

The diagnosis and management of prosthetic joint infections

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A host of technical and operative improvements have seen the rates of infection associated with joint replacement reach historic lows. However, the increasing number of operations being performed means that the absolute number of such infections remains significant. Diagnosis may be challenging and delaying appropriate treatment can lead to reduced joint function and the need for more complex, perhaps multiple, procedures. Individual centres tend to see small numbers of such cases, and in the absence of large clinical trials management varies. Early diagnosis, selection of an appropriate surgical strategy, accurate identification of the responsible microorganisms and construction of an appropriate antibiotic regimen are essential elements of any management strategy. Such packages of care are best delivered by a multidisciplinary team composed of orthopaedic and plastic surgeons, microbiologists, infectious disease physicians, specialist nurses, physiotherapists and occupational therapists. Each treatment plan must be developed in consultation with the patient, taking into account their aims and realistic goals. This review provides an overview of current understanding regarding diagnosis and treatment of prosthetic joint infections and suggests a treatment algorithm.

Keywords: joint revision, outpatient parenteral antimicrobial therapy

Introduction

The last five decades have seen a host of technical and operative improvements for the use of prosthetic joints that have reduced the risk of infection. Rates today stand at around 1% for hip and 0.7% for knee replacement.¹ However, the increasing number of joint replacements being performed means the absolute number of such infections will remain significant and pose substantial costs to healthcare systems worldwide.² Diagnosis may be challenging as symptoms are variable and diagnostic tests non-specific.³ Delayed diagnosis may lead to reduced function, increased morbidity and the need for more complex surgery, often involving multiple procedures. Individual centres tend to see small numbers of such cases and in the absence of large clinical trials management varies.

This review provides an overview of current understanding regarding diagnosis and treatment of prosthetic joint infections and suggests a treatment algorithm. The following case study demonstrates the complexity of such infections, raising the issues this review goes on to examine.

Case study

A man in his late thirties was referred to a specialist bone infection service. He had congenital hip dysplasia which had necessitated bilateral hip replacements by the age of 21 years. In his early thirties, the left prosthetic hip was revised because of mechanical problems, with the right side revised the following

year. A year later he developed bilateral discharging sinuses over the hips and underwent several incision and drainage procedures. On one occasion he developed severe sepsis as a result of hip infection and required high dependency unit care. Various bone, tissue and fluid samples grew either methicillin-susceptible *Staphylococcus aureus* (MSSA) or coagulase-negative staphylococci (CoNS), with one sample from the left hip growing methicillin-resistant *S. aureus* (MRSA). He was allergic to penicillin and linezolid. Over the next 2 years he received multiple courses of antibiotics, including a prolonged course of vancomycin. The hips remained painful, more so on the left than the right, and both were discharging thick pus through scarred wounds despite many months of appropriate antibiotic therapy.

He was referred to a multidisciplinary bone infection service. X-rays demonstrated evidence of loosening of both hips—worse on the left than the right (Figure 1a and b). A decision was made to proceed with bilateral two-stage revisions. All antibiotics were stopped and the patient was carefully monitored for signs of developing sepsis. Twelve days later the left hip prosthesis and all cement and a large amount of necrotic tissue were removed (an excision arthroplasty/Girdlestone procedure) but closure was obtained without the need for a muscle flap (Figure 1d). Post-operatively he was started on vancomycin and meropenem. Of six samples taken, five grew MSSA and two grew *Proteus mirabilis*, and his antibiotic regimen was changed to ceftriaxone only.

Two weeks after the first operation a Girdlestone procedure was performed on the right side, and previous bone graft

