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J Bone Joint Surg Am. 2007;89:871-882. doi:10.2106/JBJS.E.01070

This information is current as of March 13, 2010

Supplementary Material <http://www.ejbjs.org/cgi/content/full/89/4/871/DC1>

Supplementary Material <http://www.ejbjs.org/cgi/content/full/89/4/871/DC2>

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Publisher Information The Journal of Bone and Joint Surgery
20 Pickering Street, Needham, MA 02492-3157
www.jbjs.org

CURRENT CONCEPTS REVIEW

Antibiotic-Impregnated Cement Spacers for the Treatment of Infection Associated with Total Hip or Knee Arthroplasty

By Quanjun Cui, MD, MS, William M. Mihalko, MD, PhD,
John S. Shields, MD, Michael Ries, MD, and Khaled J. Saleh, MD, MSc, FRCS(C)

- Infection at the site of a total joint arthroplasty can be classified into four basic categories: Type I (early post-operative), Type II (late chronic), Type III (acute hematogenous), and Type IV (positive intraoperative cultures with clinically unapparent infection).
- The current standard of care for late chronic infection is considered to be two-stage revision arthroplasty including removal of the prosthesis and cement, thorough débridement, placement of an antibiotic-impregnated cement spacer, a course of intravenous antibiotics, and a delayed second-stage revision arthroplasty.
- The choice of the spacer, either articulating or nonarticulating, is based on many factors, including the amount of bone loss, the condition of the soft tissues, the need for joint motion, the availability of prefabricated spacers or molding methods, and antibiotic selection.
- Current data have demonstrated that the use of antibiotic-impregnated cement spacers has improved the outcomes of the treatment of infection associated with total joint arthroplasty.

Total joint replacement is one of the most frequent and successful types of operations in orthopaedics. Infection is a rare yet devastating complication of the procedure, with a reported prevalence of 0.5% to 3% and with a higher reported prevalence after total knee arthroplasty than after total hip arthroplasty¹⁻⁴. There is also a higher rate of infection after revision hip and knee arthroplasties than after primary hip and knee arthroplasties¹⁻⁸.

Two-stage revision surgery was first described in 1983 by Insall et al., who demonstrated the necessity of removing the implants as well as the cement and of introducing antibiotic therapy for definitive treatment⁹. This procedure has emerged as the standard of care for a late chronic infection at the site of a total joint replacement^{4,5,10-17}. Garvin and Hanssen reviewed twenty-nine studies and found that two-stage pro-

cedures without antibiotic-loaded cement had a better success rate (82% of 158 joints) than one-stage exchange arthroplasties (58% of sixty joints), although systemic antibiotics were used for both procedures¹⁸. With the addition of antibiotic cement, the rates of successful eradication of the infection increased to 91% (385 of 423 joints) for the two-stage technique and 82% (976 of 1189 joints) for the one-stage revision¹⁸.

Two-stage revision arthroplasty without the use of spacers allows complete removal of foreign materials, with later reimplantation after eradication of the infection. However, this procedure has several disadvantages as soft-tissue contractures and joint instability may develop and the patient will have difficulty with mobility. From a technical perspective, the disadvantage of the procedure is that it makes reimplantation

Disclosure: In support of their research for or preparation of this work, one or more of the authors received, in any one year, fellowship funding in excess of \$10,000 from Smith and Nephew Inc. In addition, one or more of the authors or a member of his or her immediate family received, in any one year, payments or other benefits in excess of \$10,000 or a commitment or agreement to provide such benefits from a commercial entity (Stryker Orthopaedics). Also, a commercial entity (Smith and Nephew Inc.) paid or directed in any one year, or agreed to pay or direct, benefits in excess of \$10,000 to a research fund, foundation, division, center, clinical practice, or other charitable or nonprofit organization with which the authors, or a member of their immediate families, are affiliated or associated.

TABLE I Classification and Treatment of Infection at the Site of a Total Hip or Knee Arthroplasty

Type	Presentation	Definition	Treatment
I	Acute postoperative infection	Acute infection within 4 weeks after the operation	Débridement with retention of the prosthesis, intravenous antibiotics
II	Late chronic infection	Chronic indolent infection, ≥ 4 weeks after the operation	Two-stage revision
III	Acute hematogenous infection	Acute onset of infection at the site of a previously well-functioning joint replacement	Débridement with retention of the prosthesis, intravenous antibiotics
IV	Positive intraoperative culture	≥ 2 positive intraoperative cultures	A course of appropriate antibiotics

during the second-stage operation more difficult as a result of arthrofibrosis and the loss of tissue planes^{6,9,12}. Compared with revision total hip arthroplasty for treatment of aseptic loosening and compared with primary total hip arthroplasty, two-stage revision for the treatment of infection is associated with a lengthier hospital stay, an increased number of hospitalizations, and increased perioperative morbidity¹⁹⁻²¹.

