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Chapter 9

Prosthetic Joint Infections

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Prosthetic joint implantation is among the most remarkable advances in surgery and medicine to occur during the last three decades. Although the results of this procedure are usually highly satisfactory (82, 103, 262), infection was recognized early as a serious cause of postoperative morbidity and prosthesis failure (58, 68, 319) (Fig. 1). Infection of the prosthesis occurs in only a small proportion of patients (5, 26, 101), but this dreaded complication results in major morbidity due to pain, immobility, failure, and loss of the prosthesis, reoperation, and in some cases, loss of limb or life. The cost of each episode is estimated to be 3 to 4 times the cost of a primary joint arthroplasty and to exceed $50,000 (22, 126, 278). Successful treatment of these infections is difficult, usually requiring both multiple operative interventions and prolonged antimicrobial therapy to achieve microbial sterilization, as well as a satisfactory functional result. Other implanted orthopedic foreign bodies, including a variety of fixation devices for the stabilization of fractures, are also subject to infection. While the pathogenesis and general principles of treatment are similar in many ways to those of prosthetic joints, a full discussion of these infections is beyond the scope of this chapter.

EPIDEMIOLOGY

Mechanisms of Infection

Two major mechanisms by which microorganisms cause prosthetic joint infection have been postulated. Microorganisms may colonize the prosthesis at the time of implantation, either through direct inoculation during tissue or implant manipulation or as a result of airborne contamination of the wound (171). Alternatively, microorganisms may reach a previously sterile implant either through hematogenous seeding during a bacteremia or through direct contiguous spread from an adjacent focus of infection (75, 186). Knowledge of the proportion of cases due to these different mechanisms is especially important in anticipating rational approaches to the prevention of infection.

Unfortunately, because of the sometimes long latency period between the onset of infection and the onset of symptoms and/or diagnosis, many infections are difficult to

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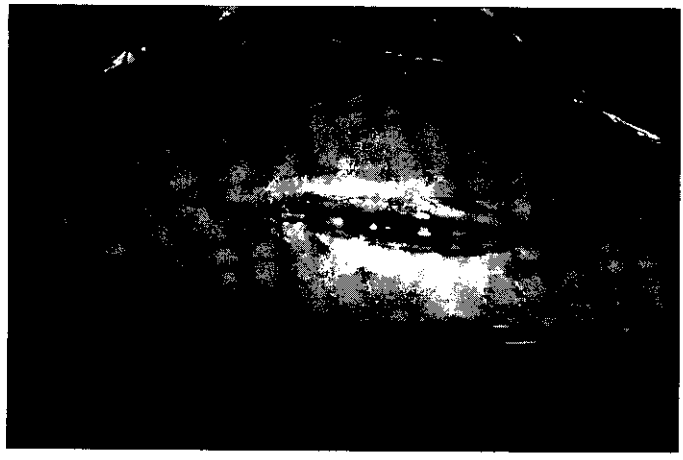

Figure 1. Infected total hip arthroplasty with four draining sinus tracts.

classify etiologically except by arbitrary definitions or assumptions (23, 273, 298). It is clear, for example, that prosthetic joint infection, like osteomyelitis, may remain asymptomatic for many years before the late occurrence of symptoms and that, conversely, hematogenous infection may occur early, in the immediate postoperative period (31, 32, 75, 285). In a recent comprehensive review of 180 published cases of presumed hematogenous infection, 50% occurred within 2 years of prosthesis implantation (75). The time after implantation at which diagnosis of infection is first made is therefore inadequate by itself to categorize the mechanisms of infection. Consequently, the relative importance of operating room-acquired infection compared with hematogenous seeding has remained controversial (75, 216).

Despite this controversy, several lines of evidence suggest that the majority of prosthetic joint infections are acquired in the operating room. First, clinical trials document that diverse types of perioperative prophylaxis—including systemic and local antimicrobial prophylaxis, as well as ultraclean operating room environments, all designed to reduce intraoperative contamination of the prosthesis—significantly decrease the incidence of prosthetic joint infection (128, 172, 194). Secondly, systemic antimicrobial prophylaxis has been shown to also reduce the incidence of late prosthetic joint infection (55), further supporting the concept that even though a prosthetic joint infection is not diagnosed until years after prosthesis insertion, the infection may be due to intraoperative contamination. Third, there is a similarity between the types of microorganisms that can be cultured from the wound at the time of surgery and that ultimately are the pathogens that cause deep periprosthetic infection. Finally, several investigators in both retrospective and prospective studies have reported a low proportion of cases acquired through hematogenous seeding when large series of patients have been critically reviewed. For example, among 490 total hip arthroplasty infections in Sweden, a hematogenous source was found for only 33 (7%) (5); in Britain, Ainscow and Denham (6) prospectively followed 1,112 total joint arthroplasties for a mean of 6 years and observed just 22 deep infections, only 3 of which were attributable to hematogenous seeding.

Incidence

Progress in understanding the epidemiology of orthopedic prosthesis infections has been hampered by methodological problems in the published literature, including the reliance on case series rather than well-designed epidemiological cohort studies, the frequent lack of an explicit case definition, incomplete case ascertainment and selection biases, and, especially, failure to account for differences in duration or completeness of follow-up, resulting in confusion between incidence (a rate) and risk (a proportion) (170). Estimates of cumulative risk (a percentage) should be interpreted or compared with caution, since it is quite difficult to estimate the true incidence rate or annual risk when the denominator for the rate (person-years) is unspecified. Studies that have longer follow-up will ultimately report higher cumulative risk, even when the true incidence in the study cohort is low; failure to account for differences in completeness and duration of follow-up between treatment groups will inevitably lead to erroneous conclusions (170).

The overall rate (hazard) of prosthetic joint infection is highest in the first 6 months postoperatively and declines continuously thereafter. In our experience, the combined incidence rates of total hip and knee arthroplasty infection during the first 2 years and years 2 through 10 postoperatively are approximately 5.9 (95% confidence interval [CI], 5.3 to 6.5) and 2.3 (95% CI, 2.1 to 2.5) infections per 1,000 joint-years, respectively (unpublished observations). The higher early incidence and subsequent declining rate of infection over time after implantation likely reflect a combination of the effects of the predominance of operating room-acquired infection (as discussed above), variable delays in symptom onset and diagnosis of infection after implantation, and the increasing resistance of prostheses to hematogenous seeding over time (31, 32, 285). The rate of total knee arthroplasty (TKA) infection is approximately twofold higher than the rate of hip arthroplasty infection at any time period after implantation (unpublished observations). There are insufficient data currently to accurately compare the true incidence rates of infection of arthroplasties in other anatomic locations, but risks (as opposed to incidence rates) with variable follow-up periods of 0 to 12% for elbows, 0.5 to 3% for shoulders, 1.5 to 5.0% for wrists, and 1.4 to 2.4% for ankles have been reported (65, 67, 118, 161, 199, 253, 276, 292, 325).

Risk Factors

Host Factors

A number of host characteristics have been implicated, either anecdotally or in controlled studies, as factors increasing the risk of foreign-body infections including prosthetic joint infection (see chapter 1). The primary factors predisposing to infection appear not to be systemic, humoral, or cellular immune defects, but rather local abnormalities of host defenses, primarily related to the presence of the foreign body itself and to the opportunities for, and degree of, exposure of the prosthesis to microorganisms. Systemic immunodeficiency states have been associated with unusual orthopedic infections (45), but opportunistic pathogens are notably uncommon causes of prosthetic joint infection.

