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# Management of Periprosthetic Hip Joint Infection

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Total hip joint replacement offers dramatic improvement in the quality of life but periprosthetic joint infection (PJI) is the most devastating complication of this procedure. The infection threatens the function of the joint, the preservation of the limb, and occasionally even the life of the patient due to long term hospitalization and high cost. For the surgeon it is a disastrous burden, which requires repeated, complicated procedures to eradicate infection and to provide a mobile joint without pain. Yet in the absence of a true gold standard, the diagnosis of PJI can be elusive. Synovial fluid aspiration, diagnostic imaging, traditional culture, peripheral serum inflammatory markers, and intraoperative frozen sections each have their limitations but continue to be the mainstay for diagnosis of PJI. Treatment options mainly include thorough irrigation and debridement with prosthesis retention, or a two-stage prosthesis exchange with intervening placement of an antibiotic-loaded spacer. Success in treating PJI depends on extensive surgical debridement and adequate and effective antibiotic therapy. Treatment in two stages using a spacer is recommended for most chronic PJI. Debridement, antibiotics and implant retention is the obvious choice for treatment of acute PJI, with good success rates in selected patients. This article presents an overview of recent management concepts for PJI of the hip emphasizing diagnosis and the clinical approach, and also share own experience at our institution.

**Key Words**: Total hip arthroplasty, Infection, Diagnosis, Debridement, Two stage reimplantation

## INTRODUCTION

Periprosthetic joint infection (PJI) after total hip arthroplasty (THA) is a serious complication that involves high costs along with physical and mental stress on the patient and the treating surgeon. PJI after arthroplasty occurs to frequency of approximately 1-2% in most hospitals despite the development of newer antibiotics and the introduction to air-cleaning systems[1,2]. In our region, particularly, the incidence of infection around artificial hip joint is still high due to antibiotic-resistant organisms caused by antibiotic abuse. Management of PJI depends upon accurate diagnosis and successful treatment, both of which are challenging. Recently, great strides have been made in improving the diagnosis of PJI, which has no 'gold standard' diagnostic tools. Proper diagnosis is essential as untreated or undetected PJI can quickly lead to biofilm formation on the implant surface depending upon the infecting organism. Microorganisms form a biofilm on the metal surface of the implant, thus penetration force of antibiotics is decreased and the

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resistance is increased. Therefore, the successful treatment of prosthetic joints is dependent on the elimination of the biofilm-dwelling micro-organisms[1,2]. Two major surgical procedures to manage the infection after arthroplasty are removal of the prosthesis to eliminate the biofilm or administration of biofilm active antibiotics with radical debridement without removing the prosthesis. In this article we will review several strategies in diagnosis and management of PJI of hip with our experiences.

## MAIN SUBJECTS

### 1. Classification

Several classifications have been proposed to defining the time at which contamination occurs and thus establishing the likely etiological agent involved and the best therapeutic strategy. The classification system most widely used today is the one proposed by Fitzgerald et al.[3] who divided infections related to arthroplasty as follows.

Stage I infections (or acute): Acute postoperative infections occurring within three months of the surgery. The etiological agents are generally of hospital origin, especially *Staphylococcus aureus* and *S. epidermidis.*

Stage II infection (or delayed): Deep late infections that appear between three months and two years after the surgery. This is more indolent and may not become apparent until several months after the joint replacement. Typically, patients who have a stage II infection have never had a pain-free interval after the operation. The etiological agents are considered to be of nosocomial origins; since the contamination probably occurred during the act of prosthesis implantation and generally consist of bacteria from the normal micro biota of the skin, such as *S. epidermidis.*

Stage III infection: These are late hematogenic infections that occur more than two years after the surgery. It includes infections frequently caused by hematogenous dissemination of micro-organisms. The joint replacement may function very well after the operation, but later the patient has increasing symptoms of pain and impaired function. Some authors categorize stage III infection as acute hematogenous infection, because most stage III infection, presents with an acute onset of symptoms of the affected prosthetic joint and it is associated with a documented or suspected bacteremia.

