# Infected Total Hip Arthroplasty: Diagnosis and Treatment

*Robert H. Fitzgerald, Jr, MD*

## Abstract

*The diagnosis of a deep infection complicating total hip arthroplasty is not difficult in most patients. When the diagnosis is not evident on the basis of the medical history, physical examination, routine blood work, and plain radiographs, indium-111–labeled leukocyte scintigraphy can be diagnostic. New immunologic techniques may allow differentiation of aseptic loosening from septic loosening of a painful total hip arthroplasty. Once the diagnosis of a deep infection about a total hip arthroplasty has been established, there are several treatment options. Oral antimicrobial therapy combining rifampin with a fluoroquinolone may prove to be an attractive alternative to surgical intervention in the treatment of some staphylococcal infections. If the causal microorganism is considered to be less virulent and does not elaborate glycocalyx, a one-stage procedure for reconstructing the hip with a cemented total hip arthroplasty incorporating antibiotics that are cidal to the microorganism has been successful in as many as 90% of patients. If the causal microorganism is considered to be virulent, a two-stage procedure with a prolonged interval between the Girdlestone resection arthroplasty and the second-stage reconstructive procedure is the treatment of choice.*

**J Am Acad Orthop Surg 1995;3:249-262**

Total hip arthroplasty has been a remarkably successful operation, restoring function and alleviating pain in the vast majority of patients. The incidence of postoperative complications has been unusually low. The most common complications include aseptic loosening, dislocation, thromboembolic disease, and postoperative sepsis. In recent years, osteolysis secondary to particulate debris of both high-density polyethylene and metal has superseded aseptic loosening secondary to use of polymethylmethacrylate as the primary complication.

## Incidence

Deep postoperative wound infections complicating total hip arthroplasty were common when the procedure was introduced by Sir John Charnley in the early 1960s. The infection rate at that time ranged from 7% to 10%[1,2] (Table 1). Improvements in operating room discipline (e.g., limiting the number of personnel, decreasing traffic, improved barrier draping, and use of sterile suction systems) and surgical technique (e.g., performing the procedure more rapidly) and more careful preoperative evaluation of patients have reduced the incidence to 0.5% or less.[1] With more intensive effort, specialized centers have further reduced the incidence of infection following total hip arthroplasty in patients with primary osteoarthrosis to 0.06%.[1,2]

Unfortunately, this reduction in the incidence of deep postoperative sepsis to such low levels has not been translated to the general community hospital. The Health Care Finance Association has reported the incidence of postoperative infection in the entire country to be greater than 1% in the Medicare patient population.[11]

## Diagnosis and Treatment Overview

In my experience, the diagnosis of deep sepsis about a total hip arthroplasty can be made on the basis of the clinical history and physical examination in approximately 25% of patients. In 50% of patients, the diagnosis of deep sepsis may require the use of extensive laboratory investigations, including radiography, nuclear imaging, examination of peripheral blood for determination of the erythrocyte sedimentation rate (ESR) and the C-reactive protein level, and aerobic and anaerobic incubation of clinical material

*Dr. Fitzgerald is Professor and Chairman, Department of Orthopaedic Surgery, University of Pennsylvania School of Medicine, Philadelphia.*

*Reprint requests: Dr. Fitzgerald, Department of Orthopaedic Surgery, Hospital of the University of Pennsylvania, II Silverstein Pavilion, 3400 Spruce Street, Philadelphia, PA 19104.*

**Table 1**
**Incidence of Musculoskeletal Infections Following Primary Total Hip Arthroplasty**

| Investigators | No. of Procedures | No. of Infections | Incidence of Infection, % |
|---|---|---|---|
| Conventional Operating Room | | | |
| Charnley and Eftekhar[3] | 190 | 13 | 6.80 |
| Wilson et al[4] | 110 | 11 | 11.00 |
| Patterson and Brown[5] | 368 | 30 | 8.20 |
| Brady et al[6] | 300* | 3 | 1.00 |
| Fitzgerald et al[7] | 3,215 | 42 | 1.30 |
| Salvati et al[8] | 765 | 12 | 2.00 |
| Lidwell et al[1] | 4,133† | 63 | 1.50 |
| Fitzgerald[2] | 1,739 | 4 | 0.23 |
| Unidirectional Airflow System | | | |
| Charnley and Eftekhar[3] | 2,152 | 12 | 0.60 |
| Hill et al[9] | 951 | 10 | 1.05 |
| Lidwell et al[1] | 3,922† | 23 | 0.60 |
| Salvati et al[8] | 1,524 | 19 | 1.20 |
| Schutzer and Harris[10] | 489 | 5 | 1.02 |
| Fitzgerald[2] | 1,628 | 1 | 0.06 |

*No antibiotics were administered prophylactically.
†Included both total hip arthroplasty and total knee arthroplasty.

obtained by aspiration of the joint. In the remaining 25% of patients, the exact diagnosis eludes detection by these commonly performed procedures. Histologic and microbiologic examination of tissue obtained by open biopsy can be used to establish the diagnosis. Newer molecular techniques for biologic and immunologic study appear to be promising.

While some believe that the use of specialized operating rooms is central to optimal treatment, preliminary analysis of a randomized, prospective study of a horizontal, unidirectional airflow system suggests that attention to detail in the preoperative assessment of the patient, operating room discipline, and the prophylactic administration of antimicrobial agents are probably the most critical factors in the further reduction of the incidence of deep postoperative sepsis.[2,9] Although there has been discussion of the superiority of one class of antimicrobial agents over another, the data from carefully studied patient populations suggest that first- and second-generation cephalosporins and semisynthetic penicillinase-resistant penicillins are equally efficacious.[1,11,12]

The appropriate treatment of a deep wound infection about a total hip arthroplasty remains controversial. A two-stage technique with total extirpation of the prosthetic components followed by delayed reconstruction has been the primary technique in North America. Buchholz et al[13,14] popularized a one-stage technique in which the components were surgically excised and the hip was reconstructed with antibiotic-impregnated bone cement during the same procedure. While antibiotic therapy alone has been reserved for patients considered too ill to withstand a major surgical procedure, newer techniques that have evolved may make such treatment a viable alternative. All three of these approaches utilize extensive healthcare resources and are extremely expensive.

## Classification

Postoperative wound infection following total hip arthroplasty has been categorized into three stages on the basis of when the symptoms begin and the clinical cause of the infection. Stage I infections include the classic fulminant postoperative infection, the infected hematoma, and the superficial infection that progresses to a deep infection. The indolent infection that usually becomes apparent 6 to 24 months postoperatively constitutes a stage II infection. Infections that develop in a previously asymptomatic total hip arthroplasty 2 or more years postoperatively and that are believed to be hematogenous in origin are stage III infections.

## Stage I Infections (Acute Postoperative Infections)

When purulent material drains from a red and swollen postoperative wound in a febrile patient (stage I infection), the diagnosis of postoperative sepsis can be easily established. However, such clinical manifestations of infection are encountered in a minority of the patients with an infected total hip arthroplasty.

The major challenge encountered is differentiating a superficial from a deep infection in a patient with persistent postoperative serous drainage from the wound or from drain sites (Fig. 1). There are no diagnostic, laboratory, radiographic, or scintigraphic techniques that permit this differentiation during the immediately postoperative period. Determining whether an early postoperative infec-

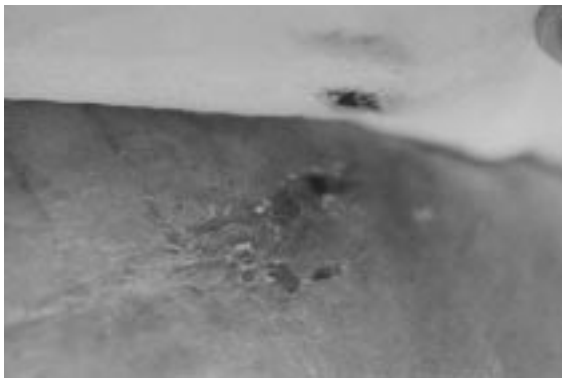


**Fig. 1** Hip wound in a 48-year-old man 7 days after revision total hip arthroplasty. Erythema, ecchymosis, and a small amount of bloody drainage from the proximal aspect of the wound are evident. Surgical debridement in the operating room revealed an infected deep hematoma. The wound healed uneventfully after debridement and parenteral antimicrobial therapy.

tion emanates from beneath the fascia can be difficult, even with direct inspection of the wound (e.g., when the patient is returned to the operating room for debridement of a draining wound or decompression of a hematoma). When no defect in the fascia is identified in the operating room, it can be assumed that the infected hematoma is superficial, and opening the fascia is therefore not surgically indicated.

