Infection after Total Hip Arthroplasty. A Study of the Treatment of One Hundred and Six Infections

DEAN T TSUKAYAMA, RUPERTO ESTRADA and RAMON B GUSTILO

The prevalence of infection following total hip arthroplasty without cement is a concern. The factors associated with subsequent aseptic loosening and the potential for recurrent infection were retained bone cement, the type of prosthesis, and the number of previous operations. The study included 106 infections, of which 49 were early postoperative, 54 were late chronic, and 3 were acute hematogenous. The most common pathogens were aerobic gram-positive cocci, anaerobes, and gram-negative bacilli. The mean duration of follow-up was 3.8 years (range, 0.3 to eleven years). A good result was noted after the initial treatment of twenty-eight (90 per cent) of the 34 patients who had early postoperative infection. Intraoperative cultures showed growth of the same organism or organisms or there was clinically apparent pus in the hip joint, or both. When the same pathogen or pathogens persisted or intermittently grew on cultures of specimens from the same joint, the infection was considered as a single ongoing infection, regardless of the number of attempts at treatment. In our experience, the treatment of infections after total hip arthroplasty can be based on their clinical presentation — that is, as an early postoperative, late chronic, or acute hematogenous infection. The fourth clinical setting that we considered in the current study was that of positive intraoperative cultures. The purpose of this study was to determine the effectiveness of the treatment protocols that we used for these four clinical settings, to identify the factors that contributed to failure of therapy, and to analyze the usefulness of common diagnostic modalities for differentiating septic and aseptic loosening of a prosthesis.

Materials and Methods

One hundred and three patients who had an infection after a total hip arthroplasty were included in the study. We reviewed all of the charts and radiographs of these patients and recorded their status with respect to infection and function of the hip at the time of the most recent clinical follow-up evaluation. Patients who had rheumatoid arthritis, diabetes mellitus, chronic renal insufficiency, or a malignant tumor were classified as potentially immunocompromised. The index operation was defined as the clean, elective hip operation that immediately preceded the infection.

Infection was diagnosed when multiple intraoperative cultures showed growth of the same organism or organisms or there was clinically apparent pus in the hip joint, or both. When the same pathogen or pathogens persisted or intermittently grew on cultures of specimens from the same joint, the infection was considered as a single ongoing infection, regardless of the number of attempts at treatment. In our experience, the treatment of infections after total hip arthroplasty can be based on their clinical presentation — that is, as an early postoperative, late chronic, or acute hematogenous infection. The fourth clinical setting that we considered in the current study was that of positive intraoperative cultures. The purpose of this study was to determine the effectiveness of the treatment protocols that we used for these four clinical settings, to identify the factors that contributed to failure of therapy, and to analyze the usefulness of common diagnostic modalities for differentiating septic and aseptic loosening of a prosthesis.
when at least two specimens that had been obtained at the time of the revision operation were positive on culture. A minimum of five cultures were performed for every revision. The diagnosis before these revisions was aseptic loosening, and infection was not obvious clinically at the time of the revision. An early postoperative infection was a wound infection that developed less than one month after the operation. A late chronic infection was one that developed one month or more after the index operation and that had an insidious clinical course. An acute hematogenous infection was associated with a documented or suspected antecedent bacteremia and was characterized by an acute onset of symptoms in the affected joint with the prosthesis.

Each infection was initially treated according to the protocol appropriate for its clinical presentation. Patients who had positive intraoperative cultures were managed with intravenous administration of antibiotics for six weeks without operative intervention. In these patients, a revision prosthesis had already been implanted for presumed aseptic loosening before the results of the intraoperative cultures were available.

Patients who had an early postoperative infection were managed with débridement, replacement of the polyethylene insert of the acetabular component, retention of the prosthesis, and intravenous administration of antibiotics for four weeks. Removal of the original polyethylene insert permitted greater access to the site of the acetabular component for débridement and removed a possible nidus of infection. Manual manipulation of the acetabular and femoral components was attempted. The duration of antibiotic therapy was arbitrarily chosen on the basis of our previous experience.

Patients who had a late chronic infection were managed with débridement, removal of all prosthetic components and bone cement; and placement of tobramycin beads, made with a mixture of 1.2 grams of tobramycin and twenty grams of polymethylmethacrylate. Approximately ninety beads, each about six millimeters in diameter, were packed in the acetabulum, and approximately ninety beads of the same diameter were placed inside the femoral canal. Antibiotics were also administered intravenously for six weeks, after which a delayed-exchange arthroplasty was performed. The time-interval between the removal of the components and the implantation of the revision prosthesis varied widely. However, in contrast with patients managed earlier in the study period, in whom the revision was typically performed six to twelve weeks after completion of the antibiotic therapy, the patients who were managed within the last five years of the study had the revision approximately two weeks after the antibiotic therapy had been discontinued. Fluid was not aspirated from the hip joint before the revision, but multiple cultures of specimens obtained during the revision were performed to confirm eradication of the infection. The tobramycin beads were removed from the joint at that time. The factors that were most important in a decision to insert the implant without cement were an age of less than sixty-five years and thinning of the cortical wall of the femur. In a previous study, we found that a thin cortical wall was associated with decreased shear strength at the bone-cement interface of revision prostheses. When cement was to be used, 1.2 grams of tobramycin was incorporated into forty grams of cement.

Patients who had an acute hematogenous infection were managed with débridement, replacement of the polyethylene insert, retention of the prosthesis if it was not loose, and intravenous administration of antibiotics for six weeks.

