Surgical Treatment of Prosthetic Joint Infections of the Hip and Knee: Changing Paradigms?

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ABSTRACT

Prosthetic joint infection (PJI) of the hip and knee remains one of the most common and feared arthroplasty complications. The impact and cost of PJI is significant, both to the patient and to the health care system. Recent reports of results of different treatment strategies have led many surgeons to modify their approach to management of PJI. This paper will explore apparent paradigm shifts, both to indications and technique, including the importance of waiting for bacterial identification, the decreasing role for irrigation and debridement (I&D) with retention of components, the increased utilization of single stage revision, and conversely a decreasing role for two-stage exchange. Strategies for treating drug-resistant organisms and management of failed treatment will also be examined.

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Options for Treatment of PJI

Successful treatment outcomes require precise assessment of the infecting organism, the immune status of the patient, and the condition of the bone and soft tissues around the joint [1]. This has led to a more deliberate assessment prior to operative treatment, as it is felt that this assessment is more important than a rapid trip to the operating room where a “conservative” treatment may be inadequate and subject the patient to the morbidity of multiple additional procedures, with perhaps decreased success of more definitive procedures [2].

Confirming Diagnosis and Stratifying Individual Patient Risk

Numerous studies have demonstrated the importance of identifying the infecting organism in PJI, and determining its antibiotic sensitivities, prior to any surgical treatment [3–5]. While Staph species grow relatively fast on culture media, many other infecting organisms do not, and additional inoculation time and special techniques outlined in the proceeding diagnosis paper are warranted. The determination of methicillin or other antibiotic resistance is critical in selecting the appropriate treatment, as virtually all studies have shown poor results for both irrigation and debridement (I&D), and one-stage revision, for antibiotic resistant PJI, even in patients with early PJI. There has been much recent work on using host biomarkers to improve diagnostic accuracy for PJI which may increase the accuracy and decrease the time for bacterial characterization [6,7]. In addition, numerous studies have identified patient risk factors that have compromised the results of I&D and single stage revision for PJI. Diagnosis of diabetes, renal failure, immunosuppression due to inflammatory conditions, HIV, or transplantation, and prior prosthetic infection should point the surgeon away from these treatment options.

Role of Irrigation and Debridement

I&D with retention of the implants involves excision of devitalized bone and soft tissue, drainage of purulent material and hematomas, and removal of any draining sinus tracts. Traditionally, this method was recommended for postoperative infections within three months of the procedure or acute hematogenous infections. In both scenarios, patients needed to have stable implants, a healthy soft tissue envelope, and the presence of symptoms for less than three weeks [8]. Irrigation and debridement was thought to be successful for these infections because the bacteria had not yet developed a glycocalyx biofilm over the implants [8]. Therefore, a thorough debridement would be able to reduce the bacterial load without significant morbidity.

An outline for I&D has been provided by an international consensus workgroup [9]. There was a 90% consensus for the following components of the surgical technique:

(1) Preoperative optimization of the patient.
(2) Good visualization and thorough debridement.
(3) Obtaining multiple culture samples.
(4) Copious irrigation (6–9 L) of the joint.
(5) Explantation of the prosthesis if indicated.
At our institution, I&Ds of knee prostheses are performed without a tourniquet. Preoperative antibiotics are always given prior to incision. We begin every I&D by performing an excision of the previous incision site. Full-thickness deep tissue flaps are created to allow for adequate visualization. Prior to the arthrotomy, synovial fluid is aspirated and sent for cell count, differential, and culture. Once the arthrotomy is completed, we perform a thorough synovectomy as a part of both the debridement and the exposure. The excised synovium is also sent for culture. Modular components are removed to allow for a thorough debridement of all interfaces and to obtain improved exposure of those areas that are difficult access (for example, the posterior capsule of the knee). A total of three to six cultures are sent from the synovium and periprosthetic tissues. Once all fibrous, devitalized, and suspicious tissue is excised, the entire surgical wound is mechanically debrided with a sterile scrub brush while soaking in 500 mL of a dilute betadine solution for approximately three minutes. The entire wound is then irrigated with 6 L of sterile normal saline solution. The surgical site is re-evaluated for any evidence of suspicious tissue or remnants of braided suture. Once the wound is judged to have been thoroughly debrided, the arthrotomy and skin are provisionally closed with monofilament suture. The entire surgical field is broken down, all of the opened trays are removed, the floors are thoroughly mopped, and all members of the surgical team change their scrubs. The operative extremity is then reperep and redraped. The incision site and arthrotomy monofilament sutures are removed, and the surgical site is irrigated with a final 3 L of saline. The previous modular components are then replaced with new implants. The arthrotomy, deep tissues, and incision site are closed in layers with monofilament sutures.