Occasionally, a patient with a painful total hip arthroplasty and radiographic evidence of loosening 6 to 18 months postoperatively will have a medical history of drainage after surgery. Such a history can be of paramount importance, providing sufficient information for the surgeon to pursue a variety of investigative diagnostic techniques to establish the presence or absence of sepsis before revision total hip arthroplasty. My recommended protocol is to routinely obtain an ESR and a C-reactive protein level as screening tests for a low-grade infection. If the patient does not have a collagen disease and the ESR and C-reactive protein concentration are elevated, indium-111–labeled autologous white blood cell (WBC) imaging is performed. If the indium study reveals evidence of sepsis, aspiration and arthrography are performed. If a causal microorganism is not recovered from the aspirate, aspiration should probably be repeated. If a second aspiration is not useful in identifying the causal microorganism and a one-stage procedure is planned, consideration should be given to a limited, open biopsy to recover the causal microorganism, determine whether it elaborates glycocalyx, and identify its susceptibility pattern.

## Stage II Infections (Delayed Deep Infections)

The patient who has a well-healed wound and a painful total hip arthroplasty, especially the patient who has had some pain from the time of surgery, represents a diagnostic dilemma for the orthopaedic surgeon. The pain may be caused by aseptic mechanical loosening of one or both components of the arthroplasty. Alternatively, it may represent a low-grade, indolent infectious process (stage II infection). In a patient without a history of fever, chills, or postoperative wound drainage, pain about a total hip arthroplasty can be caused by various pathologic conditions, including low-grade sepsis.

### Radiographic Evaluation

A radiolucent line about the bone-cement interface of one or both components frequently will be seen on routine radiographic examination of the hip. Unfortunately, such radiolucent lines usually do not permit differentiation of aseptic from septic loosening. Endosteal erosions about the femoral canal are common radiographic findings, but can occur with both aseptic and septic loosening.

Rarely, a patient will have lacy periosteal new-bone formation about the femoral cortex on plain-radiographic examination. In my experience, when seen with or without evidence of loosening of the femoral component, it is pathognomonic of a deep infection. It usually occurs at the junction of the metaphysis and the diaphysis on the medial side of the proximal femur. However, with the implantation of long stems during revision arthroplasty, it can also be seen along the medial aspect of the distal metaphysis. Unfortunately, this pathognomonic sign occurs in only 1% to 2% of patients with infections about hip implants.

### Laboratory Evaluation

The hemoglobin level, peripheral leukocyte count, differential count, serum C-reactive protein level, and ESR frequently are normal or equivocal. In my experience, up to one fourth of patients with a painful total hip arthroplasty have a normal ESR. Sanzén and Carlsson[15] have noted that neither the C-reactive protein level nor the ESR is universally elevated in patients with infection about a total hip arthroplasty. They also suggested that both laboratory studies be performed routinely. Furthermore, one fifth of the patients who undergo total hip arthroplasty have a collagen disease that can increase the ESR.

Bauer and Saltarelli[16] recently compared the serum C-reactive pro-

tein level with the ESR in patients following total hip arthroplasty. They found that the serum C-reactive protein level returned to normal more quickly and was more accurate in identifying patients with a deep infection. If this observation is corroborated by studies in other major centers with large volumes of hip surgery, determination of the C-reactive protein level should replace the ESR in the evaluation of the patient with a painful total hip arthroplasty as a screening test for the presence of a low-grade infection. However, as noted above, Sanzén and Carlsson recommend using both studies.

### Hip Arthrography and Aspiration

Arthrography of the hip can demonstrate pocketing of the radiopaque medium in the area of the pseudocapsule, which suggests infection (Fig. 2). Unfortunately, this finding is uncommon. One must be careful in the interpretation of the arthrogram, as some patients with arthrographic evidence of loosening of a total hip arthroplasty are asymptomatic.

Arthrography provides an opportunity to aspirate joint fluid. Aerobic and anaerobic incubation of the hip aspirate permits recovery of the causal organism in two thirds of cases of infected total hip arthroplasty. Furthermore, if pocketing of the dye is observed within the pseudocapsule, there is a high likelihood of a deep infection.

While arthrography and aspiration can provide important information about the status of a painful total hip arthroplasty, their routine use is not cost-effective and should be avoided.[17] I reserve arthrography and aspiration for the evaluation of patients with noninflammatory arthritis and a painful total hip arthroplasty who have an elevated ESR or an elevated C-reactive protein concentration.

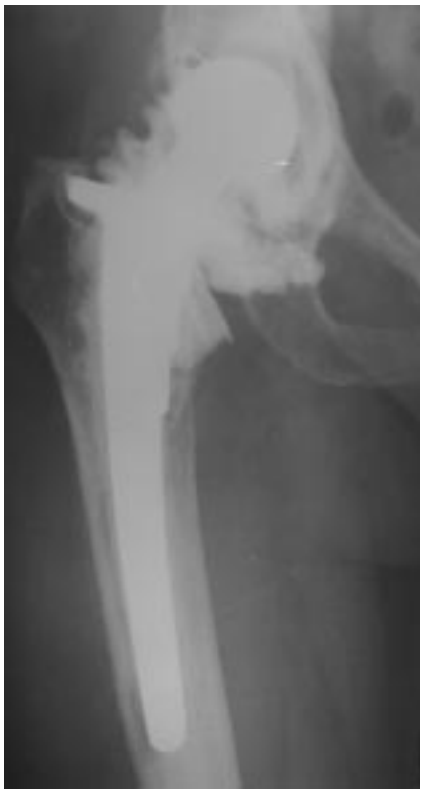


**Fig. 2** Arthrogram of a 51-year-old man with a painful, cemented total hip arthroplasty reveals pocketing of the dye in the pseudocapsule. Routine radiographs revealed a circumferential radiolucent line in Charnley-DeLee zones I, II, and III with lytic erosion of the proximal femur, particularly about the greater trochanter. There were additional lytic lesions on the table-down lateral view at the bone-cement interface at the junction of the middle and distal thirds of the femoral component. Cloudy fluid was aspirated, and both polymorphonuclear leukocytes and Gram-positive bacteria were noted on analysis.

### Scintigraphic Evaluation

For more than two decades, orthopaedic surgeons have attempted, with variable results, to use scintigraphic examination in their evaluation of the patient with a painful total hip arthroplasty. Scintigraphy has gradually become more reliable with the evolution of new diagnostic materials.