Among potential host factors predisposing to prosthesis infection, prior joint surgery, perioperative wound complications, and rheumatoid arthritis are consistently observed and well established. Poss and colleagues (238), in a review of 4,240 large joint arthroplasties with a mean follow-up of 2.5 to 3.5 years, found that the risk of deep infection was

eightfold higher among patients undergoing a revision total hip arthroplasty (THA) than among patients with primary arthroplasty. Similarly, Ahnfelt et al. found that the relative risk of deep infection increased with the number of prior hip operations and was approximately sixfold higher among hips with five prior surgeries than among those with no prior operations (5). Patients who have undergone prior knee procedures and who subsequently undergo a total knee arthroplasty are at two- to fourfold increased risk of subsequent deep infection (252, 318). The reasons for the increased risk of infection after revision surgery remain unknown.

Postoperative wound healing complications, including "superficial" infection, hematomas, delayed healing, necrosis of the wound edge, and dehiscence, occur more commonly among patients who ultimately manifest deep infection and are an important risk factor for subsequent deep infection (21, 234, 238, 252, 324). In one study, 25 of 26 patients who developed perioperative deep infections had a history of postoperative wound healing problems (238). In a carefully analyzed prospective study with short-term (1 year) follow-up, Wymenga et al. found that although multiple indicators of poor wound healing were associated with an increased risk of joint infection in univariate analyses, only superficial wound infection per se, defined as erythema more than 1 cm from the incision, and an unhealed wound at discharge were independently associated with an increased risk of deep infection in multivariate analyses (324). The relative risk of joint infection among patients with wound healing problems was increased from 13- to 20-fold after total knee arthroplasty and from 22- to 52-fold after total hip arthroplasty.

A number of studies have demonstrated a higher risk of prosthesis infection among patients with rheumatoid arthritis, including multiple concurrent prosthetic joint infections (181), with a relative risk increased approximately two- to fourfold, compared with that of patients with osteoarthritis (26, 95, 140, 238, 265, 324). This increased risk is less evident in studies with shorter follow-up (238, 324). Whether the increased risk of prosthetic joint infection among rheumatoid arthritis patients relates to the greater frequency of early wound infection (313), the greater prevalence of multiple joint surgeries, higher rates of skin and wound colonization with staphylococcal species, greater prevalence of skin ulcerations and skin infection, use of T-cell-suppressive agents, or the immunological abnormalities of rheumatoid arthritis itself cannot yet be answered with certainty.

In a recent study, Berbari and colleagues (26) examined multiple potential risk factors among 462 episodes of prosthetic joint infection and matched controls followed for a median of 11.2 years. A multiple logistic regression model analysis indicated that the largest increased risk of prosthesis infection was associated with postoperative surgical site infections that did not involve the prosthesis (odds ratio [OR], 35.9; 95% CI, 8.3 to 154.6). Additional risk factors in the multivariate analysis included the presence of malignancy diagnosed within 5 years at another anatomic site (OR, 3.1; 95% CI, 1.3 to 7.2), a National Nosocomial Infection Surveillance System score of 2 (OR, 3.9; 95% CI, 2.0 to 7.5) or 1 (OR, 1.7; 95% CI, 1.2 to 2.3), and a history of prior joint arthroplasty on the same joint (OR, 2.0; 95% CI, 1.4 to 3.0). This study is important because it provides physicians, researchers, and patients with information that will allow improved preoperative risk assessment, identifies patients in whom health care providers should have a high index of suspicion for prosthetic joint infection when a patient has a painful prosthesis, and identifies populations to be targeted for additional perioperative prophylaxis strategies.

Other host characteristics identified as risk factors for prosthesis infection in some

studies, but not in others, included diabetes mellitus, the use of steroids, obesity, extreme age, joint dislocation, poor nutrition, distant infection, psoriasis, hemophilia, sickle cell hemoglobinopathy, joint implantation for malignancy, solid organ transplantation, AIDS, dialysis dependent renal failure, and prior septic arthritis (1, 26, 95, 96, 104, 115, 134, 145, 162, 175, 203, 211, 228, 238, 246, 281, 291, 324). The data supporting an increased risk associated with these factors are less consistent than the findings associated with prior surgery or postoperative wound complications.

Implant Factors

As previously mentioned, prostheses at different anatomic sites are associated with different risks of deep infection. However, confirmation of these findings in studies utilizing formal epidemiological tools that control for potential confounders, including severity of comorbid illness (107), is lacking. Furthermore, even at the same anatomic site, different types of prostheses seem to carry different risks of infection (231, 238). For example, Poss and colleagues found that metal-to-metal hinged knee prostheses had a 20-fold increased risk of infection, compared with that of metal-to-plastic knee prostheses; and Petrie et al. found that total knee arthroplasties with metal-backed patellar components were at a threefold increased risk of late infection, compared with total knee arthroplasties with all polyethylene components (231, 238). It has been speculated that this increased risk of infection may be due to the deleterious effects of the metal debris released by these implants on local immune defense mechanisms (see below).

PATHOGENESIS

Like that of other infections of implanted materials, the pathogenesis of prosthetic joint infection involves a complex interplay among host factors, microbial factors, and the biology of foreign implanted materials. The distribution of microorganisms causing prosthetic joint infections differs from the distribution of commensal and pathogenic microorganisms that would be expected to contact these biomaterials by random exposure, through either direct inoculation or hematogenous seeding. A common characteristic of microorganisms that are pathogenic for orthopedic appliances is, however, their ability to adhere to these foreign materials (113) (see chapters 1 to 5).

Implant Factors

A number of reviews provide an excellent overview of the chemical and physical properties of various biomaterials, including metal alloys, affecting the potential for microbial adhesion and infection (20, 73, 76, 113). As is the case with biomaterials implanted at other sites, the presence of a joint prosthesis significantly lowers the number of bacteria required to establish infection. Southwood et al. demonstrated in a rabbit model of prosthetic hip replacement that only a few *Staphylococcus aureus* inoculated at the time of joint replacement were required for the development of infection, but bacteremic seeding 3 weeks after implantation was significantly more difficult (285).

The complex host responses to the presence of metal alloy and polymers commonly used in orthopedic implants have been extensively studied. An inflammatory reaction typically occurs in response to the metallic particulate and ionic debris released from arthroplasty components (28, 268, 269). The response to cement appears to be more marked

than the response to metallic debris (28). The T-cell immunological response to prosthesis-associated infection differs from the host response observed in sterile prosthesis-associated inflammation, reactive synovitis, or rheumatoid synovitis (269). While an increased risk of bland loosening may occur because of an exuberant host sterile inflammatory reaction, this reaction has also been hypothesized to decrease local immunocompetence and thus predispose to infection. Possible mechanisms include macrophage and neutrophil exhaustion due to oxidative preemption by reaction to sterile debris, resulting in diminished killing capacity in the presence of implanted biomaterials (110, 111, 113, 114, 147, 207, 268, 329). Unpolymerized polymethylmethacrylate cement has also been shown in vitro to inhibit phagocyte, lymphocyte, and complement function (227, 232, 233, 235). In vivo polymerization has been shown in an experimental dog model to reduce the number of bacteria required to establish bone infection, compared with that of prepolymerized polymethylmethacrylate or metal foreign bodies (43, 232).

In addition to the promotion of bacterial adherence and inhibition of local immune mechanisms, prosthetic arthroplasty biomaterials may also impair the activity of antimicrobial agents against microorganisms in the vicinity of the foreign body (110, 210, 214). While physical penetration through extracellular glycocalyx barriers may partially explain this phenomenon, other mechanisms have also been postulated, including phenotypic changes in adherent microorganisms (113, 268).