The most common primary sources of infection causing PJI are skin, respiratory tract, dental and intestinal and urinary tract infections. The etiological agents are of community origins and are determined by the apparent source of bacteria; dental infections are associated with bacteremia due to *S. viridans* and anaerobic bacteria, while cellulites and skin abscesses are associated with *S. aureus* or streptococci. Enterobacteria originate from the gastrointestinal and genitourinary tracts[4].

Stage IV infection has been added in the newer classification as follows: Positive intra-operative culture. This is an occult infection diagnosed after two specimens or more, obtained intra-operatively from different sites of the hip, have been cultured and found to be positive for the same organism. The infection should be treated with 6 weeks of intravenous administration of antibiotics and no operative intervention[5].

### 2. Diagnosis

Diagnosis of PJI remains a real challenge to the orthopedic community. Since no highly accurate diagnostic method exists, clinicians have yet to agree on a "gold standard" for the diagnosis of PJI. Currently, diagnosis rests on a combination of clinical suspicion, serological tests, culture results, histology, and recent basic molecular techniques, however confirming the infection and performing a correct etiologic diagnosis is more difficult; but at the same time, it is crucial for an optimized clinical management of patients.

### 3. Diagnostic Criteria

At this time, there are no single reference standard diagnostic criteria for PJI. Literature review reveals that the incidence of false-positive culture results from preoperative hip aspiration ranges from 3% to 16%[5,6]. Recent evidence shows that incidence of false-positive and false-negative culture results from total knee arthroplasty (TKA) or THA tissue biopsy is as high as 6% and 10%, respectively[7]. And also unfortunately, rates of negative intra operative cultures range from 10% to 30%; because of this, many surgeons no longer consider cultures obtained from preoperative joint aspiration or tissue biopsy to be the reference standard test for diagnosis of TKA or THA infection[8-10].

Currently, the diagnosis of PJI relies on a combination of clinical judgment, preoperative serologic testing, information obtained from TKA or THA aspiration and microbiological as well as histopathological testing of

tissue or fluid obtained at the time of surgery[7]. At present, the optimal combination of diagnostic and intra operative tests to confirm or exclude the presence of PJI has not been defined. The diagnostic criteria that have been proposed by a workgroup convened by the Musculoskeletal Infection Society[11] in 2011 (Table 1). To establish the diagnosis of PJI, one of two major criteria or three of five minor criteria must be met.

## 4. Clinical Diagnosis

The clinical diagnosis of PJI can be challenging, because the clinical presentation of PJI can be subtle in many cases, especially in chronic PJI and also other modes of arthroplasty failure can coexist with PJI[12].

PJI present characteristic clinical signs that can be divided into acute manifestations (joint pain, erythema, heat, cellulitis and surgical wound discharge and fever) and chronic manifestations (progressive pain, formation of skin fistulae, and drainage of purulent secretions, without fever). Acute infections usually have a greater number of signs and symptoms suggesting PJI. In contrast, chronic PJI has an indolent course characterized as persistent joint pain with or without early implant failure within 2-3 years after implantation[2]. Recently, it has been demonstrated that prosthetic loosened within 2 years of implantation is highly predictive of infection. Patients with chronic PJI usually do not have many of the acute signs and symptoms of PJI noted above, which makes it more difficult to distinguish from aseptic loosening of the prosthesis[2,3]. Pain is presenting symptom and when it occurs while the patient is at rest and in night, the surgeon should be alert for the possibility of infection. A history of prolonged drainage after the operation in a patient who has persistent pain can be very helpful in establishing the correct diagnosis[4,6].