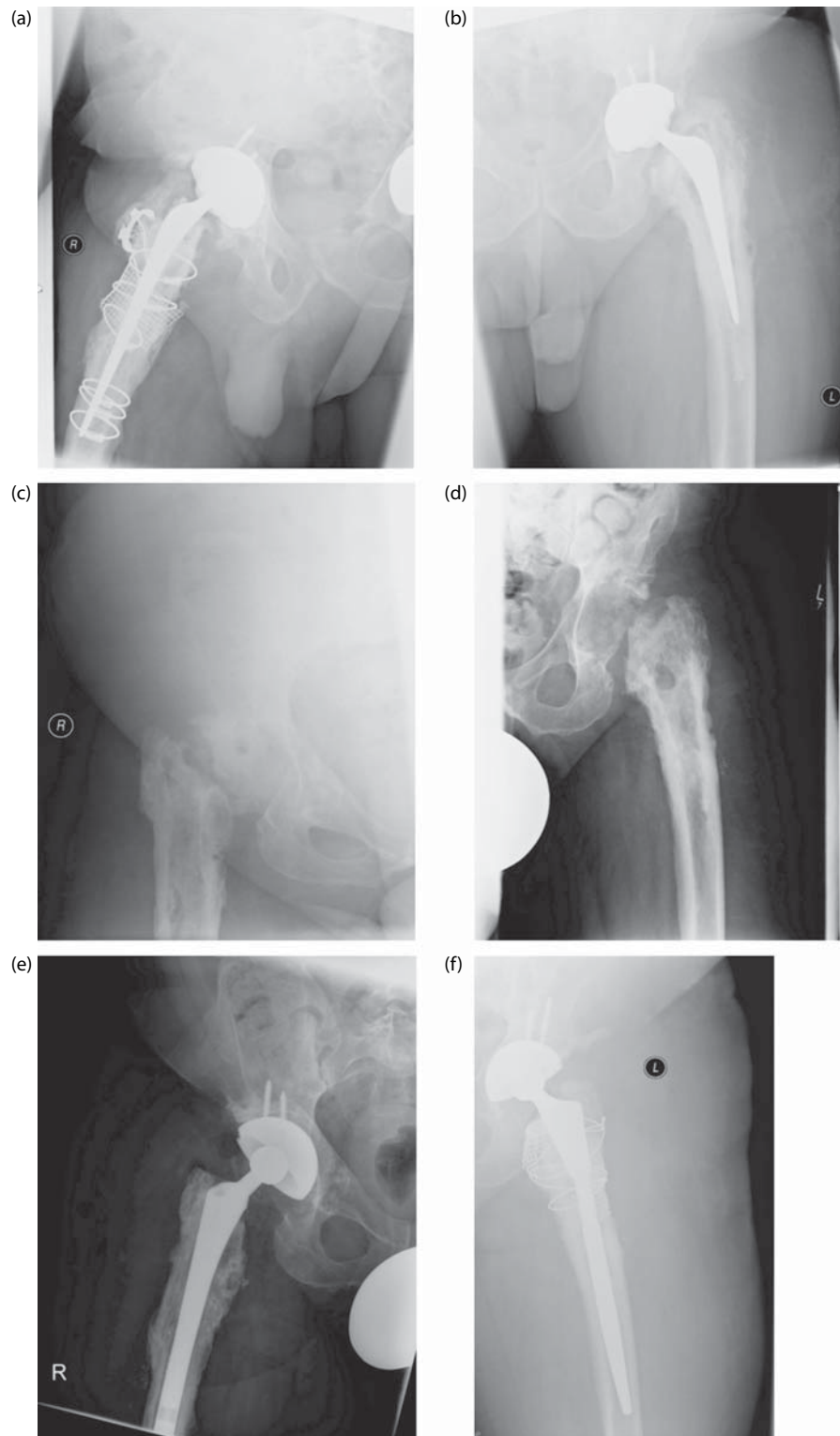


Figure 1. (a and b) Appearance of plain hip X-rays on referral to specialist infection service following bilateral hip prosthesis revisions and multiple washouts and debridements. There is severe loosening, which is particularly noticeable around the left femoral stem. (c and d) Plain hip X-rays following bilateral Girdlestone procedures. (e and f) Plain hip X-rays following reimplantation.

material and a mesh were removed. This was a difficult procedure with considerable blood loss but he recovered uneventfully (Figure 1c). He was changed back to vancomycin and meropenem pending culture results. On this occasion all seven samples taken grew CoNS. He was switched back to ceftriaxone (treating the organisms from the first operation) and continued on vancomycin. Four weeks after his second Girdlestone procedure his C-reactive protein (CRP) was 8 mg/L, and he was largely pain free. He was discharged home on suitable oral antibiotics for a further 2 weeks.

Six months after the first operation and 4 months after stopping antibiotics the left hip was re-implanted using gentamicin-loaded cement. Six samples were taken—two grew two different CoNS strains and one grew *Serratia marcescens*. These were felt to be contaminants and the empirical post-operative antibiotics were stopped. Three weeks following the implantation he became febrile and tachycardic. Blood cultures grew MSSA. An emergency left hip exploration revealed copious brown fluid and the joint was thoroughly debrided [a debridement, antibiotics, implant retention (DAIR) procedure]. All seven samples taken grew MSSA and he settled quickly with good wound healing. He was treated with iv ceftriaxone and oral rifampicin for 6 weeks, with a plan for oral ciprofloxacin and rifampicin to be given for at least 6 months (ongoing).

