

# COMBINED PROPHYLACTIC EFFECT OF ULTRACLEAN AIR AND CEFUROXIME FOR REDUCING INFECTION IN PROSTHETIC SURGERY

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One hundred seventy-four elective operations for hip and knee prostheses were undertaken in conditions of ultra-clean air and antibiotic prophylaxis (with cefuroxime), as the recent Medical Research Council multicenter study suggested that this combination was most likely to give the lowest infection rate. No acute infections of a prosthesis occurred (early infection rate < 0.6%), while the rate was 2.9% for purulent wound infection which did not involve the prostheses. Late infections, at 3 months and 1 year, occurred in only 2 patients (a rate of 1.1%), resulting from probable bacteremia, which necessitated removal of the prosthesis. These results are considered satisfactory, especially in a compromised patient population of mean age 71 years. Such low infection rates underscore the need to continue the combined use of ultraclean air and antibiotics for hip and knee prosthetic surgery, or to introduce them where absent, to prevent the occurrence of airborne staphylococcal infection; either technique alone was shown to be less effective in the Medical Research Council multicenter study.

**Keywords :** hip ; knee ; prosthesis ; infection ; prophylaxis ; ultraclean air ; cefuroxime.

**Mots-clés :** hanche ; genou ; prothèse ; infection ; prophylaxie ; air ultrafiltré ; céfuroxime.

## SAMENVATTING

L. KLENERMAN, D. V. SEAL en K. SULLENS.  
*Het gecombineerd profylactisch effect van "ultra-clean air" en cefuroxime ter vermindering van infectie in prothese chirurgie.*

Honderdvierenzeventig electieve operaties voor totale heup- en knieprothesen werden uitgevoerd onder "ultra-clean-air" installaties en met antibiotische prophylaxis (cefuroxime), gebaseerd op de resultaten van de recente Medical Research Council (M.R.C.)-studie (waarbij meerdere centra betrokken waren). Daarin werd gesuggereerd dat deze combinatie zou leiden tot het laagste percentage diepe infecties.

Een acute infectie van de prothese werd net vastgesteld (vroeg infectie percentage < 0,6%) en een purulente wondinfectie, zonder besmetting van de prothese rond of bij 2,9%.

Een late infectie, na 3 maanden en 1 jaar vond plaats bij slechts 2 patiënten (1,1%), waarschijnlijk na een bacteraemie. Bij beiden moest de prothese verwijderd worden.

Deze resultaten mogen bevredigend worden genoemd vooral in een gecompromiteerde patiëntenpopulatie met een gemiddelde leeftijd van 71 jaar. Een dergelijk laag infectiepercentage benadrukt de noodzaak het gecombineerde gebruik van "ultra-clean-air" installaties en antibiotica voor prothese-chirurgie van de heup of de knie verder te zetten en, waar niet aanwezig, in te voeren, ter preventie van "airborne" staphylokokken infecties. Het achterwege laten van één van deze twee technieken bleek minder efficiënt in eerder genoemde M.R.C.-studie.

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## RÉSUMÉ

*L. KLENERMAN, D. SEAL et K. SULLENS. Combinaison prophylactique d'air ultrafiltré et de céfuroxime dans la prévention des infections en chirurgie prothétique.*

Cent soixante quatorze arthroplasties de hanche ou de genou ont été effectuées en air ultrafiltré et sous prophylaxie antibiotique (céfuroxime), tenant compte des conclusions d'une étude multicentrique du MRC (Medical Research Council) selon laquelle cette combinaison assurerait le moindre risque d'infection. L'infection précoce d'une prothèse fut rare (0,6%), tandis qu'une infection superficielle s'est produite dans 2,9% des cas, sans atteinte de la prothèse. Une infection tardive à 3 mois et à 12 mois s'est produite chez 2 patients (1,1%) à la suite d'une bactériémie probable, ce qui a nécessité l'ablation de la prothèse. Ces résultats sont satisfaisants, surtout chez des malades âgés de 71 ans en moyenne. Un taux d'infection aussi bas nous encourage à employer cette combinaison d'air filtré et d'antibiothérapie pour les arthroplasties de hanche et de genou. Selon l'étude du MRC ces 2 mesures sont moins efficaces si elles sont employées isolément.