Use of antibiotic-impregnated polymethylmethacrylate bone-cement spacers is now considered to be the standard of care for patients with a chronic infection at the site of a total joint replacement. These spacers provide direct local delivery of antibiotics while preserving patient mobility and facilitating reimplantation surgery¹⁻¹¹. This operative treatment decreases cost and improves patient outcomes as well as addresses some of the disadvantages of two-stage revision procedures in which spacers are not used^{1-12,14-17,19-42}. We will systematically review the various types of spacers and their uses in two-stage revision arthroplasty for treatment of infection at the site of a total joint replacement.

Classification of Infection at the Site of a Total Hip or Knee Arthroplasty

Infection at the site of a total joint arthroplasty can be classi-

fied into four basic categories: Type I (early postoperative), Type II (late chronic), Type III (acute hematogenous), and Type IV (positive intraoperative cultures with clinically unapparent infection) (Table I)^{11,16,43-47}. Specific operative modalities are recommended for eradication of each type of infection, although these recommendations are not universally followed.

Early postoperative infections (Type I), both superficial and deep, are defined as wound infections that occur less than four weeks after the primary operation. Superficial Type-I infections are typically treated with débridement and a course of antibiotic therapy, and deep Type-I infections are usually treated with replacement of the polyethylene insert, retention of the metal prosthetic components, and intravenous administration of antibiotics^{11,22,46,47}. Occasionally, antibiotic-loaded polymethylmethacrylate beads are also inserted^{2,11,47}.

Late chronic infections (Type II) are defined by their occurrence more than four weeks after the operation. They typically present with worsening pain and loosening of the prosthesis and are usually treated with a two-stage reconstruction. Treatment includes removal of all prosthetic components and bone cement, débridement of necrotic and granulation tissue, placement of an antibiotic-impregnated cement spacer,



Fig. 1-A



Fig. 1-B

Anteroposterior (Fig. 1-A) and lateral (Fig. 1-B) radiographs showing a nonarticulating knee spacer hand-made with antibiotic-loaded cement in a patient with a large bone defect and patellar tendon rupture after removal of total knee components because of infection.

administration of a course of intravenous antibiotics, and delayed reimplantation arthroplasty when there is no longer evidence of infection^{11,12,16,22,23,28,44}. It is important to note that one-stage exchange arthroplasty also has been used, more commonly in Europe than in the United States, but strict patient selection and use of antibiotic-loaded cement for fixation of the prosthesis are strongly recommended^{1,2,48,49}.

Acute hematogenous infections (Type III) are defined by bacteremia and are typically managed with débridement, replacement of the polyethylene insert, and retention of the prosthesis if there is no implant loosening, followed by a course of intravenous antibiotics^{11,43-47}.

Patients with positive intraoperative cultures (Type IV) within days after the performance of a revision arthroplasty for the treatment of aseptic loosening are typically managed with a course of intravenous antibiotics with retention of the prosthesis^{11,16,43-47}.

Classification of Antibiotic-Impregnated Cement Spacers

There are two types of antibiotic-impregnated cement spacers that are typically used in two-stage revisions of total hip and knee arthroplasties: nonarticulating (block or static; Figs. 1-A

and 1-B) and articulating (mobile; Figs. 2-A through 3).

Nonarticulating spacers allow local delivery of a high concentration of antibiotics and at the same time function to maintain joint space for future revision procedures. Their disadvantages include a limited range of motion of the joint after the operation, resulting in quadriceps or abductor shortening, scar formation, and bone loss. Cohen et al.⁵⁰ and Wilde and Ruth⁵¹ reported the use of nonarticulating spacers that consisted of polymethylmethacrylate cement mixed with antibiotics and were shaped to fit the defect that had been left after the removal of a total joint prosthesis associated with infection.

In contrast, articulating spacers permit more joint motion and can improve function prior to the second-stage reimplantation. From a technical perspective, improved joint function and decreased scar formation after resection arthroplasty can facilitate exposure during reimplantation^{4,17,52}. Although the distinction between articulating and non-articulating spacers is somewhat controversial, use of a well-molded, well-fitted articulating spacer that restores soft-tissue tension and allows a greater degree of joint motion has been reported to have a better outcome than use of a nonarticulating spacer, which may limit joint freedom^{4,5,26}.



Fig. 2-A



Fig. 2-B



Fig. 2-C

Fig. 2-A Radiograph showing a total hip prosthesis associated with an infection. **Fig. 2-B** Intraoperative photograph of an articulating hip spacer hand-made with use of antibiotic-loaded polymethylmethacrylate bone cement with a Rush pin for reinforcement. **Fig. 2-C** Postoperative radiograph showing the hand-made articulating hip spacer in the same patient after removal of the total hip components that were associated with infection.

