LABORATORY STUDY

Antibiotics in the irrigating solutions reduce *Staphylococcus epidermidis* adherence to intraocular lenses

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Abstract

Purpose **To investigate the effect of antibiotics in the irrigating solutions on hydrophobicity, slime production and the adherence of *Staphylococcus epidermidis* to intraocular lenses (IOLs).**

Methods **A standard culture of *S. epidermidis* was incubated with a control phosphate-buffered saline (PBS) or PBS containing vancomycin (20 μg/ml) or gentamicin (8 μg/ml) or a combination of gentamicin and vancomycin (8 and 20 μg/ml, respectively) for 30, 60 and 120 min at 35 °C. The bacteria were harvested by centrifugation, and washed with PBS before incubation with IOLs for 1 h. Adhesion of bacterial cells to IOLs was determined by counting the viable cells attached to the lenses. Slime production on IOLs was measured using safranin staining. Hydrophobicity of the control cultures and cultures treated with antibiotics was assayed on the basis of the hexadecane droplet method.**

Results **Bacterial exposure to antibiotics produced a time-dependent significant decrease in bacterial hydrophobicity and adherence to IOLs compared with the untreated control cells ($p < 0.001$). Hydrophobicity showed a significant correlation with adherence ($r = 0.89$, $p < 0.001$). Gentamicin was significantly more effective than vancomycin, and the synergistic combination of gentamicin and vancomycin was the most effective in reducing bacterial adherence to IOLs, hydrophobicity and slime production.**

Conclusions **The use of antibiotics in the irrigating solutions during cataract surgery may be useful in reducing bacterial adherence to IOLs. Further studies are needed to determine the clinical implications of these findings in reducing the incidence of post-operative endophthalmitis associated with IOL implantation.**

Key words Antibiotics, Bacterial adhesion, Endophthalmitis, Intraocular lens, *Staphylococcus epidermidis*

Endophthalmitis following cataract extraction and intraocular lens (IOL) implantation is a serious infectious complication of ocular surgery. Coagulase-negative staphylococci, particularly *Staphylococcus epidermidis*, are the most common infectious organisms, and are the cause in up to 70% of cases.[1] Molecular biological studies in *S. epidermidis* endophthalmitis demonstrated that eyelid, conjunctiva or nose isolates were indistinguishable from intraocular isolates in up to 82% of patients with post-operative endophthalmitis, suggesting that the commonest source of infection is the patient's own flora.[2,3] Anterior chamber contamination during surgery is not infrequent and up to 43% of patients had organisms recoverable from their anterior chamber fluid at the conclusion of uncomplicated extracapsular cataract extraction or phacoemulsification.[4–6] The most commonly isolated organisms were coagulase-negative staphylococci.

The prophylactic use of antibiotics in the irrigating solutions during cataract surgery to prevent post-operative endophthalmitis is controversial. Gills[7,8] reported that no endophthalmitis developed in 25 000 patients who underwent cataract surgery when vancomycin and gentamicin were added to the infusion solution, and the infusion solution was filtered. Dickey *et al.*[9] examined post-cataract anterior chamber aspirates after surgery using gentamicin in the irrigating solution. No organisms were isolated from 28 patients' aspirates. Recently, an *in vitro* model was established in which bacterial isolates commonly implicated in infectious post-operative endophthalmitis were exposed to antibiotics in infusion fluid for a short period of time (up to 2 h), with generally no effect on the viability of these organisms.[10] Ferro *et al.*[11]

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studied the effect of antibiotics in the infusion solutions on the incidence of positive culture results from the aqueous humour after cataract surgery, and found no statistically significant differences in bacterial growth between the placebo group and the treatment group.

