Antibiotic-impregnated PMMA hip spacers
Current status

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ABSTRACT   The infection rate after primary hip arthroplasty lies at 1–2%. In the past few years, a two-stage protocol with the implantation of an antibiotic-loaded spacer has become a popular procedure in the treatment of infected hip joint arthroplasties. In this review, we pay special attention to the elution characteristics of the spacers, their mechanical stability and the clinical response. We conclude that hip spacers are an effective method in the treatment of hip joint infections, with success rates of over 90%.

Unfortunately, the recent increase in the number of antibiotic-resistant bacterial strains (Neu 1992, Cercenado et al. 1996, Krcmery et al. 1996, Wendt 1998) requires an adequate treatment strategy in order to avoid failures and multiple surgical interventions. Thus, although an antibiogram might be useful, it is not always helpful since some of the recommended antibiotics are inactivated just by mixing with the cement, or during its polymerization process (Buchholz and Engelbrecht 1970, Ger et al. 1977). Also, a low degree of antibiotic release from the cement might limit its application.

Currently, there are no established standards or clinical guidelines available for the treatment of the infected hip joint. This review covers present-day experience with antibiotic-loaded hip spacers in the treatment of hip joint infections. Specific attention is paid here to the incidence of complications and to the balance between mechanical stability and the elution characteristics of antibiotics.

One- or two-stage procedure?
Several methods of treatment can be chosen,
including a one-stage procedure, a two-stage procedure with a PMMA spacer, or a resection exchange arthroplasty/Girdlestone procedure (Wagner and Wagner 1995, Joseph et al. 2003). Before making a decision, the acuteness or chronicity of the infection, the type of infecting organism, its antibiotic sensitivity profile, its ability to manufacture glycosylx, the occurrence of severe soft-tissue damage and the extent of bone loss must be considered.

A two-stage approach permits identification of the infecting organism, determination of antibiotic sensitivity, and appropriate adjustment of antibiotic therapy before reimplantation. An adequate debridement of necrotic or infected tissues and removal of cement plus a greater flexibility in reconstructive options are also advantageous. However, the prolonged hospitalization and its associated costs, the delayed mobilization and rehabilitation, and the risk of additional surgery may be a drawback—especially in elderly patients.

Several studies have compared one-stage and two-stage procedures. Ure et al. (1998) emphasized that a direct exchange arthroplasty can only be carried out in early infections if the patient is not immunocompromized, if the infecting organism is of low virulence (no methicillin-resistant or gram-negative bacteria), if the surgeon is experienced, and if there are no major skin, soft-tissue or existing osseous defects. Delayed reimplantation procedures after a Girdlestone procedure are technically demanding due to scar formation, leg shortening, osteoporosis from disuse, and the distorted anatomy, and have thus been replaced by the implantation of spacers (Leunig et al. 1998).

**Inclusion of studies**

Data from 30 studies (26 in vivo, 4 in vitro) are presented. The studies were chosen after a Medline search (search words: hip infection, spacer(s), antibiotic-loaded) and after searching through the reference lists of the articles resulting from the Medline search. When there was more than one article published by the same author or group, the more relevant and/or recent paper was included. At least 316 hips have been treated by implanting an interim prosthesis. (Note that not every published study offers detailed data on the number of patients or hips treated). An infected total hip arthroplasty (THA) was the indication in most cases, followed by septic arthritis. In the in-vitro test studies, the static strength, the elution of antibiotics and the surface-release relation were evaluated. The clinical studies concentrated on the outcome and complications.

**Construction of antibiotic-loaded hip spacers**

Table 1 shows manufacturing details of the spacers. Hand-formed prostheses have been used in 13 studies while standardized prostheses were used in 22 studies (4 of which were PROSTALAC (prosthesis of antibiotic-loaded acrylic cement)). Most spacers function as a hemiarthroplasty, whereas only a few offer the advantages of a THA (PROSTALAC and Hsieh et al. 2004). Almost half of the studies reported fixation of the spacer by cementation to the proximal part of the femur, and the other half used snap-fit as the method of fixation.

Unfortunately, there has been no study comparing the clinical performance and the complications associated with spacers with respect to their articulation and the fixation method. Although a proximal cementation of the spacer to the femur might preserve leg length and prevent any rotation, no study has demonstrated which one of the two methods is best. Moreover, THA-like spacers may improve the congruence of the joint compared to hemiarthroplasty-like ones, but there have been no reports investigating whether clinical performance is better with THA-like spacers.