As stated earlier, antibiotic-impregnated cement spacers can maintain limb length, minimize soft-tissue contraction, facilitate reimplantation, and provide local antibiotic therapy. However, there is considerable variation in their form and function^{12,16,17,23,33,53}. A spacer may be commercially made, or it may be custom-made in the operating room. It may be made entirely of polymethylmethacrylate cement, or it may be a cement-coated metal composite or a sterile prosthesis partially coated with antibiotic-impregnated cement. Favorable results have been reported with each of these types of spacers^{2-8,10,17,27,29,33,36,38,42,52,54,55}.

Knee Spacers

The first nonarticulating knee spacers (Figs. 1-A and 1-B) were made with antibiotic-loaded cement in the operating room and were formed to fill the bone defect left after removal of a prosthesis associated with infection. Use of these types of spacers has yielded inferior results, in terms of postoperative range of motion and pain, compared with those following single-stage aseptic revisions performed because of aseptic loosening^{6,7,26,28,56}.

A number of different types of articulating spacers can be employed in the two-stage revision of a total knee arthroplasty that was complicated by infection. One commercially available system is the prosthesis of antibiotic-loaded acrylic cement (PROSTALAC) (DePuy, Warsaw, Indiana), which was originally developed for the hip and was subsequently used in the knee^{6,57}. The PROSTALAC knee system includes femoral and tibial components made of antibiotic-loaded Palacos bone cement with a small metal-on-polyethylene articular surface (Fig. 3). In a study of forty-five patients followed for an average of forty-eight months (range, twenty to 112 months) after treatment with the PROSTALAC prosthesis, Haddad et al.⁶ reported eradication of the infection in forty-one patients (91%) despite the use of the metal and polyethylene components during the first stage of the two-stage procedure. The PROSTALAC system provided an increased range of motion, minimized pain, improved function, and facilitated the second-stage procedure by maintaining soft-tissue planes^{6,17,41}.

The cost of a knee revision due to infection is twice that of an aseptic revision and three to four times that of a primary total knee replacement, with most of the increased cost due to the prolonged and repeated hospitalization⁶. While articulating spacers reduce the amount of time spent in the hospital, the cost of the PROSTALAC system, which requires an entire system of molds and instrumentation, may prohibit its use. Also, the PROSTALAC system offers a limited choice of sizes, and development of cheaper and more customizable alternatives may be beneficial.

Hofmann et al.¹² used high-dose antibiotic-impregnated polymethylmethacrylate bone cement (4.8 g of tobramycin per 40 g of cement) in an articulating spacer in fifty patients during the first stage of a two-staged procedure. The spacer was created intraoperatively by cleaning, autoclaving, and reinserting the removed femoral component, which ar-

ticulated with a new thin tibial polyethylene insert with a large amount of antibiotic-loaded cement placed between the tibial polyethylene and the bone; occasionally, a new patellar polyethylene insert was used as well. Care was taken to apply the cement early to the components and late to the bone to allow molding to the defects without adherence and interdigitation. At an average of seventy-three months (range, twenty-four to 150 months) after the reimplantation procedure (the second stage), the rate of good to excellent results was 90%, with only six of the fifty patients having a reinfection. Emerson et al.²⁶ achieved similar results using the model described by Hofmann et al. They compared twenty-six patients treated with a nonarticulating spacer (average duration of follow-up, 7.5 years) with twenty-two treated with an articulating spacer (average duration of follow-up, 3.8 years) and found a 9% reinfection rate in the patients with the articulating spacer compared with an 8% rate in those with a nonarticulating spacer. However, the range of motion of the joints with an articulating spacer was an average of 14° greater.



Fig. 3

The PROSTALAC knee system, a commercially available knee spacer, has femoral and tibial components made of antibiotic-loaded Palacos bone cement with a small metal-on-polyethylene articular surface.

Hip Spacers

As is the case for total knee arthroplasties complicated by infection, two-stage revision arthroplasty is the standard of care when total hip arthroplasties are complicated by infection^{4,5,11,14,27,33,38,42}. A PROSTALAC hip system is also commercially available. It consists of a snap-fit all-polyethylene, loosely cemented acetabular component with a metal endoskeleton, a femoral head, and a centralizer that are inserted into a mold and filled with antibiotic-impregnated cement to create the implant (Fig. 4)^{17,34,41,58,59}.

Wentworth et al.⁴¹ reported success in 83% of 116 patients treated with the PROSTALAC prosthesis. Successful treatment was defined as no growth of a microorganism on culture of any specimen obtained from the operative site at the time of the second-stage operation. Younger et al.⁸ had better results with the PROSTALAC system, with the infection eradicated in 94% (forty-five) of forty-eight patients at an average of forty-three months (range, twenty-four to sixty-three months) postoperatively. The disadvantages of this system include cost, the need for special equipment, and the limited choices with regard to the sizes of the components.

Etienne et al.²⁷ described a method to construct a prosthesis similar to the PROSTALAC system but at a lower cost. They used a spacer consisting of either the removed, autoclaved femoral component or an inexpensive modular femoral component coated with a mantle of antibiotic-loaded cement. A polyethylene acetabular liner was cemented in place with the same antibiotic-impregnated cement, so that the system temporarily functioned like a conventional total hip prosthesis. Etienne et al. reported a reinfection in only three of thirty-two patients at a mean of 1.7 years (range, one to three years) postoperatively, and they noted quick component assembly, low cost, a good range of motion, and the possibility for partial weight-bearing, which facilitated revision surgery.