Coagulase-negative staphylococci are the major cause of sepsis following prosthetic surgery of all types. This includes joint replacement, vascular grafts, cardiac valve replacement, cerebrospinal fluid shunt systems, intravascular catheters and IOL implantation.[1,12] These organisms, once attached to an implant surface, adhere strongly and become embedded in an extracellular mucoid glycocalyx or slime film which protects the embedded bacterial cells against the host's immune response and antibiotic therapy.[13–15] In addition, it is well documented that hydrophobic surface moieties play a role in bacterial adherence.[16]

Disrupting or inhibiting the initial adherence of *S. epidermidis* to IOLs would have a significant impact on reducing the incidence of endophthalmitis after lens implantation. Therefore, we have developed an *in vitro* model to investigate the activity of vancomycin (20 μg/ml), gentamicin (8 μg/ml), and a combination of gentamicin and vancomycin (8 and 20 μg/ml, respectively) in the irrigating solutions in modifying the adhering activity of *S. epidermidis* to IOLs. We also studied the effect of these antibiotics on hydrophobicity and slime production by *S. epidermidis*.

Materials and methods

A standard culture of *Staphylococcus epidermidis* (American Type Culture Collection [ATCC] #14990) with known characteristics was used in these experiments. Cells were grown in Mueller-Hinton broth (oxoid) overnight at 37 °C. Cells were harvested by centrifugation, washed three times in 0.9% saline and resuspended in phosphate-buffered saline (PBS) solution, pH 7.2, to a final cell density of 10^6 colonies forming units per millilitre (cfu/ml). One hundred and thirty-two regular polymethylmethacrylate IOLs lenses (Model 724B) provided by Pharmacia Production (The Netherlands) were used in the study.

The bacteria were incubated at 35 °C for 30, 60 and 120 min in a control PBS or PBS containing each of the following antibiotics or antibiotic combinations: vancomycin (20 μg/ml) gentamicin (8 μg/ml), and a combination of gentamicin and vancomycin (8 and 20 μg/ml, respectively). These concentrations have been recommended for irrigation solution supplementation during cataract surgery by several investigators.[7–9] After each exposure time, bacteria were harvested by centrifugation at 5000 rpm for 10 min and washed three times with PBS to remove the residual antibiotic. This step was repeated for the control culture. Thus, organisms were actually exposed to antibiotics for 40, 70 and 130 min when centrifugation time is taken into account.

Effect of antibiotics on bacterial adherence to IOLs and slime production

Following the final wash, the inocula were adjusted to a concentration of 10^6 cfu/ml. The sterile non-used lenses were suspended by fine sterile wire threaded through the dialling holes in flasks containing control cultures and cultures treated with antibiotics for 30, 60 and 120 min. The lenses were then incubated at 37 °C for 1 h. The lenses were removed and washed five times by dipping in normal saline. Bacterial adherence to IOLs was assessed using the method of viable counting. The lenses were transferred into a sterile universal container containing 10 ml of PBS, and the adherent bacteria were released from the lenses by vortexing for 3 min. This regimen was found in prior experiments to remove all adherent bacteria verified by light microscopy without affecting their viability.[17] Serial dilutions of the PBS that contained the dislodged bacteria were made and 1.0 ml from each dilution was plated on a blood agar (oxoid) plate. The plates were incubated overnight at 37 °C and the colonies counted by a masked individual. The number of viable cells per millilitre was calculated from the respective dilutions. These experiments were performed eight times.

Slime production by *S. epidermidis* was measured indirectly by determining the intensity of adherent growth on IOLs. Slime production was measured after 1 h, when the lenses were removed, washed twice in PBS and stained with safranin. The score was recorded as (+) to (+++) according to the intensity of stained adherent growth.[18] These experiments were repeated three times.

Effect of antibiotics on bacterial hydrophobicity

Control cultures and cultures treated with antibiotics for 30, 60 and 120 min (10^6 cfu/ml) were centrifuged at 5000 rpm for 10 min and the organisms were harvested and then washed twice in PBS. After the final wash the pellet was resuspended in 1 ml of PBS, and the absorbance (*A*) value was adjusted to 0.4 with additional PBS and hydrophobicity assayed on the basis of the hexadecane droplet method of Rosenberg *et al*.[19] Hexadecane, 300 μl, was added to 3 ml suspension, vortex-mixed at moderately high speed for 120 s and allowed to stand for phase separation. The change in *A* value in the aqueous phase at 530 nm was read with a spectrophotometer (Ultraspec II spectrophotometer, Pharmacia, Rockville, MD). Thus, the decrease in *A* reading caused by the addition of hexadecane reflected the surface hydrophobicity of the organism. These assays were performed eight times.

