Use of Antibiotic-Impregnated Cement in Total Joint Arthroplasty

Thomas N. Joseph, MD, Andrew L. Chen, MD, and Paul E. Di Cesare, MD

Abstract

The use of antibiotic-impregnated cement in revision of total hip arthroplasty procedures is widespread, and a substantial body of evidence demonstrates its efficacy in infection prevention and treatment. However, it is not clear that it is necessary or desirable as a routine means of prophylaxis in primary total joint arthroplasty. In the management of infected implant sites, antibiotic-impregnated cement used in one-stage exchange arthroplasties has lowered reinfection rates. In two-stage procedures, use of beads and either articulating or nonarticulating antibiotic-impregnated cement spacers also has lowered reinfection rates. In addition, spacers reduce “dead space,” help stabilize the limb, and facilitate reimplantation. Problems associated with antibiotic-impregnated cement in total joint arthroplasty include weakening of the cement and the generation of antibiotic-resistant bacteria in infected implant sites.


In 1970, Buchholz and Engelbrecht introduced the concept of impregnating acrylic bone cement with antibiotic as a possible means of preventing infection in patients undergoing total joint arthroplasty. Since then, antibiotic-impregnated cement has become more commonly used for revision total joint arthroplasty and, as antibiotic-impregnated cement spacers or beads, for treatment of infection during two-stage revision arthroplasty than it has for infection prophylaxis in primary total joint arthroplasty. Even without the contribution of antibiotic-impregnated cement, the infection rate after standard primary total joint arthroplasty in modern operating rooms has been reduced to between 0.3% and 2%. A survey from 1995 concerning orthopaedic operating room practices and equipment suggested that this reduction has been achieved by the access to laminar airflow (present in 49% of hospital operating rooms), body exhaust suits (in 69%), high airflow (in 85%), and ultraviolet lights (in 14%).

Reported infection rates after revision total joint arthroplasty vary widely because of the large number of patient variables.

Several types of acrylic bone cement in current use incorporate antibiotics, either premixed by the manufacturer or added by the surgeon in the operating room. In the United States, commonly used cements such as Palacos (Smith & Nephew, Memphis, TN), Simplex (Howmedica, Rutherford, NJ), CMW (DePuy, Warsaw, IN), and Zimmer (Zimmer, Warsaw, IN) are mixed with antibiotics by the surgeon. Commercially prepared admixtures such as AKZ (Simplex P with colistin and erythromycin), Refobacin-Palacos R (Palacos R with gentamicin cement), and Septopal (beads of Palacos R with gentamicin) are not currently available in the United States. Some hospital pharmacies (2.2%) prepackage cement with antibiotic for later use in the operating room.

A survey of 1,015 orthopaedic surgeons in the continental United States revealed that 56% have impregnated their bone cement with antibiotic for at least some cases. Surveys specializing in joint reconstruction were more likely to use antibiotic in bone cement (88%). Sixty-five percent of all surgeons surveyed reported that they adjusted antibiotic usage according to microbial sensitivity; of this group, 70% used tobramycin; 26%, gentamicin; 18%, vancomycin; 15%, cephalosporins; and 3%, combined antibiotics. Antibiotics in liquid

Dr. Joseph is resident, Department of Orthopaedic Surgery, Musculoskeletal Research Center, NYU–Hospital for Joint Diseases, New York, NY. Dr. Chen is resident, Department of Orthopaedic Surgery, Musculoskeletal Research Center, NYU–Hospital for Joint Diseases, New York. Dr. Di Cesare is Associate Professor of Orthopaedic Surgery, Department of Orthopaedic Surgery, Musculoskeletal Research Center, NYU–Hospital for Joint Diseases, New York.

Reprint requests: Dr. Di Cesare, 15th Floor, 301 East 17th Street, New York, NY 10003.

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form, generally considered to be less desirable than the powdered form (because of the effects to cement polymerization), were used by as many as 11% of the surgeons surveyed, possibly because of the general unavailability of a powdered form of gentamicin in the United States. In performing primary arthroplasties, approximately 12% of surgeons always used antibiotic-impregnated cement, 69% never used it, and 19% used it sometimes. Of those who did use it, 68% did so in less than one third of their aseptic revision total joint arthroplasties. However, over 80% used it more than two thirds of the time in septic revision total joint arthroplasty. Over half often used antibiotic-impregnated cement beads in two-stage reimplantation for infections; 32% often used antibiotic-impregnated cement spacers in hips; and 69% often used such spacers in knees. Of those using antibiotic-impregnated cement, 28% used a single-stage reimplantation in total joint arthroplasty infection, while 72% used a two-stage approach. These data suggest that no commonly accepted standard exists regarding the use of antibiotic-impregnated cement in orthopaedic surgery.