The rate of success after the first course of treatment was determined for each protocol. If the initial treatment failed, we recorded the number and type of subsequent courses of treatment that were attempted. A course of treatment was defined as a protocol that included an operation or antibiotics, or both, with the aim of eradicating the infection. In some patients, eradication was achieved only after multiple courses of treatment. A successful result was defined as no clinical evidence of infection at least two years after the end of antibiotic therapy and a functional hip with a total joint prosthesis at the time of the latest follow-up. For a hip to be considered functional, there had to be no or only slight pain with walking (with or without the use of a cane) and no radiographic findings that indicated a need for immediate or impending operative intervention.

All patients had a preoperative evaluation for infection. The evaluation included radiographs, a white blood-cell count, and determination of the erythrocyte sedimentation rate. Nuclear medicine studies were performed when loosening or infection was suspected but could not be confirmed by the initial studies. Radiographic loosening was defined as a complete radiolucent line of at least two millimeters in width at the bone-cement or prosthesis-bone interface or as evidence of migration or subsidence of a component. These criteria were also used in the evaluation of postoperative and follow-up radiographs. The postoperative radiographs were also evaluated for other evidence of mechanical loosening, such as settling of the prosthesis in a varus position, subsidence of the femoral component, or protrusion of the acetabular component. If radiographic loosening was not evident preoperatively, a technetium bone scan was done. Indium-labeled white-blood-cell scans were made when loosening of the prosthesis was evident on radiographs or bone scans or when it was not clear whether the loosening was due to a septic or aseptic process. Leukocytosis was defined as a white blood-cell count of more than 10,000 cells per cubic millimeter (10.0 x 10⁹ per liter). The erythrocyte sedimentation rate was considered high if it was more than thirty millimeters per hour. Aspiration of fluid from the hip as a means of detecting occult infection (as opposed to aseptic loosening) was not routinely done before revision operations; our experience has been in agreement with reports documenting a high rate of false-negative results in association with aspirates.

Specimens of periprosthetic tissue (including the joint capsule, synovial lining, intramedullary material from curettage, granulation tissue, and bone...
fragments) were obtained during the revision procedure or when the prosthesis was removed because of an infection of the hip joint and were evaluated histologically for evidence of inflammation. Histological examination was not done when frank pus was present, as it was in many patients who had an early postoperative infection.

The criterion for acute inflammation (more than five polymorphonuclear leukocytes per high-power field) described by Mirra et al. was used. Cultures of material obtained by swabbing of the hip joint and prosthesis as well as cultures of tissue from the joint capsule, acetabulum, and femur were performed. A minimum of five cultures were performed for each patient, and all cultures were evaluated for aerobic and anaerobic growth. Cultures that were positive in broth only were not included. Harris hip scores were calculated for patients who had had successful reimplantation of a prosthesis after treatment of an infection and were compared with the scores determined before removal of the prosthesis from the infected joint. Serial radiographs of the hip were also made and were evaluated for subsidence, migration, and radiolucent lines, with use of the same criteria that had been employed preoperatively. The duration of hospitalization was recorded, and the mean number of days was calculated for each category of infection.

Ninety-five per cent confidence intervals were calculated for the rates of successful clinical results, with reference to exact binomial probability tables. Chi-square analysis was used to evaluate the differences in the results between the patients who were immunocompromised and those who were not. The Fisher exact test was used to evaluate the effect of cement on the results of treatment of early postoperative infection.

Results
There were 106 infections in the ninety-seven patients (forty-five men and fifty-two women). The mean age of the patients at the time of the diagnosis of infection was sixty-three years (range, twenty-nine to eighty-seven years). Seven patients had two infections each, and one patient had three infections (a chronic infection bilaterally and an acute hematogenous infection). Sixty-one infections (58 per cent) were in a hip that had had a revision, and seventy (66 per cent) were in a hip in which the prosthesis had been inserted with cement.

The mean duration of follow-up was 3.8 years (range, 0.3 to eleven years). Treatment was not considered successful until there had been a minimum of two years of follow-up after completion of all operative and antibiotic treatment. The mean interval between the index operation and the diagnosis of infection was 2.6 years (range, seven days to twenty-five years). Thirty-one infections were diagnosed on the basis of positive intraoperative cultures; thirty-five were early postoperative infections; thirty-four, late chronic infections; and six, acute hematogenous infections. Fifty-eight implants (59 per cent) in fifty-seven patients were radiographically loose preoperatively.

Microbiological Findings
Staphylococci accounted for 61 per cent (eighty-nine of the 147 isolates (Table I). All thirty-three isolates of coagulase-positive staphylococci were sensitive to oxacillin, while twenty-seven (48 per cent) of the fifty-six isolates of coagulase-negative staphylococci were oxacillin-resistant. Over-all, aerobic gram-positive cocci accounted for 74 per cent (109) of the isolates; gram-negative bacilli, 14 per cent (twenty-one); and anaerobes, 8 per cent (twelve). The gram-negative bacilli included Pseudomonas aeruginosa (five isolates), Enterobacter cloacae (four isolates), Serratia marcescens (two isolates), Proteus mirabilis (two isolates), Escherichia coli (two isolates), Klebsiella pneumoniae (two isolates), Acinetobacter species (two isolates), Moraxella nonliquefaciens (one isolate), and Salmonella cholerasuis (one isolate). Anaerobic organisms were Candida albicans and Rothia dentocariosa. Most of the gram-negative isolates came from the early postoperative and late chronic infections, while isolates from the acute hematogenous infections were exclusively gram-positive cocci. Twenty-seven (25 per cent) of the 106 infections were polymicrobial, usually a combination of gram-negative bacilli and gram-positive cocci. Three patients had negative cultures, and the infection was diagnosed clinically on the basis of pus in the hip joint at the time of the operation.