Statistical analysis

All data are presented as mean ± standard deviation. Comparisons among groups were performed by one-way analysis of variance (ANOVA). ANOVA was conducted using program 7D from the BMDP Statistical Package. The Bonferroni test was used for pairwise comparisons

Table 1. *Effect of antibiotics on adherence to intraocular lenses, slime production and hydrophobicity of* S. epidermidis

Groups	Adherence (log cfu/ml)[a] (mean ± SD)	% hydrophobicity[a] (mean ± SD)	Slime production[b]
30 minutes			
Control	14.28 ± 1.05	51.35 ± 2.45	NA
Vancomycin	7.81 ± 1.03 (< 0.001)[c]	47.3 ± 0.8 (< 0.001)	NA
Gentamicin	4.4 ± 0.4 (< 0.001)	32.5 ± 1.45 (< 0.001)	NA
Gentamicin/vancomycin	2.8 ± 0.08 (< 0.001)	29.43 ± 0.95 (< 0.001)	NA
p value[d]	< 0.001	< 0.001	
60 minutes			
Control	23.35 ± 4.0	52.48 ± 3.79	++
Vancomycin	5.5 ± 0.6 (< 0.001)	42.89 ± 1.2 (< 0.001)	++
Gentamicin	3.05 ± 0.54 (< 0.001)	27.07 ± 1.27 (< 0.001)	+
Gentamicin/vancomycin	2.06 ± 0.77 (< 0.001)	24.09 ± 0.94 (< 0.001)	−
p value[d]	< 0.001	< 0.001	
120 minutes			
Control	71.0 ± 3.08	57.66 ± 1.84	+++
Vancomycin	4.02 ± 1.4 (< 0.001)	39.06 ± 0.73 (< 0.001)	+
Gentamicin	2.7 ± 0.47 (< 0.001)	23.43 ± 0.6 (< 0.001)	+
Gentamicin/vancomycin	1.57 ± 0.1 (< 0.001)	20.29 ± 0.9 (< 0.001)	−
p value[d]	< 0.001	< 0.001	

cfu, colony forming unit; NA, not applicable.
[a]Each experiment was repeated eight times.
[b]Each experiment was repeated three times.
[c]*p* values in parentheses are for treated cultures compared with untreated controls (*t*-test).
[d]*p* value for comparison among groups by ANOVA.

between group means. The *t*-test was used in addition to obtain the *p* value for each pairwise comparison. Pearson's correlation coefficient test was used to examine the correlation of hydrophobicity with adherence. The differences were considered significant if $p < 0.05$.

Results

Staphylococcus epidermidis exposure to vancomycin (20 μg/ml), gentamicin (8 μg/ml) and a combination of gentamicin and vancomycin (8 and 20 μg/ml, respectively) for 30, 60 and 120 min incubation times resulted in a significant decrease in bacterial adherence to IOLs and cell surface hydrophobicity compared with the untreated control cells (*t*-test, $p < 0.001$ for all comparisons) (Table 1). Hydrophobicity of *S. epidermidis* treated with antibiotics showed a significant correlation with adherence ($r = 0.89$, $p < 0.001$) (Fig. 1). The decrease in hydrophobicity correlated significantly with the decrease in adherence after treatment with vancomycin ($r = 0.8593$, $p < 0.001$), gentamicin ($r = 0.8624$, $p < 0.001$), and a combination of gentamicin and vancomycin ($r = 0.9496$, $p < 0.001$).

Gentamicin produced a significantly greater decrease in bacterial adherence and hydrophobicity than did vancomycin at the 30 and 60 min incubation times (*t*-test, $p < 0.001$ for all comparisons). Furthermore, gentamicin was significantly more effective in decreasing hydrophobicity than vancomycin at the 120 min time interval (*t*-test, $p < 0.001$).