The FDA takes no official position on the use of antibiotics in cement. A document issued July 17, 2002, requires that cement labeling contain the warning, “PMMA bone cement is contraindicated in the presence of active or incompletely treated infection, at the site where the bone cement is to be applied.”

**Laboratory Studies**

A number of criteria must be met for antibiotics to be effective when mixed with methyImethacrylate. The preparation must be sufficiently thermally stable to withstand the heat of polymerization. The antibiotic must not be adversely affected by body temperature and must be water soluble so that it can diffuse into surrounding tissues. The antibiotic must have a bactericidal effect at the tissue levels attained; furthermore, it must be released gradually over an appropriate time period. The preparation must evoke minimal local inflammatory or allergic reaction. Development of resistance should be rare to nonexistent; common pathogens must be considered, including *Staphylococcus aureus*, *S epidermidis*, coliform, and others, such as anaerobes. Finally, the antibiotic must not significantly compromise mechanical integrity, especially if the cement is used for implant fixation.

In vitro analyses of antibiotic elution and mechanical stability have been done with a variety of antibiotic-cement combinations. The stable incorporation of aminoglycoside antibiotics (eg, gentamicin and tobramycin) into cement and their elution therefrom are well established. Vancomycin is gaining popularity because of its effectiveness against methicillin-resistant bacteria as well as its general availability. Although penicillins and cephalosporins exhibit adequate elution and stability, they are often avoided because of their potential allergenicity. In one study, in vitro testing of vancomycin- and tobramycin-impregnated cement demonstrated elution of antibiotic for the entire 9-week study period; the highest elution rate occurred at 18 hours (between 3 and 5 times the rate that occurred at 72 hours). Ciprofloxacin, a more recent addition to bone cement, may gain in popularity because of its wide antibiotic spectrum and general availability. Ciprofloxacin elution met or exceeded the minimum inhibitory concentration for common organisms associated with osteomyelitis for up to 42 days. Recent studies indicate that ciprofloxacin may inhibit bone, ligament, and soft-tissue healing; this is a concern, particularly in total knee revision surgery.

Lipids may impede the leaching process from cement. The peptide antibiotics vancomycin and polymyxin B nonapeptide have been shown to elute for a longer period than do the nonpeptide antibiotics gentamicin, novobiocin, and erythromycin. Molecular weight also appears to play a role. One in vitro study indicated that vancomycin is eluted 10 times less efficiently than tobramycin from antibiotic-impregnated cement, probably because of its higher molecular weight. Other in vitro studies, however, found no marked difference between the two.

Palacos cement appears to provide the best elution profile for most antibiotics. A study of the elution characteristics of Palacos and CMW acrylic cements showed that CMW 1 released 24% less tobramycin and 36% less vancomycin than did Palacos; CMW 3 released 34% less tobramycin and 38% less vancomycin. Another in vitro study, in which Palacos and Simplex beads and spacers were impregnated with 4 g of either vancomycin or tobramycin in 40 g of cement, also showed antibiotic eluting from Palacos at higher levels. Concentrations remained above the minimum inhibitory concentration for *S aureus* longer in Palacos than in Simplex. In another study, elution of vancomycin, daptomycin, and amikacin from Palacos exceeded that of Simplex, Zimmer Dough-Type, and Zimmer LVC.

Commercially prepared antibiotic cement may be superior to intraoperatively mixed cement. Elution of gentamicin and tobramycin from laboratory-customized Zimmer, Simplex, or Palacos beads compared with elution from commercially prepared gentamicin-PMMA (Septopal) beads showed that more total antibiotic was eluted from the latter, and was maintained at higher con-
centrations, than it was in the beads to which antibiotics were added by the investigators.14

The results of studies of the effect on elution of combinations of antibiotics, typically vancomycin and tobramycin, are inconclusive. In one study, elution of vancomycin was minimally affected by tobramycin, while elution of tobramycin was reduced by vancomycin.10 In another study, the elution rate of tobramycin increased by 68% and that of vancomycin by 103% when these antibiotics were combined.15 In the first study,10 vacuum-mixed Simplex was used, and in the second,15 nonvacuum-mixed Palacos. In both, the most advanced means of measuring antibiotic were used. An in vivo study using the prosthesis of antibiotic-loaded acrylic cement (PROSTALAC; Smith & Nephew, Memphis, TN) demonstrated a statistically significant (P = 0.011) increase in the elution of vancomycin when the dose of tobramycin was increased from 2.4 to 3.6 g per dose of cement; Simplex was used in 12 patients and Palacos in 37.16 The investigators changed the cement early in their study after finding evidence in the literature suggesting better antibiotic elution from Palacos.

