Guest editorial

Joint prosthetic infections: A success story

The most important progress in hip and knee joint replacement surgery the last 40 years has not been in new materials and designs, but in prevention of infections and improved surgical technique.

When joint prosthetic surgery started on a larger scale in the late 1960s, an unacceptable infection rate between 5% and 10% was reported both for the hip and knee (Ahlberg et al. 1978, Bengtsson et al. 1987). Started by Charnley, this led to new aseptic procedures such as laminar airflow, body exhaust systems and closed operating rooms (Charnley 1972, Nelson 1977). Stricter pre- and perioperative routines avoiding operations on patients with ongoing infection, shorter preoperative hospitalization, improved preparation for surgery, new surgical gowns, etc., were also introduced. This was done without controlled trials, but drastically reduced the infection rate to about 3–5% (Antti-Poika et al. 1990). During the same period, the surgeons gained technical experience. The relative importance of each of these improvements is difficult to assess.

At the same time, antiseptic procedures, such as preoperative antibiotics were reported in randomized studies done under routine surgical conditions with a significant effect on the infection rates, which were reduced to 1–3% (Ericson et al. 1973, Carlsson et al. 1977, Hill et al. 1981). During the past few decades, several studies have shown that short-term prophylaxis for 1 day or less is as effective as longer regimes (Pollard et al. 1979, Nelson et al. 1983, Wymenga 1991). The prevailing schedule today is 24 hours (Walenkamp 2001).

In the early 1970s in Germany, revision of joint prosthetic infections with gentamicin bone cement was reported to give a reinfection rate similar to that of primary joint prosthetic surgery without preventive measures. This stimulated interest in evaluating the effect of gentamicin cement even in primary joint replacements. A few prospective studies were done, but with conflicting results and obvious difficulties in randomizing patient series large enough for statistical evaluation (Buchholz and Engelbrecht 1970, Pfarr and Burri 1979, Josefsson et al. 1990). Despite the lack of clear evidence, bone cement containing antibioitics is now routinely used, for instance, in the USA although the surgeons have to mix the bone cement and the antibiotic powder at surgery (van de Belt 2001).

The lack of good studies showing an effect of antibiotic-impregnated cement is one of the key statements in an article in this issue of Acta Orthopaedica Scandinavica by van de Belt and co-workers "Infection of orthopedic implants and the use of antibiotic-loaded bone cements" (pp 557–571). However, large multicenter studies have reported various preventive measures against implant infections. The largest prospective European multicenter study with over 8,000 joint replacements was done by Lidwell and co-workers (1982, 1984). It compared preventive measures in various hospitals and focused on the effect of laminar airflow and the use of body exhaust systems, but it was not randomized. They found a clear effect of combining local and systemic antibiotics in addition to the use of laminar air flow.

On the basis of Norwegian and Swedish prospective long-term register studies comprising more than 250,000 hip arthroplasties, it was shown that bone cement containing antibiotic alone is less effective than systemic antibiotics, but the combination is better, and the most cost-effective (Persson et al. 1999, Furnes et al. 2001). The latter gave an infection rate of 0.2%. There may be a synergistic effect in using a short-term systemic antibiotic together with a cement containing an antibiotic (Greene et al. 1998, Walenkamp 2001). Antibiotics also reduced the number of revisions for loosening (Persson et al. 1999). There are several explanations for this. One is that loosening in some instances is caused by an undetected low virulent infection or that killed bacteria may result in endotoxins and a more aggressive inflammatory reaction in combination with wear particles (Ragab et

al. 1999). Another possibility may be that the surgeons with the best technique are those who use antibiotics to prevent infections.

With the aseptic and antiseptic measures used today, it is possible to have infection rates of 0.3% for hips and 0.5% for knees at 10 years; an enormous progress from 10% 25 years ago (Robertsson 2000, Söderman 2000).

Animal studies have shown that cement containing antibiotics has a preventive effect on intraoperative contamination and infectious biofilm formation, but not as good as systemic antibiotics (Elson et al. 1977, Rodeheaver et al. 1983). van de Belt and co-workers report in their review in this issue that the preventive effect is very brief and related to the initial burst of antibiotics from the surface during the first days and that is related to the extent of the contact area, releasing up to at most 10% of the antibiotics present in the cement within weeks. The preventive effect regarding surgical and hematogenous infections is thus very short (Blomgren 1981, van de Belt 2001).