## 5. Laboratory Diagnosis: Serologic Study (Erythrocyte Sedimentation Rate and C-reactive Protein)

Laboratory tests that are helpful in establishing the diagnosis of a periprosthetic infection include a full blood cell count with differential, determination of the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). The serum CRP level is a sensitive indicator of postoperative infection as it returns to normal value more quickly than the ESR following surgery. A persistently elevated CRP is, therefore, more accurate in identifying patients with a deep infection. An ESR greater than 30 mm/h or a serum CRP greater than 5-10 mg/L is suggestive of PJI[13,14]. When taken together, a positive ESR or positive serum CRP provides a sensitivity and specificity of 94-98% and 59-77%, respectively, therefore serving as a useful rule-out tool. In a recent study, Parvizi et al.[15] tried to assess whether the quantification of CRP in synovial fluid was more sensitive than the serologic markers for the diagnosis of PJI. The sensitivity and specificity was 84% and 97.1% compared to 76% and 93.3%, respectively, for the serum CRP assay.

## 6. Aspiration

If the clinical sign and symptom, serological tests suggest suspicion of PJI, the next step in the diagnostic work-up is an aspiration of the hip. Synovial fluid analysis using a combination of synovial fluid culture can be useful in the diagnosis of PJIs and are more helpful than blood tests[2]. A synovial total white blood cell (WBC) count of 1,700 cells/mL or a polymorphonuclear neutrophil (PMN) percentage of >65% after the early

**Table 1.** Modified MSIS definition of PJI

| Based on the proposed criteria, definite PJI exists when: One of the Major Criteria Exists or Three Out of Five Minor Criteria Exist | |
|---|---|
| Major criteria | There is a sinus tract communicating with the prosthesis; or<br>A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; |
| Minor criteria | a. Elevated serum ESR and serum CRP concentration<br>b. Elevated synovial leukocyte count OR ++ result on leukocyte esterase test strip<br>c. Elevated synovial neutrophil percentage (PMN %)<br>d. Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or<br>e. Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at ×400 magnification |

MSIS: Musculoskeletal Infection Society, PJI: periprosthetic joint infection, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, OR: odds ratio, PMN: polymorphonuclear neutrophil.

postoperative period is a good predictor of an infected knee joint (94% sensitivity and 88% specificity)[16,17]. For the hip, the reported values were >4,200 cells/mL and >80% of PMN[18]. WBC count greater than 4,200 cells/mL had a sensitivity, specificity, and accuracy of 84%, 93%, and 90%, respectively[19]. The same analysis found that PMN % greater than 80% had a sensitivity, specificity, and accuracy of 82%, 83%, and 83%, respectively. However the interpretation of the synovial fluid analysis could be difficult in the early postoperative period because the natural increase of inflammatory markers in this period. More recently, other biomarkers of inflammation including interleukin (IL)-6, tumor necrosis factor (TNF)- $\alpha$, IL-1 $\alpha$, IL-1 $\beta$, IL-6, IL-17, granulocyte colony-stimulating factor (G-CSF) and skin-derived anti leukoproteinase (SKALP) and procalcitonin had been investigated as biomarkers of PJI and they are able to offer improved specificity and accuracy in the preliminary studies. Leukocyte esterase in the synovial fluid, easily tested using a strip common for the detection of urinary tract infections, has been found to be a highly accurate predictor of PJI[15,20].

The yield of synovial fluid culture is variable; revealing the infecting organism in 45-100%[21]. Sensitivity may be improved by inoculation into a pediatric blood-culture bottle[22]. At the time of aspiration, a “dry tap” in which fluid is not recoverable from the TKA or THA may be encountered despite appropriate anatomic location within the prosthetic hip or knee joint capsule. Absence of recoverable fluid within the joint does not imply that PJI is not present[18]. In a study investigating the utility of hip aspiration, a dry tap was present in 23% of THAs and the volume of fluid recovered from infected and sterile THAs was nearly identical[18]. In this investigation, “dry” joints were washed with non-bacteriostatic saline and culture of recoverable saline was performed. This technique yielded 83% sensitivity, 93% specificity, and 83% accuracy when compared with tissue culture obtained at the time of revision surgery[18].