Positive Intraoperative Cultures
Thirty-one infections were diagnosed on the basis of positive intraoperative cultures at the time of a revision (Table II). The thirty-one revisions represented 11 per cent of the 275 revisions done during this time-period. Preoperatively, the mean white-blood-cell count was 7900 cells per cubic millimeter (7.9 x 10^9 per liter) (range, 600 to 20,300 cells per cubic millimeter [0.6 to 20.3 x 10^9 per liter]) and the mean erythrocyte sedimentation rate was thirty-five millimeters per hour (range, five to ninety-nine millimeters per hour). Sixteen (52 per cent) of the thirty-one infections were associated with an elevated erythrocyte sedimentation rate. Acute inflammation was seen in association with one (4 per cent) of twenty-five infections in hips that had had histological examination of periprosthetic tissue specimens obtained at the time of the operation. The success rate of the treatment protocol (six weeks of antibiotics without additional operations) was 90 per cent (twenty-eight of the thirty-one infections). In the three failures of treatment, the same pathogen that had originally grown on culture was recovered again when the prosthesis was removed.

At the time of the revision, there were twenty-five prostheses that had been inserted with cement, five that had been inserted without cement, and one hybrid prosthesis (an acetabular component that had been inserted without cement and a femoral component that had been inserted with cement) in the infected joints. Because these prostheses were...
presumed to have aseptic loosening, a new prosthesis was inserted before the results of the intraoperative cultures were known. Sixteen of the revision prostheses were inserted without cement, nine were hybrid implants, and six were inserted with cement. Of the three infections that had not been eradicated after six weeks of antibiotic therapy, two were associated with insertion of a new prosthesis with cement and one, without cement. These three infections were treated with a successful delayed-exchange arthroplasty as a second procedure. The mean preoperative hip score (17) for the thirty-one hips was 45 points (range, 17 to 71 points), compared with 79 points (range, 62 to 92 points) at the latest follow-up evaluation. One femoral component and two acetabular components had evidence of loosening on the follow-up radiographs (Table III).

The mean duration of hospitalization was thirteen days (range, eight to thirty days). The patients were followed for a mean of 3.5 years (range, 0.5 to 8.6 years). Two patients had evidence of recurrent infection within two years after the completion of treatment.

**Early Postoperative Infection**

There were thirty-five early postoperative infections (Table IV). Preoperatively, the mean white-blood-cell count was 9200 cells per cubic millimeter (9.2 x 10^9 per liter) (range, 5000 to 22,300 cells per cubic millimeter [5.0 to 22.3 x 10^9 per liter]), and the mean erythrocyte sedimentation rate was fifty-two millimeters per hour (range, six to 132 millimeters per hour). No prostheses were loose at the time of débridement. After débridement and intravenous administration of antibiotics for four weeks, twenty-five infections (71 per cent) were eradicated without removal of the prosthesis.

Ten infections failed to respond to this regimen of treatment, but eight of them were ultimately eradicated. One of these eight infections was associated with retention of the original prosthesis; the infection was eradicated after a second débridement. The prosthesis was removed in association with the remaining seven infections. Of these seven infections, three were treated with a successful delayed-exchange arthroplasty; one patient had a delayed-exchange arthroplasty after an immediate-exchange arthroplasty had failed. Four of the seven infections ultimately necessitated resection of the femoral head and neck, after which there was no evidence of infection.

In two patients, the infection was never eradicated. Both patients were immunocompromised: one, because of carcinoma of the lung and the other, because of immunosuppressive medication after a renal transplantation. In the first of these patients, suppressive antibiotics were administered and the implant was not removed. The second patient had a second débridement, which failed, and the prosthesis was removed. However, the patient continued to have a draining, non-healing wound. These two patients died; their deaths were not directly attributable to the infection of the hip, and they were the only patients in the series who died.

Twenty of the early postoperative infections were associated with a primary replacement and fifteen, with a revision. Twenty-three of these infections (eleven that were associated with a primary prosthesis and twelve, with a revision prosthesis) were associated with a cemented prosthesis, and twelve (nine that were associated with a primary prosthesis and three, a revision prosthesis), with a prosthesis that had been inserted without cement. All ten of the infections that failed to respond to initial treatment were associated with a prosthesis that had been inserted without cement. This result was significantly different than that for the infections associated with a prosthesis that had been inserted with cement (p < 0.001).

For the twenty-eight hips in which the prosthesis was in place at the time of the latest follow-up evaluation and for which the hip score was calculated, the mean hip score was 70 points (range, 40 to 93 points), compared with a mean preoperative score of 39 points (range, 7 to 72 points) (Table III). At the most recent evaluation, these patients were able to walk with no or only slight pain (some with the assistance of a cane) and had no radiographic findings that indicated a need for immediate or impending operative intervention. There was radiographic loosening of one acetabular component that had been inserted with cement; this component remained clinically stable.

The mean duration of hospitalization was seventeen days (range, six to thirty-eight days). The patients were followed for a mean of 3.3 years (range, 0.3 to 6.7 years). All patients who were classified as having been managed successfully had been followed for a minimum of two years. Five patients, including the two who died, had recurrent infection within two years after the completion of treatment.

**Late Chronic Infection**

There were thirty-four late chronic infections (Table V). Preoperatively, the mean white-blood-cell count was 8800 cells per cubic millimeter (8.8 x 10^9 per liter) (range, 4000 to 19,700 cells per cubic millimeter [4.0 to 19.7 x 10^9 per liter]), and the mean erythrocyte sedimentation rate was sixty millimeters per hour (range, eleven to 129 millimeters per hour). An elevated erythrocyte sedimentation rate (more than thirty millimeters per hour) was associated with twenty-four infections (71 per cent).

Histological examination of periprosthetic tissue, obtained at the time that the prosthesis was removed, revealed acute inflammation in association with eight of thirty infections, including two of the three that had been associated with negative cultures.