After the 30 minute incubation time, the synergistic combination of gentamicin and vancomycin was significantly more effective in decreasing bacterial adherence and hydrophobicity than vancomycin or gentamicin alone (*t*-test, $p < 0.001$ for all comparisons). At the 60 and 120 min time intervals, the combination of gentamicin and vancomycin was significantly more effective than vancomycin in decreasing bacterial adherence (*t*-test, $p = 0.0022$ and 0.0078, respectively) and hydrophobicity (*t*-test, $p < 0.001$ for both comparisons). In addition, the combination of gentamicin and vancomycin was significantly more effective than gentamicin in decreasing bacterial hydrophobicity at the 60 and 120 min intervals (*t*-test, $p = 0.0094$ and < 0.001,

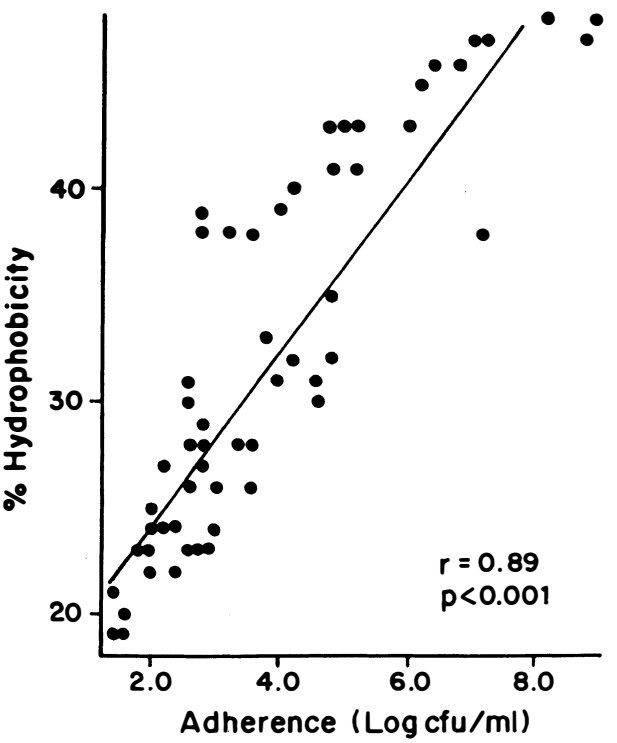

Fig. 1. *Correlation of hydrophobicity and adherence.*

respectively). Similarly, the combination of gentamicin and vancomycin was most effective in preventing slime production on IOLs (Table 1).

The reduction of bacterial adherence and hydrophobicity by vancomycin, gentamicin, or a combination of the two was time dependent (ANOVA, $p < 0.001$ for all comparisons). Exposure to antibiotics for 60 min was significantly more effective than the 30 min incubation time in reducing bacterial adherence (t-test, $p = 0.003$, < 0.001 and < 0.001, respectively) and hydrophobicity (t-test, $p < 0.001$ for all comparisons). Exposure to vancomycin and a combination of gentamicin and vancomycin for 120 min was significantly more effective than the 60 min incubation time in reducing bacterial adherence (t-test, $p = 0.0124$ and < 0.001, respectively) and hydrophobicity (t-test, $p < 0.001$ for both comparisons). In addition, gentamicin at the 120 min incubation time was more effective than at the 60 min incubation time in reducing hydrophobicity (t-test, $p < 0.001$).

Discussion

Staphylococcus epidermidis is now recognised as the most common organism responsible for infection of implanted prosthetic materials.[20] The presence of a foreign body alters the pathogenesis of the infectious process. *S. epidermidis* appears to be dependent on the presence of a foreign body to produce infection. Christensen *et al.*[21] demonstrated that these organisms are largely non-pathogenic when implanted under the skin but produce a suppurative infection when injected in the presence of a piece of an intravenous catheter material buried beneath the skin. Bacterial adherence to biomaterial is a crucial early event in the pathogenesis of infections.[16] *S. epidermidis* belongs to the ocular flora in healthy eyes.[22] An IOL can, by a presumed electrostatic surface charge, become contaminated by coagulase-negative staphylococci if it touches the ocular surface and even after exposure to the atmosphere in the operating theatre.[23,24] *S. epidermidis* secretes a bacterial glycocalyx, or slime, when adhering to an implant surface, which is thought to make the bacterial cells less accessible to human host defence systems and to decrease their antibiotic susceptibility significantly.[13–15] They can remain dormant on the material surface for a long time until the environment allows them to overgrow and clinical infection occurs. Bacteria adherent to IOLs may play a role in some forms of chronic post-operative endophthalmitis. IOLs removed because of recurrent episodes of intraocular inflammation showed *S. epidermidis* adherent to the prosthesis embedded in a matrix of extracellular slime.[25,26]