## INTRODUCTION

The recent multicentre study of 8052 patients in Britain and Sweden showed that a combination of ultraclean air and antibiotics produced the lowest sepsis rate for hip and knee prostheses of 0.06% (8, 11), an unexpected result which did not allow study of individual antibiotics nor use of antiseptics. Previously Charnley (1), in 1972, had obtained rates under 1% with ultraclean air and body exhaust suits but without antibiotics. Pollard *et al.* (14), in 1979, reduced the rates of prosthetic infection to 1.3% with the use of cephaloridine or flucloxacillin at the time of surgery but without ultraclean air. Hill *et al.* (6), in 1981, in a double-blind placebo-controlled trial of 2137 patients demonstrated both a reduction in prosthetic infection from 3.3% (placebo) to 0.9% with the use of cefazolin and a similar reduction using ultraclean air without antibiotics. This compares with a sepsis rate of 8.3% for primary Charnley hip

replacements inserted between 1968 and 1972, without specific precautions, but followed up for 10 years, when 50% of the stems appeared loose on radiographic examination because of faulty cementing technique (19). Such long-term followup is important, particularly to establish late infection rates of the prosthetic joint from bacteremia, with or without septicemia, so that appropriate prophylaxis can be considered (2). The best choice of antibiotic for surgical prophylaxis also needs to be determined, as well as whether its use in combination with ultraclean air can result in the very low infection rates achieved in the Medical Research Council study.

## PATIENTS AND METHODS

Over a period of 1 year, 174 prostheses (122 hips and 52 knees) were inserted in 64 men, average age 67 years, and in 110 women, average age 73 years, suffering mostly from osteo- or rheumatoid arthritis. The surgery was performed in an original ultraclean air theater, built by Howorth Limited for the Medical Research Council multicenter trial; it gave a lower air flow rate (0.2 m/sec) than the faster flow rates (0.4 m/sec) now produced. Body exhaust suits were not worn by the operating team. Bacteria-carrying particles (BCP) were monitored in this operating room during surgery for 114 operations by the settle plate technique, using plates of 8.5 cm diameter. They were placed on top of the diathermy machine, which was at a peripheral site within the ultraclean enclosure.

Skin preparation was begun on the ward the night before surgery with povidone iodine (steribath plus paint) or chlorhexidine (4% Hibiscrub® whole-body bathing) and was applied again in the operating room. Cefuroxime was given to patients as prophylaxis, 750 mgs IM with the premedication, 750 mgs IV on induction in the operating room, and 750 mgs IM or IV 8 hours postoperatively. This antibiotic, which is a broad-spectrum cephalosporin resistant to beta-lactamase, was continued for up to 3 days in 42 patients and more than 3 days in 33 patients because of concomitant chest, urinary or other infections. After operation wounds were covered with a dry dressing and left

undisturbed for 5 days ; suction drains were used. Surgical procedures undertaken were the Charnley and Exeter total hip replacements and the Stanmore and Kinematic total knee replacements ; antibiotic impregnated cement was used with either gentamicin or colistin and erythromycin. The operations were nonteaching, and efforts were made to keep numbers and movement of staff to a minimum.

All patients were visited before and after surgery by the Infection Control nurse to supervise prophylaxis and to investigate and quantify wound infection. Wounds were graded as 1 (erythema/slight serous discharge), 2 (purulent discharge) or 3 (deep sepsis/wound dehiscence). Patients were reviewed for up to 2 years following surgery for evidence of late infection or loosening of the prosthesis.

## RESULTS

No acute infections of a prosthesis occurred within 6 weeks, which gave an early sepsis rate of  $< 0.6\%$  (0/174). Wound infection, apparently separate from the prosthesis, occurred in 9 hip operations (7.4%) of which 5 were grade 1, 3 were grade 2 and 1 was grade 3. *Staphylococcus aureus* was isolated from one grade 2 wound and one grade 3 wound, while *Pseudomonas aeruginosa*, *Klebsiella sp.*, *Acinetobacter sp.* and *Streptococcus faecalis* were isolated from other wounds. Only 2 wound infections occurred around the knee prosthesis (3.8%), 1 grade 1 (*Escherichia coli* isolated) and 1 grade 3 (*Bacillus sp.* isolated). None of the wound infections involved the joints. There was no apparent difference in wound infection rates whether the patients had been prepared with povidone iodine or chlorhexidine whole-body bathing antiseptic, but numbers of infected patients were too small for statistical comparison.