Eight months after the first Girdlestone (and 2 months after the first re-implantation) the right hip was re-implanted. This was uneventful and there was no growth in the four microbiological samples taken (Figure 1e and f). The wound healed well and 2 weeks later he was mobilizing well on crutches and pain was improving. Careful follow-up is planned.

Presentation and pathogenesis

Prosthetic joint infections are classified as 'early' (those occurring within 3 months of implantation), 'delayed' (3–12 months after implantation) and 'late' (more than 12 months after implantation).³ Early and delayed infections are thought to be due to organisms introduced at the time of surgery, whereas late infections are more likely to be haematogenously acquired. Infecting organisms form microcolonies on the prosthesis surface, which in turn elaborate exopolysaccharides that coalesce, forming a biofilm.⁴ Once formed, organisms within the film are protected from host immune responses and may demonstrate a reduced susceptibility to antibiotics as a result of changes in metabolic processes and poor diffusion.³

Early infections may present with a persistently leaking wound or the acute onset of fever, pain, swelling, effusion and erythema at the implant site. Untreated infections may form chronic sinuses. Bacteraemia and a systemic sepsis syndrome may occur. Late infections may present more insidiously with worsening joint pain (often 'start up' in nature), and sometimes an effusion and restriction of movement. Sinuses may also occur. There may be radiological evidence of loosening but in the absence of a sinus it can be difficult to distinguish infection from aseptic loosening.⁵ Radiological loosening occurring relatively soon within the projected lifespan of a prosthetic joint may be suggestive of infection. Late infections occasionally present with an acutely inflamed joint that may be associated with systemic features of sepsis.

Risk factors

Key risk factors for prosthetic joint infection include previous joint arthroplasty, a surgical site infection not involving the joint prosthesis, the presence of malignancy and a National Nosocomial Infection Surveillance System risk score of 1 or 2.⁶ Other suggested risk factors include advanced age, diabetes mellitus, previous native joint infection, obesity, poor nutrition, skin disease and pre-existing joint disease (particularly rheumatoid arthritis).⁷ Those undergoing revision of an existing prosthetic joint are at greater risk than those undergoing primary joint replacement.⁸ A post-operative apparently superficial surgical site infection may be indicative of deeper infection involving the implant.⁶ Haematogenous seeding of a bacteraemic infection to a prosthesis is rare overall (less than 0.5% in one series).⁹ The rate of seeding to a prosthetic joint in *S. aureus* bacteraemia, however, may be as high as 34%.¹⁰

Microbiology

Staphylococci are the most frequently isolated organism at all timepoints: early, delayed and late.^{5,11} CoNS account for most of these (30%–41%) with *S. aureus* as the second most common (12%–39%).¹² Late infections are presumed to be of haematogenous aetiology and *S. aureus* seems to predominate at this point, but CoNS may still account for a third of cases. Streptococci, enterococci and diphtheroids each account for around 10% of cases. Gram-negative organisms are much less common than Gram-positive, causing around 8% of cases. Resistant organisms are still relatively uncommon in the UK and the majority of resistant and polymicrobial infections occur within the first 3 months following arthroplasty.¹¹

Diagnosis

Blood tests

Routine blood tests may suggest a diagnosis of infection (for example a raised CRP or white cell count), but these are unhelpful in the early post-operative phase as they will be raised for around 14 days after surgery. Persistent elevation, however, raises the possibility of infection. A low CRP may have a role in helping to rule out infection: Fink *et al.*¹³ reported that a CRP of less than 13.5 mg/L had a negative predictive value of 88.5% in the diagnosis of late prosthetic knee infection. A CRP above this had a positive predictive value of only 59.2%. It should be emphasized that normal results do not exclude infection and abnormal results may reflect pathology elsewhere.

Radiology

Plain radiography of the affected joint is unhelpful in early infection but may help exclude other causes of joint symptoms and signs. Chronic infection may cause bone loss and evidence of loosening around an implant but these changes are not specific to infection. Ultrasound may demonstrate effusions or synovial thickening and if joints are amenable to aspiration or biopsy this should be attempted and samples sent for histology and microbiology. MRI is not generally of value due to metal artefact. The radionuclide-based technique in most widespread use is

combined leucocyte/marrow imaging with a reported accuracy of 88%–98%;¹⁴ however, it is technically complex, expensive and takes at least 24 h to perform. An aspiration and/or biopsy yields more useful results.

Microbiology

If an acute infection is suspected blood cultures and a joint aspirate should be taken before antibiotics are administered. The latter should not delay the timely administration of antibiotics if severe systemic sepsis is present.