Seven infections for which the initial therapy had failed (three that had been diagnosed on the basis of positive intraoperative cultures, two early postoperative infections, and two acute hematogenous infections) also were treated with the delayed-exchange protocol as a second procedure. Thus, forty-one infections (the thirty-four late chronic infections and the seven just mentioned) were treated with débridement, removal of all components and cement, placement of tobramycin-impregnated
cement beads, and six weeks of antibiotics. The delayed-exchange arthroplasty was performed at a median of 110 days (range, thirty-four to 720 days) after removal of the implant. The interval between the removal of the implant and the revision decreased progressively in the later years of the study. Of the fifteen infections associated with a reimplantation that was done within sixty days after removal of the prosthesis, only one recurred. Our current practice is to perform the revision eight weeks after removal of the prosthesis, which is two weeks after the completion of antibiotic therapy.

Twenty-nine (85 per cent) of the thirty-four late chronic infections were treated successfully with the protocol for that type of infection. In addition, six of the seven infections that had not been eradicated by the initial treatment with another protocol were treated successfully with the protocol for late chronic infections. The delayed-exchange arthroplasty failed in the treatment of five of the late chronic infections and one of the seven infections that had not been eradicated previously with another treatment protocol. Four of these infections were treated successfully with a second delayed-exchange arthroplasty, and two were treated with a resection of the femoral head and neck as the second procedure. At the latest follow-up evaluation, thirty-nine (95 per cent) of the forty-one infections had been eradicated and were associated with a revision prosthesis that was in place.

Of the thirty-four late chronic infections, twenty-two were associated with a prosthesis that had been inserted with cement; seven, with a hybrid prosthesis; and five, with a prosthesis that had been inserted without cement. Twenty infections were associated with a primary replacement and fourteen, with a revision. At the time of the revision, twenty-four prostheses were inserted without cement; two were bipolar, with the femoral component inserted without cement; five were hybrid; and three were inserted with cement. The five failures after initial treatment included one prosthesis inserted with cement, two inserted without cement, and two bipolar implants.

The mean hip score before removal of the prosthesis for the hips that had had a delayed-exchange arthroplasty (including the hips from the other groups that had had failure with another protocol) was 38 points (range, 10 to 71 points), compared with 74 points (range, 48 to 95 points) postoperatively (Table III). There were two bipolar components with protrusion into the acetabulum, one loose acetabular component that had been inserted with cement, and two loose femoral components that had been inserted without cement.

The mean duration of hospitalization was thirty-two days (range, eleven to seventeen days). This included the duration of the first admission (for débridement and removal of the prosthesis) and of the second admission (for revision after eradication of the infection). The second hospitalization was typically seven to ten days. The patients were followed for a mean of 4.2 years (range, 1.3 to eleven years). All patients who were classified as having been managed successfully were followed for a minimum of two years. Five patients had recurrent infection within two years after the completion of treatment.

Acute Hematogenous Infection

There were six acute hematogenous infections (Table VI). Bacteremia was the initial source of two infections; skin infection, of two; an infection in the contralateral knee, of one; and pneumonia, of one. In patients who had an identified primary site of infection, the onset of the symptoms at that site preceded the symptoms in the hip joint by two to seven days. Preoperatively, the mean white blood-cell count was 11,700 cells per cubic millimeter (11.7 × 10⁹ per liter) (range, 4300 to 24,900 cells per cubic millimeter [4.3 to 24.9 x 10⁹ per liter]) and the mean erythrocyte sedimentation rate was eighty-one millimeters per hour (range, thirty-five to 136 millimeters per hour). Histological examination of periprosthetic tissue revealed acute inflammation in association with two of four infections.

Three of the six infections were eradicated and the prosthesis was retained. Of these three, two had caused symptoms for seven and ten days before the initiation of treatment. The duration of the symptoms was unclear with regard to the third infection, which was in a patient who had enterococcal bacteremia. The three infections for which the treatment failed had caused symptoms for two, five, and fourteen days before treatment. Of these three, one was treated successfully with delayed-exchange arthroplasty and another, with two attempts at delayed exchange. The third infection continued to recur, and eventually resection of the femoral head and neck was performed.

Of the six infections, two were associated with a cemented prosthesis and four, with one that had been inserted without cement. Of the three failures, two were in hips in which the prosthesis had been inserted with cement and one was in a hip in which it had been inserted without cement.

The mean preoperative hip score was 41 points (range, 24 to 65 points), compared with 75 points (range, 67 to 82 points) at the most recent follow-up evaluation (Table III). At the latest evaluation, there were two loose cemented acetabular components.

The mean duration of hospitalization was twenty-one days (range, eleven to forty-two days). The patients were followed for a mean of 2.6 years (range, 0.5 to 4.0 years). Two patients had recurrent infection within two years after the completion of treatment.

Immunocompromised Patients

Thirty-eight infections — nine that had been diagnosed on the basis of positive intraoperative cultures, fifteen early postoperative infections, ten late chronic infections, and four acute hematogenous infections — were in patients who were considered to be potentially immunocompromised because of underlying disease. They represented twelve (57 per cent) of the twenty-one infections for which the initial treatment had failed but only twenty-six (31 per cent) of the eighty-five that had not been eradicated previously with another treatment protocol. Three of the six infections were eradicated and the prosthesis was retained. Of these three, two had caused symptoms for seven and ten days before the initiation of treatment. The duration of the symptoms was unclear with regard to the third infection, which was in a patient who had enterococcal bacteremia. The three infections for which the treatment failed had caused symptoms for two, five, and fourteen days before treatment. Of these three, one was treated successfully with delayed-exchange arthroplasty and another, with two attempts at delayed exchange. The third infection continued to recur, and eventually resection of the femoral head and neck was performed.