Indium-111–labeled autologous WBC scintigraphy has superseded differential imaging with technetium and gallium.[18,19] It is not only more specific but also more accurate in distinguishing aseptic from septic loosening of painful arthroplasties. In a prospective study of 42 patients with suspected low-grade musculoskeletal infections, In-111–labeled WBC scintigraphy correctly identified the presence or absence of sepsis in 37 patients (88%).[18] In the same study, differential technetium and gallium scintigraphy was accurate in only 26 patients (62%) (P,0.001). The cost-effectiveness of In-111–labeled WBC scintigraphy depends on its selective application. As mentioned previously, I do not use In-111–labeled WBC scintigraphy unless the patient has an elevated ESR or C-reactive protein concentration. In a canine total hip model, In-111–labeled WBC scintigraphy was found to distinguish accurately among aseptic loosening, septic loosening, and a securely fixed arthroplasty in 14 of 15 dogs.[20]

General surgeons have found imaging with technetium-99m methylene diphosphonate–labeled leukocytes to be effective in the evaluation of abdominal abscesses.[21] Although some researchers have suggested that this imaging technique is applicable to the musculoskeletal system,[22] its use in the patient with a painful total hip arthroplasty has been disappointing. In a study of 29 patients who were treated surgically, I found this technique to be associated with an unacceptably high rate of false-positive images, especially in the evaluation of patients with a Girdlestone resection arthroplasty who were being evaluated for hip reconstruction with a two-stage technique. The sensitivity of technetium-labeled leukocyte imaging was 86%, the specificity was 65%, and the accuracy was 74%. While the predictive value of a negative examination was

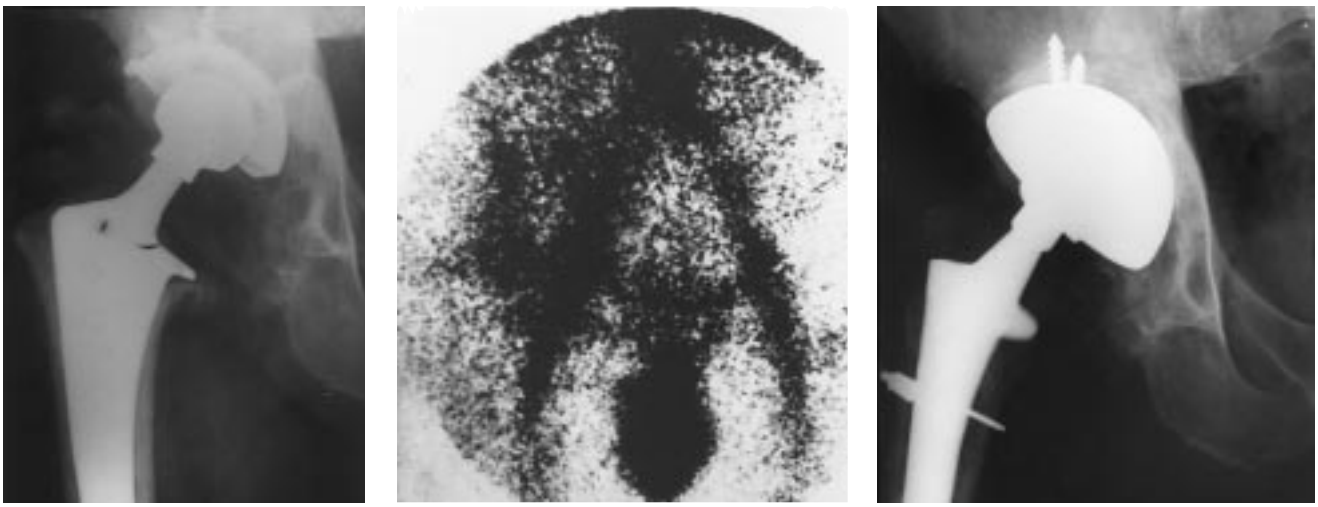
93%, the predictive value of a positive examination was only 63%. Although an advantage of technetium-labeled leukocyte scanning is its ease of use for the nuclear radiologist, with less exposure to blood products by the nuclear radiology laboratory personnel, this scintigraphic examination does not compare favorably with In-111–leukocyte scintigraphy.

### New Scintigraphic Modalities

There are two new diagnostic scintigraphic agents currently undergoing Food and Drug Administration (FDA)-controlled evaluations in the United States. In-111–labeled immunoglobulin G (IgG) is a new agent that can be used for the diagnosis of low-grade sepsis about a painful implant (Fig. 3).[23,24] While this technique is new in the United States (but will receive FDA approval in the near future), experience in Europe suggests that it will enhance the diagnosis of musculoskeletal infections if there is no inflammatory reaction from particulate debris.

Unfortunately, the most frequent differential diagnosis in the patient with a painful total joint arthroplasty includes both aseptic loosening and low-grade infection. In a preliminary FDA-controlled study, I did not encounter false-positive images in patients with aseptic loosening of total joint arthroplasties. False-positive images were encountered in one patient with a retained sponge and in two patients with a Girdlestone resection arthroplasty. This study suggests that the particular polyclonal antibody being used in the United States may obviate the problem encountered in Europe with an earlier version of the antibody or a different antibody. In-111–labeled IgG scintigraphy will require further study to determine whether it can differentiate these two conditions. It does, however, appear to hold promise in the diagnosis of a low-grade infectious process about an orthopaedic implant.

Another new scintigraphic agent currently undergoing FDA evaluation is Tc-99m monoclonal antibody. The early experience with this agent suggests that it may be more accurate than the In-111–labeled IgG polyclonal antibody. Both of these diagnostic agents will need widespread application in a variety of environments before their overall efficacy and cost-effectiveness can be evaluated.



A B C

**Fig. 3** Images of a 60-year-old man with a painful revision total hip arthroplasty who experienced prolonged drainage (3 weeks) after the primary procedure. **A,** Anteroposterior radiograph reveals a cementless total hip arthroplasty 18 months after surgery. There are erosions of the lateral femoral cortex about the distal third of the femoral stem. The patient complained of groin and thigh pain predominantly with weight-bearing but also with rest and during the night. His ESR (Westergren) was 40 mm/hr. **B,** An image obtained with In-111–labeled IgG (polyclonal) reveals increased uptake about the proximal femur and acetabulum, consistent with low-grade sepsis. Two species of *Staphylococcus epidermidis* were isolated from a hip aspirate: one was β-lactamase–positive, glycocalyx-negative, and methicillin-susceptible; the other was β-lactamase–positive, glycocalyx-negative, and methicillin-resistant. **C,** Anteroposterior radiograph obtained 18 months after a two-stage reconstruction. Six months after Girdlestone resection arthroplasty, the hip was reconstructed with a cementless total hip arthroplasty with hydroxyapatite coating on the proximal third of a calcar-buildup femoral component. The patient has returned to normal activities without pain, and the prosthetic-cement interfaces appear stable without erosions or other evidence of an ongoing infectious process.

### Histologic and Microbiologic Evaluation

In a few patients, all preoperative examinations will fail to differentiate mechanical from septic problems. A limited open biopsy of areas with radiographic evidence of erosion of the endosteal surfaces of the acetabulum and femur can prove helpful. Tissue for both pathologic (histologic) and microbiologic (aerobic and anaerobic incubation) examination can be diagnostic. In some cases, the final diagnosis can be based on histologic examination of multiple frozen-section deep-tissue specimens obtained from the pseudocapsule and the femoral and acetabular membranes during surgical treatment of the painful arthroplasty.

In addition, adjacent surgical specimens should be sent to the microbiology laboratory for aerobic and anaerobic incubation to confirm the pathologic diagnosis. It is important to send several specimens to both laboratories. I routinely send three specimens—one from the pseudocapsule, one from the membrane between the bone and the acetabular component or acetabular bone-cement interface, and one from the membrane between the femoral component and the femur or the femoral bone-cement interface and the femur. If the pathologic and microbiologic findings do not correlate, the availability of both microbiologic and histologic data about adjacent tissues provides the surgeon with additional information on which to base decisions. For example, the isolation of *Staphylococcus epidermidis* in the adjacent tissue specimen without the presence of polymorphonuclear leukocytes, which would reflect a foreign-body reaction, suggests that the microorganism is a contaminant.

Only rarely does one encounter histologic evidence of an infectious process without bacterial growth on either the aerobic or the anaerobic media. Frequently in such cases, the patients received antimicrobial therapy before the surgical procedure. If the results of microbiologic analysis are to be of value in the decision-making process, antimicrobial therapy must be withheld until clinical material has been analyzed by the microbiology laboratory.