The majority of studies have used Palacos bone cement. Cephalosporins, penicillin G, aminoglycosides and glycopeptides have been added to the cement, the two latter being used most often. While 25 spacers had mechanical support from metallic components, 7 spacers only consisted of antibiotic-impregnated cement.

**Diagnostic steps**

Many authors have emphasized the value of clinical history and physical examination, radiological evaluation and laboratory data, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and leukocyte blood account in confirming the diagnosis (Koo et al. 2001, Takahira et al. 2003, Durbhakula et al. 2004, Hsieh et al. 2005). An ESR of > 30–40 mm/h combined with a CRP level of > 10–20 mg/L is considered highly suggestive of infection (Durbhakula et al. 2004, Hsieh...
Table 1. Manufacturing details of hip spacers

| Study                          | In vivo/ in vitro | Antibiotic (per 40 g PMMA) | Infecting organism | Design | Metallic components |
|-------------------------------|-------------------|-----------------------------|-------------------|--------|---------------------|
| Abendschein (1992)            | v                 | tobramycin                  | n.r.              | m      | none                |
| Affatato et al. (2003)        | t                 | gentamicin, vancomycin      | MRSA, E. faecalis | s      | cylindrical rod of SS |
| Anagnostakos et al. (2005)    | t                 | gentamicin, vancomycin      | MRSA, E. faecalis | s      | none                |
| Barrack (2002)                | v                 | 3.6 g tobramycin            | n.r.              | m      | 1 Rush pin          |
| Bertazzoni Minelli et al. (2004) | t               | gentamicin, vancomycin      | n.r.              | s      | hollow cylindrical rod |
| Desmukh et al. (1998)         | v                 | unknown                     | n.r.              | m      | Küntcher nail       |
| Duncan et al. (2003)          | v                 | 2.4 g tobramycin            | E. coli, Streptococcus | s      | SS endoskeleton     |
| Durbhakula et al. (2004)      | v                 | 2.4 g tobramycin            | SA, SE, E. coli, Streptococcus | s      | 1 Rush pin          |
| Greene et al. (1998)          | t                 | 4 g tobramycin              | SA, SE, E. coli, Streptococcus | s      | none                |
| Haddad et al. (1999)          | v                 | 2.4–3.6 g tobramycin        | B. subtilis       | s      | SS endoskeleton     |
| Holton et al. (1998)          | t                 | 4 g vancomycin              | B. subtilis       | s      | none                |
| Hsieh et al. (2004)           | v                 | vancomycin, gentamicin, teicoplanin, aztreonam, piperacillin | mostly staph. species | s      | >2 K-wires          |
| Isiklar et al. (1999)         | v                 | 2–3 g vancomycin            | SA, MRSE          | m      | 2–3 Steinmann pins  |
| Ivarsson et al. (1994)        | v                 | gentamicin                  | Enterococcus, Klebsiella, Propionibacteria, Streptococcus | m      | none                |
| Jahoda et al. (2003)          | v                 | gentamicin                  | n.r.              | m      | 1 K-Wire            |
| Kelm et al. (2001)            | v                 | n.r.                        | n.r.              | s      | none                |
| Koo et al. (2001)             | v                 | 1 g gentamicin              | Enterobacter cloacae | s      | none                |
| Kraay et al. (1992)           | v                 | 2 g tobramycin              | 1 × SE (rest: unknown) | m      | cerclage wire       |
| Leunig et al. (1998)          | v                 | 1 g gentamicin              | SA, CNS           | m      | plates, screws      |
| Magnan et al. (2001)          | v                 | 0.95 g gentamicin           | SA, SE, P. aeruginosa | m      | hollow cylindrical rod of SS |
| Masri et al. (1998)           | v                 | 1.2–4.8 g tobramycin        | 1–2 g vancomycin | s      | SS endoskeleton     |
| McGrory et al. (2002)         | v                 | 1.5 g vancomycin            | MRSA              | m      | endoprosthetic head |
| Morimoto et al. (2003)        | v                 | 40 mg gentamicin            | MRSA              | m      | gamma locking nail |
| Pearle et al. (2002)          | v                 | tobramycin                  | n.r.              | s      | 2 Steinmann pins    |
| Ries et al. (1999)            | v                 | 1.2–3.6 g tobramycin        | n.r.              | s      | intramed. nail/pins |
| Schöllner et al. (2003)       | t                 | 0.5 g gentamicin            | n.r.              | s      | 2 K-Wires           |
| Shin et al. (2002)            | v                 | n.r.                        | n.r.              | s      | femoral endoprosthes |
| Takahira et al. (2003)        | v                 | 1.5 g gentamicin            | SA, SE, MRSA, E. coli | m      | 2 K-Wires           |
| Yamamoto et al. (2003)        | v                 | 0.5 g gentamicin + 1 g vancomycin | 4 × CNS, 4 × SE, 3 × MRSA, P. aeruginosa | m/s    | with cerclage wires |
| Younger et al. (1997)         | v                 | tobramycin, penicillin G, teicoplanin, streptomycin | 24 × SE, 7 × SA, 11 × Enterococcus, etc. | s      | SS endoskeleton     |
| Wentworth et al. (2002)       | v                 | 3.6 g tobramycin            | 34 × SA, 30 × SE | s      | SS endoskeleton     |
| Zilkens et al. (1990)         | v                 | gentamicin                  | SA, P. mirabilis | m/s    | metallic telescopic shaft |
et al. 2005). However, these values may be false-negative if the patient has already been treated with antibiotics. Radiological findings depend on the stage of the infection, and may be normal. A preoperative hip aspiration has been performed routinely by some authors (Isiklar et al. 1999, Takahira et al. 2003), whereas others have found it to be of minor value, since the reported rates of negative preoperative aspiration are in the 7–50% range (Koo et al. 2001). Also, intraoperative findings may suggest an infection despite a negative preoperative aspiration (Kraay et al. 1992). Multiple biopsy samples from the infected area should help to clarify and distinguish a contamination from an infection of any clinical significance.