Of the six infections, two were associated with a cemented prosthesis and four, with one that had been inserted without cement. Of the three failures, two were in hips in which the prosthesis had been inserted with cement and one was in a hip in which it had been inserted without cement.

The mean preoperative hip score was 41 points (range, 24 to 65 points), compared with 75 points (range, 67 to 82 points) at the most recent follow-up evaluation (Table III). At the latest evaluation, there were two loose cemented acetabular components.

The mean duration of hospitalization was twenty-one days (range, eleven to forty-two days). The patients were followed for a mean of 2.6 years (range, 0.5 to 4.0 years). Two patients had recurrent infection within two years after the completion of treatment.
of the three failures of initial treatment of infection diagnosed on the basis of positive intraoperative cultures, five of the ten failures of treatment of early postoperative infection, four of the five failures of treatment of late chronic infection, and two of the three failures of treatment of acute hematogenous infection were in immunocompromised patients.

Final Result

One hundred and four (98 per cent) of the 106 infections were ultimately eradicated, and after the final, successful treatment of ninety-seven (93 per cent) of these 104 infections a prosthesis was in place (Table VII). Seven infections led to a resection of the femoral head and neck. The prosthesis was in place in one additional patient, who had advanced cancer, but the infection was never eradicated. Four of these seven infections were caused by coagulase-negative staphylococci, and four, by coagulase-positive staphylococci.

The two patients who had had failure of initial treatment (débridement) of the early postoperative infection and had underlying immunosuppression died. One, who had had a renal transplantation, died of nosocomial superinfections although the coagulase-positive staphylococci that originally grew on culture from a specimen of the wound was no longer present. The other patient who died was the one who had advanced cancer (small-cell carcinoma of the lung); coagulase-positive staphylococci had also caused the infection in this patient.

Functional Hip Score and Mechanical Loosening

The mean preoperative hip score for the entire series was 41 points (range, 7 to 72 points). This score was calculated before the revision arthroplasty (for presumed aseptic loosening) for the hips with positive intraoperative cultures, before the index replacement for the hips with early postoperative infection, and before operative intervention for the hips with late chronic infection and those with acute hematogenous infection. The mean postoperative hip score, calculated for the hips with a prosthesis in place at the latest follow-up evaluation, was 74 points (range, 40 to 95 points). In some hips the original prosthesis had been successfully retained, while in others the revision prosthesis was in place. A limp, slight discomfort in the hip, and use of a cane contributed to the lower scores for many hips.

There appeared to be no substantial differences, among the four treatment groups, with respect to the hip scores. Nine prostheses had radiographic evidence of mechanical loosening after two to ten years of follow-up. Six infections were associated with a revision for aseptic loosening after they had been eradicated. These revisions included two of the thirty-six acetabular components inserted with cement, one of the fifty-eight acetabular components inserted without cement, and one of the fifty-seven femoral components inserted without cement. Only two bipolar cups were implanted in our series; both were revised because of protrusion into the acetabulum. All six infections were associated with negative intraoperative cultures at the time of the latest operation.

Reinfection

Of the ninety-seven infections associated with a retained or successfully replaced implant, one was in a hip that became reinfeeted with a different pathogen during the course of the study. This hip had been treated successfully for an early postoperative infection with coagulase-positive staphylococci after insertion of a prosthesis with cement. The hip was revised without cement eight years later, and coagulase-negative staphylococci grew on intraoperative cultures. Treatment with antibiotics alone was unsuccessful, and a delayed-exchange arthroplasty was performed two years later to treat the persistent coagulase-negative staphylococcal infection. No hip had recurrence of the infection with the same pathogen more than two years after the follow-up period.

Discussion

Our series included 106 infections that occurred after total hip arthroplasty or that were diagnosed on the basis of positive intraoperative cultures during revision total hip arthroplasty for presumed aseptic loosening. The treatment of these infections, including the decision to remove or retain the prosthesis, was guided by the clinical setting in which the infection had occurred. We reviewed our results to determine whether a classification scheme based on the four clinical settings described in this study was a useful guide to treatment.

We had found that other classification schemes did not fulfill the role of guiding therapy. For example, one such scheme defines an early infection as occurring within three months after the index operation, a subacute infection as occurring within one year after the operation, and a late infection as occurring after one year. Anti-Poika et al. recommended débridement for the treatment of early infections (those occurring within three months after the operation) but cited a 0 to 4.5 per cent rate of success with this procedure in their review of seven reported series. We believe that our success rate of 71 per cent (twenty-five of thirty-five early postoperative infections) after treatment with débridement is due in part to limiting the use of this procedure to patients who had a shorter duration of infection (one that occurred within one month after the operation). Late infections have traditionally been regarded as necessitating removal of the prosthesis, but this is not always the case for acute infections, presenting either early or late after implantation of the prosthesis, that are the result of hematogenous seeding.

Of the categories that we have defined, that of positive intraoperative cultures caused the most problems. These patients had had a direct-exchange arthroplasty for presumed aseptic loosening. When the intraoperative cultures were subsequently found to be positive, the clinical question that arose was whether the joint with the newly implanted prosthesis needed any treatment and whether such treatment was indicated.
should include additional operations. It may be very
difficult to decide whether bacteria that grow on
culture of specimens from a revision hip operation
represent infection or contamination\(^{(13)}\). In order to
minimize the chance that a laboratory contaminant
would be inappropriately considered a pathogen, we
required that positive cultures be obtained from at
least two intraoperative specimens and we
disregarded cultures that were positive in only the
broth medium. Others have recommended recovery of
bacteria from all specimens\(^{(25)}\) or have required at
least five colonies per plate\(^{(39)}\) as a definition of
meaningful cultures.