In more chronic infections, ultrasound-guided joint aspiration is usually straightforward and can be performed under local anaesthesia. Studies report widely varying sensitivities (12%–100%).¹³ A peri-prosthetic biopsy under fluoroscopy is an alternative and may increase the chances of sampling the area with the highest density of organisms in chronic infections (the bone/cement or bone/prosthesis interface). Multiple arthroscopic synovial biopsies may be useful in the diagnosis of chronic prosthetic knee infection.¹³ If a prosthetic joint requires revision and infection is suspected, an attempt at pre-operative identification of the infecting organisms may confirm the diagnosis and guide the choice of surgical strategy and the constituents of antibiotic-loaded cement where relevant. Superficial or sinus swabs may highlight the presence of resistant organisms such as MRSA but are not useful in diagnosis.

The diagnosis of infection is made by a combination of clinical, histological and biopsy or intra-operative microbiological criteria. Surgical samples or aspirates are more likely to be culture-negative if the patient has received any antibiotics in the preceding 3 months.¹⁵ Where possible, antibiotics should be withheld until all diagnostic microbiological tests have been completed. It is not clear how long a patient should be off antibiotics prior to a diagnostic procedure or joint revision but it is our practice and that of others to recommend at least 14 days.¹⁵ Clearly, administration of pre-operative antibiotics may have to be accepted in those cases where sepsis or deteriorating local disease demands immediate antibiotic therapy.

When a joint is revised, multiple intra-operative specimens should be taken.¹⁶ The growth of an indistinguishable organism from at least three samples is strongly associated with infection when histology is used as the criterion standard.¹⁷ It is recommended that five distinct samples are taken using separate instruments, thus reducing the chance of false positivity by cross-contamination. Histological samples from equivalent sites are also useful for predicting infection.¹⁸ Intra-operative frozen sections may be helpful for surgical planning in some cases.^{19–21} Recently, most clinical studies have used a composite clinico-pathological definition where a result of two or more samples positive with an indistinguishable organism constitutes a positive microbiology result.

It is recommended that microbiology specimens are cultured for at least 5 days.¹⁶ Certain organisms, such as *Propionibacterium* spp. and *Corynebacterium* spp., however, may require longer incubations. Schäfer *et al.*²² demonstrated that only 73.6% of infections were detected by 7 days of culture, the remainder being detected during the second week of culture. Sonication of a removed implant may increase the culture yield by disrupting adherent bacterial biofilm, an effect most notable in samples

from patients who have recently received antibiotics.²³ It does not replace the need for careful multiple sampling and where this is done the sensitivity is comparable.

The development of nucleic amplification techniques shows promise and studies demonstrate they are capable of detecting new and fastidious pathogens. However, at present they do not appear to demonstrate significant advantage over meticulous culture techniques.²⁴

Treatment

Effective treatment requires a combination of an appropriate surgical strategy with, in most cases, suitable antibiotic therapy. This is most effectively delivered through multidisciplinary teams involving orthopaedic and plastic surgeons, microbiologists and infectious disease specialists as well as physiotherapists and occupational therapists experienced in rehabilitation. Where infections are long-standing or complicated it may be appropriate to consider referral to surgeons or units with expertise in managing such cases. This can be of benefit to both the patient and the referring surgeon. The importance of selecting the appropriate surgical strategy for the individual patient cannot be overemphasized. This will be influenced by their co-morbidities, life expectancy, personal expectations and goals—these should be explored carefully. Some individuals will have experienced multiple operations, prolonged discomfort and immobility with the psychological co-morbidity that entails.

Surgical strategy

In some cases pursuing a surgical ‘cure’ of infection may not be practical or appropriate. For example, an elderly frail individual with a functional infected prosthesis may be best managed with a stoma bag over a discharging sinus and/or long-term antibiotic suppression. Options for management include, but are not limited to, no surgery (with or without antibiotic suppression), amputation, joint fusion or removal, prosthesis retention with debridement and antibiotics, and joint revision in either one or two stages.

No surgery

Some patients, particularly those with multiple co-morbidities, or in whom a curative procedure is likely to be technically challenging, may be best managed conservatively. This may be by long-term antibiotic suppression, acceptance of a chronically discharging sinus, or indeed deliberate formation of a sinus.

Joint removal or fusion

It may be inappropriate to subject an individual to a revision when, even with a functional prosthesis, they will remain immobile for other reasons—for example, someone wheelchair-bound with neurological illness. Such cases may be best managed by prosthesis removal. In other cases repeated attempts at revision and salvage may fail to eradicate infection, and again an excision arthroplasty with removal of all foreign material may be appropriate.