Pathogenic organisms

Most of the reported infections were caused by *Staphylococcus aureus*, *Staphylococcus epidermidis*, methicillin-resistant *Staphylococcus aureus*, and *Eschericia coli* (Table 1). In a few cases, a polymicrobial infection has been diagnosed. Depending on the profile of the infecting organism, the local therapy has been complemented with a wide range of oral and/or parenteral antibiotics, amongst which cephalosporins have been administered most frequently (Table 2).

Clinical experience

In one of the latest reports by the PROSTALAC team, Haddad et al. (1999) described healing of the infection in 77 of 81 hips. The mean Harris hip score increased from 34 points before spacer implantation to 56 during stages and 76 at the time of reimplantation. In a study prior to that, the great majority of patients (43/48) were reportedly satisfied with the outcome of the treatment (Younger et al. 1997). Such subjective reports have been supported by the study of Koo et al. (2001) who used the Merle d’Aubigne hip score and found an increase from 5.9 to 14.6 points. Takahira et al. (2003) reported a similar improvement after spacer implantation using the hip score of the Japanese Orthopaedic Association (an increase from 30 to 73 points).

Only one study has appeared that has compared the two procedures of the two-stage protocol (Girdlestone and spacer implantation) (Hsieh et al. 2004). It could be shown that the spacer implantation had a significantly lower complication rate. Between stages, the patients achieved a higher hip score rate, and at re-implantation there was a shorter operative time, less loss of blood, and a lower transfusion requirement, indicating that the spacer is probably the superior technique in the treatment of late hip joint infections.

Furthermore, the treatment of infection by using a spacer seems to offer great advantages, even in cases with massive bone loss of the proximal femur or the acetabulum (Duncan et al. 1993, Younger et al. 1998, Isiklar et al. 1999, Hsieh et al. 2005). The prosthesis re-implantation can be a technically demanding procedure due to leg length discrepancy, soft-tissue shortening and disuse osteoporosis. The implantation of a spacer in such cases gives the patient a functional joint during the interim period. Duncan et al. (1993) and Hsieh et al. (2005) reported encouraging results in the treatment of hip infections by spacer implantation followed by reconstruction with allografts. None of the patients had any recurrence of infection, and the joint function was enhanced between stages.

In addition to the material properties of the spacers, an optimal interaction and articulation between the bone and the spacer favors a positive result of the joint replacement. The insertion of a standardized, articulating and antibiotic-impregnated prosthesis into the bone reduces the risk of crepitus during hip mobilization and helps to preserve the bone stock (Ries and Jergesen 1999, Shin et al. 2002). This method has been reported to increase hip mobility and reduce pain during stages and after re-implantation (Duncan and Beauchamp 1993, Younger...
et al. 1997, Koo et al. 2001, Magnan et al. 2001, Takahira et al. 2003).