MICROBIOLOGY

Several investigators have published data on the microbiology of prosthetic joint infection (139, 239, 266). However, because of a lack of a uniform definition of infection, different methods of intraoperative culture ascertainment, variable reporting of microbiological data, small sample size, and a variety of selection biases among different investigations, these data are difficult to interpret.

Five hundred seventy-eight cases of total hip and total knee prosthetic arthroplasty infections seen at the Mayo Clinic between 1992 and 1997 were classified as definite infections according to a strict case definition. A case was defined as a definite prosthetic joint infection if at least one of the following criteria was satisfied: (i) two or more cultures from sterile joint aspirates or intraoperative cultures were positive for the same organism, (ii) purulence was observed at the time of surgical inspection, (iii) acute inflammation consistent with infection was present on histopathologic examination of intracapsular tissue, or (iv) a sinus tract that communicates with the joint space was present. The pathogens identified in these cases are shown in Table 1.

The majority of infections (65%) are caused by aerobic gram-positive cocci, most commonly *S. aureus,* coagulase-negative staphylococci, beta-hemolytic streptococci, viridans group streptococci, and enterococci. Multiple strains of staphylococci can be present in a single prosthetic joint infection (69), and antibiotic resistance among staphylococci is increasing (144). Aerobic gram-negative bacilli, including members of the family *Enterobacteriaceae* (*Escherichia coli, Proteus mirabilis,* and others) and *Pseudomonas aeruginosa,* cause infection less frequently. Anaerobes such as peptostreptococci account for 4% of infections in our series, consistent with other investigators' experience (139, 239). *Bacteroides* spp. are an unusual cause of anaerobic infection. Polymicrobial infections account for 12% of cases.

Table 1. Microbiology of 578 prosthetic joint infections seen at Mayo Clinic between 1992 and 1997

Microorganism(s)	No. (%) of PJI[a]
Coagulase-negative staphylococci	172 (30)
S. aureus	135 (23)
Polymicrobial[b]	71 (12)
Unknown[c]	64 (11)
Streptococci[d]	51 (9)
Gram-negative bacilli[e]	32 (6)
Anaerobes[f]	23 (4)
Enterococci	16 (3)
Other microorganisms[g]	14 (2)
Total	578 (100)

[a] PJI, prosthetic joint infections.

[b] Includes coagulase-negative staphylococci (n = 51), *S. aureus* (n = 26), *Propionibacterium* spp. (n = 15), enterococci (n = 13), *Corynebacterium* spp. (n = 12), peptostreptococci (n = 11), viridans group streptococci (n = 7), *Bacteroides* spp. (n = 5), group B streptococci (n = 4), *Aspergillus* spp. (n = 3), *Penicillium* spp. (n = 2), *Actinomyces* spp. (n = 2), anaerobic gram-positive cocci (not otherwise specified) (n = 2), *Enterobacter cloacae* (n = 2), *Candida albicans* (n = 2), group D streptococcus (n = 1), beta-hemolytic streptococcus (not otherwise specified) (n = 1), *Pseudomonas aeruginosa* (n = 1), *Pseudomonas picketti* (n = 1), *Citrobacter freundii* (n = 1), *Morganella morganii* (n = 1), *Clostridium subterminale* (n = 1), *Serratia marcescens* (n = 1), gram-positive bacillus (not otherwise specified) (n = 1), gram-positive coccus (not otherwise specified (n = 1), *Prevotella bivia* (n = 1), *Alcaligenes xylosoxidans* (n = 1), *Stenotrophomonas maltophilia* (n = 1), and *Acinetobacter* sp. (n = 1).

[c] Includes cases in which there was no growth on routine bacterial cultures, routine bacterial cultures were not obtained, or microbiological information was not available.

[d] Includes group B streptococci (n = 20), viridans group streptococci (n = 19), group G streptococci (n = 7), group C streptococci (n = 2), nutritionally variant streptococci (n = 2), and *Streptococcus pneumoniae* (n = 1).

[e] Includes *Pseudomonas aeruginosa* (n = 11), *E. coli* (n = 8), *Enterobacter* spp. (n = 5), *Proteus mirabilis* (n = 4), *Klebsiella* spp. (n = 2), *Serratia marcescens* (n = 2), *Morganella morganii* (n = 1), and *Salmonella* sp. (n = 1).

[f] Includes *Propionibacterium* spp. (n = 9), peptostreptococci (n = 8), *Bacteroides* spp. (n = 5), anaerobic gram-positive coccus (not otherwise specified) (n = 1), *Prevotella melaninogenica* (n = 1), and *Veillonella parvula* (n = 1).

[g] Includes *Candida albicans* (n = 5), *Corynebacterium* spp. (n = 3), *Neisseria meningitidis* (n = 2), *Brucella* sp. (n = 1), *Mycobacterium fortuitum* (n = 1), *Mycobacterium genavense* (n = 1), and *Haemophilus influenzae* (n = 1).

Rare microbial causes of prosthetic joint infection that have been reported and should be considered in the correct clinical and epidemiological setting include *Haemophilus parainfluenzae* (240), *Pasteurella multocida* (218), *Chryseomonas luteola* (258), *Achromobacter xylosoxidans* (295), *Candida* spp. (300), *Histoplasma capsulatum* (97), *Brucella melitensis* (2, 187), *Mycobacterium tuberculosis* (25), *Mycobacterium fortuitum* (35), *Mycobacterium avium-m. intracellulare* (193), *Mycobacterium bovis* (166), *Mycobacterium chelonae* (242), bacillus Calmette-Guérin strain (59), *Echinococcus* spp. (304), *Gemella haemolysans* (83), *Yersinia enterocolitica* (217), *Campylobacter* spp. (326), *Listeria monocytogenes* (7), *Aspergillus* spp. (17), *Mycoplasma hominis* (282), *Oerskovia xanthineolytica* (124), *Tropheryma whippelii* (99), and *Clostridium difficile* (244).

Although some authors have suggested that the microbiology of prosthetic joint infection may vary with time after implantation (139, 239), the proportion of cases due to any one particular microorganism in 130 primary total hip arthroplasty infections seen at our institution between 1969 and 1987 was not significantly different between early and late infections (Table 2) (L. Carbone, J. M. Steckelberg, and W. R. Wilson, 5th Eur. Congr. Clin. Microbiol. Infect. Dis., 1991) This information suggests that the mechanisms of infection of early and late postoperative infections may be similar. If, on the other hand, hematogenous infections were the major source of late infections, one would expect to

Table 2. Microbiology of early and late primary THA infections at the Mayo Clinic from 1969 to 1987

Microorganism(s)	No. (%) of infections		
	Early[a]	Late[b]	Total
Coagulase-negative staphylococci	12 (18)	10 (15)	22 (17)
S. aureus	18 (28)	17 (26)	35 (27)
Other	35 (54)	38 (58)	73 (56)
Total	65 (100)	65 (100)	130 (100)

[a] 0 to 24 mo.
[b] >24 mo.

see an increased proportion of site-specific pathogens in later postoperative infections. These data are also useful in guiding empirical antimicrobial therapy while waiting for the results of cultures and antimicrobial susceptibility testing (see below).