The absolute contraindication to I&D with retention of implants is the inability to close a wound. Soft tissue defects create an ideal environment for persistent contamination which can result in chronic colonization [9]. Additionally, these scenarios are also more likely to have a polymicrobial infection [10]. Relative contraindications to irrigation and debridement include highly virulent organisms, presence of a polymicrobial infection, immunocompromised host status, and the presence of a draining sinus tract [3].

There is increasing evidence of the substantial morbidity and cost of I&D as a treatment for prosthetic joint infection. Many centers report poor results when this treatment is utilized [11–13]. While most studies demonstrate a success rate of between 40% and 50% [13–17], some have published successful outcomes in as few as 10–20% of their patients [11,18,19]. Furthermore, there is concern for an increased risk of failure in two stage techniques after an initial failed I&D. While there is no literature that describes outcomes of two stage procedures after a failed I&D in total hip arthroplasty, there are two studies that provide pessimistic results in total knee arthroplasty. One study reported that 34% of their patients who had undergone a two stage exchange after a failed I&D required subsequent procedures for persistent infection [20]. Another group reported a 42% failure rate for two stage procedures following a failed I&D [17].

Several factors may be responsible for these failure rates. One factor is the high level of drug resistant bacteria that are isolated from patients with confirmed prosthetic joint infection treated with I&D [21,22]. In a series of 112 patients treated between 1998 and 2003, 44% grew Coagulase Negative Staph species – 60% of these species were resistant to methicillin. Additionally, 8% of the isolates were positive for MRSA. Altogether, over 30% of the cases in this series were resistant to methicillin [23]. Infections with resistant bacteria have been historically more difficult to treat [24,4,25,26,5,22]. Bradbury et al found a failure rate of 82% when patients with acute periprosthetic MRSA infections were treated with I&D [4].

There is evidence that between 14% and 39% of prosthetic joint infections are polymicrobial [10,17,27]. Polymicrobial prosthetic joint infection treatment has a high failure rate when treated with I&D alone [10,27,5], showing relatively consistent success rates of 53% compared with 78% for two stage procedures in some series [10]. In addition to the virulence of two different pathogens, some data has demonstrated that polymicrobial infections have higher rates of MRSA and anaerobic bacteria when compared to prosthetic joint infections with a single pathogen [10]. The second area contributing to failure of I&D may include host comorbidities. Many comorbidities compromise the immune system, limiting the host response to the infecting organisms. Choong et al found patients with a BMI of greater than 30, more than two comorbidities, and diabetes as independent risk factors for failure [28]. Other studies have shown an increased failure rate in those who carry a diagnosis of rheumatoid arthritis [29], are immunosuppressed [30], and have a history of previous infection within the same joint [31,32]. Additionally, patients over the age of 65 have been found to be at an increased risk for polymicrobial infections [10], which, as previously described, are more difficult to eradicate. Despite these findings, some studies have found no difference in their patient characteristics (including BMI, age, ASA score, inflammatory arthropathy, diabetes, malignancy, or heart disease) and the success of this procedure [14,32,17]. Despite the inconsistency in the literature, the consensus from Proceedings of the International Consensus on Periprosthetic Joint Infection workgroup is that patients receive optimization of all preoperative comorbid conditions prior to undergoing any surgical intervention for a PJI [9].

A third factor implicated in poor results of I&D is the chronicity of symptoms prior to surgical intervention [14,18,15,10,32]. Despite the large amount of literature describing the importance of the duration of symptoms, discrepancies remain with regard to the threshold for optimal outcomes. Studies have demonstrated the ideal timing to be within 8 days, 2 weeks, 3 weeks, or 4 weeks [32,14,18,10,15,27]. Despite these conflicts, the international workgroup decided to use the threshold described by Zimmerli et al of three weeks from the onset of symptoms [3]. Furthermore, this workgroup advocates addressing all preoperative comorbidities and complications, and the use of acute surgical intervention only in cases where patients demonstrate signs of sepsis [9].