## 7. Microbiological Studies

Until now, the culture of periprosthetic tissues has been considered the gold standard for the diagnosis of PJI. Synovial fluid is a sterile sample that can be obtained from different joints before surgery. Its value from a microbiological point of view is high, because every organism that grew in culture is considered a potential pathogen if the sample is not contaminated. The main problem of culturing this sample is its low sensitivity, especially in chronic infections, where the microorganisms are embedded in biofilm and the synovial fluid could be sterile. Trying to increase the sensitivity, it has been suggested that inoculation into blood culture bottles can be useful for this purpose. However, the main problem of this methodology is the same that for blood cultures; it is difficult to discriminate between contamination and a true positive with some microorganisms.

The culture of samples taken during the surgery is still the best available methodology for the diagnosis of PJI. Even today, the gold standard for the etiological diagnosis in many guidelines and reviews[2,23,24] is the culture of several samples of periprosthetic tissue taken during surgery. For this purpose, several samples (between 3 and 6) must be obtained and processed separately to perform the proper evaluation of the results. According to the classical scheme of Atkins et al[25], the isolation of the same organism in three or more samples has a specificity of 99.6%. However, the significance of the organism must take into account the species (probably true pathogens must be considered even if a low number of samples are positive). Trying to improve the performance of cultures, different modifications of the protocol have been studied, including bead mill grinding of the sample[26] or prolonged incubation up to 15 days[27].

The other surgical sample available is, obviously, the retrieved implant; recently the use of ultrasounds aiming for removal of the bacterial biofilm became an interesting approach. Nevertheless, despite the important advance of sonication, there are still some patients without diagnosis. The improvement in sensitivity was most profound (45%) when performed in patients with recent administration of antibiotics[28]. Schäfer et al.[27] studied the effect of prolonged periprosthetic hip tissue culture duration on both sensitivity and specificity. They found that extension of culture duration from 7 days to 2 weeks identified an additional 26.4% of revision cases that would otherwise have been categorized as aseptic.

## 8. Radiographic Evaluation

Radiographic evaluation of the joint may be helpful in the diagnosis of a periprosthetic infection if radiolucent

lines, focal osteolysis, or periosteal bone formation are present. Of these radiographic findings, periosteal bone formation is strongly suggestive of a deep periprosthetic infection because of its high rate of association with this finding. The presence of radiolucent lines does not usually permit differentiation of aseptic from septic loosening. Endosteal erosions about the femoral canal are common radiographic findings, but can also occur with both aseptic and septic loosening. Unfortunately, the absence of any of these findings does not rule out the presence of an infection. The use of special radiographic techniques, such as nuclear scanning, to confirm the diagnosis is less well established. Nuclear scintigraphy (either with technetium-99 m-labeled scan or gallium-67-labeled WBC scan) has a high sensitivity but low specificity for PJI[29]. As nuclear scintigraphy detects inflammation in periprosthetic tissue, these scans may lead to false positive up to 12 months following surgery due to periprosthetic bone remodeling, or in cases of aseptic loosening because of the inflammation caused in the periprosthetic tissue by the moving prosthesis.