Fifteen patients (9 hips, 6 knees) were lost to follow-up after surgery, while 4 patients (2 hips, 2 knees) died within 10 days of surgery from noninfectious causes. For prosthetic hips, 95% were satisfactory at 6 months ; 5 patients were then lost to follow-up at one year, and 8 at 2 years, but all others (93 patients) except those described

below remained satisfactory at 2 years. Within 6 months, 2 patients had developed dislocation of the prosthetic hip, 2 had developed "loose" hips (managed conservatively without further surgery), while one developed infection of the prosthesis with group G beta-hemolytic *Streptococcus* (BHS). In the latter patient pain and instability began around the prosthesis 3 months after operation following two episodes of cellulitis near the wound (4) ; the prosthesis was removed after 6 months and the organism was isolated, but the patient died 2 months later from carcinoma of the rectum.

Forty-four prosthetic knees were satisfactory at 6 months. Two patients were then lost to follow-up at 1 year and 2 at 2 years, but all except 1 (39 patients) remained satisfactory at 2 years. This one patient, who had bilateral hip and knee prostheses for severe rheumatoid arthritis, presented with late infection of a knee prosthesis at 1 year. Pus was drained from it, which gave no growth on culture, and he was treated with antibiotics ; after a further year the prosthesis had to be removed, and the knee was arthrodesed. *S. aureus* and *P. aeruginosa* were cultured from swabs collected during the operation.

For 114 operations the average count of airborne bacteria-carrying particles (BCP), at a site near the wound, was  $25/m^3$ , which is within acceptable limits for the settle-plate method used. The settling rate of BCP in an ultraclean operating room was assumed, from a study by Lidwell *et al.* (9), to be 1.3 cm/sec, which is double the rate of a traditional turbulently ventilated operating room. This allowed  $0.3 m^3/h$  of air to be sampled on each plate, which is less accurate than bigger volumes collected by the slit-sampling technique, but has the advantage of simplicity of use. *S. aureus* was isolated from these settle plates on two occasions when a surgeon had early folliculitis ; despite shedding skin scales containing the organism near the wound, the patients were not infected. On another two occasions, a single colony of *S. aureus* was isolated on each settle plate. Neither patient developed a wound or hip prosthesis infection, probably because the pattern of air flow generated in an ultraclean air operating room results in BCP being removed from the site of the wound to the periphery of the operating

room and then excluded in the air filtration system.

Cefuroxime prophylaxis was well tolerated except for 2 patients who had prolonged therapy for 8 and 26 days, respectively. They each developed diarrhea from which *Clostridium difficile* was isolated, and, as a result, the prosthetic hip became dislocated. No hypersensitivity reactions occurred.

## DISCUSSION

Multicenter studies, such as that of Lidwell *et al.* (11), are needed to show real differences in infection rates between 1 and 0.06%. As the latter figure of almost zero infection was obtained by using both ultraclean air and antibiotics together, smaller trials are needed in District Hospitals to assess the combination in practice. Cefuroxime was chosen for antibiotic prophylaxis because it is bactericidal and effective against *S. aureus* and *S. epidermidis* as well as gram-negative coliform flora, excluding *P. aeruginosa*. It has been shown to give good penetration into the femoral head, lower femur, and hip and knee capsules (7). It was used in a trial for prosthetic surgery by Hughes *et al.* (7), as antibiotic prophylaxis without ultraclean air. In this study, a prosthesis infection rate of 1.9% (2 out of 106 patients) was obtained, but both infections occurred late at 6 months and 1 year. Such absence of acute infection did not occur however in their second trial of 295 prostheses (13), also performed without ultraclean air, when 3 acute infections of prostheses developed within 3 weeks of surgery, necessitating removal of 2 of them; the *S. aureus* and coryneform bacteria isolated were probably acquired by the airborne route.