Debridement, antibiotics and implant retention (DAIR)

Conservative surgical management involves debridement of a joint with exchange of modular components and/or liners but retaining the prosthesis itself, combined with prolonged antibiotic therapy (the DAIR strategy). Whether debridement should be an open surgical procedure or may be performed as effectively arthroscopically is a matter of some debate. Some studies of prosthetic knee infection have implied that arthroscopic debridement is as effective as open debridement in those joints that are well fixed with little cement.²⁵ However, more recent data suggest higher rates of failure when arthroscopic washout is used compared with open debridement, particularly in those cases where *S. aureus* is isolated.²⁶ This presumably reflects the less adequate debridement and the inevitable retention of modular components. In some cases, for example those with a sinus, achieving adequate debridement may necessitate soft tissue reconstruction using a muscle flap.

A retrospective review of 112 prosthetic joint infections managed by DAIR demonstrated a success rate of 82% (mean antibiotic duration 1.5 years, mean follow-up 2.3 years).²⁶ Failure was associated with arthroscopic debridement, previously revised joints and cases in which *S. aureus* was isolated. Antibiotics were administered intravenously for 6 weeks, and then switched to an appropriate oral regimen. The author's analysis suggested that whilst there was an increased risk of relapse once antibiotics were stopped, extending antibiotic duration beyond 6 months did not significantly increase the chance of a cure. Rates of relapse were highest in the 4 months after cessation of antibiotic therapy.

Which patients are suitable for DAIR? Outcomes are best in those patients with a short duration of symptoms, a well-fixed and functional implant and ideally with well-characterized microbiology demonstrating a highly susceptible organism.²⁷ Those with rheumatoid disease, undergoing debridement of a previously revised joint or infected with *S. aureus* may do less well.²⁸ It has been suggested that those with Gram-negative infections fare worse than those with Gram-positive ones, but larger studies are needed.²⁹ DAIR may also be an appropriate surgical strategy for selected patients with more chronic presentations.²⁶

Implant revision

Joint revision may be performed as either a one- or two-stage procedure. A one-stage procedure involves sampling, removal of the infected joint and all cement, thorough debridement followed by re-scrubbing, re-draping and insertion of a new prosthesis. A two-stage procedure separates sampling, joint removal, thorough debridement and closure (the first-stage) from subsequent re-insertion by weeks or months. A cement spacer is essential for knee joints and may be used for hips. There are commercially available antibiotic-impregnated cements and a range of other antimicrobials can also be added to cement provided they are heat-stable.³⁰ Some units recommend a pre-operative aspirate to try to define the microbiology in order to guide selection of the antibiotic components of the cement.³¹ Most units administer systemic antibiotics for up to 6 weeks post-operatively before insertion of a new prosthesis 2 or more months later.³² Some advocate the use of an

appropriate antibiotic-impregnated cement and do not use any systemic therapy beyond standard surgical prophylaxis.³³ This is discussed in more detail below.

The role of effective debridement at the first stage, which should include removal of all cement, cement restrictors and prosthetic material, cannot be overemphasized. A good outcome is probably as dependent upon this as on antibiotic therapy.³⁴ Intra-operative samples for culture and histology are taken from joint fluid, joint capsule (hip), and synovium (knee), infected collections and membrane from each interface as prosthetic components are removed. All samples should be obtained with separate instruments and placed into separate containers. Sinuses should be excised and bone ends and cavities must be debrided of all infected, necrotic and foreign material. It may be necessary to conduct some procedures with plastic surgeons to ensure that the adequacy of the debridement is not compromised as a result of concern regarding wound closure. In some cases a second or even further debridement may be required to achieve adequate surgical clearance (Figure 2).

Two-stage revisions are the most widely favoured. However, they are demanding for healthcare facilities and the patient in terms of the repeated procedures and the limited mobility between stages. They allow effective debridement and the option of local antibiotic delivery by drug-eluting cement spacers. Antibiotics may be delivered locally, systemically (either intravenously or oral) or both. What few data exist suggest that outcomes are broadly similar regardless of the means of antibiotic delivery—this is discussed in more detail below.

One-stage revision may be appropriate for selected cases and is common practice in some centres. In particular it may be appropriate for those too frail to withstand two procedures and the demanding rehabilitation that follows a long period of relative immobility. It may not be advisable in those with resistant or difficult-to-treat organisms. What evidence exists suggests outcomes are broadly similar to those with two-stage revision,³⁵ but trials are needed.