Although there is literature describing the importance of symptom duration, there is conflicting data when comparing outcomes based on the interval between arthroplasty and the development of infection [32,15,33,14]. Confounding these results is the fact that many infections are indolent. Not all patients report longstanding symptoms prior to their presentation with a chronic infection. In fact, systemic symptoms are often subtle or absent. The identification of infection in what may appear to be acute cases may simply be a manifestation of the accumulation of a critical bioburden that has rendered the patient acutely ill. This means that the time course of infection can be difficult to pinpoint, as few PJIs cases have a defined inciting event.

Another factor which may contribute to the poor results of I&D is the historical lack of uniform consensus on the details of appropriate surgical technique. Poor or incomplete surgical technique during I&D may leave behind significant bacterial burden or biofilm. The importance of adequate debridement has been noted by the EndoKlinik group [34]. Even with the consensus that a thorough debridement is imperative, numerous techniques have been described, even within the same study [17]. Surgical procedures have included methods for mechanical disruption (scrubbing and/or lavage), chemical disruption (dilute betadine, chlorhexidine washes, Dakin’s solution), and isolation of contaminated surgical equipment.

Even with multiple variables, the international workgroup has been able to determine that there is no role for arthroscopic washout in an established PJI [9]. Data has demonstrated that arthroscopic I&Ds are significantly less successful than open debridement (47% and 88%, respectively) [31], likely because of the limited ability to access all of the interfaces [9].

The international workgroup advocates for the exchange of modular components despite only a small amount of literature demonstrating improved outcomes [35,30]. They believe that the removal of modular
components allows improved access to all interfaces, especially the posterior capsule in total knee arthroplasties. However, there is no data to support or refute the replacement of the same modular components after thorough debridement and sterilization. Laffer et al’s description of reimplantation of the same polyethylene during the irrigation and debridement of total knee arthroplasties led the workgroup to conclude that this practice may be a reasonable and potentially less expensive option [36,9].

Additionally, several authors have provided a description of specific methods for I&D. Hansen and Parvizi published their regimen of five specific steps. Their first step is to soak the surgical site in either Dakin’s solution or hydrogen peroxide for 3 minutes. Following this, they thoroughly irrigate the wound with 3 liters of sterile saline. After this irrigation, the authors describe placing a solution of 0.3% dilute betadine solution for another three minutes while continuing to mechanically scrub and debride the surgical site. After this three minute period, the surgical site is again irrigated with 3 liters of sterile saline. The final step is to irrigate the site with 3 liters of saline containing 500,000 units of polymyxin B and 50,000 units of bacitracin [37].

At this time, there is no evidence beyond their level V description to support or refute this process. The only consensus with regard to the specifics of the actual irrigation and debridement includes the mechanical debridement of all surfaces with an aseptic solution and the use of low pressure pulse lavage or bulb irrigation to copiously irrigate the surgical site [9]. The workgroup prefers low pressure irrigation given that high pressure may spread infection to deeper regions [38,39].

Further means to bolster the effect of I&D includes the use of local antibiotics. The rationale for local antibiotics was to create an environment of high antibiotic concentration to further reduce the bacterial burden without the systemic adverse side effects [40-42]. One method to provide high doses of local antibiotic therapy is to use continuous antibiotic infusion. Aside from Whiteside et al’s success with aggressive debridement with reimplantation of noncemented total knee components [43], there is a paucity of mid and long term outcomes for patients treated with irrigation and debridement with continuous infusion [40,41]. Given the lack of evidence to support its use, potential for drug reactions, increased expense, potential to develop resistance, and the need for further surgery to remove the delivery device, the international workgroup could not support the use of this method [9].

The recent evolution of biodegradable drug delivery implant systems has led to increased interest in their use for infection, particularly in single stage irrigation and debridement. The two forms of implant system currently available include beads and sponges. While the use of these systems has demonstrated promising outcomes when combined with irrigation and debridement (success ranging from 75–100%) [44-47], this data is derived from small, non-randomized studies. Furthermore, each of these delivery methods has potential complications. Concerns for these delivery devices include the formation of a biofilm after elution of all of the antibiotics [48] and prolonged wound secretion [46] due to the formation of exudates [98,99]. Given the paucity of data to support their use with the potential for complications, the international workgroup could not justify the use of local antibiotic therapy as an adjunct to irrigation and debridement [9].