DIAGNOSIS

The clinical presentation of prosthetic joint infection is highly variable, ranging from the syndrome of acute septic arthritis with the sudden onset of joint pain, erythema, swelling, fever, and systemic symptoms to a syndrome of indolent loosening and chronic pain, which is difficult to distinguish from aseptic loosening on the basis of symptoms and clinical examination alone. Typically, the pain associated with chronic prosthetic joint infection is usually present from the time of joint implantation and is persistent throughout the day, whereas pain due to aseptic loosening often begins after a pain-free interval and occurs only with movement or weight bearing. Many patients with chronic prosthetic joint infection will have had wound complications or superficial wound infections in the early postoperative period (26). Patients with a sudden onset or a new painful prosthesis should be questioned about possible sources of hematogenous infection, such as a recent cellulitis, pneumonia, urinary tract infection, or dental infection (75).

A fulminant presentation is more common with virulent organisms such as *S. aureus* or pyogenic beta-hemolytic streptococci, while a chronic indolent course is more typical of infection with less-virulent microorganisms such as coagulase-negative staphylococci (41, 280). Laboratory, radiographic, and scintigraphic evaluations provide the most value in the diagnosis of infection and planning operative decisions such as staged reimplantation in situations where the diagnosis of infection is not obvious (e.g., a draining sinus tract is not present) and there is an intermediate pretest probability of infection. What follows is a discussion of the utility of various diagnostic tests used to diagnose prosthetic joint infection.

Laboratory Studies

The leukocyte count, the erythrocyte sedimentation rate, and C-reactive protein are the most commonly used screening laboratory blood tests in the diagnosis of prosthetic joint infection. Unfortunately, these tests do not have a positive or negative predictive value sufficiently high to allow the physician to rely on the results of these tests alone to predict

the presence or absence of infection (71, 271, 286, 287, 298). The results of a recent prospective study of 178 patients (202 revision hip replacements) would suggest that the C-reactive protein is a more sensitive and specific test for the diagnosis of prosthetic joint infection than the erythrocyte sedimentation rate (286). In this study, the probability of prosthetic joint infection was 0% (95% CI, 0.0 to 4.0%) when the clinical history was not suggestive of prosthetic joint infection and the C-reactive protein and the erythrocyte sedimentation rate were normal. In this clinical setting, Spangehl et al. did not advocate additional diagnostic tests to exclude infection.

Radiologic Studies

The principal imaging modalities useful for detecting infection of a prosthetic joint include plain radiographs or tomograms, arthrograms, and radioisotopic imaging, particularly (111m) indium and technetium (^{99m}Tc) scanning. Abnormalities associated with infection on plain radiography are not specific for infection but may include loosening of the prosthesis, lucency at the bone-cement interface, periostitis, or other evidence of osteomyelitis (Fig. 2) (71, 183). Arthrograms (or sinograms in the presence of a sinus tract) may demonstrate communication between the joint space and the bone-cement interface, thus confirming the presence of a loose prosthesis (183). Nuclear scintigraphy may detect periprosthetic inflammation and suggest infection on the basis of characteristic combinations and timing of abnormalities. Technetium (^{99m}Tc) bone scintigraphy, while sensitive for infection, lacks specificity and is frequently abnormal because of arthritis, fracture, previous surgery, and heterotopic bone formation, as well as infection. In addition, activity can persist for long periods (81, 132, 154, 220). Johnson et al. reported an accuracy of 65% for the detection of prosthesis infection by indium-111-labeled leukocyte scanning alone (148). The accuracy of scintigraphy was increased to 93% when sequential technetium and indium-111-labeled leukocyte scans were correlated (Fig. 3) and may be increased even more with the addition of sulfur colloid marrow scintography (148, 157, 224, 225). Indium-111-labeled immunoglobulin scintigraphy was found to have a high sensitivity (100%) but specificity of only 80 and 50% for hip and knee arthroplasty infection, respec-

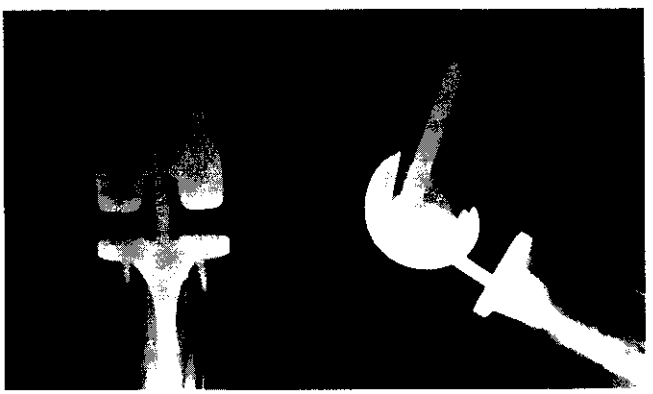

Figure 2. Plain radiograph of an infected TKA illustrating lucency at the bone-cement interface of both the femoral and tibial components.

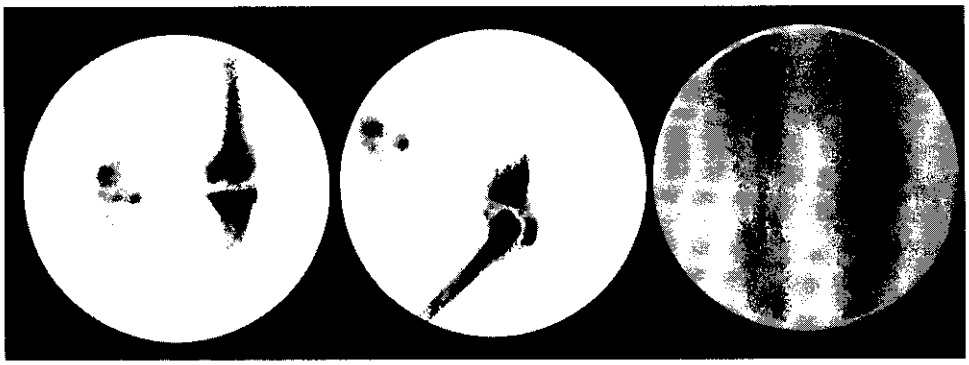

Figure 3. Technetium-99 bone scan and indium-labelled leukocyte scan demonstrating uptake around both components of the infected TKA shown in Fig. 2.

tively (215). False-positive results with this method occurred more than a year after implantation. Technetium-labeled leukocyte scintigraphy has also been studied and is more specific, but less sensitive than 3-phase technetium bone scintigraphy (61). Further study of the clinical utility of fluorine-18-FDG positron emission tomography scanning in the diagnosis of prosthetic joint infection is warranted (117). The advantages and disadvantages of available scintigraphic imaging techniques have been extensively reviewed (29, 48, 87, 311). Computed tomography and magnetic resonance imaging are not routinely used to diagnose prosthetic joint infection because of the imaging artifacts caused by the metal prostheses (40, 197).

Microbiological Studies

Optimal antimicrobial therapy depends on identifying the specific etiologic microorganism(s) and antimicrobial susceptibility testing. Adequate deep culture specimen collection and handling, preferably without recent antimicrobial pretreatment, are therefore essential. Multiple positive cultures, either from aspiration or from intraoperatively obtained tissue, are diagnostic and in our experience provide the single most useful diagnostic and therapeutic information. Cultures of drainage from sinus tracts do not reliably identify the etiologic microorganism(s) (184).