Specially designed reusable silicone or metal molds have been fabricated as temporary articulating spacer endoprostheses, with a metal endoskeleton for support^{4,10,42}. Durbhakula et al.⁴ used a Rush pin as the endoskeleton and reported no reinfections in twenty patients followed for an average of thirty-eight months (range, twenty-six to sixty-seven months); eighteen patients had a successful two-stage revision. Yamamoto et al.⁴² used two 2.0-mm bent Kirschner wires as the endoskeleton and also reported good results, with eradication of the infection in all of seventeen patients followed for a mean of three years and two months (range, fourteen to sixty-two months); however, there was one periprosthetic fracture and one dislocation.

Antibiotics in Polymethylmethacrylate Spacers

Implantation of antibiotic-loaded polymethylmethacrylate bone cement has become a useful technique in the treatment of infections at the sites of total joint arthroplasties (see Appendix). Spacers formed with use of antibiotic-loaded cement deliver high doses of antibiotics at the site of the infection and can achieve local concentrations higher than those achieved

with systemic antibiotics alone, with little effect on serum or urine levels^{12,34,39,60,61}. Because they achieve high concentrations of antibiotics at the site of an infection, spacers can be used to treat infected avascular bone that is isolated from systemic antibiotics while avoiding the potential systemic toxicity that can result from intravenous use^{2,11,16,39,43,61}.

Choice of Antibiotics

The choice of antibiotics is limited to those that are thermostable, as the polymerization of cement is an exothermic reaction that generates a substantial amount of heat³¹. The antibiotic also must be water-soluble, to permit diffusion into surrounding tissues while allowing a gradual release over time for a sustained bactericidal effect². The most commonly used antibiotics include tobramycin, gentamicin, vancomycin, and cephalosporins. These can be combined to provide broad-spectrum coverage^{2,61}. Most periprosthetic infections involve gram-positive organisms (*Staphylococcus aureus* and *Staphylococcus epidermidis*), and when the pathogen and antibiotic



Fig. 4

The PROSTALAC hip system consists of a snap-fit all-polyethylene cemented acetabular component with a metal endoskeleton, a femoral head, and a centralizer that are inserted into a mold and filled with antibiotic-impregnated cement to create the implant.

sensitivity are clearly identifiable one antibiotic should be used³¹. When the pathogen is unknown, treatment becomes more difficult, and a combination of antibiotics may be required to completely eradicate the infection. In the study by Koo et al.³¹, with an average duration of follow-up of forty-one months (minimum, twenty-four months), infection was eradicated in twenty-one of twenty-two patients treated with 2 g each of vancomycin, gentamicin, and cefotaxime per 40 g of cement. The vancomycin covers methicillin-resistant *Staphylococcus aureus*, the gentamicin covers Enterobacteriaceae and *Pseudomonas aeruginosa*, and the cefotaxime kills gentamicin-resistant organisms. It is important to keep in mind that, if antibiotic-loaded cement had been used for the primary procedure, bacteria involved in the infection may have already survived a high concentration of that antibiotic and will likely be resistant if the same antibiotic is used in the spacer cement⁶².

Fungal infections are extremely rare at the sites of total joint arthroplasties and are difficult to treat. In most reported cases, the offending organism has been a member of the *Candida* species^{28,63,64}. An in vitro analysis of antifungal-impregnated polymethylmethacrylate bone cement showed that amphotericin B and fluconazole remained active with zones of inhibition, while 5-flucytosine did not⁶⁵. Fungal infection at the site of a total joint arthroplasty has been treated successfully with antibiotic-impregnated polymethylmethacrylate bone-cement spacers and staged reimplantation^{28,63,66,67}.

Factors Affecting Elution of Antibiotics from Polymethylmethacrylate Spacers

The elution of antibiotics from bone cement depends on several factors. The type of antibiotic, the amount and number of antibiotics, the porosity and type of cement, and the surface area of the spacer all play a role in the release^{4,5,11,34,68}. Stevens et al.⁴⁰ studied the in vitro elution of antibiotics from Simplex and Palacos bone cements and found Palacos to be a more effective vehicle for local drug delivery. In a study of the long-term elution of antibiotics from polymethylmethacrylate bone cement in vivo in forty patients, Masri et al.³⁴ found that effective levels of antibiotics remained four months after the operation. This observation is consistent with the suggestion that at least 3.6 g of tobramycin per 40 g of bone cement, with the addition of 1 g of vancomycin, is an effective antibiotic regimen in this setting. With effective levels of vancomycin not present four months after the operation, Masri et al. determined that the two antibiotics acted synergistically with one another to increase the elution rates but vancomycin should not be used alone. This finding was consistent with the results of an in vitro study that showed that combining tobramycin and vancomycin in polymethylmethacrylate bone cement improved the elution rates of both antibiotics⁶⁹.