### Immunologic and Molecular Diagnostic Techniques of the Future

Circulating mononuclear cells from patients with aseptic loosening of a cemented total hip or knee arthroplasty have been demonstrated to have a T-cell response with concomitant elaboration of cytokines during in vitro exposure to polymethylmethacrylate particles measuring less than 10 mm; this response is statistically different (P,0.05) from that encountered in patients with painless, functioning total joint arthroplasties.[25] Preliminary studies also suggest that patients with aseptic loosening have a different response from those with septic loosening: the patients with sepsis displayed elevated interleukin-2 levels (P,0.003); the patients with aseptic loosening had elevated levels of gamma interferon, but this elevation was not statistically significant (P = 0.15). These preliminary results suggest a role for immunologic techniques in accurately differentiating aseptic from septic loosening. While further studies remain to be performed, this may prove to be the best method to use in cases in which the diagnosis is not obvious from routine studies. Recent laboratory investigations have suggested that certain subsets of the T-cell repertoire respond to musculoskeletal infections and may be different from those that respond to aseptic loosening. If such findings are confirmed with clinical experience, this may be the ideal diagnostic test.

Another new technique, polymerase chain reaction, relies on the identification in the tissues of DNA fragments from microorganisms that have been phagocytosed and partially digested. When the fragments are amplified, the genetic code of the causal microorganism can be identified. This technique is exquisitely sensitive. A negative test may be the most important finding at this time because most, if not all, surgical wounds are contaminated at the time of surgery; thus, bacterial DNA remnants would not be surprising.

## Stage III Infections (Late Hematogenous Infections)

Diagnosis of stage III infections poses little difficulty. The patient will frequently have had a recent surgical treatment, dental manipulation, or remote infection. The infectious process will be heralded by the classic symptoms, including the acute onset of pain with a febrile response. Laboratory evaluation will reveal elevations of the ESR and C-reactive protein concentration, as well as elevation of the peripheral WBC count with a shift to the left. Purulent material can be obtained by means of aspiration.

## Microbiology of the Infected Total Hip Arthroplasty

During the past decade, multidrug-resistant microorganisms have been isolated with increasing frequency from postoperative infections complicating cardiovascular, thoracic, and general surgical procedures. For this reason, some cardiovascular surgeons have recommended the prophylactic administration of a combination of a second-generation cephalosporin and an aminoglyco-

side to combat resistant *Staphylococcus* organisms.[26] Others have suggested the routine use of vancomycin in patients receiving any type of biomedical implant.

The microbiologic characteristics of infections following total joint arthroplasty have also changed in recent years, but in a different fashion from those attributed to cardiovascular thoracic surgery. In my experience in the past 3 years, the overall distribution of the microorganisms recovered from 105 patients with an infected total joint arthroplasty has not changed from that previously documented over the previous two decades (Table 2). Gram-positive isolates were recovered from almost three fourths of the patients. However, when one studies the microbiologic findings in greater detail, the patterns of resistance were quite distinct from those reported by other surgical subspecialists. *Staphylococcus epidermidis* has become the most frequently isolated causal organism, recovered almost twice as frequently as *Staphylococcus aureus.* While methicillin resistance was uncommon among the isolates of *S epidermidis* recovered during the past 3 years (occurring in only 17% of cases), the vast majority of the isolates (93%) elaborated β-lactamase, which would render them resistant to any of the antimicrobial agents containing a β-lactam ring. In contrast, half of the isolates of *S aureus* were found to be methicillin-resistant, and 100% of the isolates tested elaborated β-lactamase.

**Table 2**
**Microorganisms Isolated From 105 Patients With Infected Total Joint Arthroplasty, 1989–1992**

| Microorganisms | No. of Isolates |
|---|---|
| Gram-positive bacteria | |
| *Staphylococcus epidermidis* | 30 |
| *Staphylococcus aureus* | 19 |
| Group D *Streptococcus* (*Enterococcus*) | 5 |
| *Peptostreptococcus* species | 4 |
| *Streptococcus agalactiae* | 3 |
| *Streptococcus sanguis* | 2 |
| *Streptococcus faecalis* | 2 |
| *Streptococcus* species | 1 |
| *Streptococcus viridans* group | 1 |
| β-Hemolytic *Streptococcus* | 1 |
| *Micrococcus* species | 1 |
| Gram-negative bacteria | |
| *Pseudomonas aeruginosa* | 6 |
| *Enterobacter cloacae* | 3 |
| *Acinetobacter calcoaceticus* | 2 |
| *Escherichia coli* | 2 |
| *Enterobacter agglomerans* | 1 |
| *Morganella morganii* | 1 |
| *Proteus mirabilis* | 1 |
| *Serratia marcescens* | 1 |
| *Xanthomonas maltophilia* | 1 |
| Anaerobes | |
| *Corynebacterium* species | 6 |
| *Propionibacterium acnes* | 2 |
| *Clostridium sporogenes* | 1 |
| *Lactobacillus* species | 1 |
| Fungi and mycobacteria | |
| *Aspergillus fumigatus* | 2 |
| *Mycobacterium tuberculosis* | 1 |
| *Candida albicans* | 1 |
| *Sporotrix schenckii* | 1 |

Although one can postulate that the extensive prophylactic administration of a first-generation cephalosporin over the past 15 years may be responsible for the emergence of the β-lactamase–producing causal organisms, there appears to be no need to make drastic alterations in the antimicrobial agents administered prophylactically. I have documented that the incidence of postoperative sepsis following primary total hip arthroplasty has been reduced to less than 0.5% in patients with idiopathic coxarthrosis.[2] This reduction in deep sepsis following this commonly performed surgical procedure reflects many changes that have taken place over two decades, and the prophylactic administration of antimicrobial agents continues to be one of the more critical aspects of therapy implemented by orthopaedic surgeons. However, the reduction in the incidence of deep sepsis by one to two orders of magnitude from the time of the introduction of total hip arthroplasty into the United States appears to have come at the price of the emergence of a new type of resistance, namely, the elaboration of enzymes that render the causal organism resistant to commonly administered agents that have a relatively high degree of safety. Even in view of this change in resistance, there appears to be no need to change the type of antimicrobial agent administered prophylactically during surgery. The low incidence of postoperative sepsis detailed above suggests that there is no need to alter the use of an antistaphylococcal agent.

Another subtle form of resistance involves the creation of a biofilm layer, which is a collection of exogenous host factors, microorganisms, and extracellular microbial products that promotes development and persistence of orthopaedic implant-related infections.[27] It has been known for some time that the virulent organism *S aureus* produces extracellular products that play a role in infection. Fibronectin and plasma proteins appear to combine with *S aureus* to assist in the adherence of the microorganism to biomaterials, including polymethylmethacrylate, chrome-cobalt alloys, titanium, and high-density polyethylene. The adherence of *S aureus* organisms to orthopaedic implants decreases their susceptibility to killing by polymorphonuclear leukocytes.

*Staphylococcus epidermidis* organisms and other coagulase-negative staphylococci are also capable of elaborating an extracellular polysaccharide, which is referred to as glycocalyx, or slime. This extracellular glycoprotein provides a binding

mechanism for these microorganisms to adhere to orthopaedic implants. Interestingly, glycocalyx does not have virulent properties in the absence of a foreign body or dead tissue that can behave as a foreign body. In the evaluation of the 105 patients with infections of a total joint arthroplasty referred to above, 52% of the isolates of *S epidermidis* and 28% of the isolates of *S aureus* elaborated glycocalyx.

The mechanism by which glycocalyx creates resistance to antimicrobial therapy has been thought to involve either (1) inhibition of the penetration of the antimicrobial agent through a thick material by the chemical composition of the biofilm or (2) inactivation of the inhibitory or cidal activity of the antimicrobial agent by the microenvironment of the biofilm or the metabolic state of the microorganism within the biofilm. Recent in vitro studies documented that antimicrobial agents such as vancomycin and rifampin could penetrate biofilm and achieve bactericidal concentrations at the surface of implants.[28] Nevertheless, these agents were not capable of sterilizing an implant with 72 hours of treatment, even though in vitro susceptibility testing indicated that the causal microorganism was susceptible to both.