Recently, the usefulness of a single positive culture from a joint aspiration for the diagnosis of total hip arthroplasty infection was reviewed (287). The reported sensitivity and specificity of joint aspiration in the studies reviewed by Spangehl et al. ranged from 50 to 93% and 82 to 97%, respectively. Results are similar for joint aspiration prior to revision total knee arthroplasty, but fewer studies are available (19). This wide range of results was attributed to different definitions of a positive and negative result, the number of samples taken during aspiration, the inclusion of results of repeat aspiration in some studies, and the unrecognized or unreported use of antibiotics prior to aspiration. Recent antibiotic treatment may cause false-negative culture results, and re-aspiration, after antibiotics have been discontinued, increases sensitivity (19). Spangehl et al., in a recent prospective study of 180 aspirations prior to revision hip replacement in which the prior use of antibiotics was excluded, found the sensitivity and specificity of aspiration for the diagnosis

of prosthetic joint infection to be 86% (95% CI, 63 to 96%) and 94% (95% CI, 89 to 97%) (287).

Surveillance cultures (that is, cultures obtained intraoperatively when there is no clinical suspicion of infection) have very low predictive value in the setting of primary arthroplasties (D. R. Osmon, J. M. Steckelberg, B. S. P. Ang, A. D. Hanssen, and W. R. Wilson, 31st Intersci. Conf. Antimicrob. Agents Chemother., 1991). The predictive value of a single positive surveillance culture, when multiple intraoperative specimens have been sent for culture at the time of revision arthroplasty for a failed prosthesis, is unknown; such a result requires careful correlation with the clinical context (16, 222). A recent prospective study by Atkins et al. (16) of 253 total hip and 44 total knee revisions in 297 patients in which there were 41 prosthetic joint infections based on histologic criteria found that the highest post-test probability of prosthetic joint infection (96.4%) was achieved when 3 or more specimens yielded the same organism. The post-test probability for infection when one of many intraoperative specimens was positive was only 10.6%. In contrast, the post-test probability of infection for a single positive culture was higher (33%) when the culture was obtained from a prosthesis that failed within 2 years of implantation.

Because of the critical importance of making a microbiological diagnosis, in most nonacute cases antimicrobial therapy should be withheld until all aspirate and/or intraoperative specimens for culture have been obtained from the joint. If antimicrobial therapy has already been started, it should be stopped when possible for 10 to 14 days prior to any diagnostic procedure, to avoid false-negative culture results. As much fluid as possible should be obtained for culture at the time of diagnostic joint aspiration. If sterile saline is used for aspiration, a nonbacteriostatic formulation should be used.

Intraoperative cultures should include tissue from the bone-cement interface, if possible, as well as samples of any purulence or sequestrum that may be present (251). Furthermore, when prosthesis debridement or removal is performed, the surgeon should obtain multiple tissue samples. Because of an increased risk of surgical site infection if perioperative prophylactic antibiotics are withheld until after incision time in clean orthopedic surgery, prophylactic antibiotics should be given routinely at the time of revision arthroplasty unless there is a high index of suspicion of prosthetic joint infection preoperatively. If there is a high index of suspicion of prosthetic joint infection at the time of revision arthroplasty, prophylactic antibiotics should be held until after culture ascertainment to avoid false-negative culture results. One recent report suggests that transport in anaerobic conditions, ultrasonication, and culture of the entire prosthesis result in increased detection of microorganisms (301). All microbiological specimens should be sent promptly to the microbiology laboratory and processed as recently reviewed (116).

The clinical significance of detecting bacterial DNA using molecular techniques such as polymerase chain reaction, when there is no other evidence of prosthetic joint infection, remains unknown (189). Concern has been raised about false-positive results due to amplification of background *E. coli* DNA present in test reagents (130). However, when specific primers designed not to hybridize and amplify background *E. coli* DNA were used to evaluate 63 patients who had undergone revision total hip arthroplasty in which the prevalence of prosthetic joint infection was 17%, the sensitivity and specificity of polymerase chain reaction compared with conventional culture techniques were 71 and 49%, respectively. We agree with Hoeffel et al. that additional research is needed before molecular diagnostic techniques will become useful in the diagnosis of prosthetic joint infection.

We suggest routinely obtaining specimens to culture for aerobic and anaerobic bacteria in suspected prosthetic joint infection, unless the causative organism is already known at the time of specimen collection. Intraoperative Gram stains are not useful for the diagnosis of prosthetic joint infection and therefore should not be routinely performed (16, 62, 287). When the history, physical examination, or intraoperative findings suggest the possibility of unusual infection, special culturing techniques for organisms such as fungi, mycobacteria, *S. aureus,* or *E. coli* small-colony variants (243, 260), or other unusual organisms may be required. Failure to obtain specimens for these cultures at the time of initial debridement may result in unnecessary procedures to obtain further culture material or, ultimately, treatment failure. The pathologist, although primarily looking for the presence or absence of acute inflammation suggestive of infection, may also find evidence of a specific type of inflammation (e.g., granulomas) that may provide a clue to the etiology of the infection. In this circumstance, it is useful to perform additional tissue stains for fungi or mycobacteria.

Once the microorganism responsible for the infection has been identified, antimicrobial susceptibility tests should be performed (66, 208, 209). An MIC obtained by broth or agar dilution is the best guide to therapy (66). Some investigators have suggested that the minimal bactericidal concentration (MBC) of bacteria adherent to prostheses may be higher than those reflected by standard testing (110, 210). When only disk-diffusion (Kirby-Bauer disk) sensitivities are available, antimicrobial agents with intermediate or resistant results should not be used. Some investigators also advocate determining a serum bactericidal titer (SBT) (312, 320). However, the results of these tests are difficult to consistently reproduce within and among laboratories, and we do not advocate their use (66).

PATHOLOGY

Frozen Section

For patients undergoing revision total joint arthroplasty, pathological examination of intraoperative frozen sections is useful in selected cases to detect infection. The amount of acute inflammation in submitted specimens that provides the best combination of sensitivity, specificity, and positive and negative predictive value remains controversial (15, 91, 92, 180, 196, 221, 226). The presence of acute inflammation (more than 5 neutrophils per high-power field) has a sensitivity for infection of 82 to 84%, and a specificity of 93 to 96% (180, 221). The positive predictive values were 70 to 82% (180, 221). The use of a higher cut-off (10 neutrophils per high-power field) increased specificity and increased the positive predictive value to 89% (180). The negative predictive value with either cut-off was 98% (180). Other investigators have suggested that $\leq$1 neutrophil per high-power field after examination of at least 10 high-power fields is highly suggestive of prosthetic joint infection (226). Pathologists performing intraoperative frozen sections should be experienced in preparing and interpreting specimens since substantial interobserver variation among pathologists who are less experienced in interpreting tissue obtained from failed prosthetic joints has been reported (287).

MANAGEMENT

There are no adequately designed, randomized, controlled, prospective trials with sufficient follow-up comparing different combinations of medical and surgical alternatives for

the treatment of infected joint arthroplasties. Nonetheless, a number of medical and surgical approaches have been described. Surgical management and medical decisions about the duration and intensity of antimicrobial management are closely related. The optimal, but not always attainable, goal of treatment is a pain-free, functional joint with satisfactory mobility. Eradication of infection is often the most direct method of achieving this goal, but in selected cases, chronic antimicrobial suppression may be an appropriate alternative. Basic treatment options that have been proposed include, in addition to chronic suppressive antimicrobial therapy, surgical debridement with retention of the prosthesis, resection arthroplasty, arthrodesis, one- or two-stage reimplantation, and amputation. Antimicrobial agents may be delivered locally via antibiotic-impregnated polymethylmethacrylate, as well as systemically.