Our primary objective was to study the capacity of vancomycin and gentamicin in the irrigating solutions to alter *S. epidermidis* adherence to IOLs. We developed an *in vitro* model, attempting to mimic the situation that occurs when the patient undergoes cataract surgery with an antibiotic-containing irrigating solution. Antibiotics induced a significant time-dependent reduction in bacterial hydrophobicity, slime production and adherence to IOLs. The synergistic combination of vancomycin and gentamicin was the most efficacious. Hydrophobic moieties, which play a significant role in bacterial adherence,[16] significantly correlated with *S. epidermidis* adherence to IOLs. The reduction in adherence after drug treatment had an accompanying decrease in hydrophobicity and slime production. Ferro *et al.*[11] determined the intraocular antibiotic concentration in the early post-operative period after using vancomycin (20 μg/ml) and gentamicin (8 μg/ml) in the irrigating solutions. They observed that 2 h post-operatively, 47% of the initial concentration of vancomycin and 32% of the original concentration of gentamicin remained in the anterior chamber. Combining both antibiotics, these figures were greater than the minimum inhibitory concentration for all bacteria responsible for causing post-operative endophthalmitis.

The short exposure of bacteria to high antibiotic concentrations can result in prolonged suppression of bacterial growth, termed the post-antibiotic effect (PAE).[27] Bacteria that are in a suppressed or 'PAE' state may have altered virulence characteristics due to impaired adherence, diminished tissue invasion or inhibited toxin release. Several studies have demonstrated the capacity of antibiotics to reduce *S. epidermidis* adherence to implanted biomaterial surfaces.[28–30] In addition, coating catheters with antibiotics inhibited *S. epidermidis* colonisation on catheter surfaces.[31] These results indicate that antibiotics modify the interaction of *S. epidermidis* wth foreign surfaces. It is possible to hypothesise that vancomycin, by inhibiting bacterial cell wall synthesis, induces alteration of bacterial wall structures, probably surface adhesins which mediate bacterial adherence. Gentamicin, by inhibiting bacterial protein synthesis, may suppress the formation and expression of bacterial surface adhesins, and may induce the formation of functionally aberrant adhesins.[32] In addition, pretreatment of bacteria with antibiotics induces a marked increase in the phagocytosis of bacteria by phagocytes, and pretreatment of the phagocytes with antibiotics causes significant increase in phagocytosis of bacteria.[33]

The present data suggest that there may be an application of PAE in the prophylactic use of antibiotics in the irrigating solutions at the time of cataract surgery. The antibiotics studied were chosen because they have been recommended for irrigation solution supplementation by several investigators.[7–9] The administration of a short course of high-dose antibiotics could induce a state of decreased microbial virulence through impaired adherence.[27] Using quantitative counting, Ferro *et al.*[11] concluded that antibiotics in the irrigating solutions did not significantly reduce the incidence of positive post-operative intraocular cultures. Nevertheless, the odds of having a positive culture result in their study were 2.51 times greater for the placebo group. Similarly, Gritz *et al.*[10] found that exposure to

antibiotics for a short period of time, such as during intraocular surgery, has no effect on the viability of organisms commonly responsible for endophthalmitis. In fact, our results indicate that antibiotics in irrigating solutions may have effects on bacteria that alter their virulence properties responsible for adherence beyond simply reducing their capacity for growth or killing them.

Recently, serious concerns about the prophylactic use of vancomycin emerged because of increased occurrence of vancomycin-resistant organisms. The Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, recently published guidelines for controlling vancomycin hydrochloride resistance in hospitals.[34] It was reported by the CDC's National Nosocomial Infectious Surveillance System that the percentage of vancomycin-resistant enterococcal infections increased from 0.3% to 7.9% between 1989 and 1993. Of major concern is the potential for plasmid-born resistance of vancomycin being transferred to other gram-positive organisms, including *S. aureus* and *S. epidermidis*.[35] However, cataract patients, often operated on in an ambulatory setting, do not correspond with the patients described by the CDC.[36] Nevertheless, alternative antibiotics should be considered for routine surgical prophylaxis.