Antibiotic therapy

There is little evidence to guide the choice of the route or duration of antibiotic therapy and there is great variation in practice.³⁶ The antibiotic can be delivered systemically or locally to the joint, usually through the use of loaded cement.³⁷ If local delivery is to be relied upon, it is useful for the causative organisms and their susceptibilities to be defined pre-operatively. If systemic delivery is selected, a suitable empirical regimen must be designed whilst the results of intraoperative cultures are awaited. This should be guided by local organism susceptibilities and must be active against staphylococci and a wide range of nosocomial multiresistant Gram-negative organisms (for example, a glycopeptide and a carbapenem).¹¹

Two-stage revisions

Local antibiotics can be delivered via a cement spacer. Caution must be exercised in deciding which antibiotic to use and how much as they may alter cement characteristics such as strength and viscosity,³⁸ although this is of less concern with a temporary spacer in a two-stage procedure than it might be in a single stage operation. It is possible for antibiotic levels to remain at

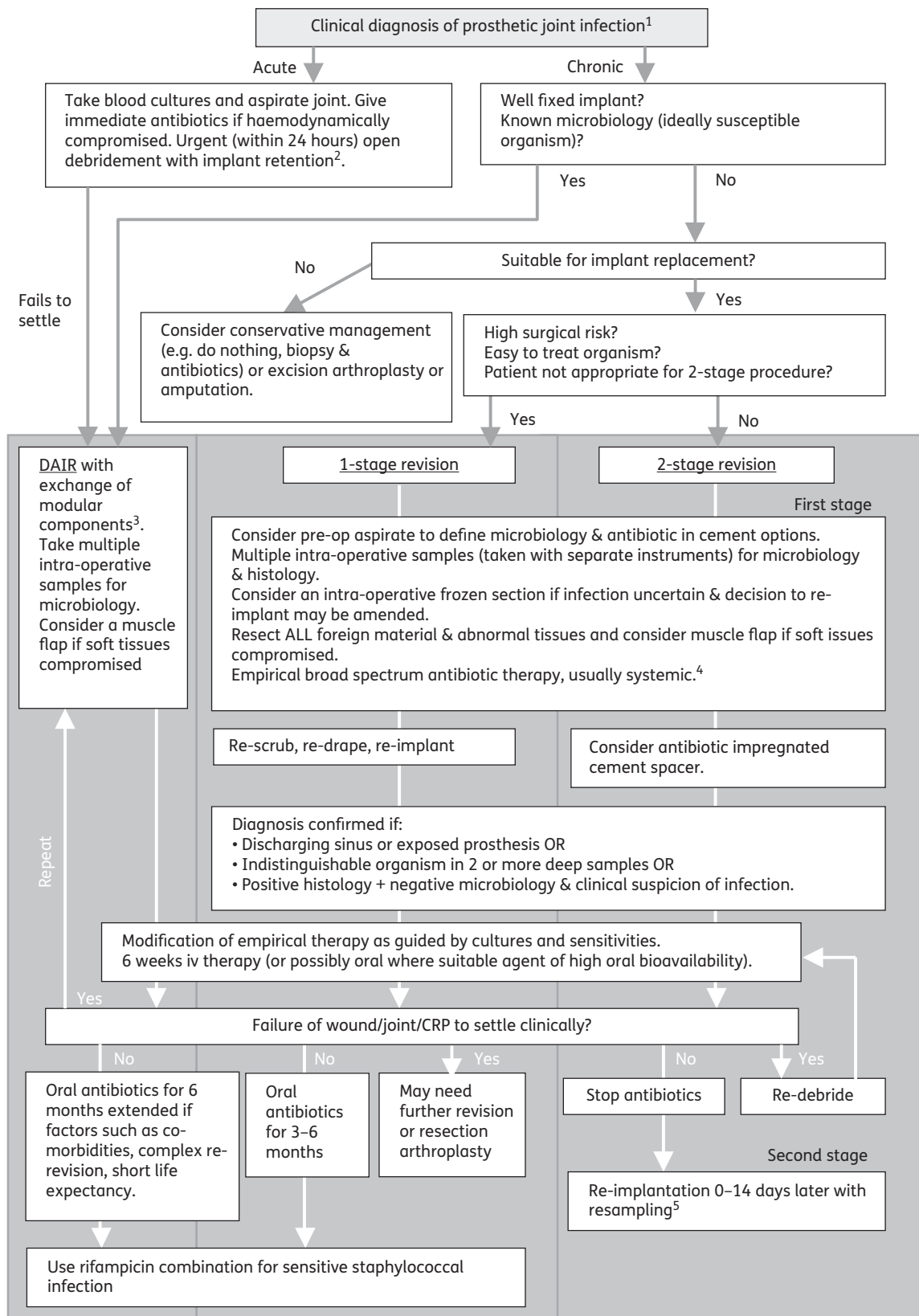


Figure 2. Flowchart summarizing the selection of an appropriate management strategy for an infected prosthetic joint. Drawn on the evidence summarized in the text and clinical experience at the Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford, UK. This scheme refers to systemic