Klekamp et al10 demonstrated that compressive and fatigue strength decreased with the addition of vancomycin or tobramycin to cement. Cement impregnated with 1, 2, or 3 g of vancomycin failed at 90%, 70%, and 50%, respectively, of the number of cycles to failure for antibiotic-free cement. Likewise, cement with 1.2 and 2.4 g of tobramycin failed at 80% and 60%, respectively, of the number of cycles to failure for controls. Although fatigue strength data were statistically significant (P < 0.05), the results of compressive strength tests demonstrated a decreasing trend yet were not statistically significant. Routinely used lyophilized vancomycin was found to greatly reduce cement fatigue strength. The authors suggested using vancomycin P (an ultrafine powder) in bone cement intended for prosthesis fixation because it has less detrimental effect on cement strength. Askew et al17 found that the addition of 1 g of either tobramycin or vancomycin resulted in nominal bending strength reductions (6% and 1%, respectively, compared with controls). Another study confirmed that the addition of 1.2 g of tobramycin to 40 g of Simplex powder did not significantly decrease fatigue strength.18 Vancomycin L (lyophilized) should be finely ground when used for prosthesis fixation to prevent mechanical weakening; however, large crystals should not be completely pulverized when preparing beads or spacers because the crystals facilitate antibiotic elution.

Morita and Aritomi19 showed no reduction in tension and bending strengths of cefuzonam-impregnated cement when <3 g was used. Earlier studies showed similar results with respect to compressive and tension strengths of cement impregnated with gentamicin, oxacillin, and cefazolin.20 Addition of more than 4.5 g of gentamicin has been shown to substantially weaken cement to a level below that appropriate for implant fixation.21 Reduction of no more than 10% in bone cement strength is considered acceptable for use in total joint arthroplasty fixation; however, weaker antibiotic-impregnated cement may be used in beads and spacers. Table 1 lists appropriate doses of antibiotic impregnation in cement for prosthesis fixation and for spacers and beads.

Vacuum mixing, which reduces the number of voids in bone cement, improves the mechanical properties of antibiotic-impregnated cement. When cylindrical cement-vancomycin specimens were subjected to fatigue testing (uniaxial mode), cycles to failure were 15% to 58% greater in vacuum-mixed specimens than in those mixed at atmospheric pressure. Fracture of antibiotic-impregnated cement specimens during cyclic testing was reduced up to tenfold with vacuum mixing or with vigorous pulverizing of the antibiotic before mixing.10 Another study showed vacuum mixing also reduced fivefold the radiographically apparent porosity of antibiotic-impregnated cement specimens but may inhibit antibiotic release.17

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose for Prosthesis Fixation</th>
<th>Dose for Spacers and Beads</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>1 g</td>
<td>2 g</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>NR</td>
<td>4 to 8 g</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>3 g</td>
<td>NR</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>1.5 to 3 g</td>
<td>NR</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>NR</td>
<td>4 to 8 g</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0.5 to 1 g</td>
<td>NR</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>1 g</td>
<td>2 to 5 g</td>
</tr>
<tr>
<td>Ticarcillin</td>
<td>Not appropriate</td>
<td>5 to 13 g</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>1.2 g</td>
<td>2.4 to 9.6 g</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1 g (vancomycin P)</td>
<td>3 to 9 g (vancomycin P or L)</td>
</tr>
</tbody>
</table>

P = ultrafine powder, L = lyophilized, NR = not reported in the literature.
one study, vancomycin vacuum-mixed with Simplex (1:40 ratio) released slightly less than half the antibiotic that air-mixed cement did; no antibiotic release was detectable after 48 hours.\textsuperscript{13} Another study, however, found adequate antibacterial activity lasting for 21 days.\textsuperscript{17}

Dextran has been used to enhance porosity and thus improve the elution of antibiotic. One preparation with dextran released approximately 4 times as much antibiotic as did a dextran-free preparation, and elution remained detectable for 10 days versus 7 days, respectively.\textsuperscript{13} However, dextran degrades the mechanical properties of cement; therefore, its use for prosthetic fixation should be extremely limited. Centrifugation, another preparation technique, markedly increased the fatigue life of Simplex both with and without tobramycin by a factor of eight.