In conclusion, exposure of *S. epidermidis* to vancomycin (20 μg/ml) and gentamicin (8 μg/ml) significantly reduced bacterial adherence to IOLs. Gentamicin was more effective than vancomycin, and the synergistic combination of the two antibiotics was the most efficacious. Our results suggest that the addition of vancomycin and gentamicin to the irrigating solutions during cataract surgery could reduce the incidence of post-operative endophthalmitis and intraocular inflammation associated with IOL implantation. Further experimental and clinical studies are needed to prove the usefulness of the prophylactic use of antibiotics in the irrigating solutions, and to determine the efficacy and safety of alternative antibiotics.

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References

1. Han DP, Wisniewski SR, Wilson LA, Barza M, Vine AK, Doft BH, Kelsey SF and The Endophthalmitis Vitrectomy Study Group. Spectrum and susceptibilities of microbiologic isolates in the endophthalmitis vitrectomy study. Am J Ophthalmol 1996;122:1–7.
2. Speaker MG, Milch FA, Shah MK, Eisner W, Kreiswirth BN. Role of external bacterial flora in the pathogenesis of acute postoperative endophthalmitis. Ophthalmology 1991;98:639–50.
3. Bannerman TL, Rhoden DL, McAllister SK, Miller JM, Wilson LA, for the Endophthalmitis Vitrectomy Study Group. The source of coagulase-negative staphylococci in the endophthalmitis vitrectomy study: a comparison of eyelid and intraocular isolates using pulsed-field gel electrophoresis. Arch Ophthalmol 1997;115:357–61.
4. Sherwood DR, Rich WJ, Jacob JS, Hart RJ, Fairchild YL. Bacterial contamination of intraocular and extraocular fluids during extracapsular cataract surgery. Eye 1989;3:308–12.
5. Dickey JB, Thompson KD, Jay WM. Anterior chamber aspirate cultures after uncomplicated cataract surgery. Am J Ophthalmol 1991;112:278–82.
6. Samad A, Solomon LD, Miller MA, Mendelson J. Anterior chamber contamination after uncomplicated phacoemulsification and intraocular lens implantation. Am J Ophthalmol 1995;120:143–50.
7. Gills JP. Antibiotics in irrigating solutions [letter]. J Cataract Refract Surg 1987;13:344.
8. Gills JP. Filters and antibiotics in irrigating solution for cataract surgery [letter]. J Cataract Refract Surg 1991;17:385.
9. Dickey JB, Thompson KD, Jay WM. Intraocular gentamicin sulphate and postcataract anterior chamber aspirate cultures. J Cataract Refract Surg 1994;20:373–7.
10. Gritz DC, Cevallos AV, Smolin G, Whitcher JP Jr. Antibiotic supplementation of intraocular irrigating solutions: an *in vitro* model of antibacterial action. Ophthalmology 1996;103:1204–9.
11. Ferro JF, de-Pablos M, Logrono MJ, Guisasola L, Aizpuru F. Postoperative contamination after using vancomycin and gentamicin during phacoemulsification. Arch Ophthalmol 1997;115:165–70.
12. Jansen B, Peters G. Modern strategies in the prevention of polymer-associated infections. J Hosp Infect 1991;19:83–8.
13. Sugarman B, Young EJ. Infections associated with prosthetic devices: magnitude of the problem. Infect Dis Clin North Am 1989;3:187–99.
14. Gristina AG, Jennings RA, Naylor PT, Myrvik QN, Webb LX. Comparative *in vitro* antibiotic resistance of surface-colonizing coagulase-negative staphylococci. Antimicrob Agents Chemother 1989;33:813–6.
15. Pascual A, de Arellano ER, Martinez LM, Parea EJ. Effect of polyurethane catheters and bacterial biofilm on the *in vitro* activity of antimicrobials against *Staphylococcus epidermidis*. J Hosp Infect 1993;24:211–8.
16. Jansen B, Peters G, Pulverer G. Mechanisms and clinical relevance of bacterial adhesion to polymers. J Biomat Appl 1988;2:520–43.
17. Abu El-Asrar AM, Shibl AM, Tabbara KF, Al-Kharashi SA. Heparin and heparin-surface-modification reduce *Staphylococcus epidermidis* adhesion to intraocular lenses. Int Ophthalmol 1997;21:71–4.
18. Kadry AA, Tawfik AF, Abu El-Asrar AM, Shibl AM. Reduction of mucoid *Staphylococcus epidermidis* adherence to intraocular lenses by selected antimicrobial agents. Chemotherapy 1999;45:56–60.
19. Rosenberg M, Gutnick D, Rosenberg E. Adherence of bacteria to hydrocarbons: a simple method for measuring cell-surface hydrophobicity. FEMS Microbiol Lett 1980;9:29–33.
20. Jansen B, Peters G. Modern strategies in the prevention of polymer-associated infections. J Hosp Infect 1991;19:83–8.
21. Christensen GD, Simpson WA, Bisno AL, Beachey EH. Experimental foreign body infection in mice challenged with slime-producing *Staphylococcus epidermidis*. Infect Immun 1983;40:407–10.
22. Perkins RE, Kundsin RB, Pratt MV. Bacteriology of normal and infected conjunctiva. J Clin Microbiol 1975;1:147–9.
23. Vafidis GC, Marsh RJ, Stacey AR. Bacterial contamination of intraocular lens surgery. Br J Ophthalmol 1984;68:520–3.
24. Doyle A, Beigi B, Early A, Blake A, Eustace P, Hone R. Adherence of bacteria to intraocular lenses: a prospective study. Br J Ophthalmol 1995;79:347–9.
25. Dilly PN, Sellors PJ. Bacterial adhesion to intraocular lenses. J Cataract Refract Surg 1989;15:317–20.
26. Jansen B, Hartmann C, Schumacher-Perdreau F, Peters G. Late onset endophthalmitis associated with intraocular lens: a case of molecularly proved *S. epidermidis* aetiology. Br J Ophthalmol 1991;75:440–1.
27. Craig WA, Gundmundsson S. The post-antibiotic effect. In: Lorain V, editor. Antibiotics in laboratory medicine. Baltimore: Williams & Wilkins, 1986:515–36.