Most spacer patients were mobile during stages, either on crutches with toe touch and/or partial weight bearing. Leunig et al. (1998) reported dislocations of the hip in 5 of 12 patients, Magnan et al. (2001) reported a dislocation rate of 1/10, and Duncan et al. (1993) reported dislocations in 3 of

Table 2. Clinical response, complications and follow-up

| Study            | Hips | Antibiotics p.o./i.v. | Complication                                      | Weeks between stages | Follow-up (months) |
|------------------|------|-----------------------|---------------------------------------------------|----------------------|--------------------|
| Abendschein (1992) | 1    | n.r.                  | none                                              | 34                   | 24                 |
| Barrack (2002)   | 12   | n.r.                  | none                                              | 6–12                 | 24–48              |
| Desmukh et al. (1998) | 5    | n.r.                  | none                                              | n.r.                 | n.r.               |
| Duncan et al. (1993) | 15   | n.r.                  | 3 × dislocation 1 × sciatic paresis (resolved) 1 × peroneal paresis (resolved) | 4–40                 | 25–54              |
| Durhakula et al. (2004) | 20   | n.r.                  | 2 × fractures 2 × dislocations                   | 10–21                | 26–67              |
| Haddad et al. (1999) | 81   | n.r.                  | n.r.                                              | n.r.                 | 24–114             |
| Hsieh et al. (2004) | 58   | n.r.                  | 2 × fracture 1 × infection recurrence 2 × dislocations 2 × fractures | 7–40                 | 24–96              |
| Isiklar et al. (1999) | 10   | rifampicin vancomycin ceftazidime cephalosporin clindamycin cloxacillin | 1 × spacer dislocation 1 × femur fracture | 3–14                 | 16–36              |
| Ivarsson et al. (1994) | 5    | n.r.                  | 1 × spacer dislocation 1 × subtrochanteric fracture | 3–8                  | 9–24               |
| Jahoda et al. (2003) | 29   | n.r.                  | 1 × infection persistence 2 × fractures 5 × dislocations none | 6–28                 | n.r.               |
| Kelm et al. (2001) | 7    | n.r.                  | 2 × femur fracture (intraop.) 2 × peroneal paresis 3 × heterotopic ossification | n.r.                 | 8                  |
| Ko et al. (2001)  | 22   | vancomycin, cefotaxime ciprofloxacin, cefamandole | none | 6–12                 | 24–78              |
| Kraay et al. (1992) (average) | 7    | n.r.                  | 5 × dislocation 1 × protrusion 1 × fracture   | n.r.                 | 15                 |
| Leunig et al. (1998) | 12   | n.r.                  | 2 × infection persistence 2 × fractures 5 × dislocations none | 8–30                 | 27                 |
| Magnan et al. (2001) | 10   | teicoplanin, ciprofloxacin | 2 × acetabular bone graft 1 × dislocation | 13–39                | 24–48              |
| Masri et al. (1998) | 49   | n.r.                  | n.r.                                              | 6–46                 | n.r.               |
| McGrory et al. (2002) | 1    | nafcillin, rifampicin | none                                              | n.r.                 | 12                 |
| Morimoto et al. (2003) | 1    | n.r.                  | none                                              | 6                    | 30                 |
| Pearle et al. (2002) | n.r. | tobramycin            | n.r.                                              | n.r.                 | n.r.               |
| Ries et al. (1999) | n.r. | n.r.                  | n.r.                                              | n.r.                 | n.r.               |
| Shin et al. (2002) | 8    | n.r.                  | none                                              | n.r.                 | n.r.               |
| Takahira et al. (2003) | 9    | n.r.                  | 1 × reinfection 1 × fracture                      | 6–19                 | 10–55              |
| Yamamoto et al. (2003) | 17   | n.r.                  | 1 × fracture 1 × dislocation 1 × periprosthetic fracture 5 × dislocation 4 × reinfection | 13–40                | 14–62              |
| Younger et al. (1997) | 61   | vancomycin cefamandole | none                                              | 5–42                 | 24–63              |
| Wentworth et al. (2002) | 135  | n.r.                  | 15 × dislocation 12 × infection                   | none                 | 26                 |
| Zilkens et al. (1990) | 1    | wide-spectrum penicillin | none                                              | 26                   | 43                 |

n.r.: not reported.
13 patients. Ries and Jergesen (1999), Koo et al. (2001), Shin et al. (2002) and Takahira et al. (2003) did not observe any dislocation during implantation of the spacer (Table 2).