## 9. Intraoperative Diagnosis of PJI

It will be easy to confirm the PJI, if gross purulence is observed intra-operatively. However usually it is impossible to take intra operative diagnosis of infection grossly in many cases even in hand of experienced surgeons. Intraoperative histopathological examination of periprosthetic tissue samples is a highly reliable diagnostic test provided that a pathologist, skilled in interpretation of periprosthetic tissue is available even though some institutions do not perform histological analysis of frozen sections intra-articular samples[30]. It should be performed at the time of revision prosthetic joint surgery, when available, if the presence of infection is in doubt based on the clinical suspicion of the surgeon and the results will affect management, for example, in deciding between revision arthroplasty and two-stage exchange surgery. At least 3 and optimally 5 or 6 periprosthetic intra operative tissue samples or the explanted prosthesis itself should be submitted for aerobic and anaerobic culture at the time of surgical debridement or prosthesis removal to maximize the chance of obtaining a microbiologic diagnosis. Morawietz et al.[31] quantified neutrophils in 147 periprosthetic membranes from cases of aseptic loosening as well as infection, and correlated the morphologic results with the results of microbiologic cultures and clinical diagnoses. Using the receiver-operating characteristic curves, the authors suggested an optimum threshold of a total of 23 neutrophils in 10 high power fields. This threshold yielded a sensitivity of 73% and a specificity of 95% using microbiologic cultures as the benchmark, and a sensitivity of 77% and a specificity of 97% using clinical impression as the reference standard for infection. Our experience support a recommendation for use of intra operative frozen sections for diagnosis of septic versus aseptic loosening in revision hip surgery to rule in or rule out infection.

## 10. Management of Infection

The decision with regard to the ideal treatment procedure for management of PJIs of the hip joint is made based on several factors such as time of infection manifestation, duration of symptoms, local soft-tissue condition, number of prior surgeries, identification of pathogenic organism, its virulence and antibiotic resistance profile as well as patient's co morbidities.

## 11. Debridement, Implant Retention and Antibiotics Therapy

Surgical debridement with antibiotic therapy and implant retention may be considered in patients with early type I and type III infections. Debridement, antibiotics and implant retention is the primary treatment for acute PJI, and should be performed as soon as possible after the development of symptoms.

Debridement with prosthesis retention is known as a relatively simple treatment with some advantages that include less morbidity, shorter hospital stay and lower costs compared to revision surgery. However, the reported success rate of debridement with prosthesis retention and long-term antibiotics is highly variable and has a wide range[8-10]. The reported rate of eradication varies from 21-89%[32,33], but also in very recent ones, success rate 92.8% has been reported[24,34].

Literature review showed that the most important factors contributing to treatment failure are longer duration of symptoms, a longer time after initial arthroplasty, the need for more debridement procedures and the type of infective microorganism and available antibiotics is also a key factor. *Staphylococcus* infection, high American Society of Anesthesiologists score and

intra-articular purulence, contribute to a substantial increase in failed treatments[35]. Other important factors related to debridement are the surgical risk in patients with co morbidities, the soft tissue status and the potential to implant or not a new prosthesis, which depends on the patient's bone stock. Therefore, this procedure should be reserved for a well-defined population of patients. If the following conditions are fulfilled, the success rate is similar to the one for exchange surgery[9,36]. The requirements are: (1) a stable implant; (2) a pathogen with susceptibility to antimicrobial agents active against surface-adhering microorganisms; (3) a duration of symptoms of infection of less than 4-6 weeks. Many patients with early or late acute-onset hematogenous infection qualify for this procedure.

The optimal antibiotic treatment (the choice and duration) of PJIs is, might be, also important factor in the result of debridement but is still unknown. The antibiotic used for PJI is based on the acquired culture results, potentially combined with rifampicin in the case of a staphylococcal infection. However, very few studies have been published regarding the choice of antibiotics when the cultures are not yet known. Vancomycin appears to be a possible antibiotic option though a definite recommendation cannot be made. Total duration of antibiotic therapy ranges for six weeks to six months, and treatment should be adjusted whenever necessary, based on microbiological results. When antibiotics levels fall to sub-therapeutic levels, surviving bacteria can slowly re-establish a community, which can serve as a nidus for biofilm formation. More specifically, controlled-release systems generate supra-therapeutic levels of antibiotics for a short time, after which the antibiotic concentration falls below the minimum inhibitory concentration; when this occurs, there is concern that resistant strains can emerge. Very high levels of antibiotic can also interfere with stem cell recruitment and commitment and osteoblast function, and thus block osteointegration.