Treatment Options

Suppressive Antimicrobial Therapy

Antimicrobial therapy without concomitant surgical intervention is not considered standard therapy for prosthetic joint infection. In one study of 25 patients, no patient had a satisfactory functional outcome after a mean of 1.3 years of follow-up (146); another study found that only 3 of 13 prostheses were retained after a mean of 37.6 months among patients treated with chronic antimicrobial suppression (299). Success, defined as suppression of symptoms and maintenance of a functioning joint, is greater with carefully selected patients (108), especially when suppression can be combined with initial debridement. Chronic antimicrobial suppression might be contemplated when (i) removal of the prosthesis is not feasible, (ii) the microorganism is of low virulence and highly susceptible to orally administered antimicrobial agents, (iii) there are no signs of systemic infection, (iv) the patient is compliant and tolerant of the antimicrobial agent, and (v) the prosthesis is not already loose (44, 108, 252). The oral antibiotic used for chronic suppression should be chosen based on susceptibility test results, long-term tolerability, and cost (263).

Surgical Debridement with Retention of the Prosthesis

Historically, attempts to salvage a prosthesis by debridement and aggressive initial antibiotic therapy have generally been disappointing, with relapse rates as high as 77 to 88% by 2 to 4 years (274, 318). Infection with *S. aureus* or gram-negative organisms, late onset, and chronicity of infection (longer than 2 to 3 weeks) appear to be particularly poor prognostic indicators. Recently, reports have suggested that with careful patient selection, this method may salvage some prostheses, especially when infection is fulminant, it occurs early after prosthesis implantation, and/or debridement can occur within 24 to 36 hours (37, 41, 47, 52, 70, 77, 78, 125, 156, 198, 252, 274, 279, 290, 296, 298, 314, 330). Rifampin-containing combination regimens or chronic antibiotic suppression may be advantageous against implant-associated infections due to susceptible staphylococci (77, 78, 279, 314, 330). In a recent, randomized blinded placebo-controlled study that included 33 patients with both prosthetic joints ($n = 15$) and fracture fixation devices ($n = 18$), among the 24 patients who completed the study according to protocol, those patients who received a combination of ciprofloxacin and rifampin ($n = 12$) for 3 to 6 months were significantly less likely to relapse after a median follow-up of 35 months (range, 24 to 36 months) than patients who received a combination of placebo and ciprofloxacin ($n = 12$) (0 versus 42%; $P < 0.05$) (330). All patients were symptomatic

less than 3 weeks, had stable implants, and received initial therapy with intravenous flucloxacillin or vancomycin plus rifampin or placebo for 2 weeks. Twenty-eight percent (5 of 18 patients) in the rifampin-containing group developed adverse events related to rifampin.

Prosthesis Removal

To consistently achieve a microbiological cure in prosthetic joint infection, it is necessary to remove the prosthesis and all associated cement and completely debride devitalized tissue and bone. Options after resection arthroplasty depend on the joint site and include arthrodesis or one- or two-stage reimplantation arthroplasty.

Resection arthroplasty. Prior to the development of techniques that allowed successful reimplantation of an infected prosthesis, resection arthroplasty was the traditional therapeutic modality used to treat infected prostheses. The procedure involves complete removal of the infected prosthesis and any associated cement, as well as infected bone or synovial tissue, and the administration of intravenous antibiotics for 4 to 6 weeks.

Resection arthroplasty results in successful eradication of infection in 58 to 100% of cases of THA infection (Table 3) (4, 29, 34, 39, 53, 54, 57, 64, 74, 109, 153, 188, 192, 236, 272). Microbiological cure seems to correlate with the extent of debridement and the thoroughness of removal of the residual methylmethacrylate cement (54). After resection arthroplasty, hip function is often severely compromised. This limits the procedure's usefulness (109, 153, 236). For THA infection, this procedure is currently recommended only in situations in which exchange arthroplasty is not feasible—for example, patients who have major bone loss due to infection or prior surgery, nonambulatory patients, patients with recurrent infections, and patients with infections due to organisms for which effective antimicrobial therapy is unavailable (104).

Less information is available regarding the utility of resection arthroplasty as definitive

Table 3. Success of resection arthroplasty for the treatment of THA infection

Author (yr published)	Reference	No. of THA infections	No. (%) without recurrent infection	Follow-up (yr) (range [mean])
Clegg (1977)	64	30	24 (80)	1–6 (N/A)[a]
Mallory (1978)	188	10	10 (100)	3–5 (N/A)[a]
Campbell (1978)	53	45	33 (71)	≥0.5 (2.2)
Petty (1980)	236	21	16 (76)	1–8 (2.8)
Ahlgren (1990)	4	19	11 (58)	1–5.7 (3.3)
Bittar (1982)	29	14	11 (79)	0.17–4 (1.5)
Canner (1984)	54	33	27 (82)	0.5–9 (4.1)
McElwaine (1984)	192	22	18 (82)	1.2–9 (N/A)[a]
Bourne (1984)	39	33	32 (97)	3–13 (6.2)
Kantor (1986)	153	41	24 (59)	1–10 (3.9)
Grauer (1989)	109	33	30 (91)	2–10.5 (3.8)
Bohler (1991)	34	20	18 (92)	1–7.3 (3.9)
de Laat (1991)	74	23	22 (96)	2–15 (4.9)
Scalvi (1995)	272	27	26 (96)	1–20 (6.8)
Castellanos (1998)	57	78	67 (86)	(5)
Total		449	369 (82)	

[a] N/A, not available.

surgical therapy for TKA infection (38, 89, 156, 200). Falahee et al. reported that 89% of 28 TKAs were free of infection 6 months after the procedure (89). Three knees continued to have chronic drainage for up to 9 years. The mean length of antimicrobial therapy was 7.5 months. Fifteen (54%) patients walked independently following the procedure; six (21%) patients were unsatisfied with the procedure and elected to undergo arthrodesis. Resection knee arthroplasty is most often used for patients who have minimal ambulatory demands or who, because of poor bone stock or some other technical reason, are unable to undergo arthrodesis or reimplantation (247).

Arthrodesis. Until exchange arthroplasty was found to be a viable alternative, arthrodesis was the therapy of choice for TKA infection. A successful arthrodesis outcome depends on the ability to achieve adequate healthy bone apposition (159, 247). Thus, patients with large hinged knee prostheses, which sacrifice large amounts of bone, or patients who have had multiple revisions will have a decreased chance of a successful arthrodesis (46). Bone grafting can sometimes be performed in these situations (160).

The two surgical techniques most often utilized to provide a stable arthrodesis are implant removal with subsequent external fixation by use of a multiplaner external fixator (200, 250) or prosthesis removal with delayed internal fixation with an intramedullary nail (38, 84, 160, 245). Other techniques that have been reported to be effective but for which there is less experience are immediate external fixation with an intramedullary nail or fixation with a vascularized rotatatory graft (163, 254). The advantages and disadvantages of these procedures have recently been reviewed (247). External fixation is recommended in cases of active TKA infection, although an intramedullary nail can be used as part of a two-stage procedure (160).

Arthrodesis is associated with prolonged periods of immobility. Time to achieve union can range from 2.5 to 22 months (46, 79). Success rates vary considerably from study to study, likely because of differences in operative technique, patient population, and length of follow-up. In one recent study with a mean 3.8-year follow-up period, Morrey et al. reported a 70% efficacy of arthrodesis in 43 selected patients (200). There was evidence of recurrence of infection in two (6%) patients who had achieved union. Despite adequate fusion, 9% of patients experienced residual pain after the arthrodesis.

Arthrodesis is often the treatment of choice for TKA infection when patient mobility is important and reimplantation of a prosthesis is not feasible for technical reasons (247). When arthrodesis is the surgical therapy of choice, we recommend 4 to 6 weeks of parenteral antimicrobial therapy (223). In some instances, further oral antimicrobial therapy may be useful. This aggressive approach is dictated by the goal of achieving a microbiological cure and is used because persistent infection is a serious cause of arthrodesis failure (250).