clinically effective levels locally for a prolonged period and rarely reach significant levels within the bloodstream.^{39–41} Some practitioners rely on local antibiotics alone, suggesting there is no additional benefit from the co-administration of systemic therapy. Their published cure rates are similar to those obtained by adopting a systemic approach.^{31,42,43} An attempt at isolating the infecting organism by joint aspiration prior to the first-stage procedure is of particular importance with this strategy.³¹

The more widely accepted practice is to give empirical systemic antibiotics after the first-stage operation whilst awaiting culture results.^{3,44} Specific antibiotic therapy is then given for up to 6 weeks, usually intravenously but orally if an agent of suitable oral bioavailability is available. Failure of inflammatory markers or clinical signs of infection to settle during this time raises the possibility of persistent infection and re-debridement is essential. An antibiotic-free period of around 2 weeks may be considered following completion of therapy prior to the re-implantation second stage to allow microbiological sampling at operation.⁸ Empirical antibiotics are given peri-operatively and stopped if cultures are negative.

The significance of positive cultures from samples taken at re-implantation is not clear. A retrospective series of 152 patients gave an overall new joint retention rate of 83% at 5.75 years—better for those undergoing their first revision (89%) and worse for the second (73%). Positive microbiological sampling of the joint space at the second stage did not predict outcome, although the majority of such patients did receive further antibiotics.³² If there are significant microbiology cultures at re-implantation it may be reasonable to give oral antibiotics of suitable bioavailability for 3–6 months post-operatively with the rationale of preventing biofilm formation in the new joint.⁴

One-stage revisions

The optimum duration of antibiotic treatment following a one-stage revision is not known and reports range from 1 week to several months.⁴⁵ Most series report outcomes broadly similar to those with two-stage revisions, most likely reflecting that a thorough and extensive debridement is the most critical predictor of success.

Debridement, antibiotics and implant retention (DAIR)

In the studies quoted above long courses of antibiotics were administered, up to 6 weeks intravenously and then an oral equivalent for a mean of 1.5 years. Zimmerli *et al.*³ suggest much shorter courses of between 3 months for a hip and 6 months for a knee. Stopping antibiotics runs the risk of relapse but continuing beyond 6 months does not appear to significantly increase the chance of a cure.²⁶ However, in selected patients at high risk of relapse it would seem reasonable to continue antibiotics long term with a strategy of suppression rather than

cure. Many units use up to 2 years of oral antibiotics and in selected high-risk patients there may be individualized decisions to go longer, or even indefinitely. More trials are needed to define optimum antibiotic durations.

Intravenous or oral

Where systemic antibiotics are used there is no clear evidence to support one route over another at present. Recommendations vary, with some centres giving intravenous antibiotics only as the empirical regimen whilst awaiting culture results and others routinely giving them for up to 6 weeks. Oral therapy may be an option in those cases where both organism and patient permit the use of an agent with equivalent oral and intravenous bioavailability. Where prolonged intravenous courses are required it is preferable that patients are treated in the community. This should be under the supervision of a specialist outpatient parenteral antimicrobial therapy (OPAT) team trained in both the management of intravenous long lines, the agents administered and safe monitoring and follow-up. Within this context OPAT has been widely demonstrated to be safe and effective.^{46,47} The British Infection Society and the BSAC are currently in the process of producing standard national guidelines for the safe implementation of OPAT services.⁴⁸

Specific agents

The evidence for the use of specific antibiotics in the setting of prosthetic joint infection is limited.^{37,49} Most studies have examined the treatment of staphylococcal infection. Experimental data support the use of regimens based on rifampicin, as this is an agent with excellent oral bioavailability that achieves high concentrations in biofilms. Used alone, resistance emerges rapidly through a single point mutation in the DNA-dependent RNA polymerase. Animal and clinical data have demonstrated its effectiveness in combination therapy with ciprofloxacin^{50,51} (another agent of high oral bioavailability) or fucidin.⁵² It has also been used in combination with trimethoprim and doxycycline.⁴⁴ MRSA isolates demonstrating quinolone resistance have been successfully treated with rifampicin and linezolid⁵³ or rifampicin and daptomycin.⁵⁴ The duration of linezolid therapy is limited by a high risk of haematological and neurological side effects. Linezolid alone is probably as effective as teicoplanin—indeed it appears to be more effective at the initial clearance of MRSA⁵⁵—but is less well tolerated. Experimental evidence suggests that when used alone, teicoplanin is not as effective as vancomycin in producing a reduction in viable MRSA counts. It could be combined with another agent such as rifampicin⁵⁶—particularly in those instances in which a prosthetic device has been retained—or used at high dose: trough levels of >20 mg/L are recommended, requiring at least 600 mg a day in most individuals.⁵⁷ Co-trimoxazole has been shown to be effective in the treatment of MRSA *in vitro*⁵⁸ and