Our institution's treatment algorithm provides an opportunity for irrigation and debridement with antibiotics therapy for PJI occurring during the acute postoperative period (within six weeks). We have performed radical debridement with retention of prosthesis from January 2000 to May 2011 for early PJI of hip arthroplasty in 20 patients (11 men and 9 women). The average time took to implement radical debridement after hip arthroplasty was 31.3 days (range, 18-48 days) and average follow-up period was 55 months (range, 12-178 months). Pathogens were isolated from 11 hips methicillin-resistant *S. aureus* (MRSA) in three, methicillin-resistant *S. epidermidis* (MRSE) in two, methicillin-sensitive *S. aureus* (MSSA) in one, *Acinetobacter baumannii* in two, *Enterococcus faecalis* in two patients, and *Enterococcus, Citrobacter* species in one). We performed radical debridement which included removal of infected granulation tissue in every interface space and betadine topical solution (povidone, iodine topical solution 10%) soaked gauze was packed into all surgical sites for 5-10 minutes and then repeating the irrigation with 3 L normal saline for already matured biofilm on the surface of the implant.

After radical debridement, vancomycin, vancomycin/aminoglycoside antibiotics and/or a combination with levofloxacin was given. In patients with isolated and sensitivity-tested pathogens, other antibiotics were used either alone or in combination (e.g., ciprofloxacin, ampicillin, sulbactam, teicocin, tazocin, and rifampin). The average duration for intravenous antibiotic administration was 43.5 days (range, 28-62 days). Recurrence of infection was not observed in any case during follow up period in our series. Our experience showed that the key point to success is the aggressiveness of surgical debridement and the surgeon's ability to reduce the bio burden. All the infected tissues and synovial significant deep areas, synovial and peri-implant tissues must be thoroughly removed[37]. The present literature review with our results shows that debridement, irrigation, antibiotic therapy, change of modular prosthesis components and prosthesis retention is an acceptable solution in the management of early and acute hematogenous PJI of hip.

## 12. One-stage Revision

One-stage revision or direct exchange arthroplasty has obvious advantages in the management of infected THA. With one major procedure, the patient is exposed to lower, cumulative perioperative risk. A functional revision is completed without exposure to the complications associated with spacers. There are also benefiting both financially and in terms of resource allocation. It is intuitive that a successful one-stage exchange will be drastically less expensive than a two-stage exchange; however, when incorporating the

increased failure rate it is very difficult to illicit the cost-benefit of the single-stage exchange. Literature review showed that factors associated with success were (1) absence of wound complications after the initial THA, (2) good general health, (3) sensitive *Staphylococcus* or *Streptococcus* species, and (4) organisms sensitive to the antibiotic in the cement while factors associated with poor outcomes were (1) polymicrobial infection, (2) Gram-negative organisms, especially pseudomonas, and (3) MRSA and group D *Streptococcus*. Our institution has no experience of one-stage exchange procedure for PJI because most of these chronic PJI in our institution were resistant organisms.

## 13. Two-stage Revision

Two stage reconstructions are considered a technique to ensure complete eradication of infection and to achieve a good success rate. It consists of debridement and removal of implant, insertion of spacer and then final implantation. It has several advantages, the infective load is removed, and the residual causative bacteria under the biofilm are exposed after debridement, the antibiotic elusion from spacer at high concentration helps in complete eradication. Furthermore, articulating spacers help to maintain partial joint mobility, proper limb length and soft tissue tension between stages, and improving the functional outcome[38]. But, several question remains, particularly the timing of antibiotic administration, the appropriate use of articulating spacer and timing to reimplantation.

