivery of high concentrations of local antibiotics can be achieved through use of antibiotic impregnated cement beads (Fig. 1) or antibiotic loaded cement spacers. Antibiotic loaded spacers can either be of the static variety or articulating. Static spacers are antibiotic loaded cement dowels loosely inserted into the femoral shaft and a corresponding spacer ball loosely inserted into the acetabulum (Fig. 2). Although some movement is possible at the hip joint it is restricted and there is associated discomfort favoring scar formation and soft tissue contracture over the interval between stages. Articulating spacers consist of femoral and acetabular components that are covered by antibiotic loaded cement with conventional articulating bearings (PROSTALAC), or more simply, a one-piece femoral component with a large head made of antibiotic loaded cement (Fig. 3). Articulating spacers allow maintenance of
range of motion in the hip during the interval period, and ultimately an easier reimplantation procedure. Off-the-shelf pre-molded spacers are also available but these are generally fabricated with low levels of antibiotic within the cement (Fig. 4). Novel approaches include sterilisation of the removed prosthesis, coating with antibiotic loaded cement and use as a spacer.

Hsieh et al.\(^{32}\) compared use of cement beads with a cement spacer prosthesis in 128 patients followed-up for an average of 4.9 years. The use of the spacer prosthesis was associated with a higher hip score, a shorter hospital stay, and better walking capacity in the interim period; a decreased operative time, less blood loss and a lower transfusion requirement at the time of re-implantation. The infection-free rates were similar in both groups.

The choice of antibiotic is predicated on pre-operative cultures and sensitivities. Antibiotics loaded onto the cement should be thermostable and they should not adversely affect the properties of the cement. In vitro studies have demonstrated that combining two antibiotics in the cement improves elution of both, suggesting bi-antibiotic spacers may be better than mono-antibiotic spacers.\(^{33}\) Koo et al.\(^{34}\) recommend use of a combination of vancomycin, gentamicin and cefotaxime impregnated cement in two-stage revisions when the causative organism is not identified in preoperative cultures.

**Decision making regarding proceeding to re-implantation**

The decision to proceed to re-implantation in the staged procedure is based on the general condition of the patient,
the condition of the wound and special investigations. The patient’s condition should be optimised with respect to addressing immuno-incompetence, nutritional deficiencies and fitness to undergo further surgery. The wound should be healed, clean and without discharge or active sinuses.

Blood investigations

A trend indicating a fall in both ESR and CRP during the interval period of antibiotic treatment is a reassuring sign that infection is being eradicated. Both these markers should be within normal range before proceeding to re-implantation. IL-6 may prove to be invaluable in guiding re-implantation as levels rapidly return to normal after total joint surgery in the absence of infection.

Aspiration

Preoperative hip aspiration is useful in excluding ongoing infection. Continuing infection necessitates further surgical debridement or modification of antibiotic therapy. Aspiration is a particularly useful investigation in patients with active inflammatory disorders where the ESR and CRP would otherwise remain elevated despite eradication of infection.

Frozen section

This investigation is appropriate in cases where infection eradication remains doubtful because of equivocal ESR, CRP and hip aspiration results. Della Valle et al. demonstrated that a negative finding on intraoperative analysis has a high predictive value with regard to ruling out the presence of infection. However, the sensitivity of the test for detection of persistent infection was poor (sensitivity of 25%, specificity of 98%, positive predictive value of 50%, negative predictive value of 95% and accuracy of 94%).

Salvage procedures

Although arthrodesis, definitive excision arthroplasty and amputation remain in our armamentarium, these procedures are appropriate only in a select few patients in modern orthopaedics.

Arthrodesis

Arthrodesis is indicated as a salvage procedure in young patients. Infection should be completely eradicated at the time of arthrodesis and the technique for fusion should ideally spare the abductors to enable reconversion to hip arthroplasty in later years. Long-term complications of hip arthrodesis include back pain, which dramatically improves on conversion to hip arthroplasty. Arthrodesis is contraindicated in patients with contralateral hip pathology, lumbar spine pathology and ipsilateral knee instability. Achieving hip fusion in the correct plane and sparing the abductors is a challenge in the arthroplasty patient because of pre-existing bone loss.

Girdlestone’s arthroplasty

Planned definitive excision arthroplasty in the form of a Girdlestone’s arthroplasty is a reliable treatment option for eradicating infection (98%, 43 of 44 patients) and pain at the cost of functional compromise. The combination of a Trendelenburg gait and limb shortening makes for difficult walking and patients tire easily. Bourne et al. reported satisfaction rates of 79% in 33 patients followed for 6.9 years. They noted that results improved with time. Where cost constraints preclude further reconstructive surgery, Girdlestone’s arthroplasty is a reasonable salvage procedure in treating the chronically infected hip arthroplasty. The excision arthroplasty can be converted to hip arthroplasty when circumstances change, provided infection is eradicated. Occasionally, planned two-stage reimplantation surgery proceeds no further than the first stage due to patient infirmity leaving the patient with effectively an excision arthroplasty.

Hip disarticulation

Disarticulation is associated with high morbidity and a very poor functional outcome with most patients confined to a wheelchair. The procedure may rarely be indicated in cases of overwhelming life threatening hip arthroplasty sepsis, as a last resort. It may also be considered in patients with intractable infection together with either major vascular insufficiency or massive bone loss, who are not deemed candidates for reconstructive surgery.