Despite these findings, there still may be a role for isolated irrigation and debridement in PJI. Its role will be better defined as surgeons are able to identify and control for the confounding factors that have been associated with poor outcomes. Potentially, I&D can be used in patients with few medical comorbidities (for example, not immunosuppressed), acute PJI, appropriate pathogens (single, non-resistant bacteria with low virulence), stable components, and a healthy soft tissue envelope. There has been a change in the paradigm for the treatment of an “acutely infected” prosthetic joint infection. Treating these infections has shifted from surgical urgencies/emergencies to optimizing patient comorbidities and establishing an accurate diagnosis. Although the threshold for appropriate timing of irrigation and debridement has never been absolutely delineated, the continued improvements in the speed and ability to both diagnose a prosthetic joint infection and identify the specific pathogens will direct the treatment plan.

Furthermore, future directions should focus to standardize an appropriate surgical technique. Although a thorough debridement to significantly reduce the bioburden is necessary, the role for adjunct therapy will need to be better established. The role for specific aseptic solutions (dilute betadine, chlorhexidine, Dakin’s solution, and hydrogen peroxide), continuous antibiotic infusion, and biodegradable drug delivery devices have to be proven with well-designed studies. Also, while most authors suggest that I&D be accompanied by 6 weeks of antibiotic therapy [12], future studies should evaluate the appropriateness of systemic therapy, especially if I&D techniques become standardized. Finally, future studies will need to define the value in chronic antibiotic suppression, as its role remains unclear after I&D for acute PJI.

One-Stage Revision for PJI

The predominant treatment in North America for chronic PJI has been two-stage revision, largely due to results from several centers which showed somewhat better results for two-stage than for one-stage. However, centers in Europe have reported results of single stage revision for both infected hip and knee arthroplasties that approach reported results for two-stage revision [34,51-54]. These centers feel that careful patient selection and adherence to specific surgical principles are responsible for good results from this treatment. There is consensus that the ideal scenarios for one-stage revision should be studied with randomized controlled trials.

In 2014, an international consensus group of arthroplasty surgeons and researchers reached strong consensus (78%) on which patient groups should not have one-stage exchange [55]:

1. The presence of generalized sepsis.
2. Infections in which the bacteria is not identified.
3. Infection caused by a drug resistant bacteria.
4. The presence of a sinus tract.
5. The presence of severe soft tissue deficiency over the joint.

The corollary to this consensus was that patients who do not have any of these factors may be considered for one-stage revision for PJI. The arguments for one-stage revision for PJI are decreased morbidity and increased function for the patient [56,57]. These centers feel that patients who do not have one-stage exchange [55]:

- Decreased time to return to normal activity (50% less)
- Decreased hospital stay (3 days)
- Decreased number of follow up visits

For surgeons considering increased use of one-stage exchange it is prudent to minimize patient and wound comorbidities in patient selection. Those patient comorbidities predisposing to infection mentioned previously (diabetes, obesity, immunosuppression, renal disease, smoking, severe cardiac disease, and metastatic carcinoma) are likely to compromise the results of one-stage revision, just as they increase the risk of failure of I&D and primary arthroplasty in patients with those conditions. Similarly, joints with compromised skin flaps including multiple separate incisions and multiple recent surgical insults should not be considered.

In addition to careful patient selection, there is ample evidence in the literature that meticulous surgical technique is important. Haddad et al described a technique for single stage knee revision for PJI that included aggressive debridement of all devitalized tissue, followed by instillation of hydrogen peroxide and betadine solutions followed by pulsatile lavage with saline [59]. Following this the wound is soaked in aqueous betadine and the skin edges are loosely approximated. The entire room is then cleaned and a new set of surgical instruments and tables are set. The entire surgical team rescrubs and dows new gowns, and the patients’ extremity is prepped and draped. The surgical team then implants new knee components using antibiotic laden cement at a volume of antibiotic cement < 5% of the weight of the cement powder (often using 1 gram of tobramycin and 1 gram of vancomycin per 40
grains of cement powder). Another aspect of their treatment regimen is continuing antibiotics for at least 6 weeks after revision in some combination of intravenous and oral.