This information suggests that alteration of the microenvironment or an altered state of bacterial metabolism is responsible for the resistance afforded to the bacteria that elaborate biofilm. Furthermore, it supports the difficulty that can occur when laboratory studies report the inhibitory effect of antimicrobial agents with reference to planktonic bacteria (free-living individual organisms). The sessile forms of bacteria found in biofilm (which attach themselves to surfaces) are generally more resistant than their planktonic counterparts to killing by antibiotics. It has been proposed that the "biofilm-eradicating concentration" would be a more appropriate indicator in estimating in vitro antimicrobial activity than the more traditional minimal inhibitory concentration.

If the causal microorganism elaborates glycocalyx, it is highly likely that microorganisms will remain after surgical extirpation of the total hip arthroplasty and debridement of the hip. At the present time, it seems warranted to avoid a one-stage reconstruction in a patient with an infected total hip arthroplasty in whom a glycocalyx-elaborating microorganism has been isolated. While we do not know for certain, as the appropriate testing was not performed in the past, glycocalyx may be responsible for the reported 20% to 25% incidence of recurrence following one-stage reconstructions.[9] Thus, it is imperative that the surgeon obtain microbiologic information before proceeding with a proposed one-stage procedure in the treatment of a patient with an infected total hip arthroplasty. This necessitates the isolation of the causal microorganism by means of either a hip aspiration or a limited open biopsy to obtain clinical material for aerobic and anaerobic incubation. The microbiology laboratory should also be asked to determine whether the isolated staphylococci elaborate glycocalyx.

The test for glycocalyx, which is based on the procedure of Christensen et al,[29] is easily performed in the microbiology laboratory. Several colonies of the organism to be tested are inoculated into 5 mL of trypticase soy broth, and the culture is incubated at 35°C for 48 hours without shaking. The contents of the test tube are then aspirated and replaced with safranin stain for 2 minutes. The safranin solution is aspirated, and the inside wall of the test tube is examined for the presence of the stain, which indicates the elaboration of glycocalyx by the microorganism under study.

## Treatment

### Antimicrobial Therapy

Suppressive antibiotic therapy without concomitant surgery has been used in the past for patients with significant medical problems considered to be at too high a risk for surgical treatment of an infected total hip arthroplasty. Goulet et al[30] introduced the concept of antimicrobial therapy alone in the treatment of a select group of such patients who they believed could not medically tolerate either a one-stage or a two-stage arthroplasty. Although they reported that 50% of 36 patients treated with this technique retained their prosthetic devices for at least 3 years, they subsequently found that generalized sepsis later developed in some patients. Tsukayama et al[31] found that this technique failed in 10 of 13 patients followed up for 2 or more years.

More recent reports from researchers in Europe suggest that a combination of rifampin and fluoroquinolone administered for a minimum of 6 months can be efficacious in a patient with an infected total hip or knee replacement. Widmer et al[32] and Drancourt et al[33] independently reported the successful treatment of such infections with rifampin plus either ofloxacin or ciprofloxacin without concomitant surgery in up to two thirds of their patients. Unfortunately, the clinicians who performed these two studies failed to follow up all of their patients for a minimum of 2 years on completion of the antimicrobial therapy. Thus, the final results are likely to be less optimistic than those reported after the preliminary observations. While the number of patients treated to date is small and the follow-up is unaccept-

ably short, the results are impressive, deserving an extended multicenter clinical trial.

**Surgical Treatment**

The surgical treatment of the infected hip prosthesis varies with the type (i.e., the stage) of the infection. In most cases, surgical extirpation of the prosthetic components is necessary to eradicate the infection. Infected hematomas are an exception. Aggressive surgical debridement of both superficial and deep hematomas and administration of specific parenteral antimicrobial therapy can lead to resolution of the infection and also salvage a functional joint.

Most other types of deep infection must be treated with surgical removal of all foreign bodies and debridement of the wound, followed by 4 weeks of specific parenteral therapy. McDonald et al[34] recently demonstrated that patients with a relatively more virulent infection (Table 3) who received 4 weeks of specific parenteral therapy had a lower incidence of recurrent sepsis with delayed reconstruction than did patients who received less than 28 days of such therapy (1 of 13 patients versus 3 of 7 patients [P,0.06, log-rank test, Kaplan-Meier actuarial survival curves]). In patients with infections with less virulent organisms, a relationship between the duration of therapy and the incidence of recurrent sepsis with reconstructive arthroplasty was not observed.

*One-Stage Surgical Treatment*

Buchholz and Gartmann[14] introduced the one-stage exchange arthroplasty. This procedure includes excision of the infected components, surgical debridement, and immediate reconstruction with a cemented total hip arthroplasty. The basis of this procedure is the addition of antibiotics in powdered form to polymethylmethacrylate (acrylic bone cement). Buchholz et al[13] reported an extensive experience with this technique in 1981, noting successful eradication of infection in 449 of 583 patients.

Garvin et al[35] recently reported their experience with the one-stage procedure performed with the use of gentamicin-impregnated Palacos acrylic cement (Merck, Darmstadt, Germany) as treatment of infections in 211 arthroplasties in 204 patients. Of the 211 arthroplasties, 76 were definitely infected. At the minimum 2-year follow-up, 19 of 21 hips (90%) in 21 patients were considered to have been successfully treated. In contrast to the philosophy of Buchholz et al[13] that all patients with an infected total hip arthroplasty should be treated with a one-stage procedure, these 21 patients were highly selected and thought to have a less virulent infection.

As previously stated, the success of this technique may be influenced by the ability of staphylococci to elaborate glycocalyx. Thus, in addition to the preoperative isolation of the microorganism and the identification of its susceptibility pattern, the microbiology laboratory should test for the ability of the causal organism to form a biofilm. If the causal organism does not elaborate glycocalyx and is susceptible to antibiotics that can be incorporated into acrylic bone cement, a one-stage procedure may be the appropriate treatment for a patient with an infected total hip arthroplasty (Fig. 4).

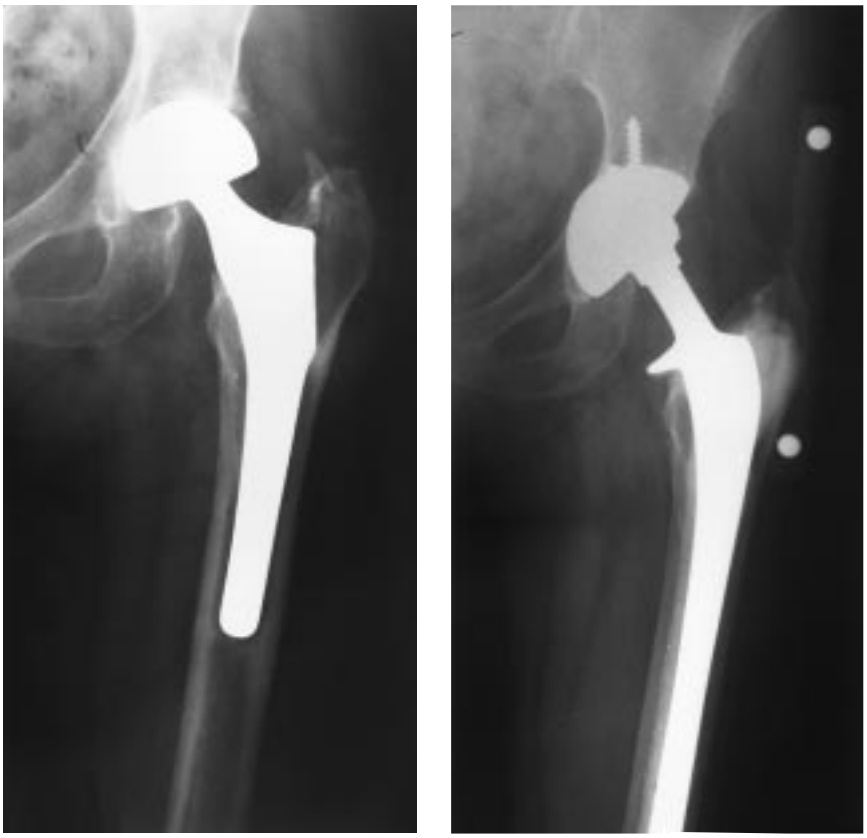
**Table 3**
**Virulence of Causal Microorganisms**

| |
|---|
| Less virulent |
| *Staphylococcus epidermidis* (methicillin-susceptible, non-glycocalyx-forming) |
| *Staphylococcus aureus* (methicillin-susceptible, non-glycocalyx-forming) |
| Anaerobic Gram-positive cocci |
| Streptococci (other than enterococci) |
| More virulent |
| Gram-negative bacilli |
| *Staphylococcus epidermidis* (methicillin-resistant, glycocalyx-forming) |
| *Staphylococcus aureus* (methicillin-resistant, glycocalyx-forming) |
| Group D streptococci (enterococci) |