The period between stages varied. Based on laboratory data and the progress of each infection, the re-implantation was carried out after a mean period of 3–4 months. Usually, no difficulties were reported at the time of spacer removal. Re-infections—either with the primary organism or with another bacterium—were rare and were only found in two studies (Table 2). A prolonged implantation period might actually endanger the outcome of the treatment since subtherapeutic levels of antibiotic(s) might be eluted from the spacer, and the antibiotic-impregnated cement itself provides an excellent environment for the development of resistant bacterial strains (Duncan and Masri 1994, Thomes et al. 2002).

On the whole, the overall success rates of the hip replacements were reported to be 80–98% (data not shown).

**Antibiotic elution**

Masri et al. (1994) measured intraarticular antibiotic concentrations in the first days after the insertion of vancomycin/tobramycin-loaded spacers. They confirmed the in-vitro results reported by Greene et al. (1998) and showed that tobramycin eluted better than vancomycin. Peak concentrations on day 1 were 107 µg/mL for tobramycin and 19 µg/mL for vancomycin, determined from the wound drainage fluids. These concentrations were 10–30 fold higher than the MICs of the infecting organisms. An increase in the tobramycin dose enhanced the elution of tobramycin and vancomycin, whereas an increase in the vancomycin concentration lacked such an effect (Masri et al. 1998).

A sufficient degree of elution of antibiotics from PROSTALAC could be measured over a period of at least 4 months (Masri et al. 1998). The duration of the spacer implantation did not have a significant effect on the elution characteristics of either antibiotic.

Isiklar et al. (1999) reported mean concentrations of 57 µg/mL vancomycin on day 1 from vancomycin-impregnated spacers in the treatment of orthopedic implant-related *Staphylococcus epidermidis* infections, also determined from the drainage fluid.

A recent in-vitro study has investigated the efficacy of single antibiotic- and bi-antibiotic-loaded spacers with regard to bacterial growth inhibition and antibiotic release (Anagnostakos et al. 2005). Gentamicin/vancomycin-loaded spacers were the most effective in growth inhibition of *S. epidermidis* and MRSA, whereas gentamicin/teicoplanin-impregnated spacers showed the best results against *E. faecalis* and *S. aureus*.

Reports on the elution characteristics of spacers are encouraging, but require further investigations about the exact nature of the release mechanism in vivo. In-vivo (Masri et al. 1998) and in-vitro studies (Anagnostakos et al. 2005) have shown a sufficient degree of antibiotic elution; however, both of these studies have limitations. In the first study, no data were reported on the antimicrobial properties at specific antibiotic concentrations, and in the latter one, the experimental conditions were different from normal conditions in vivo. An in-vivo animal model might perhaps solve this question.

Some concerns have been expressed regarding the ideal re-implantation time, and whether spacer removal that is too early or too late with prostheses re-implantation might be associated with persistence or recurrence of infection. Bertazzoni Minelli et al. (2004) studied antibiotic elution from explanted spacers. 0.05–0.4% gentamicin and 0.8–3.3% vancomycin (of the initial amounts present) were released in vitro over a time period of 10 days, indicating that a sufficient degree of antibiotic release can persist over several months.

Following surgery, the outcome of infections can be particularly dramatic because of the extent of soft tissue, and therefore systemic antibiotic therapy should be given. Unfortunately, such supporting antibiotic treatments are not without risks—as reported by Koo et al. (2001). In that study, the authors described the occurrence of a transient liver dysfunction and bone marrow depression following the simultaneous implantation of an antibiotic-loaded spacer and intravenous treatment with antibiotics.

Holtom et al. (1998) found a positive correlation between the surface area of the vancomycin-loaded spacers and their elution characteristics in vitro. By increasing the surface-to-volume ratio from 0.24 (control-spacer) to 0.30, a 40% enhancement in
antibiotic release could be achieved. Greene et al. (1998) showed that tobramycin showed a higher release rate than vancomycin, and that Palacos allowed higher antibiotic elution than Simplex.

**Mechanical stability**

The mechanical stability of spacers is determined and influenced by many parameters, including geometry, ageing, storage, type of cement, the type and content of antibiotic(s), the presence of an endoskeleton, and standardization of its preparation (such as atmospheric composition during mixing and the frequency and duration of the particular mixing process) (Murray 1984, Leunig et al. 1998). Mechanical stress experiments with gentamicin-loaded spacers showed an average failure load of 1.6 kN (Schöllner et al. 2003). The inclusion of K-wires into the spacers prevented any dislocation of the fragments, but did not improve the mechanical properties significantly. In contrast to that, Kelm et al. (2001) reported an average failure load of 20 kN with antibiotic-loaded cement, not including any supporting metal components. Recently, Affatato et al. (2003) investigated in an in-vitro model for the changes in PMMA polymer conformation induced by wear. Although the wear behavior varied with the area of the spacer and the amount of debris was higher than in tests with no temporary prostheses, the authors concluded that partial weight bearing can be allowed, since at the time of prosthesis re-implantation any particle debris can be removed by jet lavage.