By careful patient selection and these techniques, Haddad et al reported results that were better than their results for two-stage revisions for PJI, presumably due to the high rate of comorbidities and resistant bacteria in their two-stage revision group.

Other authors have described similar results with one-stage revision for prosthesis hip infection using antibiotic cement to fix the femoral component [60,34,56,61,62]

There are numerous questions that should be answered by well-designed clinical trials including the ideal patient and bacterial ID for one-stage revision, what is the importance of instilled agents such as a betadine and hydrogen peroxide, what is the importance of pulsatile lavage, what is the importance of reprep and drape, what is the importance of antibiotic cement, and can similar results be achieved with cementless implants.

Nonetheless there appears to be a compelling argument to use one-stage revision for PJI in appropriately selected patients using appropriate surgical technique, and it also appears that the use of this technique is growing.

Two-Stage Revision for PJI

At the 2014 International Consensus Group conference, an even stronger consensus (93%) on the indications for two-stage revision, with criteria which were virtually the same as the contraindications for one-stage revision mentioned in the prior section:

1. The presence of generalized sepsis.
2. Culture negative PJI.
3. Cultures revealing antibiotic resistant or difficult to treat bacteria.
4. Sinus tract.
5. Severe soft tissue deficiency.

There is emerging consensus that two-stage exchange should be utilized on the more difficult patients; i.e., those with significant comorbidities, resistant bacteria, or compromised wounds. It is quite possible that when patients are stratified the results of two-stage revision for PJI will be worse than one-stage revision, as some authors have shown [59].

Several authors have suggested that the surgical technique of a two-stage revision be similar to a one-stage, in that the procedure includes a rescrub and reprep once the infected implants and debridement of devitalized tissue is completed. Any technique which decreases the bioburden certainly makes theoretical sense but it will be up to controlled trials to demonstrate any practical efficacy.

The question of what should be implanted in the first stage of a two-stage revision for PJI is a controversial topic. Most surgeons agree on utilization of antibiotic loaded cement spacers, but there is considerable disagreement on the dose of antibiotics, and whether these spacers should be static or articulating [63-65]. Many surgeons have had the experience of implanting an articulating spacer as the first stage of a two-stage revision for infection only to have the patient do so well (or the patient be so debilitated from other medical conditions) that the articulating implant becomes a one-stage revision. This may be the way that many two-stage surgeons begin to adopt one-stage revisions. To do this the articulating spacer must be durable and capable of reasonable survival. Implants fashioned out of polymethylmethacrylate (PMMA) have the risk of wear, fracture, and crepitus and are not amenable to an articulating spacer that may become a one-stage revision in older, more debilitated patients not able to tolerate the morbidity of a second stage. Low cost implants such as a cobalt chrome femoral component and an all poly tibia in the knee, or a cemented cobalt chrome femoral stem and an all poly acetabular component in the hip, are reasonable selections if there is relatively little bone loss and the surgeon is not sure the patient will tolerate a second surgery.

Another area of controversy in two-stage revision is the length of time between the stages. Most surgeons prefer the wound completely healed with edema resolved, many like to see serology trending down with no exacerbation of symptoms if antibiotics are stopped prior to replantation. There is some evidence that time periods of greater than 6 months between stages is not associated with increased efficacy but is associated with decreased function [66].

Another area of controversy in two-stage revisions for PJI is the use of antibiotics. Most sources support the use of antibiotics after the first stage but there is debate on the length of antibiotic treatment, from 2 weeks to 6 weeks, but many authors recommend a period of antibiotic cessation before the second stage procedure of at least 2 weeks to verify that the infection is controlled [67]. However, the 2014 Periprosthetic Infection Consensus group reached strong consensus (74%) that there was no good data to support an antibiotic holiday prior to replantation, so this is another area that will require controlled study [55]. This will be further discussed in the section on antibiotic therapy.

Management of Treatment Failure

Multiple treatment failures or recurrences prompt consideration for options other than repeat reconstruction. It is important to understand the cause of failure in order to determine if additional salvage options are possible. First, radical debridement should be undertaken. Failure to remove prior prosthetic components, devitalized bone, cement or permanent sutures may have predisposed the patient to failure. Optimized nutritional parameters may be helpful. In addition to debridement, addressing the local soft-tissue environment with measures such as local or free tissue transfer (gastrocnemius flap, e.g.) may enable salvage TJA in some cases.