*Two-Stage Surgical Procedure*

The two-stage technique has been the treatment of choice in the United States for the past two decades. McDonald et al[34] reported that their initial experience with a two-stage procedure was that it was successful in approximately 85% of the patients treated. If all of the polymethylmethacrylate is carefully removed, antibiotics are administered for at least 4 weeks, and there is an interval of 1 year between the Girdlestone resection arthroplasty and the reconstruction, the percentage of patients without recurrent infection will increase. In my recent experience with a two-stage procedure, which included careful surgical removal of all of the polymethylmethacrylate and the administration of parenteral antimicrobial therapy for 4 weeks, the treatment was successful in 94% of cases (unpublished data).

Some surgeons have found that the surgical implantation of antibiotic-loaded polymethylmethacrylate beads into the wound at the time of closure can enhance the eradication of the remaining microorganisms.[36] A prospective study addressing this technique has not yet been performed. Initially, it was recommended that the beads be pulled from the wound one per day beginning 2 weeks after surgery. This has proved to be painful for the patient, leading many surgeons to leave the beads in place until the time of reconstruction. Surgical



A B

**Fig. 4** Anteroposterior radiographs of a 66-year-old woman with severe weight-bearing pain. A bipolar arthroplasty of the left hip had been performed as the definitive treatment of an acute intracapsular hip fracture. The operative wound healed without drainage. **A,** Image obtained 15 months after surgery, when the patient complained of pain both at rest and with weight-bearing activities. Her ESR (Westergren) was 32 mm/hr. Group D *Streptococcus (Enterococcus)* organisms were isolated from a preoperative aspiration specimen. The radiograph reveals a radiolucency about the distal stem of the femoral component, with healing and periosteal new-bone formation. **B,** Postoperative anteroposterior radiograph obtained 3 years after one-stage treatment of the enterococcal infection with tobramycin and erythromycin incorporated into Palacos acrylic cement. There is no clinical evidence of an ongoing infectious process. The patient was extremely active without pain.

excision of the beads at the time of reconstruction of the hip can be difficult and is tedious.

Once the infectious process has been arrested after the Girdlestone resection arthroplasty, the patient must wear a 2.5-inch heel lift and use crutches for ambulation. Thus, it is not surprising that many patients seek hip reconstruction as soon as possible. The ideal timing of the second stage remains to be defined. For example, should the interval between resection arthroplasty and hip reconstruction be longer for patients with more virulent infections? Unfortunately, a database of sufficient size to address this question does not yet exist. My preference for dealing with this problem has been to perform reconstruction 3 or more months after resection arthroplasty in patients with less virulent infections, but to delay reconstruction for at least 1 year in patients with more virulent infections. Others have reported success with shorter intervals between the Girdlestone resection arthroplasty and reconstruction of the hip. The In-111–labeled autologous WBC scintigraph must be negative and the ESR must be normal before proceeding with the second stage.

It is frequently necessary to implant a long-stem femoral component to achieve interdigitation of the polymethylmethacrylate within the femur. Depending on the degree of destruction of the acetabulum by the infectious process before the Girdlestone resection arthroplasty, structural allografts may be necessary to achieve a mechanically stable acetabular component during the reconstructive procedure (Fig. 5).

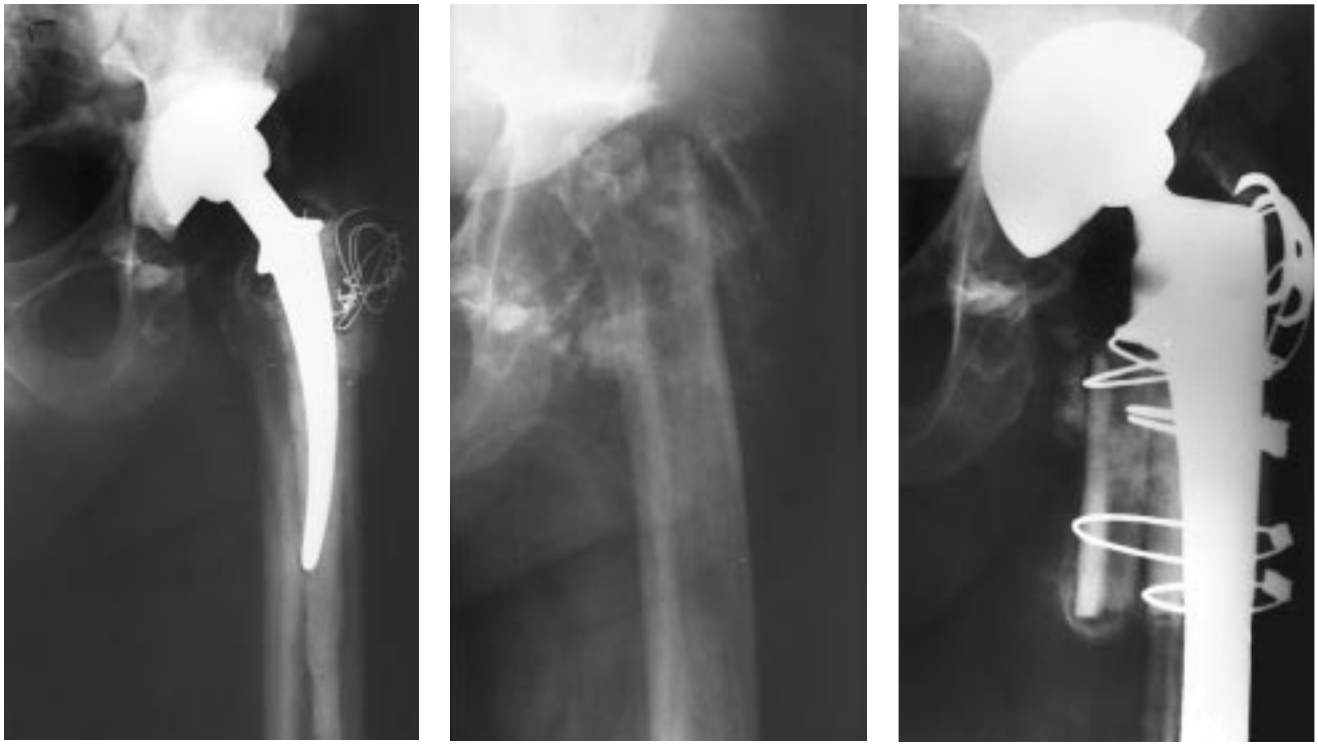
There is little data available on which to judge the advantages of mixing antibiotics with the polymethylmethacrylate used for fixation in a two-stage reconstruction of an infected total hip arthroplasty.[14] Most surgeons place the antibiotic in Simplex P (Howmedica, Rutherford, NJ) rather than in Palacos acrylic cement. Palacos affords both a higher local concentration of the antibiotic and a more sustained release. Simplex P is more commonly used in the United States because it is easier to inject, which is especially useful when multiple batches are necessary to cement the femoral component. Thus, while Palacos has theoretical advantages for a two-stage reconstruction of an infected total hip arthroplasty when antibiotic-impregnated polymethylmethacrylate is thought to be advantageous, Simplex P may be the wiser choice, because the cement can be injected in a low-viscosity state.