Although we are concerned that we may be
managing some patients who do not have an
infection, the danger of overlooking an occult
infection in a patient who has a loose, painful hip
prosthesis is also very real\(^{(22)}\). Our failures of
treatment were instructive in this regard. Three of the
thirty-one infections that had been diagnosed on the
basis of positive intraoperative cultures failed to
respond to six weeks of antibiotic therapy,
necessitating removal of the prosthesis that had been
implanted just before the intraoperative cultures were
found to be positive. In these three infections, the
same pathogen that had been found originally when the
prosthesis had been implanted was recovered again
when the prosthesis was removed. These
failures illustrate that intraoperative cultures of
specimens obtained from revision hip operations can
indicate infection even when the clinical evidence is
not present and that the specific pathogen recovered is
also important. Dupont reported that fifteen (15 per
cent) of ninety-eight joints had positive
intraoperative cultures after a revision total hip
arthroplasty\(^{(12)}\). Six of these fifteen hips had an
infection, compared with one (1 per cent) of eighty-
three hips that had had negative intraoperative
cultures.

We believe that our treatment protocol of six
weeks of antibiotic therapy without any additional
operative intervention warrants consideration as an
option with a great potential benefit and a relatively
low risk. A larger series of patients will be needed to
decide whether this protocol is appropriate for all
patients who have positive intraoperative cultures of
specimens obtained during revision for presumed
aseptic loosening. The determination of methods to
identify patients with positive intraoperative cultures
who do not need antibiotic therapy is also an
important goal for future investigation.

The success rate of irrigation and débridement in
the treatment of early postoperative infection has
ranged from 0 to 100 per cent\(^{(4,20,29,30)}\). Nolan et al.
reported that this procedure was successful for all of
six infections diagnosed within two weeks after an
index total hip arthroplasty\(^{(30)}\). In general, it appears
that the longer that the infection has been present in
the hip, the more difficult it is to eradicate it without
removal of the prosthesis. Our definition of an early
postoperative infection as one that occurs within one
month after the operation is based on our experience
that infections that become evident longer than one
month after the operation, unless they are associated
with hematogenous seeding from another site of
infection, are not likely to respond to treatment that
does not include removal of the prosthesis. However,
our initial rate of failure of 29 per cent (ten of thirty-
five infections) in this group shows that further
advances in treatment are needed. The finding that all
of the failures of treatment of the early postoperative
infections were in hips in which the prosthesis had
been inserted without cement was unexpected but, on
further review, it was consistent with what has been
found with other prosthetic devices, such as polymer
vascular grafts\(^{(11)}\). None of these components that had
been inserted without cement had been loose at the
time of the débridement. It may be that porous
surfaces, before the ingrowth of host tissue, can
provide a sanctuary for bacteria, enabling them to
evade débridement, antibiotic therapy, and host
defense cells. Our results, although not conclusive,
suggest that implants that have been inserted without
cement should be removed at the time of débridement
from patients who have an early postoperative
infection. Additional investigation is needed to
determine whether our findings can be confirmed in a
larger group of patients.

Good results have been obtained with delayed-
exchange arthroplasty in the treatment of chronic
infections of the hip\(^{(8,17,18,27,34,38)}\). Our rate of success
of 85 per cent (twenty-nine of thirty-four infections)
is comparable with that reported by others\(^{(8,17,18,27,34,}
38)\). Delayed-exchange arthroplasty with use of the
protocol for late chronic infection was also highly
successful as a second course of treatment for six of
seven infections in the other clinical settings for
which the initial therapy had failed.

Both acute hematogenous infection and late
chronic infection can occur long after the prosthesis
has been implanted. The key to diagnosis is the
acuteness of the symptoms. An acute hematogenous
infection is one that is recently acquired in
association with a previous arthroplasty. The patient
has an abrupt onset of symptoms, including fever and
acute pain and swelling of the affected joint. If
treatment is initiated promptly, it is possible to
eradicate the infection without removal of a stable
prosthesis. In contrast, the subacute or indolent
presentation of a late chronic infection almost always
means that the infection will be well established by
the time that a diagnosis can be made and treatment
can be started. In this setting, the prosthesis must be
removed. It is worth noting that only three of the six
acute hematogenous infections in the current series
were treated successfully with retention of the
prosthesis. Although there were too few infections in
this group to support any conclusions, a high rate of
success may not be possible with our current protocol
for the treatment of acute hematogenous infections.
Alternatively, the deficiency may lie in our inability
to distinguish acute from chronic infections, which
leads us to choose the wrong protocol for treatment.

The classification of infection on the basis of the
clinical setting allows prediction of the most likely
pathogens. Infections that were diagnosed on the
basis of positive intraoperative cultures were
predominantly caused by coagulase-negative
staphylococci; early postoperative and late chronic infections were usually caused by coagulase-positive staphylococci, coagulase-negative staphylococci, or gram-negative bacilli; and acute hematogenous infections were caused by gram-positive cocci. This information is valuable when choosing the appropriate antibiotic therapy on an empirical basis, before the results of cultures are available, and in the infrequent situation in which bacteria do not grow on culture despite a clinically apparent infection. Buchholz et al. reported that 12 per cent of 667 infections after total hip arthroplasty were associated with negative cultures, despite the presence of draining sinuses or an elevated erythrocyte sedimentation rate. In the current series, three infections were diagnosed on the basis of a finding of pus in the joint during the operation, although the cultures were negative.

The literature suggests that infections caused by gram-negative organisms are more difficult to treat than those caused by gram-positive isolates; however, we did not find this to be the case. All thirteen infections in our series that were caused by gram-negative bacilli, which represented 12 per cent of the total of 106 infections, were eventually treated successfully, almost all after one course of therapy. We attribute this success to the availability of new antimicrobial agents that are more effective against these pathogens and less toxic to patients. The use of tobramycin-impregnated polymethylmethacrylate beads, which can achieve high local concentrations of antibiotic, may have also contributed to the successful treatment of gram-negative infections.