28. Schadow KH, Simpson WA, Christensen GD. Characteristics of adherence to plastic tissue culture plates of coagulase-negative staphylococci exposed to subinhibitory concentrations of antimicrobial agents. J Infect Dis 1988;157:71–7.
29. Schmitt DD, Edmiston CE, Krepel C, Gohr C, Seabrook GR, Bandyk DF, *et al*. Impact of postantibiotic effect on bacterial adherence to vascular prostheses. J Surg Res 1990;48:373–8.
30. Elliott TS, D'Abrera VC, Dutton S. The effect of antibiotics on bacterial colonisation of vascular cannula in a novel *in vitro* model. J Med Microbiol 1988;26:229–35.
31. Raad I, Darouiche R, Hachem R, Sacilowski M, Bodey GP. Antibiotics and prevention of microbiol colonization of catheters. Antimicrob Agents Chemother 1995;39:2397–400.
32. Shibl AM. Effect of antibiotics on adherence of microorganisms to epithelial cell surfaces. Rev Infect Dis 1985;7:51–65.
33. Van den Broek PJ. Antimicrobial drugs, microorganisms and phagocytes. Rev Infect Dis 1989;11:213–45.
34. Hospital Infection Control Practices Advisory Committee (HICAC). Recommendations for preventing the spread of vancomycin resistance. Infect Control Hosp Epidemiol 1995;16:105–13.
35. Fiscella RG. Vancomycin use in ophthalmology. Arch Ophthalmol 1995;113:1353–4.
36. Sunaric-Megevand G, Pournaras CJ. Current approach to postoperative endophthalmitis. Br J Ophthalmol 1997;81:1006–15.