Despite optimum care, a certain percentage of patients will experience treatment failure. If multiple attempts to eradicate infection have failed, chronic suppression may be a consideration. Chronic suppressive antibiotics can cause the development of drug resistance, and there is a risk of secondary side effects or complications, like antibiotic-associated diarrhea, renal or hepatic dysfunction, or marrow suppression. Patients who have a chronically draining sinus may have some element of protection against developing systemic sepsis, but may be at risk for squamous cell carcinoma.

Resection arthroplasty is the most common treatment for failed or recurrent PJI about the hip. Patients with a resection arthroplasty may bear weight and can be ambulatory with an assistive device. It is essential that a thorough debridement of all infected or devitalized tissue is done at the time of resection. Generally, all prosthetic material and permanent sutures are removed, but antibiotic-loaded cement may be left in the femur and/or acetabulum. Resection is less commonly used for knees, and some patients may develop a functional pseudoarthrosis at the knee. Permanent bracing is usually required. The longer lever arm of a knee resection may provide some degree of mechanical advantage for transfer and ambulation compared to above-knee amputation.

Arthrodesis can be a useful salvage option in the case of multiple treatment failures, especially with extensor mechanism deficiency about the knee. Arthrodesis can be done using long antegrade intramedullary nails, modular intramedullary nails, plate fixation, or external fixation. There are advantages and disadvantages to each approach [68,69]. Length is an important consideration, and lengthening may be performed simultaneously if an Ilizarov type fixator is used [70].

If the arthrodesis will result in excessive overall limb shortening, an above-knee amputation may be more mechanically suitable for ambulation but arthrodesis generally results in better ambulatory status than amputation [71]. Bony fusion is not a requirement for success with intramedullary nailing [72].

Bone loss from multiple prior operations limits the applicability of arthrodesis for failed PJI treatment in the hip, but may be considered if adequate bone is available for fusion.
Above-knee amputation is reserved for multiple failures or if the limb is not felt to be reconstructable due to excessive bone loss, soft-tissue deficit, or severe vascular disease. Six prior attempts at treatment of infection have been reported as an endpoint that leads to consideration of AKA [73]. Only about half of patients who undergo above-knee amputation for treatment of TKA infection are able to regain functional ambulation [74, 71].

Antibiotic Rx during Surgical Treatment

Antibiotics, among other factors, play a vital role in the management of PJI. Workup and diagnosis of a PJI follows the criteria set forth by the Musculoskeletal Infection Society (MSIS) and/or from the International Consensus Meeting on Periprosthetic Joint Infection [75, 79]. As discussed previously, management options vary depending on the diagnosis and/or suspicion of PJI. If surgical intervention is chosen as part of the treatment plan for PJI, confusion can sometimes exist regarding the role of perioperative antibiotics prior to skin incision. Studies have demonstrated that administration of preoperative antibiotics to patients with a positive preoperative joint aspiration did not interfere with isolation of the infecting organism from intraoperative culture samples more than when antibiotics were withheld [76–78]. Therefore, perioperative antibiotics should be given within one hour prior to incision regardless of infection or not and should follow the standard criteria for appropriate antibiotic selection based on patient characteristics.

Traditionally, PJI is treated with a pathogen specific intravenous (IV) antibiotic regimen in order to obtain the minimum inhibitory concentration (MIC) in the shortest time possible. Unfortunately, the ideal length of antibiotic treatment is not known. Clinicians tend to use a combination of clinical signs and symptoms as well as inflammatory markers and joint aspirations as a way to monitor response to treatment. Antibiotic holiday periods prior to reimplantation have also been suggested to monitor for the eradication of an infection however no evidence conclusively supports the need for an ideal length of such a holiday period [9]. Literature suggests between 6 and 12 weeks of antibiotic therapy, however variability does exist. One prospective non-randomized study concluded that 6 weeks of antibiotic treatment was sufficient to control infection however this study included only one week of an IV antibiotic regimen as well as groups of patients treated with irrigation and debridement (I&D), single stage and two-stage exchange arthroplasty [79]. Conversely, another study showed an 87% eradication rate using an IV antibiotic regimen of 2 weeks duration after I&D and placement of an antibiotic spacer [80]. This highlights a couple of considerations. The first consideration involves the use of an oral antibiotic regimen. Decreased financial burden to the patient and payers, reduced risks associated with vascular access and the increased possibility of home-based therapy make oral antibiotic therapy an attractive option for sensitive pathogens. Darley et al. [81] showed no relapse with a treatment plan consisting of 14 days of an IV regimen followed by 6 to 8 weeks of oral therapy.