The mechanism underlying the formation of an infectious biofilm on acrylates, release mechanisms and properties of antibiotic-loaded cement in clinical use have been extensively reviewed by van de Belt et al. and others (Törholm et al.1983, Costerton et al. 1999, van de Belt 2001). The sustained release over longer periods depends on the porosity and channels in the cement. Subsequent cracking of the bone cement due to fatigue or at revision causes leaking of small amounts of antibiotics (Powles et al. 1998). van de Belt et al. state that these low levels can increase antibiotic resistance— i.e., to gentamicin and become an ecological and environmental threat. This may be possible, but it has not been demonstrated. Bacteria within a biofilm on a plain polymer are several hundred times more resistant to antibiotics (Bayston and Wood 1997, Gilbert and Allison 1999). There are also reasons to believe that both coagulase-positive and coagulase-negative staphylococci (CNS) have either resistant clones already present (phenotypic variation) or the genetic capacity to transform rapidly into resistant strains when cultured on a foreign material (Arizono et al 1992, Kendall et al 1996, Merritt et al. 1998, Tunney et al. 1998a, b). Development of resistant strains occurs shortly after exposure to the material and also on bone cement or a polymer without gentamicin. It is important to realize that gentamicin resistance has not been shown to be commoner in countries using bone cement containing antibiotics. Resistance to antibiotics occurs frequently also in other, nonsurgical, medical fields. It should also be remembered that more than half of the total production of antimicrobial agents worldwise is used in animal husbandry (Wilcox 1998).

The most important question to be answered is whether the patients to be operated on with a primary joint replacement have bacteria with increased resistance to the antibiotics used for prophylaxis in a specific geographical area. This has not been shown, but Sanzén and Walder (1988) found an increased resistance to gentamicin in patients after joint replacement.

van de Belt et al. have also studied revision and the use of intermediate treatment with cement spacers and beads containing antibiotics. The obvious advantages of using a molded spacer on extraction of a prosthesis are easier mobilization of the patient and less demanding secondary replacement surgery. The most difficult problem to overcome is multiresistant infections mainly caused by CNS, in some countries now representing almost half of the positive cultures occurring in joint prosthetic infections (Lidgren 1994, Gaine et al. 2000, Ostendorf et al. 2001). CNS infections should be treated with at least two antibiotics, in the bone cement and preferably in combination with systemic treatment to prevent the development of antibiotic resistance (Lidgren 2000).

Conclusion

With the low rate of infection seen in many countries today, 30 hip prosthetic infections and 50 knee infections per 10,000 operations in Scandinavia, the treatment of infected arthroplasties should be centralized, not only for the sake of more surgical experience, but also for detecting a change in bacterial resistance. This should be done at centers with facilities having appropriate techniques, as shown in the article by van de Belt and co-workers. Genetic probes for PCR analyzing joint fluid and tissue, serological detection, ultrasound treatment of implant and soft tissue for release of bacteria into the culture media, rapid transport, using anaerobic culture media and cultures over long periods

to detect slow growing low virulent bacteria are all in clinical use and important for making a correct diagnosis and selecting antibiotic treatment (Mariani et al. 1996, Barrack et al. 1997, Lidgren 2000, Rafiq et al. 2000).

The concomitant risk of hepatitis and more serious viral infections in patients with joint replacements is increasing and constitutes a risk for the surgical staff, especially using high-speed water-irrigated instruments for removal of prostheses and cement. This may lead to the bacterial and viral spread in aerosols and the return of protective shields and body exhaust system, but now to protect the surgeon from the patient.

There is weak evidence for the preventive effect of antibiotic-loaded bone cement in primary replacements, except when given in addition to systemic antibiotic prophylaxis (Persson et al. 1999, Furnes et al. 2001). Today, however, it is almost impossible to do additional randomized studies that prove the efficacy in primary replacements.

The need for continuous monitoring of bacterial and resistance patterns remains. The data should be collected in registers on a national/regional level. To show the efficacy of various treatments in revision surgery, multinational, multicenter very costly studies have to be done to obtain series for valid statistical analyses.

Laboratory studies analyzing surface properties, bacterial adhesion, biofilm, tissue integration, etc., are important when new materials are introduced since they may cause new adverse effects. Today, as is often the case, we try to explain why and how materials that we are already using work.

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