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Improved antibiotic therapy for elimination and prevention of prosthetic hip infection

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Total hip replacement is one of the most successful and cost-effective surgical operations ever introduced with over 50,000 hip replacements performed annually in the UK. Bacterial infection is a significant complication following this procedure, with 22% of revision operations in a recent study resulting from implant infection (Tunney et al 1998). Failure of the second implant post-revision, however, is due to infection in up to 40% of cases (Dupont 1986). It has been suggested that this higher rate of infection post-revision may be due to the fact that bacteria colonising the surface of implanted biomaterials grow predominantly within adherent biofilms which confer a level of resistance to antibiotics and may render current antibiotic therapy ineffective. In Musgrave Park Hospital, antibiotic treatment to reduce the risk of recurrent infection includes the use of gentamicin-impregnated bone cement for prosthesis fixation at revision surgery and the intravenous administration of either cefamandole or erythromycin peroperatively. We have previously shown resistance of planktonic *Staphylococcus* spp. isolated from orthopaedic implants to these three antibiotics (Tunney et al 1997). The aim of the present study was, therefore, to determine if treatment of hip implant infection could be improved by the use of alternative antimicrobial agents or combinations of antimicrobial agents.

A total of 49 clinical isolates (30 *Staphylococcus* spp., 19 *Propionibacterium acnes*) recovered from retrieved prosthetic hip implants were tested. Planktonic minimum inhibitory concentrations (MIC), Planktonic minimum bactericidal concentrations (MBC) and sessile MBC's were determined as described previously (Tunney et al 1997). Paired combinations of antibiotics were cross-titrated using the chequerboard technique to investigate possible synergy. The summation of fractional inhibitory concentrations (ΣFIC) was calculated to provide an indication of the combined effect of the antibiotics (Hallender et al 1982).

All isolates tested were sensitive to vancomycin and ciprofloxacin (Table 1). Resistance of several aerobic isolates to fusidic acid was however apparent. Ciprofloxacin was the most effective bactericidal agent followed by vancomycin and fusidic acid in decreasing order of efficacy. Synergy between cefamandole and gentamicin was observed for five of the eight isolates tested. In contrast, a combination of vancomycin and ciprofloxacin was synergistic for only one isolate and antagonistic for a further four isolates. On the basis of MBC's, sessile populations of a range of isolates adherent to bone cement exhibited greater resistance to gentamicin, cefamandole and vancomycin compared with planktonic bacterial suspensions. In contrast, sessile populations of seven of the eleven isolates tested showed no increase in resistance to ciprofloxacin.

Table 1. Susceptibility of isolates to antibiotics

		MIC(μg/mL)		
Isolate	Test agent	Range	50%	90%
Staphyl	Vancomycin	0.25-2	1	2
ococcus	Ciprofloxacin	0.125-2	0.5	1
spp.	Fusidic acid	0.125-16	0.25	16
P.	Vancomycin	0.125-1	0.5	0.5
acnes	Ciprofloxacin	0.5-1	1	1
	Fusidic acid	0.125-1	1	2

This study has shown that the use of vancomycin and ciprofloxacin peroperatively and in bone cement could be more effective for the eradication of implant infection and for the prevention of further infection. It has also shown that the elimination of bacterial biofilm is particularly difficult, but that ciprofloxacin is much superior to other antibiotics in this respect.

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