Increase in the surface area of antibiotic-impregnated cement spacers has been shown to increase elution of antibiotic in vitro. Holtom et al\textsuperscript{22} demonstrated that fenestrated spacers with a 40% greater surface area resulted in a 20% higher elution rate of vancomycin from Palacos cement than from standard or donut-shaped spacers. Masri et al\textsuperscript{23} demonstrated a significant ($P = 0.05$) increase in the elution of tobramycin over 1 week with the use of Simplex-impregnated blocks that had a 9% increased surface area-to-volume ratio.

Antibiotics in liquid form mixed with cement dilute the catalyst that is needed for the cement curing process, thereby adversely affecting both the curing time and final mechanical properties of cement; accordingly, they are not recommended. Table 2 lists antibiotics that can be mixed with cement.

**In Vivo Studies**

The penetration of antibiotics released from antibiotic-impregnated cement into surrounding tissues has been evaluated in both animal and human studies. Concentrations of antibiotic in hematoma, granulation tissue, and bone vary according to antibiotic. Local concentrations, however, have been found to be consistently higher than serum concentrations and usually exceed the minimum inhibitory concentrations for target pathogens.

The elution of several antibiotics from Simplex cement was measured in samples from dogs over a 28-day period.\textsuperscript{24} Clindamycin, vancomycin, and tobramycin exhibited elution characteristics that reached consistently high levels in bone and granulation tissue. Cefazolin and ciprofloxacin were maintained at high concentrations in granulation tissue but at low levels in seroma and bone. Ticarcillin showed unfavorable elution characteristics in granulation tissue, seroma, and bone.

Experimentally produced paraspinous wounds (fractured, infected spinous processes) in rabbits were treated with either a chain of tobramycin antibiotic-impregnated cement beads, beads without antibiotics, systemic antibiotics only, or nothing.\textsuperscript{25} At 5 days, no recoverable organisms were found in six of eight animals treated with antibiotic-impregnated cement beads. Six of eight rabbits receiving systemic tobramycin had wound infections. All five animals in which nonantibiotic-impregnated cement beads were implanted had significant infections; one died from sepsis. All four animals that received no treatment were infected.

Antibiotic concentrations were measured in wound drainage fluid, urine, and serum from 50 patients who underwent primary total hip arthroplasty (THA) and received tobramycin or vancomycin delivered either in antibiotic-impregnated cement or by intravenous administration (not both).\textsuperscript{26} No significant differences were found between

<table>
<thead>
<tr>
<th>Antibiotics Used in Antibiotic-Impregnated Cement</th>
<th>Decreased Activity Because of Cement Heat</th>
<th>Adversely Affected by Cement Curing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can Be Mixed With Cement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>Cefuzonam</td>
<td>Penicillin</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Cephalothin</td>
<td>Polymyxin B</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Ciprofloxacin (powder)</td>
<td>Streptomycin</td>
</tr>
<tr>
<td>Bacitracin</td>
<td>Clindamycin (powder)</td>
<td>Ticarcillin</td>
</tr>
<tr>
<td>Cefamandole (powder)</td>
<td>Lincomycin</td>
<td>Tetracycline</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>Methicillin</td>
<td>Colistimethate</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>Colistin</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td></td>
<td>Daptomycin</td>
<td>Colistinmethate</td>
</tr>
<tr>
<td></td>
<td>Oxacillin</td>
<td>Tetracycline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liquid gentamicin, clindamycin, etc</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(because of aqueous content)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rifampin</td>
</tr>
</tbody>
</table>

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**Table 2**

Antibiotics Used in Antibiotic-Impregnated Cement

*Thomas N. Joseph, MD, et al*
Simplex and Palacos surgeon-prepared antibiotic-impregnated cement. Serum and urine antibiotic levels were significantly ($P \leq 0.05$) higher in the intravenous group than in the impregnated-cement group. Wound drainage fluid levels of tobramycin were significantly ($P \leq 0.05$) higher in the antibiotic-impregnated cement group than in the intravenous group, whereas the vancomycin intravenous group had higher antibiotic levels in wound drainage fluid than did the vancomycin cement group. In the cement group, tobramycin exhibited a consistently high level of bioactivity against *S. epidermidis* in wound drainage fluid, while vancomycin lost all bioactivity by 24 hours. In 30% of cases, no vancomycin was detected in the wound drainage fluid of the cement group. Overall, tobramycin exhibited adequate local tissue levels and released antibiotic effectively, whereas vancomycin exhibited inadequate elution properties.