Two-stage revision is generally regarded as the gold standard for the treatment of infected THA. Eradication rates over 90% have consistently been reported[39]. The principles of two-stage revision are the removal of all components including cement with radical debridement of all possible infected tissues and bone. However, despite the success of the two-stage revision in the treatment of failed septic primary hip arthroplasties, not all bacteria can be successfully treated especially resistant microorganism, so this is an rising concerning the antibiotic resistance pattern of the isolated bacteria and an increasing number of patients are presenting with complicated, difficult to eradicate infections even though repeated two-stage reimplantaion procedures. 50% failure rate in 12 patients with methicillin-resistant *Staphylococcus* infection was reported by Salgado et al[40]. A 48% of success rate in 19 patients who underwent two-stage reimplantation without the use of antibiotic-loaded cement in resistant bacteria-infected hip and knee arthroplasty was reported by Kilgus et al[41]. Uchiyama et al.[38] also reported that 10 of 31 hips (32.3%) became reinfected after staged reimplantation using antibiotic-impregnated cement spacers for periprosthetic infections. Although a few studies have shown maintenance of antibiotic levels above the minimum inhibitory concentration for common pathogens for several months after implantation[39], but the relative hydrophobicity of bone cement allows only 10% of the antibiotic to elute effectively[42].

Our institution has performed two-stage reimplantation in 62 patients with chronic PJI between August 2003 and March 2014. Of these 62 consecutive patients, 5 were excluded from the study because they died of causes unrelated to our surgery during follow-up. Of the remaining 57 cases (36 men and 21 women), 21 had undergone primary THA; 24, bipolar hemiarthroplasty; and 12, revision THA. Extensive debridement followed by removal of hardware as well as infected necrotic tissues and synovial sheath were performed in all the cases. During debridement, after initial irrigation, gauze soaked in 10% povidone-iodine solution (povidone-iodine solution Sungkwang®, Chungnam, Korea) was packed in the operative wound for 3-5 minutes followed by pulsatile lavage with 3-6 L of isotonic sodium chloride solution without antibiotics. In cases where gram-positive bacteria were identified and also in cases with negative bacterial culture, 3 g of vancomycin was mixed with 40 g of bone cement (Surgical Simplex-P; Stryker, Allendale, NJ, USA); a combination of 2-3 g of vancomycin and 2 g of fortimicin with 40 g of bone cement was used in cases of Gram-negative bacteria or mixed infection. Our treatment regimen consisted of extensive debridement and removal of the prosthesis in the first stage followed by appropriate intravenous antibiotic therapy (usually for 6-8 weeks) and second-stage reimplantation depending on patient status. If clinical signs of infection persisted and the CRP level did not recover to the normal level even 6-8 weeks after first-stage debridement, one or more additional debridement was performed with the consent of the patients. Infection-causing organisms were cultured in 46 patients (80.7%), of which 38 (66.7%) were infected with resistant organisms. Infection was controlled in 51 patients (89.5%) after the first stage. Second-stage reimplantation was possible in 51 patients (89.5%), and

there was no evidence of infection recurrence in 48 (84.2%). Two or more first-stage debridements were performed in 20 patients (35.1%). A mean of 1.8 (range, 1-7) debridements was required to control infection. An increased frequency of debridement was significantly correlated with increased comorbidity ($P$<0.001), low preoperative Harris hip score ($P$<0.001), antibiotic resistance, and polymicrobial culture results ($P$<0.001). Repeated debridements were performed at least twice in 20 patients. Of these, 13 patients required a second, 1 required a third, 5 required a fourth, and 1 patient required a seventh debridement with reinsertion of an antibiotic-loaded cement spacer to control infection. In 5 of 20 patients, the organisms observed after the latter debridements were different from the original ones and 3 became infected with multiple bacterial organisms. More frequent repeated debridements were required in patients who had chronic periprosthetic infection caused by resistant organisms as well as in the patients who had medical co- morbidities.

Our experience show that two stage reimplantation procedure can be effective for treating chronic periprosthetic infection of the hip, but repeated debridement is necessary in patients with high-risk factors such as poor health with co-morbidities and infection with virulent resistant pathogens.

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