Our acute infection rate of prostheses of < 0.6% (0 out of 174 operations), using ultraclean air and cefuroxime, is considered satisfactory, particularly as such patients were elderly or had rheumatoid arthritis. Because of the smaller number of patients in our study, these figures are not better than those for surgery in conventional operating rooms together with the use of antibiotic prophylaxis, when a prosthesis infection rate was obtained of 0.65% (3) and 0.9% (6). In the study of Fitzgerald *et al.* (3) *S. aureus* was isolated from half the acute

infections together with anaerobic and Gram-negative bacteria expected to be sensitive to cefuroxime. Ultraclean air, as shown by Charnley (1), reduces the airborne contamination of wounds, while a bactericidal antibiotic such as cefuroxime further reduces the numbers of bacteria able to multiply in tissue. A minimum number of organisms is required to cause a clinical infection, so that it is not surprising that the combined approach of ultraclean air and antibiotics has been shown to significantly reduce acute (or early) prosthetic infection to a rate of 0.06% (11).

The late infection rate was 1.1% (2 out of 174 operations) or 1.35% (2 out of 148 operations) excluding those 26 lost to follow-up at 1 year. The late infections involved 1 hip at 3 months and 1 knee at 1 year, both in high-risk patients. The former was infected with BHS group G which was resistant to gentamicin in the bone cement; such BHS infections are associated with neoplasia, which the patient was later shown to have, and followed two episodes of cellulitis in the thigh below the prosthesis. The latter patient had severe rheumatoid arthritis and was taking steroids. Both patients were probably infected by hematogenous spread, as described by others (2, 12, 15, 18), although Fitzgerald *et al.* (3) classified late infections as occurring after a long asymptomatic period up to 23 months or more following surgery. The importance of giving antibiotic treatment to patients with prostheses who have intercurrent infections should be emphasized (18), as small inocula of bacteria can cause infections of "foreign bodies". The choice of antibiotic depends on the type of intercurrent infection, but treatment must be given early; it should be remembered that beta-hemolytic streptococci are resistant to gentamicin, often used in cement. Both our late infections occurred in patients in whom antibiotic cement had been used. Such cement is considered to have a dubious prophylactic effect owing to the slow release of antibiotic which often yields levels below those required for inhibition of bacteria.

Failure rates, apparently unassociated with infection, have been reported to reach 5% after 7 years (10), which is similar to our figure. Loosening of the joint is difficult to differentiate from chronic infection due to bacteria of low virulence such as

*S. epidermidis*. Such prostheses can yield no bacterial growth by ordinary culture techniques but have been shown by Gristina and Costerton (5) to be colonized by a polymicrobial population within an adherent biofilm. Bone samples require homogenizing and treating in a cleaning sonicator for successful culture, with care taken to avoid contamination. Electron-microscopy can usefully demonstrate bacteria on the surface.

Monitoring the numbers of airborne bacteria can be useful in older ultraclean air operating rooms, or in those without ultraclean air, for detecting shedding of skin scales containing *S. aureus*, but it is not usually required when the air-flow rate reaches 0.4 m/sec. New experimental ultraclean air theaters have been constructed that function without restrictive walls, depending instead on "air barriers" (16, 17). They prevent bacterial entrainment toward the wound, and they should reduce the occurrence of airborne staphylococcal infection. For the surgeon they do not necessitate wearing a body exhaust suit, with special gowns and helmets, which thereby permits more freedom of movement. With an air-flow rate of 0.4 m/sec., used in new ultraclean operating rooms, little additional benefit in preventing airborne staphylococcal infection can be expected from the use of body exhaust suits by the surgical team, especially if the patient receives antibiotics, as there is rapid clearance of shed skin scales; these scales are then removed by the high efficiency filters (17). In turbulently ventilated nonultraclean operating rooms, however, the wearing of body exhaust suits by the surgical team can be expected to contribute to a significant reduction in airborne Staphylococcal infection (1, 8).

#### Acknowledgments

We are very grateful to Mrs. Maureen Gibson for valuable assistance with this study, as well as to the medical and nursing staff of Evelyn and Eliot wards.

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