Duncan and Beauchamp[37] have described another technique, which obviates the patient's having to ambulate with a short and difficult-to-control extremity in the interval between resection arthroplasty and reconstruc-

tion. These investigators implant an articulated spacer, which is constructed from antibiotic-impregnated Palacos acrylic cement about a femoral stem and polyethylene acetabulum. The initial experience with this technique is small and limited to one center, but it is quite promising.

With the introduction of the uncemented total hip arthroplasty and the less-than-optimal results following revision cemented total hip arthroplasty (for aseptic mechanical loosening), it was only natural for reconstructive arthroplasty with uncemented components to be extended to patients with a resection arthroplasty performed as treatment of an infection (Figs. 3, C, and 5). Of course, such procedures must be performed in a delayed or staged fashion. The optimal timing of reconstruction to avoid recurrent sepsis remains unknown. McDonald et al[34] noted that procedures performed less than 1 year after resection arthroplasty were associated with recurrent sepsis in 7 of 26 patients (26.9%), compared with only 4 of 56 patients (7.1%) in whom reconstruction was performed 1 or more years after resection arthroplasty (P,0.01). However, the database was not sufficiently large to identify the ideal time for reconstruction after a Girdlestone resection arthroplasty.

In my own experience, 16 of 17 patients with an infected total hip arthroplasty were successfully treated with the use of uncemented components for reconstruction. In the past 6 years, an additional 44 patients have been successfully treated with this technique and followed up for at least 2 years. Sepsis recurred in only 1. Thus, 59 of 61 patients (97%) have undergone suc-



A B C

**Fig. 5** Images of a 50-year-old man with a painful cemented total hip arthroplasty 10 years after surgery. Group D *Streptococcus (Enterococcus)* and *S epidermidis* (β-lactamase–positive, glycocalyx-positive, and methicillin-susceptible) organisms were recovered from a preoperative aspirate and from intraoperative tissue specimens. He was treated with a two-stage technique. **A,** Preoperative anteroposterior radiograph reveals a circumferential radiolucent line in Charnley-DeLee zones I, II, and III measuring 1 to 2 mm. The acetabular component has migrated cephalad since the early postoperative radiographs. There is erosion of the proximal femur, but the cement mantle about the femoral component shows minimal erosion about the bone-cement interface. **B,** Anteroposterior radiograph obtained following Girdlestone resection arthroplasty. The proximal femur was found to have been destroyed by the resection arthroplasty down to the level of the lesser trochanter. **C,** Anteroposterior radiograph obtained 1 year after a cementless total hip arthroplasty, which was performed 12 months after the Girdlestone resection arthroplasty. A calcar-replacement femoral component was used to correct the leg-length inequality and, in conjunction with strut allografts, to reinforce the thin proximal femur.

cessful reconstruction with this technique. In contrast, a recent review of this technique by several surgeons, albeit from a single institution, was not able to demonstrate any difference in the incidence of recurrent sepsis after reconstruction of the Girdlestone resection arthroplasty with either a cementless or a cemented arthroplasty.[38]

*Three-Stage Reconstruction*

Unfortunately, most patients who have undergone extirpation of a total hip arthroplasty and surgical removal of the acrylic bone cement have little remaining trabecular bone. Quite frequently, even the gross osseous architecture has been significantly distorted. Such problems have led to the development of a three-stage arthroplasty involving the following steps: (1) surgical extirpation of the device and debridement of the wound, followed by 4 weeks of specific parenteral antimicrobial therapy; (2) a bone-grafting procedure on the acetabulum and proximal femur with use of a mixture of autologous iliac bone graft and allograft bone 3 to 12 months after the resection arthroplasty; and (3) the implantation of porous-ingrowth prosthetic devices into the femur and acetabulum once the bone graft has become incorporated and has matured.

The concept of a three-stage reconstruction of the infected hip arthroplasty developed incrementally. The initial experience with uncemented femoral components implanted into femoral canals damaged by aseptic loosening suggested that press-fit stems could function satisfactorily in environments devoid of the cancellous bone usually encountered in a primary total hip arthroplasty. In the young patient with considerable bone loss from an infection about a cemented total hip arthroplasty, the introduction of structural allografts precipitates apprehension, especially since the recent report of high failure rates by Jasty and Harris.[39] However, reconstruction of the anatomy can permit more conventional restoration of hip function in otherwise healthy young patients who have normal life expectancies. Because the amount of bone graft that can be harvested from each patient is limited, it seems reasonable to combine autogenous and allograft bone in particulate form. Limited clinical experience suggests that it requires 6 to 12 months for this bone to be vascularized and to mature sufficiently to support a prosthesis. Even in a healthy bone bed, this combination of graft materials has been noted to be quite soft 6 months after implantation. Preliminary experience indicates that at least 9 months should elapse after implantation of bone grafts before insertion of the prosthetic devices.

Although these techniques are new and may require custom prostheses, the preliminary experience indicates that a pain-free functional arthroplasty is provided. If bone ingrowth can be achieved through the use of simultaneous bone grafting or a separate preparatory bone-grafting procedure, the prosthetic devices can be securely anchored to the acetabulum and femur. This should provide long-term mechanical stability. If sepsis recurs with the implantation of these large foreign bodies, bone ingrowth will not occur. Removal of the foreign bodies can be accomplished without the destruction of bone that so frequently occurs with efforts to surgically remove retained acrylic bone cement.

### Cost Considerations

The treatment of a patient with an infected total hip arthroplasty utilizes an extensive array of hospital resources to successfully eradicate the infectious process and restore function to the involved extremity. Septicemia can develop during the initial surgical debridement, which can be a prolonged procedure with extensive blood loss. In my experience over the past 3 years, the hospital provides $50,000 worth of nonreimbursed medical care when a two-stage technique is used in the treatment of patients with total hip arthroplasty infections, even when patients with fixed-reimbursement insurance are mixed with those who have indemnity health-care insurance. Since patients with total hip arthroplasty infections are commonly referred to major medical centers for treatment, referral centers have assumed a large financial loss. With the changes that are occurring in the health-care industry, such losses are unacceptable. A one-stage technique will reduce this loss for the hospitals, but at what cost to the patient?

Orthopaedic surgeons need to know whether the limited experience reported by Garvin et al[35] will translate into broader experience. Alternatively, should we continue with the two-stage technique, for which the success rate has been pushed to 94%? There is a need for a national database, as no one surgeon or group of surgeons has sufficient experience to address the multitude of clinical and financial questions about the treatment of infected total hip replacements.

## Summary

The incidence of deep postoperative wound infections complicating total hip arthroplasty has decreased significantly with improvements in operating room discipline and surgical technique, more assiduous preoperative assessment of the patient,

and the prophylactic administration of antimicrobial agents. The diagnosis of deep sepsis can be made on the basis of the clinical history and physical examination in approximately 25% of patients, but in the remainder, laboratory and imaging studies and, in the most elusive cases, histologic and microbiologic examination of biopsy specimens may be necessary.

The appropriate treatment of a deep wound infection about a total hip arthroplasty remains controversial. Oral antimicrobial therapy combining rifampin with a fluoroquinolone has been used in Europe and may prove to be an attractive alternative to surgical intervention in the treatment of *S aureus* infections. A one-stage procedure for reconstructing the hip with a cemented total hip arthroplasty incorporating antibiotics has been successful in as many as 90% of patients with less virulent infections. A two-stage technique involving total extirpation of the prosthetic components followed by delayed reconstruction is most commonly used in North America. In the younger patient with extensive bone destruction, a three-stage procedure that includes an intervening bone-graft procedure permits restoration of the osseous anatomy and the implantation of cementless devices.

In spite of the improvements in the treatment of deep sepsis, there is still a need for more research addressing the multitude of clinical and financial issues pertaining to this condition.