Compared with commercially available antibiotic-loaded cement, hand-mixed cement is associated with a decreased release of antibiotics, whereas vacuum-mixing has been shown to result in only a minor reduction in antibiotic release⁷⁰⁻⁷⁴. Unlike antibiotics that are commercially mixed in

cement, hand-mixed antibiotics do not have a homogeneous distribution in the cement, which decreases their rate of elution from a given surface area^{70,71,73}. Vacuum-mixing decreases the porosity of the cement, which also decreases the rate of elution of the antibiotics⁷¹. The elution of antibiotics from polymethylmethacrylate bone cement is determined by a combination of surface area and porosity^{60,71,73}. One study showed that increasing the surface area of polymethylmethacrylate bone cement by 40% resulted in a 20% higher rate of elution of vancomycin⁶⁸. Dextran has been added to cement to enhance porosity and increase antibiotic elution rates. Kuechle et al. found that the addition of 25% dextran to cement increased the release of antibiotics in the first forty-eight hours approximately four times compared with that associated with routine preparation and increased the duration of the elution to up to ten days compared with only six days with routine preparation⁷⁵.

For decades, hand-made polymethylmethacrylate bone-cement spacers containing high doses of antibiotics have been used successfully in the treatment of established infections at the sites of prosthetic joints, and they can release high levels of antibiotics locally¹⁻¹¹. It is important to note that the Food and Drug Administration has approved commercial production of only low-dose antibiotic-loaded bone cements. These include Simplex P (Stryker Howmedica Osteonics, Mahwah, New Jersey), which contains 1 g of tobramycin; SmartSet GHV and MHV (DePuy Orthopaedics, Warsaw, Indiana), which contain 1 g of gentamicin; and Palacos G (Biomet, Warsaw, Indiana), which contains 0.85 g of gentamicin^{28,60,61}. These low-dose antibiotic-loaded cements are not suitable for treatment of established infections at the sites of prosthetic joints, although they may be used prophylactically for high-risk patients undergoing a total knee or hip arthroplasty with cement or in the second stage of a two-stage revision total joint arthroplasty after the initial infection has been eradicated^{11,31,60,61}. Therefore, surgeons need to add antibiotics to the cement in order to achieve the high doses suggested for the treatment of periprosthetic joint infection^{2,18,34,61}.

Method for Mixing Antibiotic-Impregnated Cement

Hanssen and Spanghel⁶¹ proposed a method for adding high doses of antibiotic powder to bone cement. The polymethylmethacrylate monomer and powder must first be mixed together to form the liquid cement, and then the antibiotic is added. It is important to leave as many large crystals intact as possible to create a more porous mixture to increase the antibiotic elution rate. The opposite is true when cement with prophylactic antibiotics is used for prosthetic fixation, as the crystals also weaken the cement. Once the cement is formed, care should be taken when it is applied to bone. Cement should be applied in the late stage of polymerization to prevent interdigitation into bone while still allowing the surgeon some freedom to shape the articular surface of the bone^{12,29}. Tapered cement dowels for intramedullary insertion may be fashioned with use of the nozzle of a cement gun as a mold or simply by rolling the cement by hand⁶¹.

Changes in Biomechanical Properties

Because the inclusion of antibiotics produces additional defects in the cement matrix, the ingredients and the mixing of the cement in the operating room play a role in the antibiotic release rate and the mechanical properties of the spacer^{58,61}. The addition of high doses of antibiotics (>4.5 g of powder) substantially weakens bone cement, and such cements should not be used for prosthetic fixation⁵⁸. Liquid antibiotics are typically not used as they have been shown to decrease cement strength, as compared with that associated with their crystalline counterparts, as a result of the dilution of the catalyst needed for cement curing^{2,76,77}. Seldes et al.⁷⁷ found that the addition of liquid gentamicin to antibiotic-free cement decreased compressive strength by 49% and decreased tensile strength by 46% whereas the addition of powdered tobramycin had no significant effect as compared with control values. In one study, hand-mixing of antibiotics into bone cement decreased the strength of the cement by 36% as compared with that of commercially prepared antibiotic-loaded bone cement, while the strength of the commercial antibiotic-loaded cement was no different from that of the antibiotic-free cement⁷⁸. Vacuum-mixing of antibiotic-impregnated bone cement improves its mechanical properties by decreasing porosity^{75,79}, and, while it was shown to decrease the rate of fractures during cyclic loading by up to tenfold⁷⁹ and to decrease the apparent porosity on radiographs by up to fivefold⁸⁰, it may also decrease antibiotic elution rates⁷⁵.