One- or two-stage reimplantation. The best functional results in the treatment of prosthetic joint infection have been achieved with reimplantation of a new prosthesis (101, 104, 247). Unfortunately, no randomized prospective studies compare the various reimplantation regimens utilized by different investigators. Thus, the clinician is left to compare the published results of various case series to determine the optimal approach to reimplantation for any given patient. Because case series often differ in patient population, surgical technique, duration and type of antimicrobial therapy, length and thoroughness of follow-up, and definition of an unsuccessful outcome (reinfection with a different organ-

ism, relapse of the original organism, reinfection and relapse, or a painful joint), these comparisons can sometimes be difficult.

Issues about reimplantation that remain controversial include the optimal time between resection and reimplantation, the role of antibiotic-impregnated cement, the need for antibiotic-impregnated polymethylmethacrylate spacers in two-stage reimplantation, the optimal type and duration of administration of intravenous and oral antimicrobial agents, and the feasibility of a second attempt at reimplantation if the first attempt results in reinfection. Although several authors in recent years have reviewed the issues of time to reimplantation and the in vitro characteristics and clinical usefulness of antibiotic-impregnated polymethylmethacrylate (80, 101, 112, 185, 191, 247, 297, 321), relatively little attention has been paid to the optimal type and duration of parenteral therapy needed to eradicate prosthetic joint infection (42, 191, 264, 320).

THA infection. Surgical options that have been evaluated most extensively include one- and two-stage exchange arthroplasty. One-stage exchange arthroplasty involves removal of the infected prosthesis and associated cement, debridement of all devitalized tissue and bone, and immediate reimplantation of a second prosthesis during the same procedure. Success rates with variable lengths of follow-up have ranged from 38 to 100% (Table 4) (49, 54, 56, 60, 85, 133, 152, 195, 201, 202, 204, 255–257, 264, 270, 298, 302,

Table 4. Success of one-step exchange arthroplasty for THA infection

Author (yr published)	Reference	No. of THA infections	No. (%) without recurrent infection	Follow-up (yr) (range [mean])
Without antibiotic-impregnated cement				
Jupiter (1981)	152	17	14 (82)	2–6 (3.7)
Salvati (1982)	264	32	29 (91)	6–10 (N/A)[a]
Miley (1982)	195	101	94 (92)	≥2.7 (N/A)[a]
Cherney (1983)	60	5	4 (80)	3.0–7.25 (6.0)
Canner (1984)	54	5	4 (80)	0.5–9 (4.1)
Wilson (1989)	317	7	6 (86)	2–5 (3.4)
Morscher (1990)	201	47	27 (57)	1.0–6.0 (7.6)
Total		214	178 (83)	–
With antibiotic-impregnated cement				
Carlsson (1978)	56	59	54 (91)	≥0.5 (N/A)[a]
Murray (1981)	204	13	5 (38)	N/A (N/A)[a]
Buchholz (1984)	49	825	645 (78)	≥2 (N/A)[a]
Wroblewski (1986)	323	102	93 (91)	2.2–5.2 (2.2)
Sanzen (1988)	270	72	55 (76)	2–9.75 (6.0)
Hope (1989)	133	72	63 (87)	0.4–10 (3.75)
Raut (1994)	256	57	49 (86)	2.0–12.6 (7.3)
Raut (1995)	257	183	154 (84)	2.0–8.7 (7.75)
Raut (1996)	255	13	13 (100)	1.0–13 (8.0)
Mulcahy[b] (1996)	202	15	15 (100)	2.0–7.0 (4.4)
Ure (1998)	303	20	20 (100)	3.5–17.1 (9.9)
Elson (1994)	85	235	209 (89)	2–12 (N/A)[a]
Total		1666	1375 (83)	
Positive intraoperative culture				
Tsukayama (1996)	298	31	28 (90)	0.5–8.6 (3.5)

[a] N/A, not available.
[b] Number with antibiotic-impregnated cement not known.

303, 317, 323). Most investigators have used antibiotic-impregnated cement, most often with gentamicin or tabramycin, in combination with intravenous and oral antimicrobial therapy based on in vitro susceptibility testing. The duration of systemic antimicrobial therapy has been extremely variable (49, 54, 56, 60, 133, 152, 195, 204, 264, 270, 302, 323). One-stage exchange procedures that are inadvertent and result from diagnosis of prosthetic joint infection after revision for presumed aseptic loosening are most often due to coagulase-negative staphylococci and have a good prognosis (Table 4) (298). Six weeks of directed parenteral antimicrobial therapy without chronic oral antimicrobial therapy was utilized in this study.

Two-stage exchange arthroplasty involves at least two separate operations. The first operation is a standard resection arthroplasty. Four to six weeks of intravenous antimicrobial agents, chosen on the basis of in vitro susceptibility testing, are then usually administered (42, 191, 219, 264). Use of antibiotic-impregnated spacers to manage dead space and allow easier mobility prior to reimplantation is becoming more common (100, 123, 133, 135, 169, 270, 327, 328). Some investigators also use oral antimicrobial therapy for several weeks after the conclusion of intravenous therapy. Following a variable period of time, typically 3 to 6 months but ranging from weeks to several years, a new prosthesis is reimplanted. Antibiotic-impregnated cement may or may not be utilized with the reimplanted joint. Success rates have varied from 53 to 100% with variable lengths of follow-up (Table 5) (27, 56, 60, 90, 100, 123, 133, 135, 137, 138, 164, 169, 174, 191, 204, 205, 264, 270, 298, 309, 317, 327, 328). The use of implantable pumps to deliver local antimicrobial therapy has also been reported (230).

In one early, small study involving 82 infected THAs reimplanted using a two-stage technique without antibiotic-impregnated cement, McDonald et al. (191) investigated factors associated with recurrence of infection. Variables studied included presence of retained cement after resection arthroplasty, reconstruction less than 1 year after resection arthroplasty, intravenous antimicrobial therapy for less than 28 days, and infection due to aerobic gram-negative bacilli or enterococci. In univariate analysis, all factors were significant. In the multivariate analysis, only reimplantation within 1 year of resection arthroplasty was statistically significant, although the statistical power was limited.

Reinfection following reimplantation arthroplasty for THA infection leads to permanent prosthesis removal in the majority of cases (223). The final outcome of 34 THA infections following reinfection after reimplantation for prosthetic joint infection in a recent study was 21 hips with a resection arthroplasty, 8 hips with a retained prosthesis on chronic antibiotic suppression, 4 well-functioning arthroplasties, and 1 hip disarticulation. Of the 11 patients who had an attempt at reimplantation of another prosthesis, 3 of 5 (60%) undergoing two-stage exchange and 1 of 6 (17%) undergoing one-stage exchange were successful.

TKA infection. Most investigators have favored delayed two-stage exchange arthroplasty with reimplantation 4 to 6 weeks after joint resection for the treatment of established TKA infection (106, 247, 320). Reasons for this opinion have included the relatively low probability of microbiological cure with immediate and early (less than 3 weeks) reimplantation (Table 6) and the lack of a satisfactory functional outcome reported by some authors after early reimplantation (116, 249). Additionally, staged reimplantation provides the opportunity to perform multiple debridements and to identify the responsible microorganisms in order to direct antimicrobial therapy prior to reimplantation (247).