## References


1. Lidwell OM, Lowbury EJL, Whyte W, et al: Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: A randomised study. *Br Med J* 1982; 285:10-14.
2. Fitzgerald RH Jr: Total hip arthroplasty sepsis: Prevention and diagnosis. *Orthop Clin North Am* 1992;232: 259-264.
3. Charnley J, Eftekhar N: Postoperative infection in total prosthetic replacement arthroplasty of the hip-joint: With special reference to the bacterial content of the air of the operating room. *Br J Surg* 1969;56:641-649.
4. Wilson PD Jr, Amstutz HC, Czerniecki A, et al: Total hip replacement with fixation by acrylic cement: A preliminary study of 100 consecutive McKee-Farrar prosthetic replacements. *J Bone Joint Surg Am* 1972;54:207-236.
5. Patterson FP, Brown CS: The McKee-Farrar total hip replacement: Preliminary results and complications of 368 operations performed in five general hospitals. *J Bone Joint Surg Am* 1972; 54:257-275.
6. Brady LP, Enneking WF, Franco JA: The effect of operating-room environment on the infection rate after Charnley low-friction total hip replacement. *J Bone Joint Surg Am* 1975;57:80-83.
7. Fitzgerald RH Jr, Nolan DR, Ilstrup DM, et al: Deep wound sepsis following total hip arthroplasty. *J Bone Joint Surg Am* 1977;59:847-855.
8. Salvati EA, Robinson RP, Zeno SM, et al: Infection rates after 3175 total hip and total knee replacements performed with and without a horizontal unidirectional filtered air-flow system. *J Bone Joint Surg Am* 1982;64:525-535.
9. Hill C, Mazas F, Flamant R, et al: Prophylactic cefazolin versus placebo in total hip replacement: Report of a multicentre double-blind randomised trial. *Lancet* 1981;1:795-796.
10. Schutzer SF, Harris WH: Deep-wound infection after total hip replacement under contemporary aseptic conditions. *J Bone Joint Surg Am* 1988;70:724-727.
11. *Vital and Health Statistics: National Hospi--tal Discharge Survey—Annual Summary, 1990.* Hyattsville, MD: US Department of Health and Human Services, Series 13 (Data From the National Health Survey), No. 112, DHS Publication No. (PHS) 92-1773, June 1992.
12. Mauerhan DR, Nelson CL, Smith DL, et al: Prophylaxis against infection in total joint arthroplasty: One day of cefuroxime compared with three days of cefazolin. *J Bone Joint Surg Am* 1994;76:39-45.
13. Buchholz HW, Elson RA, Engelbrecht E, et al: Management of deep infection of total hip replacement. *J Bone Joint Surg Br* 1981;63:342-353.
14. Buchholz HW, Gartmann HD: Infection prevention and surgical management of deep insidious infection in total endoprosthesis [in German]. *Chirurg* 1972;43:446-453.
15. Sanzén L, Carlsson AS: The diagnostic value of C-reactive protein in infected total hip arthroplasties. *J Bone Joint Surg Br* 1989;71:638-641.
16. Bauer TW, Saltarelli MG: Infection vs aseptic loosening in revision arthroplasty: Predictive value of frozen section and other laboratory tests. *Orthop Trans* 1993;17:1054.
17. Barrack RL, Harris WH: The value of aspiration of the hip joint before revision total hip arthroplasty. *J Bone Joint Surg Am* 1993;75:66-76.
18. Merkel KD, Brown ML, Dewanjee MK, et al: Comparison of indium-labeled-leukocyte imaging with sequential technetium-gallium scanning in the diagnosis of low-grade musculoskeletal sepsis: A prospective study. *J Bone Joint Surg Am* 1985;67:465-476.
19. Magnuson JE, Brown ML, Hauser MF, et al: In-111-labeled leukocyte scintigraphy in suspected orthopedic prosthesis infection: Comparison with other imaging modalities. *Radiology* 1988;168:235-239.
20. Merkel KD, Fitzgerald RH Jr, Brown ML: Scintigraphic examination of total hip arthroplasty: Comparison of indium with technetium-gallium in the loose and infected canine arthroplasty, in Welch RB (ed): *The Hip: Proceedings of the Twelfth Open Scientific Meeting of the Hip Society, 1984.* St Louis: CV Mosby, 1984, pp 163-192.
21. Pullman W, Hanna R, Sullivan P, et al: Technetium-99m autologous phagocyte scanning: A new imaging technique for inflammatory bowel disease. *Br Med J* 1986;293:171-174.
22. Winker KH, Reuland P, Weller S, et al: Diagnosis of infection in surgery of the locomotor system with Tc-99m-HMPAO leukocyte scintigraphy [in German]. *Langenbecks Arch Chir* 1989;374:200-207.
23. Rubin RH, Fischman AJ, Callahan RJ, et al: $^{111}$In-labeled nonspecific immunoglobulin scanning in the detection of focal infection. *N Engl J Med* 1989;321:935-940.

24. Oyen WJ, Claessens RA, van Horn JR, et al: Scintigraphic detection of bone and joint infections with indium-111-labeled nonspecific polyclonal human immunoglobulin G. *J Nucl Med* 1990; 31:403-412.
25. Chadha HS, Wooley PH, Fitzgerald RH Jr: Cellular proliferation and cytokine responses to polymethylmethacrylate (PMMA) following joint arthroplasty. *Orthop Trans* 1993;17: 600-601.
26. Kaiser AB. Petracek MR, Lea JW IV, et al: Efficacy of cefazolin, cefamandole, and gentamicin as prophylactic agents in cardiac surgery: Results of a prospective, randomized, double-blind trial in 1030 patients. *Ann Surg* 1987;206:791-797.
27. Marshal KC: Biofilm: An overview of bacterial adhesion, activity, and control at surfaces. *Am Soc Microbiol News* 1992;58:202-207.
28. Dunne WM Jr, Mason EO Jr, Kaplan SL: Diffusion of rifampin and vancomycin through a Staphylococcus epidermidis biofilm. *Antimicrob Agents Chemother* 1993;37:2522-2526.
29. Christensen GD, Simpson WA, Bisno AL, et al: Adherence of slime-producing strains of *Staphylococcus epidermidis* to smooth surfaces. *Infect Immun* 1982;37:318-326.
30. Goulet JA, Pellicci PM, Brause BD, et al: Prolonged suppression of infection in total hip arthroplasty. *J Arthroplasty* 1988;3:109-116.
31. Tsukayama DT, Wicklund B, Gustilo RB: Suppressive antibiotic therapy in chronic prosthetic joint infections. *Orthopedics* 1991;14:841-844.
32. Widmer AF, Gaechter A, Ochsner PE, et al: Antimicrobial treatment of orthopedic implant-related infections with rifampin combinations. *Clin Infect Dis* 1992;14:1251-1253.
33. Drancourt, M, Stein A, Argenson JN, et al: Oral rifampin plus ofloxacin for treatment of Staphylococcus-infected orthopedic implants. *Antimicrob Agents Chemother* 1993;37:1214-1218.
34. McDonald DJ, Fitzgerald RH Jr, Ilstrup DM: Two-stage reconstruction of total hip arthroplasty because of infection. *J Bone Joint Surg Am* 1989;71:828-834.
35. Garvin KL, Fitzgerald RH Jr, Salvati EA, et al: Reconstruction of the infected total hip and knee arthroplasty with gentamicin-impregnated Palacos® bone cement. *Instr Course Lect* 1993;42:293-302.
36. Wahlig H, Dingeldein E, Bergmann R, et al: The release of gentamicin from polymethylmethacrylate beads: An experimental and pharmacokinetic study. *J Bone Joint Surg Br* 1978;60:270-275.
37. Duncan CP, Beauchamp CP: A temporary antibiotic-loaded joint replacement system for management of complex infections involving the hip. *Orthop Clin North Am* 1993;24:751-759.
38. Nestor BJ, Hanssen AD, Ferrer-Gonzalez R, et al: The use of porous prostheses in delayed reconstruction of total hip replacements that have failed because of infection. *J Bone Joint Surg Am* 1994;76:349-359.
39. Jasty M, Harris WH: Salvage total hip reconstruction in patients with major acetabular bone deficiency using structural femoral head allografts. *J Bone Joint Surg Br* 1990;72:63-67.