The mechanical strength of cement is not only influenced by the type of antibiotic and atmospheric pressure, but also by the ratio in which the antibiotics are mixed into the cement (Lautenschlager et al. 1976). Proportional weights of up to roughly 5% have a negligible influence on the mechanical strength of the resulting cement (Levin 1975, Lautenschlager et al. 1976, Murray 1984), whereas larger amounts of antibiotic powder will make the cement harder to mix and increase the possibility of lack of homogeneity. There is no quantitative information available regarding the ideal antibiotic/cement ratio, but most surgeons do not exceed a ratio of 10%. However, Hsieh et al. (2005) recently reported an antibiotic mixture ratio of up to 20% and had no difficulty in fabricating the prosthesis.

In addition to the manufacturing process, other factors might compromise the function of the spacer, including the residual bone quality after the first surgery, or deficient soft tissue. Although numerous initial strength tests for antibiotic-impregnated cement blocks or discs have been carried out (Lautenschlager et al. 1976, Lidgren et al. 1987, Askew et al. 1990, Armstrong et al. 2002, Lewis 2003), only the studies by Kelm et al. (2001) and Schöllner et al. (2003) attempted to provide hard static data on these constructs. Unfortunately, the clinical relevance of these reports is hampered by the limited number of spacers investigated and the experimental conditions (an axial strength test does not represent the stress that a spacer is being exposed to in the human body). The mechanical strength of the spacers could be increased by the addition of a metallic endoskeleton, although the benefits of such a construct have not been thoroughly determined. Also, a spacer fracture exposing the metal may lead to bacterial recolonization and/or re-infection. In addition, studies should be conducted to investigate the antibiotic elution profile of spacers with metal, in order to detect any possible alteration in the release characteristics.

**New techniques**

The increase in the popularity of spacers during the treatment of hip joint infections in the past years has fostered the search for new techniques for quick and simple intraoperative manufacture. Ries and Jergesen (1999) and Shin et al. (2002) recommended the use of a rubber bulb portion of an irrigation syringe as a mold to shape the proximal end of the spacer, while Barrack (2002) manufactured different spacers by using rod pins of various lengths and diameters. Such an approach would enable the surgeon to build up a stock of premanufactured spacers, from which the appropriate shape could be selected during surgery. Ries and Jergesen (1999), Barrack (2002) and Shin et al. (2002) reported using such spacers for successful eradication of infection—and preservation of articulation between the spacer and the acetabulum in conjunction with satisfying mechanical strength of the prosthesis.

**Conclusion**

A choice between one-stage and two-stage proce-
dures must be made in the treatment of an infection of the hip joint. Should the patient undergo a two-stage protocol, the implantation of antibiotic-loaded spacers is currently the most commonly used method. Here, we have reviewed the current data available and our conclusions can be summarized as follows:

- Standardized spacers appear to be superior to hand-made spacers
- The combination of two antibiotics is advisable, due to the enhanced elution of both agents and the wider antimicrobial spectrum
- For an aminoglycoside-glycopeptide combination, the glycopeptide should be included at a higher dose due to its inferior release characteristics
- The total (additive) dose of the two antibiotics should not exceed 10% of the weight of the cement, in order to maintain the mechanical strength of the spacer
- Insertion of metallic components into the cement during the spacer’s manufacturing process may increase its stability, but the release of antibiotics after metal insertion has not been evaluated
- A complementary, systemic antibiotic treatment during the first weeks between stages is necessary to prevent an infection due to hematogenous spread, but it should be noted that the selected antibiotics ought to differ from the spacer’s antibiotics.

Better data on all of these issues are clearly desirable. The ideal ratio of antibiotic and cement for hip spacers is still unknown and requires quantification. In addition, future studies more attention should be paid to possible improvements in the mixing process, which may result in a more homogeneous antibiotic/cement mixture. We would also welcome further investigations into the enhanced strength of spacers by inclusion of metal endoskeleton at different antibiotic concentrations. It should, however, be noted that despite the importance of in vitro studies for all these parameters, clinical trials are imperative to confirm and substantiate the results.

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