**Clinical Studies**

**Primary Total Joint Arthroplasty**

Because of the low rates of infection experienced with total joint arthroplasty procedures, researchers seeking to demonstrate statistically significant differences with the prophylactic use of antibiotic-impregnated cement require a very large sample size with multicenter participation. A prospective, randomized study in Sweden combined results from nine orthopaedics departments (1,688 consecutive THAs) to compare the prophylactic effect of systemic antibiotics to that of gentamicin-impregnated cement alone. At a mean follow-up of 10 years, the infection rate was 1.6% in the systemic antibiotic group and 1.1% in the gentamicin-impregnated cement group, a difference that was not statistically significant.11 No cases of nephrotoxicity, ototoxicity, or allergic reaction were reported.

More than 10,000 primary cemented total hip replacements done for osteoarthritis and reported to the Norwegian arthroplasty registry were studied retrospectively.27 Four groups were compared: patients receiving antibiotic prophylaxis both systemically and locally in antibiotic-impregnated cement, those receiving antibiotics only systemically, those receiving only antibiotic-impregnated cement, and those receiving no antibiotic prophylaxis. The antibiotic-impregnated cement was either Palacos with gentamicin or AKZ (erythromycin and colistin with Simplex). The rate of revision done for any reason was 2.0% (94/4,586) in patients receiving only systemic antibiotics, 4.2% (10/239) for antibiotic-impregnated cement only, 1.2% (70/5,804) for the combined regimen, and 2.5% (7/276) for no antibiotics. Among cases that subsequently required revision for infection, the lowest revision rate, 0.14% (8/5,804), was in patients who received both antibiotic-impregnated cement and systemic antibiotics.

A prospective, randomized clinical trial of 401 patients in two British centers compared the effect of cefuroxime-impregnated cement and cefuroxime administered systemically on infection after total joint arthroplasty.28 No statistically significant difference was found between the two groups with respect to incidence of superficial wound infection or early deep infection (1% in both groups). There were no late deep infections after 2-year follow-up.

Hope et al29 found at least one strain of gentamicin-resistant coagulase-negative staphylococcus in 30 of 34 cases of deep infection (88%) in which cement containing gentamicin had been used. In contrast, only 9 of 57 patients (16%) in whom antibiotic-free cement was used exhibited gentamicin-resistant coagulate-negative staphylococcus.

**Revision Arthroplasty**

Revision arthroplasty usually is accompanied by rates of infection significantly higher than rates for primary arthroplasty. Revision arthroplasties done for infection are either one- or two-stage procedures. Two-stage revisions are more common, but they can be technically demanding because of scar formation, limb shortening, disuse osteoporosis, and altered anatomy. Although advocates of two-stage reimplantation cite infection rates lower than those of one-stage revisions, carefully selected patients can be treated with comparable success with one-stage revisions using antibiotic-impregnated cement. In one review of the literature, success rates of one-stage exchange with and without the use of antibiotic-impregnated cement were 81% and 71%, respectively; the success rates of two-stage reimplantation with and without antibiotic-impregnated cement were 93% and 82%.30

One-stage Revision for Infection

One-stage exchange arthroplasty using antibiotic-impregnated cement has been advocated in defined instances for the treatment of an infected total joint arthroplasty. In a multicenter comparison of one- and two-stage exchange arthroplasties for infection conducted in the 1970s, a success rate of approximately 80% was found for both methods.31 Gentamicin-loaded Palacos and 6 months of systemic antibiotics were used in all procedures. The results were slightly better for one-stage exchanges; however, follow-up was relatively short (0.5 to 3.5 years). In a study of 235 one-stage exchanges for THA infection using antibiotic-impregnated cement, 11% with persistent infection failed; another 3% of cases with suspected infection failed.32 Of the 61 two-stage exchanges, which used antibiotic-
impregnated cement beads for periods of from 6 weeks to 9 months, 5% failed from reinfection. Hope et al reviewed a series of 91 patients with deep infection of a cemented THA caused by coagulase-negative staphylococcus. In this series, 72 patients were treated with one-stage exchange arthroplasty; 9 (13%) failed because of recurrence of infection. Gentamicin was used in combination with other antibiotics based on organism sensitivities. The other 19 patients underwent a two-stage exchange without any failures.