therapy only—the use of local antibiotics is discussed in the text. It should be remembered that certain frail patients with poor mobility for other reasons may gain little from a new prosthesis and conservative (non-surgical) management or an excision arthroplasty may be all that is appropriate.¹ A negative aspiration does not rule out infection.² Consider endocarditis and metastatic osteomyelitis particularly if *S. aureus* is isolated.³ DAIR, debridement, antibiotics, implant retention. If a prosthesis is found to be unexpectedly loose it may be necessary to change to a one- or two-stage revision intra-operatively and patients should be consented appropriately.⁴ Empirical antibiotics should be selected on the basis of local susceptibility data.⁵ Excision arthroplasty alone may be appropriate in certain patients for either social or technical reasons.

anecdotal data and a prospective study suggest it is effective clinically.^{59,60} No randomized trials have specifically assessed its role in joint infection and treatment failure has been associated with settings in which the bacterial burden is high, emphasizing the importance of thorough operative debridement.⁶¹

Daptomycin is a novel cyclic lipopeptide with activity against MRSA, glycopeptide-intermediate *S. aureus* and glycopeptide-resistant enterococci. *In vitro* studies demonstrate an efficacy equivalent to that of vancomycin and it demonstrates synergy with rifampicin against vancomycin-resistant enterococci⁶² and MRSA.⁵⁴

The evidence supporting any specific antibiotic regimen for the treatment of Gram-negative joint infection is lacking. The combination of ceftazidime and ciprofloxacin has been successful in the treatment of *Pseudomonas aeruginosa* infection,⁶³ and the use of ciprofloxacin may be associated with a better outcome when treating any susceptible Gram-negative organism.⁶⁴ It is our practice to treat many Gram-negative prosthetic joint infections with a suitable intravenous agent for 4–6 weeks (for example ceftriaxone, ertapenem or meropenem) according to identification and susceptibility and, where indicated, continue with an oral agent.

Culture-negative infections

Even with meticulous sampling, around 7%–11% of prosthetic joint infections confirmed by histology are culture-negative and this may reflect prior antibiotic exposure.¹⁵ Agents should be selected on the basis of the clinical history, the presence of resistant organisms (for example MRSA colonization) and any previously positive samples. Empirical treatment with a glycopeptide and/or cephalosporin may be as effective as specific therapy in those cases in which the organism is known.¹⁵

Prevention

The high infection rates associated with prosthetic joint implantation in the 1970s have fallen dramatically as a result of improvements in patient selection and preparation, surgical technique, theatre design, prophylactic antibiotics and anaesthesia. The introduction in 2005 of the UK Department of Health's 'Saving Lives' delivery programme for acute hospitals was designed to help organizations to reduce healthcare-associated infections. This programme now includes a care bundle aimed at the prevention of surgical site infection.⁶⁵ MRSA screening and decolonization is now mandatory for all elective orthopaedic admissions in the UK.⁶⁶

There has been controversy over the role of dental prophylaxis for patients with joint replacements. There is no evidence that dental procedures are a risk factor for prosthesis infection, nor that prophylaxis impacts infection rates.⁶⁷ Therefore prophylactic antibiotics prior to dental procedures in patients with prosthetic joints should not be recommended.

Future developments

The future will no doubt see technical advances in areas such as microbiological diagnostics and biofilm-resistant prosthetics. Today, much of current best practice is supported largely by consensus opinion and data from observational studies or small

trials. Ideally, multicentre randomized trials are needed to tackle the big unanswered questions regarding the diagnosis and treatment of these difficult infections. In which cases is it safe to do a one-stage revision for infection? Are local antibiotics delivered via loaded cement as effective as systemic therapy? Are oral antibiotics as effective as intravenous treatment? How long should antibiotics be continued after a DAIR procedure?

Bone and joint infection is increasingly seen as a specialty in its own right. Individual orthopaedic surgeons see relatively few complex cases and it is to be hoped that the future will see the development of further specialist centres capable of providing the multidisciplinary expertise required.

Transparency declarations

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