Antibiotic Doses for Polymethylmethacrylate Spacers

The proper dosage of a specific antibiotic to be used in polymethylmethacrylate bone cement for the treatment of an established infection at the site of a prosthetic joint is not yet standardized, although impregnation of cement with two antibiotics has proven to be superior to the use of a single antibiotic^{61,81}. In the literature, doses of the most commonly used antibiotics range from 2.4 g of tobramycin with 1 g of vancomycin per 40 g of cement to 4 g of vancomycin with 4.6 g of tobramycin per 40 g of cement. All of these doses have been associated with similar repeated success rates of >90%^{4,7,28}. As the amount of antibiotic powder introduced is increased, the strength of the cement is reduced^{58,61}. It has been reported that 8 g of antibiotics per 40 g of bone cement is the highest ratio that can be introduced and still allow the cement to be molded and formed¹⁰.

In one study, Fehring et al.²² observed effective results with the use of 1.2 g of tobramycin per 40 g of bone cement alone. The average duration of follow-up was thirty-six months (range, twenty-four to seventy-two months) for the patients who received a static spacer and twenty-seven months (range, twenty-four to thirty-six months) for those treated with an articulating spacer. Three patients who had received a static spacer had a reinfection, and the final infection eradication rate was 88% (twenty-two of twenty-five). One patient who had received an articulating spacer had persistent drainage after the implant was removed and required an arthrodesis, leading to an infection eradication rate of 93% (fourteen of fifteen) in this group.

As stated previously, fungal infection at the site of total joint replacement represents a very difficult challenge. However, Evans successfully treated fungal infections with polymethylmethacrylate bone-cement spacers containing 500 mg of amphotericin B followed by second-stage reimplantation in six patients²⁸. Similar techniques have been used by other authors^{66,67}. Phelan et al.⁶³ used staged reimplantation arthroplasty and systemic administration of antifungal agents to treat four *Candida* infections at the sites of total joint arthroplasties. They also identified an additional six cases in the literature that had been treated with the same regimen. In addition to resection arthroplasty, eight patients received amphotericin B, either alone or in combination with other antifungal therapy, and one patient received fluconazole alone. Eight of the patients did not have a recurrence of the infection at a median of 50.7 months (range, two to seventy-three months) following reimplantation arthroplasty.

Safety Issues

The safety of antibiotic-impregnated polymethylmethacrylate bone cement has been well documented^{128,39,58,61,82}. Evans²⁸ used 4 g of vancomycin and 4.6 g of tobramycin powder per 40-g batch of polymethylmethacrylate cement in forty-four patients with a total of fifty-four periprosthetic joint infections. Follow-up at a minimum of two years showed no renal, vestibular, or hearing changes. Springer et al.³⁹ studied the systemic safety of high-dose antibiotic-loaded cement over time and described average doses of 10.5 g of vancomycin and 12.5 g of gentamicin as being clinically safe, with no evidence of acute renal insufficiency or other systemic side effects. However, van Raaij et al.⁸³ reported a case of acute renal failure that developed in an eighty-three-year-old woman after treatment with 2 g of gentamicin in a 240-g block of cement combined with seven chains of polymethylmethacrylate beads also impregnated with gentamicin. Serum gentamicin levels were high, which led to the removal of the spacer and the eventual return of normal renal function. Koo et al.³¹ reported transient liver dysfunction and bone marrow suppression and Ceffa et al.⁸⁴ reported two cases of *Mucoraceae* infection after treatment with antibiotic-loaded cement spacers. In our opinion, these reported cases represent unusual events. However, the surgeon must be aware of these potential complications.

Outcomes of Utilization of Antibiotic Spacers

The use of antibiotic-loaded polymethylmethacrylate bone cement in spacers offers not only a more effective treatment for periprosthetic infection, with eradication rates in the literature ranging from 90% to 100%, but also improved function, decreased pain, increased patient satisfaction, shorter hospital stays, and decreased cost^{4,8,12,16,17,28,31,61,85}.

Outcome Studies of Knee Cement Spacers

Meek et al.¹⁷ retrospectively analyzed the outcomes of two-staged reimplantation, with use of a PROSTALAC articulating spacer in the first stage of the procedure, in forty-seven patients with an infection at the site of a total knee arthro-