Although it has been suggested that a contraindication to one-stage reimplantation is infection with a gram-negative organism, a study of 15 patients with gram-negative infection treated with one-stage THA revision found only 1 recurrence (6.7%) at a mean follow-up of 8 years. Palacos cement with gentamicin was used in 13 of 15 patients, with other antibiotics added to cement as appropriate. In a larger study of 183 patients with similar follow-up (mean, 7.75 years), one-stage revision with both antibiotic-impregnated cement and systemic antibiotics was used for deep infection of a THA. Twenty-nine of these patients (16%) had evidence of persistent infection and 154 (84%) were free of infection on follow-up. None of the 29 patients who experienced failure was infected with a gram-negative organism.

For patients undergoing revision arthroplasty, Garvin et al developed a classification system of high-risk, suspicious, and definite infection categories. These were based on Gram stains, cultures, intraoperative findings, clinical diagnoses, radiographic findings, and laboratory results. In a prospective clinical study, gentamicin-impregnated Palacos was used for prosthesis fixation in 67 high-risk, 32 suspicious, and 31 definite infections. All but one of the high-risk patients underwent one-stage procedures; those with suspicious or definite infections underwent either one- or two-stage procedures plus 6 weeks of intravenous antibiotics. Postoperative infection occurred in 5 of the 92 one-stage patients (5.4%) and in none of the 38 two-stage patients. Of the 67 high-risk patients, 3 (4.5%) developed postoperative infections; one was then revised with a successful two-stage procedure. Of the 32 patients suspicious for infection, 19 underwent one-stage implantation; one of them developed a postoperative infection. The other 13 patients with suspicious infection underwent successful two-stage implantation. Of patients with definite infection, 7 of 31 underwent one-stage implantation, with one of them developing a postoperative infection; 24 patients had a successful two-stage implantation.

To test that one-stage revisions can be successful if rigid criteria are met, Ure et al prospectively followed 20 consecutive patients undergoing one-stage THA for infection between 1979 and 1990. Surgical management included meticulous débridement, use of antibiotic-impregnated cement, and systemic antibiotic therapy. Patients were excluded from this treatment when they were immunocompromised, had an infection with a known resistant gram-negative or methicillin-resistant organism, or had a major skin, soft-tissue, or osseous defect. At a mean follow-up of 9.9 years, no patient had experienced recurrence of infection. Two patients required revision for aseptic loosening. Parenteral antibiotics were administered postoperatively for a mean of 4.7 months.

**Two-Stage Revision for Infection**

By reducing dead space, cement spacers help stabilize the limb awaiting reimplantation (Fig. 1). Complications include bone loss, dislocation, continued pain, decreased mobility, and (rarely) fracture. Local antibiotic delivery with cement spacers, cement beads, or a PROSTALAC has been used after component removal in a two-stage procedure. Additionally, antibiotic-impregnated cement can be used for prosthesis fixation during reimplantation in the second stage.

Antibiotic-impregnated cement spacers used in the first stage of two-stage reimplantation can deliver a high concentration of antibiotics to the infected area. In a retrospective study, Calton et al treated 25 infected total knee prostheses in 24 patients with débridement, component removal, and insertion of an antibiotic-impregnated cement block. Intravenous antibiotics were administered for 6 weeks; patients’ knees were kept immobilized with no weight bearing. The success rate was 92% (2 failures) at a mean follow-up of 36 months; 15 of 25 knees exhibited either tibial or femoral bone loss caused by invagination of the cement spacer block into the cancellous bone. Leunig et al reported on 12 patients with deep infections of hip implants who underwent two-stage revision and were treated using gentamicin-loaded cement. Spacers were used for a mean of 4 months; during that period, six spacers failed, five by dislocation and one by fracture. At a mean follow-up of 27 months after reimplantation arthroplasty, all patients were mobile and infection free.