Several factors that have previously been identified as potentially contributing to failure of treatment appeared to be important in our study as well, although their importance could not be confirmed statistically. The first such factor was retained bone cement. Two patients needed additional débridement to remove bone cement deep in the acetabulum, even after resection of the femoral head and neck, before the infection was finally controlled. The difficulty in eradicating bacteria that are adherent to foreign bodies has been well described. The need to remove all hardware and cement in the treatment of infections adjacent to prosthetic joints has also been well documented, although others have reported mixed results. The second factor that may have contributed to the failures of treatment in our series was a history of multiple operations on the hip. The hips that had a resection of the femoral head and neck had had a mean of 3.1 previous operations, compared with 1.6 operations for those that ultimately had retention or replacement of the prosthesis. This difference might be attributed to the increased scarring and poor wound-healing as well as to the threefold increase in the rate of infection associated with multiple operations.

Evaluation of the final result of treatment should include an assessment of function of the hip (we used the Harris hip score), the rate of aseptic loosening, and the rate of recurrent or subsequent infection in the joint that had a revision arthroplasty. With respect to function, the mean postoperative hip score of the patients who were managed successfully was approximately 10 to 15 points less than what we would have anticipated after primary total hip arthroplasty without infection, but it did show an 80 per cent improvement compared with the mean preoperative score (74 compared with 41 points). Six infections (6 per cent) were associated with a later revision for mechanical loosening, two to ten years after the operation. Only one hip was reinfected with another pathogen, and no hip that had been followed for more than two years had recurrent infection with the original pathogen. James et al. reviewed the results of 1063 total hip revisions, in eleven series, that had been performed after current or quiescent infection, and they found an over-all rate of reinfection of 17 per cent. The high rate was attributed in part to unrecognized occult infections that were present at the time of the revision, a finding that supports the treatment of patients who have positive intraoperative cultures.

As a result of the data obtained in the current study, we have incorporated several changes into our treatment of infections after total hip arthroplasty. Our perioperative regimen of antibiotics after revision arthroplasty consists of vancomycin and tobramycin. With the knowledge that coagulase-negative staphylococci are the most frequent pathogens isolated from the sites of prosthetic joints associated with an infection that may not be apparent at the time of revision, vancomycin is administered intravenously after the operation until the results from intraoperative cultures are known. Use of antibiotics is discontinued if there is no growth of organisms. Tobramycin is given intravenously for two days as prophylaxis against gram-negative bacilli, which accounted for eight (16 per cent) of the fifty-one bacterial isolates from our patients who had an early postoperative infection. When an infection occurs in the early postoperative period, antibiotic treatment is directed against coagulase-positive staphylococci and gram-negative bacilli. The duration of antibiotic therapy for the early postoperative infections was four weeks; this duration was arbitrarily chosen on the basis of our previous experience. We currently administer antibiotics for six weeks after débridement in an attempt to improve our success rate of 71 per cent (twenty-five of thirty-five) in the treatment of early infections. If the pathogen is unknown, treatment of a late chronic infection with antibiotics does not begin until intraoperative specimens have been obtained for culture, at which point treatment with vancomycin and, often, a second antibiotic directed against gram-negative bacilli is started. The antibiotics are later adjusted on the basis of the results of the cultures. Porous ingrowth acetabular cups, rather than bipolar cups or those inserted with cement, are used in all revisions after an infection. Two young patients in the current study had protrusion of the bipolar cup three and five years after revision.

We realize that the treatment protocols used in this study should not be considered the standard of care for infections after a total hip arthroplasty or for those diagnosed on the basis of positive intraoperative
cultures of specimens obtained during a revision total hip arthroplasty for presumed aseptic loosening. A consensus on the optimum treatment can be reached only when our results have been compared with the data of other investigators reporting on alternative treatment protocols for the clinical settings that we have described.

In summary, we found that preoperative evaluation was not helpful in differentiating septic from aseptic loosening of a hip prosthesis. When cultures of multiple specimens obtained at the time of a revision were positive, the hip was considered to be infected and was treated accordingly. Late chronic infections were treated with removal of the prosthesis, but many hips that had an early postoperative infection, positive intraoperative cultures, or an acute hematogenous infection were treated successfully with retention of the prosthesis. Although twenty-one (20 per cent) of the 106 infections needed more than one course of therapy, 104 (98 per cent) were eradicated and ninety-seven (92 per cent) were treated successfully with retention of the prosthesis.

References: (1-39)

Orthop 1983; 181:92-98.


36. Surin, V. V.; Sundholm, K.; and Bäckman, L.: Infection after total hip replacement. With special reference to a discharge from the wound. J. Bone and Joint Surg 1983; 65-
TABLE I
NUMBER OF ISOLATES RECOVERED ACCORDING TO CLINICAL SETTING

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive cocci (n = 109)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulase-positive staphylococci (n = 33)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulase-negative staphylococci (n = 56)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptococcus (n = 14)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterococcus (n = 6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram-negative bacilli (n = 21)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteric gram-negative bacilli (n = 16)</td>
<td>2</td>
<td>18</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Pseudomonas (n = 5)</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Anaerobes (n = 12)</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Miscellaneous (n = 5)</td>
<td>-</td>
<td>2</td>
<td>3</td>
<td>-</td>
</tr>
</tbody>
</table>

TABLE II
INFECTIONS DIAGNOSED ON THE BASIS OF POSITIVE INTRAOPERATIVE CULTURES

<table>
<thead>
<tr>
<th>Results</th>
<th>No. of Infections</th>
<th>Success</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>First treatment biotics (6 wks.)</td>
<td>31</td>
<td>28(90%)*</td>
<td>3(10%)</td>
</tr>
<tr>
<td>Second treatment:</td>
<td></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Final result</td>
<td>31</td>
<td>31(100%)*</td>
<td></td>
</tr>
</tbody>
</table>