The second consideration involves the combination of the surgical plan and the antibiotic regimen. In regard to a single stage exchange arthroplasty, the recently published guidelines of the Infectious Diseases Society of America (IDSA) recommend 2 to 6 weeks of pathogen specific IV antimicrobial therapy in combination with oral rifampin, followed by 3 months of oral rifampin and ciprofloxacin or levofloxacin for staphylococcal PJI and only an initial course of IV therapy for 4 to 6 weeks for non-staphylococcal organisms [82]. The role of rifampin is not a new idea. Zimmerli et al. [83] evaluated the clinical efficacy of a rifampin combination in staphylococcal infections associated with stable orthopedic implants through a randomized, placebo-controlled, double-blind trial. Thirty three patients with culture proven staphylococcal infection associated with stable orthopedic implants and a short duration of symptoms were randomized into treatment groups involving an initial debridement, implant retention, and a 2-week course of IV fluvoxacinil or vancomycin with rifampin or placebo, followed by either ciprofloxacin-rifampin or ciprofloxacin-placebo long-term therapy (3–6 months). The ciprofloxacin-rifampin group had a 100% cure rated compared to a 58% cure rate in the ciprofloxacin-placebo group.

A special situation involves those with culture negative PJI. Culture-negative PJI has an incidence ranging from 3% to 35%. Culture negativity may not be a negative predictor of failure and most infectious disease specialists recommend combinations of vancomycin and either ceftriaxone or a fluoroquinolone [84]. Another unique group involves those with a fungal PJI. High-risk host factors include immunosuppression, malignancy, drug abuse, prolonged use of antibiotics, presence of indwelling catheters, diabetes, malnutrition, rheumatoid arthritis, history of multiple abdominal surgeries, severe burns, tuberculosis, and preceding bacterial infection of the prosthesis [9]. Two-stage exchange arthroplasty is the recommended treatment for fungal PJI. Pathogen specific systemic therapy is chosen and continues for a minimum of 6 weeks with no good data to support antifungal agent administration after reimplantation [9]. The two most common antifungals used in antifungal spacers are amphotericin B (200 mg/40 g cement) and voriconazole (300–600 mg/40 g cement). As with any antibiotic or antifungal, whether it is oral, IV or mixed in cement, the dose needs to be individualized for each patient based on the organism profile, antibiogram and patient characteristics including allergies and renal function.

Antibiotic Spacers

The International Consensus Meeting on Periprosthetic Joint Infection found that, in regard to infection, there was no difference with regard to control of infection with use of articulating or non-articulating spacers in the hip and knee. When it comes to antibiotic selection, several factors have to be recognized. Some antibiotics become deactivated during the exothermic setting of polymethylmethacrylate (PMMA). Most infections can be treated with vancomycin (1–4 g/40 g cement) and gentamicin or tobramycin (2.4–4.8 g/40 g cement). However, each treatment needs to be individualized to the patient. One must also recognize that each PMMA cement has specific antibiotic elution profiles, which therefore affects the concentration of intraarticular antibiotic. High-viscosity cements containing MA-MMA copolymers have better elution profiles than other acrylics. Also, the larger the surface area of the spacer, the higher the antibiotic elution will be from the given spacer. The goal is to generate high local concentrations of antibiotic without associated systemic toxicity. The highest elution of antibiotics occurs within the first 24 to 72 hours followed by a prolonged release over several weeks, which correlates with the concentration of antibiotics within the cement itself [85, 86]. Higher concentrations increase the porosity once the antibiotic dissolves which changes the surface of the cement allowing for increased elution [87]. Hand mixing of cement and antibiotic powder in a bowl without a vacuum is recommended as bubbles facilitate elution of antibiotics by increasing surface area [88]. Increasing the amount of antibiotic powder increases the amount of antibiotic available for elution however the addition of more than 4.5 g/40 g cement compromises the mechanical strength of the cement itself.

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