Single-stage vs. two-stage reimplantation

The obvious advantages of single-stage reimplantation over two-stage surgery are the cost savings and reduced patient morbidity of a single procedure as opposed to two major procedures. In addition, single-stage reimplantation is a technically easier procedure. Proponents of the single-stage approach point to a higher incidence of mechanical complications including fracture, dislocation and limb length discrepancy with staged treatment. The disadvantages include less flexibility and lower success rate for curing infection. There is less flexibility in choice of high dose local antibiotic. There is only one opportunity, for instance, to choose the correct antibiotic to be impregnated into the cement at the time of reimplantation. Staged surgery allows revision of the antibiotic impregnated spacer should intraoperative cultures reveal infection by organisms resistant to the chosen antibiotic. There is also a documented lower success rate for curing infection in single-stage reimplantation procedures. Consistently high success rates have been reported for eradication of infection in two-stage reimplantations, making this treatment strategy currently the standard of care.

Jackson et al. performed a literature review to determine when direct exchange was most likely to be successful. They found an 83% success rate at average 4.8 years follow-up of 1299 hips. The procedure was likely to be successful if the following criteria were met: patients who were generally of good health, absence of wound complications following the initial hip replacement, and if the
infecting organisms are of low virulence and sensitive to antibiotic mixed into the bone cement used in the re-implantation. Polymicrobial infections, gram negative infections and infections by methicillin resistant organisms were associated with failure. The authors concluded that indications for direct exchange were limited as methicillin resistant organisms are common nowadays and current revision techniques use cementless implants.

**Interval between stages**

Hansen and Rand\(^4\) combined results of multiple studies in order to investigate the effect of delay in reimplantation on the success rate of eradication of infection. They found that the timing of reconstruction and the use of antibiotic impregnated cement were closely linked variables. The results of two-stage reimplantation using cement without antibiotic were superior to those of single stage revision using cement without antibiotic and similar to those of single stage revision using antibiotic laden cement. An interval period between stages by itself seems to be beneficial. The ideal length of interval between stages has not been determined but by convention we wait a minimum of 6 weeks. Ketterl et al.\(^4\) found that reimplantation carried out early (<4 weeks (average 2.1 weeks) was better than reimplantation >4 weeks (average 12.7 weeks), with respect to function, mortality and cure of infection.

**Cementless vs. cemented implants**

The advantage of using cement lies in the ability to add antibiotic, which elutes over time, keeping infection in check. Indeed, early successful reimplantations involved use of antibiotic laden cemented prostheses. Buccholz et al.\(^4\) introduced the concept of antibiotic impregnated cement and popularised its use in Europe for single stage revision surgery, reporting infection cure rates of 77% in his series. Raut et al.\(^4\) reported a success rate of 84% using the same treatment strategy. A review of published series comparing use of plain bone cement and antibiotic impregnated cement in single-stage revisions found cumulative success rates of 60% and 83%, respectively, strongly suggesting there was no role for single-stage cementless revisions.\(^4\)

The superiority of cementless hip revisions over cemented implants in aseptic loosening led investigators to consider their use in two-stage reimplantations. The limited time-dependant ability of antibiotic to elute from bone cement in sufficient quantities to overcome infective bacteria coupled with the negative long-term effects of cement on the function of polymorphonuclear cells supported the move towards cementless two-stage reimplantations. Fehring et al.\(^4\) demonstrated a success rate of 92% (25 patients) at average 41 months follow-up using a two-stage cementless reimplantation approach. The authors highlighted the importance of using implants of appropriate design to ensure bone ingrowth of the femoral component. They used proximally milled cementless implants in cases where proximal femoral bone stock was adequate and extensively coated stems to obtain diaphyseal stability where there was proximal structural bone loss. Other authors have reported similar experience: Haddad et al.\(^4\) (50 patients) reported a 92% success rate at 5.8 years follow-up; Kraay et al.\(^4\) (33 patients) reported a 93% success rate. Reported success rates for two-stage cemented reimplantations range from 90% to 95%.

**Bone grafting**

It is not unusual for the infected hip arthroplasty to present with significant bone loss. During debridement additional bone that is deemed to be non-viable is sacrificed, compounding bone stock deficiency (Fig. 5). In the past, there were concerns about the use of bone graft with fears that it may encourage persistence of infection or even introduce new infection. Patients with significant bone loss were treated with definitive resection arthroplasty, rendering them severely functionally compromised. The safety of bone grafts, including structural allografts (Fig. 6) in second-stage reimplantation has now been reported in a number of studies with a reasonable length of follow-up.\(^4\)

**The future**

A single investigation with 100% sensitivity and specificity is required to diagnose infected hip arthroplasties. Different generations of radionuclide tests have been touted to fulfil this purpose, only to be found inadequate on further clinical testing. However, with further refinement radionuclide tests may still come close to 100% sensitivity and specificity. Molecular biology techniques like PCR continue...

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**Figure 5** Radiograph of the right hip illustrating severe femoral bone stock deficiency in a young patient following first-stage surgery for an infected revision hip replacement.
to hold promise, but again need refinement. A technique for covalently tethering antibiotic to titanium surfaces has been developed. Facilitating high dose local antibiotic delivery may revolutionise treatment of chronic infections. This would make it possible to use cementless antibiotic coated revision implants and acceptable to dispense with staged treatment. The change in the microbiology of infecting organisms towards increased virulence is discouraging the move towards shorter antibiotic treatment times and use of more convenient oral antibiotics. Studies on biofilm organisms will hopefully lead to development of effective agents that can be taken orally. One of the biggest impediments in advancing management of the infected hip arthroplasty seems to be the falling incidence of infections. Studies with adequate numbers of patients are only possible in large referral centres that specialise in this particular complication, or combined multiple centres. There is certainly a need for these centres to rigorously evaluate new investigative and treatment modalities.

References

1. Salvati EA, Della Valle AG, Masri BA, Duncan CP. The infected total hip arthroplasty. AAOS Instruction Course Lecture 2003; 52:223–45.


Suggested Further Reading