*95 per cent confidence interval, 70 to 96 per cent.
†95 per cent confidence interval, 88 to 100 per cent.
### TABLE III
FUNCTION OF THE HIPS WITH REVISION PROSTHESSES

<table>
<thead>
<tr>
<th>Group*</th>
<th>Positive Intraop. Cultures</th>
<th>Early Postop. Infect.</th>
<th>Late Chronic Infect.</th>
<th>Acute Hematogenous Infect.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harris hip score (points)</td>
<td>Preop. 45 (17-71)</td>
<td>39 (7-72)</td>
<td>38 (10-71)†</td>
<td>41 (24-65)</td>
</tr>
<tr>
<td></td>
<td>Postop. 79 (62-92)</td>
<td>70 (40-93)</td>
<td>74 (48-95)†</td>
<td>75 (67-82)</td>
</tr>
<tr>
<td>Loose components</td>
<td>Inserted with cement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetabular (n = 36)</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Femoral (n = 39)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Inserted without cement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetabular (n = 58)</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Femoral (n = 57)</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Bipolar (n = 2)</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
</tbody>
</table>

*The score is given as the mean, with the range in parenthesis.
†These scores were determined after treatment of the thirty-four late chronic infections that had not responded to the protocols for their respective groups and were subsequently treated with the protocol for the late chronic infection group.

### TABLE IV
EARLY POSTOPERATIVE INFECTIONS

<table>
<thead>
<tr>
<th>Result</th>
<th>No. of Infections</th>
<th>Success</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>First treatment: débridement</td>
<td>35</td>
<td>25 (71%)*</td>
<td>10 (29%)</td>
</tr>
<tr>
<td>Second treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed-exchange arthroplasty</td>
<td>2</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Immediate-exchange arthroplasty†</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Second débridement</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Resection of femoral head and neck</td>
<td>4</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Suppressive antibiotics</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Final result</td>
<td>35</td>
<td>29 (83%‡)</td>
<td>6 (17%)</td>
</tr>
</tbody>
</table>

*95 per cent confidence interval, 53 to 85 per cent.
†A delayed-exchange arthroplasty was done after this treatment failed.
‡95 per cent confidence interval, 63 to 92 per cent.
TABLE V
**LATE CHRONIC INFECTIONS**

<table>
<thead>
<tr>
<th>Result</th>
<th>No. of Infections</th>
<th>Success</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>First treatment:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed-exchange arthroplasty</td>
<td>34</td>
<td>29 (85%)*</td>
<td>5 (15%)</td>
</tr>
<tr>
<td>Persistent infection</td>
<td>7 †</td>
<td>6‡</td>
<td>1</td>
</tr>
<tr>
<td>Second treatment:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed-exchange arthroplasty</td>
<td>4</td>
<td>4 (100%)</td>
<td>—</td>
</tr>
<tr>
<td>Resection of femoral head and neck</td>
<td>2</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>Final result</td>
<td>41</td>
<td>39 (95%)$</td>
<td>2 (5%)</td>
</tr>
</tbody>
</table>

*95 per cent confidence interval, 69 to 95 per cent.
†These seven infections (three that had been diagnosed on the basis of positive intraoperative cultures, two early postoperative infections, and two acute hematogenous infections) had had failure of treatment with the protocols for their respective groups and were subsequently treated with the protocol for the late chronic infection group.
‡95 per cent confidence interval, 42 to 99.6 per cent.
§95 per cent confidence interval, 83 to 99.4 per cent.

TABLE VI
**ACUTE HEMATOMOUS INFECTIONS**

<table>
<thead>
<tr>
<th>Result</th>
<th>No. of Infections</th>
<th>Success</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>First treatment:</td>
<td>6</td>
<td>3*</td>
<td>3</td>
</tr>
<tr>
<td>débridement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed-exchange arthroplasty</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Resection of femoral head and neck</td>
<td>1</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Third treatment:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>delayed-exchange arthroplasty</td>
<td>1</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Final result</td>
<td>6</td>
<td>5†</td>
<td>1</td>
</tr>
</tbody>
</table>

*95 per cent confidence interval, 12 to 88 per cent.
†95 per cent confidence interval, 22 to 99.6 per cent.

TABLE VII
**RESULTS OF TREATMENT OF THE ONE HUNDRED AND SIX INFECTIONS**

<table>
<thead>
<tr>
<th>Group</th>
<th>Positive Intraop. Cultures (N = 31)</th>
<th>Early Postop. Infect. (N = 35)</th>
<th>Late Chronic Infect. (N = 34)</th>
<th>Acute Hematogenous Infect. (N = 6)</th>
<th>Over-All (N = 106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful first treatment</td>
<td>28 (90%)</td>
<td>25 (71%)</td>
<td>29 (85%)</td>
<td>3</td>
<td>85 (80%)*</td>
</tr>
<tr>
<td>Infection eradicated</td>
<td>31 (100%)</td>
<td>33 (94%)</td>
<td>34 (100%)</td>
<td>6</td>
<td>104 (98%)$†</td>
</tr>
<tr>
<td>Functional hip</td>
<td>31 (100%)</td>
<td>29 (83%)</td>
<td>32 (94%)</td>
<td>5</td>
<td>97 (92%)$‡</td>
</tr>
</tbody>
</table>

*95 per cent confidence interval, 71 to 87 per cent.
†95 per cent confidence interval, 93 to 99.8 per cent.
‡95 per cent confidence interval, 83 to 95 per cent.