Table 5. Success of two-stage exchange arthroplasty for THA infection

Author (yr published)	Reference	No. of THA infections	No. (%) without recurrent infection	Follow-up (yr) (range [mean])
Without antibiotic impregnated cement				
Hunter (1979)	138	49	26 (53)	≥0.5
Hughes (1979)	137	13	10 (77)	2.7–6.9 (4.3)
Salvati (1982)	264	18	18 (100)	2.0–6.0 (4)
Cherney (1983)	60	28	19 (68)	0.17–7 (4.1)
McDonald (1989)	191	82	71 (87)	2–13 (5.5)
Wilson (1989)	317	22	20 (91)	2–5 (3.3)
Berry (1991)	27	17	15 (88)	2.0–8.1 (4.2)
Lieberman (1994)	174	17	15 (88)	2.0–6.0 (3.3)
Total		246	194 (79)	
With antibiotic-impregnated cement				
Carlsson (1978)	56	77	69 (90)	0.5–3.5 (N/A)
Murray (1981)	204	22	21 (96)	1–20 (N/A)[a]
Murray (1984)	205	51	47 (92)	N/A[a]
Lieberman (1994)	174	15	14 (93)	2.0–6.2 (3.3)
Wang (1997)	309	22	21 (96)	1.0–20.0 (N/A)[a]
Total		187	172 (92)	
With antibiotic-impregnated cement plus antibiotic-impregnated spacers or beads				
Hovelius (1979)	135	3	3 (100)	0.5–1.5 (1.2)
Sanzen (1988)	270	30	22 (73)	2–9.75 (6)
Hope (1989)	133	8	8 (100)	0.17–8 (1.75)
Harle (1989)	123	76	69 (91)	≥2
Elson (1994)	85	61	58 (95)	2–12 (N/A)[a]
Garvin (1994)	100	16	16 (100)	2–10 (5)
Younger (1997)	328	48	45 (93)	2.0–5.25 (3.6)
Younger (1998)	327	28	27 (96)	2.0–9.3 (3.9)
Leunig[b] (1998)	169	12	12 (100)	2.2[a]
Total		282	260 (92)	
Uncemented prosthesis				
Tsakuyama (1996)	298	24	22 (92)	1.3–11.0 (4.2)
Lai (1996)	164	39	34 (87)	2.0–5.7 (4.0)
Fehring (1999)	90	25	23 (92)	2.0–8.2 (3.4)
Total		88	79 (90)	

[a] N/A, not available.
[b] No. with antibiotic-impregnated cement is unknown.

Investigators have used various surgical techniques when reporting their results of delayed two-stage exchange arthroplasty. The use of antibiotic-impregnated polymethylmethacrylate cement and spacers, as well as the time to reimplantation, has varied from series to series (Table 6). The overall success rate combining the results of numerous series is 88% (Table 6) (24, 30, 36–38, 51, 98, 105, 106, 115, 121, 129, 131, 141, 143, 200, 213, 249, 261, 277, 296, 307, 308, 310, 315, 318, 320, 322). In one recent retrospective study of 89 TKA infections in which there was an 11% reinfection rate, the use of antibiotic cement at the time of reimplantation arthroplasty was the only variable analyzed that significantly improved the reinfection rate (121). However, definitive recommendations

Table 6. Success of various surgical procedures of TKA infection

Author (yr published)	Reference	No. of TKA infections	No. (%) without recurrent infection	Follow-up (yr) (range [mean])	Wk to reimplantation (range [mean])
One-state exchange procedures					
Freeman (1985)	98	8	8 (100)	1–3.3 (N/A)[a]	0[b]
Bengston (1986)	21	8	2 (25)	1.1–9.7 (5)	0[b]
Borden (1987)	37	3	3 (100)	2.5–4.5 (3.5)	0[b]
Teeny (1990)	296	1	1 (100)	>2 (N/A)[a]	0[c]
Buechel (1990)	51	12	11 (92)	0.17–9.1 (6.1)	0[b]
Goksan (1992)	105	18	16 (89)	1–10 (5.0)	0
Scott (1993)	277	10	7 (70)	N/A[a]	0
Total		60	48 (80)		
Two-stage reimplantation					
Early reimplant (<3 weeks)					
Rand (1983)	249	14	8 (57)	2–4.7 (3.3)	<2[c]
Grogan (1986)	115	2	2 (100)	6.6–8.1 (7.3)	<3[c]
Total		16	10 (63)		
Without antibiotic cement					
Nelson (1982)	213	5	5 (100)	N/A[a] (N/A)[a]	N/A[a] (6)
Insall (1983)	141	11	10 (91)	2.8 (1–6)	5.4–11.7 (6)
Woods (1983)	322	3	3 (100)	N/A[a] (N/A)[a]	12–24 (N/A)[a]
Walker (1984)	307	11	9 (82)	2.7–7.4 (4.5)	2–114 (38.3)
Morrey (1989)	200	15	8 (53)	1–10 (8.0)	2–114 (N/A)[a]
Jacobs (1989)	143	7	7 (100)	2–4.17 (3)	N/A[a] (6)
Wilson (1990)	318	12	11 (92)	2–5 (2.8)	6–24 (12)
Teeny (1990)	296	9	9 (100)	2–6 (3.5)	4–>12 (N/A)[a]
Windsor (1990)	320	29	26 (90)	2.5–6 (4)	6–11 (7.14)
Goldman[d] (1996)	106	64	58 (91)	2–17.0 (7.5)	6–26.3 (8.0)
Wasielewski[e] (1996)	310	50	44 (92)	2.0–10.3 (5.2)	3–12 (N/A)[a]
Total		216	190 (88)		
With antibiotic cement					
Bliss (1985)	30	5	4 (80)	0.75–3 (1.6)	>6 (N/A)[a]
Rosenberg (1988)	261	24	24 (100)	1–5.8 (2.5)	6–8 (6)
Wilson (1990)	318	8	5 (63)	2–5 (2.8)	6–24 (12)
Total		37	33 (89)		
Antibiotic cement plus antibiotic-impregnated spacers or beads					
Bengston (1986)	21	5	3 (60)	1.1–9.7 (5)	4–8 (N/A)[a]
Borden (1987)	37	18	17 (100)	>1 (N/A)[a]	N/A (3)
Wilde (1988)	315	10	9 (90)	1–4.7 (2.6)	3–12 (6)
Booth (1989)	36	25	24 (96)	0.5–5 (2)	3–204 (16)
Scott (1993)	277	7	7 (100)	N/A[a]	N/A[a]
Hanssen[f] (1994)	121	89	79 (89)	0.5–10.5 (4.3)	0–18.7 (5.5)
Hofmann (1995)	131	25	25 (100)	1.0–5.8 (2.6)	2.1–39.3 (11.7)
Bose (1995)	(38)	6	6 (100)	2.0–8.0 (4.3)	4–6 (N/A)[a]
Wang (1997)	308	7	7 (100)	1.0–5.75 (2.3)	4–12 (N/A)[a]
Hirakawa (1998)	129	54	40 (75)	2.3–12.2 (5.2)	(N/A)[a] 6
Total		246	217 (88)		

[a] N/A, not available.
[b] Antibiotic-impregnated cement used.
[c] No antibiotic-impregnated cement used.
[d] Seven patients with antibiotic-impregnated spacer.
[e] Fourteen patients with antibiotic-impregnated spacer.
[f] Sixty-four (72%) patients with antibiotic-impregnated cement; 50 (56%) patients with antibiotic-impregnated spacer or beads; 18 patients implanted within 3 weeks of resection arthroplasty.