An articulating spacer used in two-stage revision for infected total knee arthroplasty may improve patient mobility and allow partial weight bearing. This would promote healthier soft tissues, improve wound healing, allow easier reimplantation, improve bone quality and range of motion, and reduce complications. Hofmann et al treated 26 patients who had late-infected total knee arthroplasties with two-stage revision using an articulating spacer with tobramycin-
impregnated cement. The spacer was prepared by cleaning, autoclaving, and reinserting the femoral component. A new tibial polyethylene insert and in some cases a new all-polyethylene patellar component were used to place a large amount of antibiotic-impregnated cement between each insert and bone. Patients were treated with 6 weeks of intravenous antibiotic therapy. Reimplantation was performed 6 to 12 weeks after placement of the spacer. All but one patient (who died of systemic complications) underwent successful reimplantation (96%). At a mean follow-up of 31 months, knee scores had improved and no recurrence of infection was found.

Complications of early articulating spacers included tibiofemoral instability and patellar instability; results subsequently have improved with design modifications. A recent study by Fehring et al. failed to show any difference in range of motion or knee scores between articulating and static antibiotic-impregnated cement spacers used in two-stage revisions. The articulating spacers were custom-prepared using a stainless steel femoral component mold and stemmed tibial baseplate of antibiotic-impregnated cement. Nevertheless, reimplantation was facilitated, and less bone loss occurred with articulating spacers than with static antibiotic-impregnated spacers.

Lai et al. reported on 40 infected hip prostheses treated with component removal, intravenous and oral antibiotics for 8 weeks, and delayed reimplantation (mean, 48 weeks) with cementless components. At mean of 4 years’ follow-up, 5 patients (13%) had experienced recurrent infection: 2 of 33 from the group treated with Septopal (gentamicin) beads, and 3 of 6 of those treated without antibiotic-impregnated cement beads. A prospective, randomized, multicenter study of 6 infected total knee and 22 infected hip arthroplasties in 28 patients compared two-stage reimplantation using gentamicin-impregnated cement beads with that using conventional parenteral systemic antibiotic therapy for 6 weeks postoperatively. At a mean follow-up of 3 years, infection recurred in 2 of 15 patients treated with gentamicin-impregnated cement beads (13%) and in 4 of 13 patients treated with conventional systemic antibiotic therapy (31%); however, this was not statistically significant. Whiteside used allograft technique with cementless revision arthroplasty for massive tibial and femoral defects in 33 chronically infected total knee arthroplasties. Treatment included implant removal, débridement, and rigidly fixed antibiotic-soaked bone graft followed by 6 weeks of antibiotic-impregnated cement beads and intravenous antibiotics. The success rate of the two-stage procedure was 85%. Infection recurred in five knees; however, repeated procedures allowed successful revision in all but one, which required an above-the-knee amputation. Although use of antibiotic-impregnated cement beads or spacers is common in two-stage revisions, one study showed that their use in two-stage revisions was not correlated with cure rate for infection.

The PROSTALAC, introduced in 1989, is a temporary hip prosthesis composed of a thin polyethylene acetabular cup and a stainless steel femoral component, both of which are loosely cemented with antibiotic-impregnated cement (Fig. 2). Benefits include early mobilization, accelerated rehabilitation, and early hospital discharge. The device maintains soft-tissue planes and leg lengths and has made second-stage procedures easier to perform. Younger et al. reviewed 48 patients who had treatment.
undergone two-stage arthroplasty of an infected hip replacement using the PROSTALAC. All but three patients were free from persistent infection, for an eradication rate of 94%. More recently, Younger et al evaluated PROSTALACs with a cement-on-cement articulation and with a custom metal-on-polyethylene articulation. Of 28 infected total hips followed for a minimum of 2 years, 96% exhibited no evidence of infection.

In a retrospective study of 89 revision procedures for infected total knee arthroplasties, persistent infection occurred in 10 knees (11.2%).\(^\text{44}\) No standardized protocol was used for treatment. In 64 knees, antibiotic-impregnated cement was used for implant fixation; in 25, no antibiotic-impregnated cement was used. Antibiotic-impregnated beads were used in 20 patients, antibiotic-impregnated spacers in 23, both used in 4, and neither used in 42 patients. When use of antibiotic-impregnated cement for implant fixation was factored in, the results were statistically significant. Of the 25 knees without antibiotic-impregnated cement, 7 (28%) developed recurrent infection, compared with only 3 (5%) of the 64 knees treated with antibiotic-impregnated cement \( (P < 0.01). \) Although antibiotic-impregnated cement beads or spacers appeared to be beneficial, their use was not statistically significant. We are not aware of any prospective randomized study comparing antibiotic-impregnated cement beads or spacers to antibiotic-impregnated cement in prosthetic fixation.