Fig. 5-A

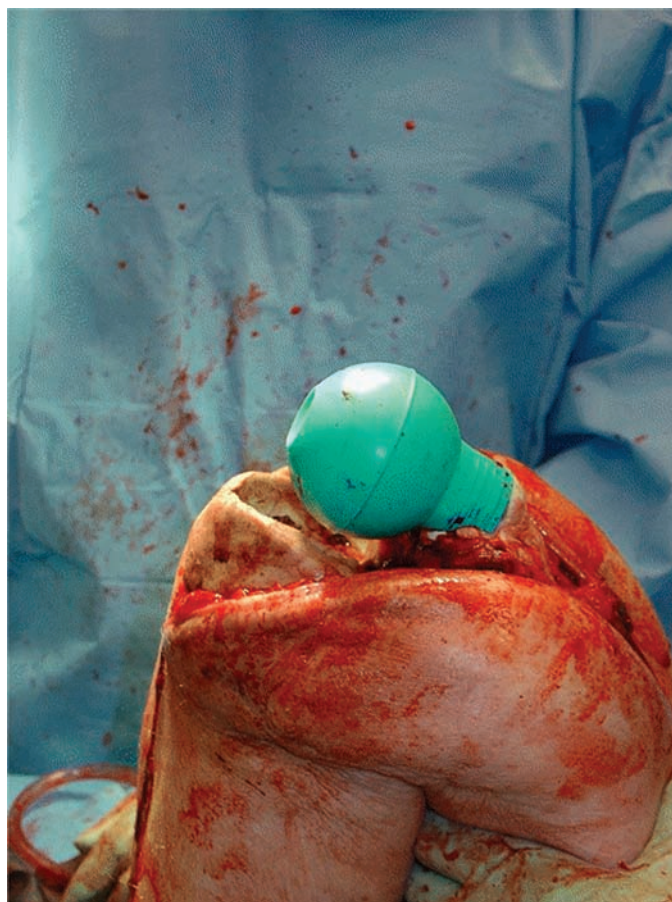


Fig. 5-B

Figs. 5-A, 5-B, and 5-C A hand-made articulating knee spacer used in a patient with a large bone defect after removal of total knee components because of infection. **Fig. 5-A** Molding of the tibial cement cup. **Fig. 5-B** Molding of the distal femoral spacer, which is ball-shaped to articulate with the tibial cup.

plasty. After an average of forty-one months, assessments with the WOMAC (Western Ontario and McMaster Universities Osteoarthritis), Oxford-12, and SF-12 (Short Form-12) instruments as well as a satisfaction questionnaire demonstrated that use of an articulating spacer was associated with improved function and satisfaction scores. Two patients had a recurrence of the infection, so the eradication rate was 96%.

In a retrospective review, Calton et al.⁵⁶ found scarring and capsular contractions with bone loss in 60% of twenty-four patients in whom an infection at the site of a total knee replacement had been treated with a nonarticulating spacer. On the average, 6.2 mm of bone loss was noted in the tibia, while 12.8 mm was noted in the femur, frequently with invagination and migration of the spacer. The authors recommended intramedullary extension of the spacer to prevent migration, adequate thickness of the spacer to tense the collateral ligaments to prevent contracture, and a wide-enough block to rest on the cortical rim and prevent invagination into the cancellous bone. There was no difference in the infection rate, operating time, or functional outcome between the pa-

tients treated with the nonarticulating spacer and those treated with an articulating spacer.

A study of twenty-five static and thirty mobile spacers demonstrated that the articulating spacers facilitated reimplantation and were not associated with bone loss²². Emerson et al.²⁶ reported a greater range of motion with articulating spacers than with static knee spacers, with knee flexion averaging 107.8° and 93.7°, respectively, and no evidence of higher complication rates.

Durbhakula et al.⁷ reported on twenty-four patients treated with a two-stage revision involving use of an antibiotic-loaded articulating cement spacer formed with vacuum-injected silicone molds that had been designed to fabricate articulating femoral and tibial components. With such a system, there is no need for a metal-on-polyethylene articulating surface and the cost is reduced by the employment of reusable molds that cost approximately \$300 each. Durbhakula et al. reported no problems with dislocation, fracture, or fragmentation of the spacer, and the infection eradication rate was 92% at an average of thirty-three months.

Goldstein et al.²⁹ designed a low-cost, all-cement system

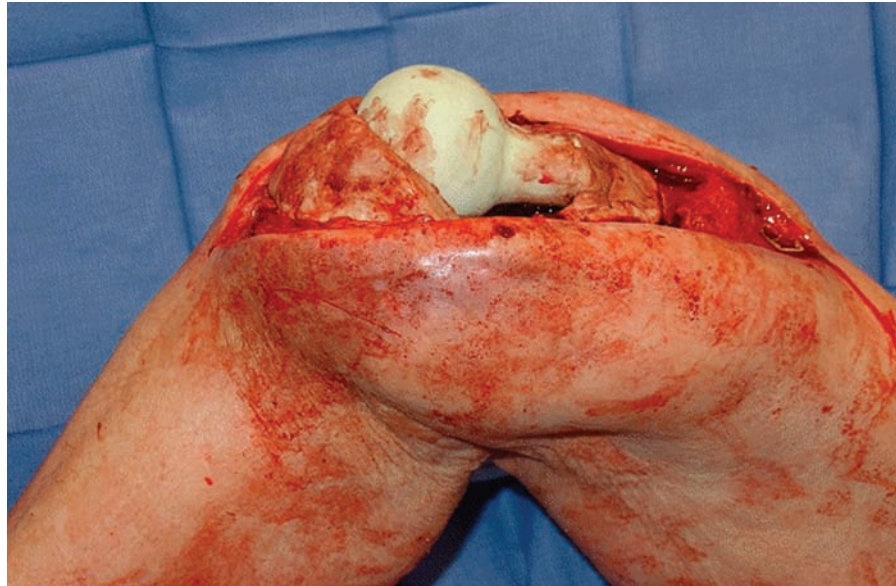


Fig. 5-C
The final hand-made articulating knee spacer.

that could be formed with instruments and supplies that are available at most hospitals. They described a technique in which heavy aluminum foil was used to form the osseous anatomy, hand-molded cement was applied around the foil to prevent interdigitation, and a layer of sterile lubricant was used in between for easy removal of the foil. The femoral condyles were molded with the trial tibial insert, and the tibial insert was used to approximate the size and thickness of the cemented tibial component. The authors reported early success in five patients.