**Antibiotics in Revision Arthroplasty Without Infection**

Although the use of antibiotic-impregnated cement in revision arthroplasty without evidence of infection has been advocated, the literature on the subject is scant and equivocal. Lynch et al\(^\text{47}\) reported notably better results with gentamicin-containing cement for aseptic revisions than with cement alone (systemic antibiotics not used), a reduction from 3.5% to 0.8%. A retrospective analysis with minimum 2-year follow-up reported that in aseptic revision THAs or conversion from upper femoral prosthesis (prophylactic systemic antibiotics not used), infection rates were 0.5% for gentamicin-impregnated cement and 2.8% for cement alone.\(^\text{47}\) The authors concluded that low-virulence organisms that are difficult to culture may be present in some cases thought to be aseptic loosening and that the local antibacterial effect is responsible for the effective prevention and treatment of infection in these patients.

**Experimental Cement-Antibiotic Combinations**

Ceramic composites have been considered for use as a vehicle for antibiotic delivery. In one laboratory study of a novel bioactive bone cement (15% bisphenol-\(\alpha\)-glycidyl methacrylate, 15% triethylene-glycol dimethacrylate resin, and 70% apatite- and wollastonite-containing glass-ceramic powder) containing cephalixin in the form of pellets, antibiotic release was initially rapid, slowed markedly after 24 hours, and was released continuously thereafter for 2 weeks.\(^\text{48}\) The strength of the cement with cephaloxin was approximately twice that of acrylic antibiotic-impregnated cement. The authors suggested that this material may be suitable for prosthetic fixation as well as in beads or spacers. Another study tested the efficacy of a calcium hydroxyapatite ceramic with gentamicin in the form of blocks implanted adjacent to stainless steel tibial inserts in rats that had been injected with \(S\) aureus.\(^\text{49}\) Suppression of infection in the ceramic-gentamicin–treated animals was superior to that in controls, including those in which acrylic antibiotic-impregnated cement was used.

Biodegradable antibiotic-impregnated material offers a potential means of local antibiotic delivery for infection control or treatment without obligation for later removal. A biodegradable cement (composed of tricalcium phosphate and calcium carbonate with a matrix phase of polypropylene fumarate cross-linked with methylmethacrylate monomer) containing gentamicin and vancomycin was evaluated for treatment and prophylaxis of \(S\) aureus osteomyelitis in rat proximal tibias.\(^\text{50}\) The treatment group exhibited significantly \( (P < 0.01) \) fewer colony-forming units than did controls. Sites treated prophylactically developed no infections. No significant difference was found between biodegradable cement and PMMA used as a carrier for antibiotics. Another study showed that the tensile strength of the material and the biologic activity of the antibiotic were maintained when gentamicin was added to a resorbable calcium phosphate cement composed of \(\beta\)-tricalcium phosphate, monocal-

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*Figure 2 Anteroposterior radiograph of the PROSTALAC in a two-stage revision THA.*
Antibiotic-Impregnated Cement in Total Joint Arthroplasty

Summary

Since its introduction in 1970, antibiotic-impregnated cement has been used in total joint arthroplasty in a variety of situations. In both one- and two-stage revision procedures for infection, antibiotic-impregnated cement clearly reduces the reinfection rate. The antibiotic should be chosen based on the infecting organism or, if preoperative cultures are unavailable, by assessment of likely pathogens. In two-stage procedures, the use of articulating spacers implanted with antibiotic-impregnated cement may improve reimplantation results as well as quality of life in the period between procedures. There is some suggestive evidence that if cement is to be used in apparently aseptic revision surgery cases, the cement should be antibiotic-impregnated because of the possibility that these culture-negative cases are indeed contaminated. Because of the low rate of infections with established perioperative and intraoperative protocols and the risk that using antibiotics will lead to the development of antibiotic-resistant bacteria, the routine use of antibiotic-impregnated cement appears to be unnecessary in primary total joint replacement surgery. The future of antibiotic-impregnated cements may include stronger composites with more sustained release of a wide array of antibiotics. Bioabsorbable antibiotic-impregnated cements may further reduce reinfection rates in one-stage procedures by supplying additional local delivery of antibiotic via materials that do not require later removal.

References

20. Marks KE, Nelson CL, Lautenschlager