MacAvoy and Ries⁵² described an inexpensive molding method to fabricate a “ball-and-socket” articulating spacer. The relatively constrained articulation between the spacer components may be particularly useful for patients with large amounts of bone loss and instability (Figs. 5-A, 5-B, and 5-C). The technique was used in twelve patients who had an infection at the site of a total knee arthroplasty complicated by severe comorbidities. At an average of twenty-eight months postoperatively, the infection was eradicated in nine of thirteen knees. All patients were able to walk with the spacer in place with minimal assistance. The average knee flexion was 98° (range, 45° to 135°) at the time of follow-up. With the spacer in place at the time of reimplantation, the average range of motion of the knee was 79° (range, 40° to 100°).

Outcome Studies of Hip Cement Spacers

Hsieh et al.¹⁰ used three or more 2.4-mm Kirschner wires as the endoskeleton for a molded antibiotic-loaded cement spacer in forty-two patients and reported a success rate of 95% at an average of 55.2 months. The authors attributed their success to complete removal of the prosthetic components and cement and thorough débridement, high doses (8 g) of organism-appropriate antibiotics in the cement, and

use of the erythrocyte sedimentation rate and C-reactive protein level to monitor and judge the timing of the second-stage revision. Molded cement stems with a metal endoskeleton are able to withstand partial weight-bearing, as reported by Schoellner et al.³⁷, who tested five spacers with double Kirschner wires under cranial-caudal loading of 20 N/s and observed failure at a load of 1550 N. The forces acting on a hip are about 2.5 times that of body weight but can increase to eight times that with a stumble; thus, a fall may lead to fracture of one of these spacers⁸⁶.

In order to fill bone defects resulting from the removal of components associated with infection, Leunig et al.³³ created customized, inexpensive, hand-molded implants with gentamicin-loaded cement and placed them in the area of the femoral neck or medullary canal. The implants were reinforced by inserting plates and/or screws into the cement before polymerization. While the authors reported complete eradication of infection in twelve patients followed for an average of 2.2 years, they also reported five dislocations and one fracture, suggesting a weakness in the design.

Barrack⁵ used a Rush pin to reinforce hand-molded, antibiotic-loaded cement to make a temporary prosthesis. Twelve patients so treated had no fractures or dislocations and were free of infection at a minimum of two years postoperatively. The advantage of using Rush pins is that they are available in numerous lengths and diameters, which allows the surgeon to produce hand-made prostheses with a wide range of lengths and offsets. This technique is a cost-effective alternative to the use of a commercially available hip spacer.

Overview

An infection at the site of a total hip or knee arthroplasty is a challenging clinical problem. The gold standard of treatment

for late chronic infections is two-stage revision arthroplasty, which includes placement of an antibiotic-impregnated cement spacer after removal of the prosthesis and thorough débridement, followed by a course of intravenous antibiotics and delayed second-stage revision total joint arthroplasty. The choice of the spacer is based on many factors, including the amount of bone loss, the condition of the soft tissues, the need for joint motion, the availability of prefabricated spacers or molding methods, and the selection of the antibiotics. Thermostable, water-soluble, susceptibility-directed antibiotics should be used. Hand-mixing of additional antibiotics into antibiotic-impregnated bone cement is preferred to increase the antibiotic dosage. The cement should be mixed first, and the antibiotics should then be added. Articulating spacers should be the first option since they appear to provide a better functional outcome.

Appendix

 Tables summarizing the results of the use of antibiotic-loaded cement spacers in the hip and knee as reported in

the literature are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on "Supplementary Material") and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM). ■

Quanjun Cui, MD, MS
William M. Mihalko, MD, PhD
John S. Shields, MD
Department of Orthopaedic Surgery, University of Virginia, Box 800159,
Charlottesville, VA 22908

Michael Ries, MD
Department of Orthopaedic Surgery, University of California San Francisco Medical Center, 500 Parnassus Avenue, San Francisco, CA 94143

Khaled J. Saleh, MD, MSc, FRCSC
Department of Orthopaedic Surgery and Health Evaluative Sciences,
University of Virginia, 400 Ray C. Hunt Drive, Charlottesville, VA, 22903.
E-mail address: Saleh@Virginia.edu

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