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Bacterial adhesion to intravenous cannulae: influence of implantation in the rabbit and of enzyme treatments

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SUMMARY

Comparison was made of the adhesion of *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella aerogenes* and *Pseudomonas aeruginosa* to six types of intravascular cannula material. Adhesion to materials removed from rabbit tissues did not differ significantly between types of material or between bacterial species. In contrast, major differences were found when unimplanted materials were examined; the overall rank order of adhesiveness of bacteria to unimplanted materials (*S. epidermidis* > *P. aeruginosa* > *S. aureus* ⩾ *K. aerogenes* > *E. coli*) was highly significant ($F = 13{\cdot}0$, $P < 0{\cdot}0005$), and although no single material was consistently least attractive to all micro-organisms, FEP-Teflon and PTFE-Teflon showed significantly lower overall affinity for bacteria than other materials ($P < 0{\cdot}001$); all species showed a significant preference for a silicone polymer ($P < 0{\cdot}0005$). The nature of the bacterial surface structures responsible for adhesion were investigated by the actions of pronase and mixed glycosidase, which produced significant respective decreases and increases in adhesion of staphylococci to unimplanted materials; their effects on the Gram-negative bacilli were less consistent.

INTRODUCTION

Since the introduction of plastic intravenous cannulae shortly after the Second World War an increasing variety of synthetic polymers has been used for the manufacture of these devices. The precise choice of materials from which a cannula is to be made is determined by the required degree of flexibility, tissue compatibility and conformation to the specifications of licensing bodies. Propensity to infection is not normally asessed during materials selection, but obviously may be a limiting factor in the useful life of an implanted device, and in the case of intravascular cannulae is of particular importance where long-term vascular access is required for parenteral nutrition, cytotoxic drug administration, etc.

Naturally, infection of a cannula becomes evident whilst is is present within the tissue, but as with other implanted devices, it is rarely possible to decide whether the infection has been initiated at the time of implantation or afterwards. There are many case reports of devices which have become infected after implantation,

and the source has been a presumed bacteraemia due to a distant focus of sepsis (Downes, 1977; Liñares *et al.* 1985). However, organisms which enter the tissues along with an implant may also be responsible for infection, for example Lidwell *et al.* (1982) found that manipulation of operating theatre environment reduced the incidence of later sepsis in prosthetic joints.

It is recognized that the implantation of a foreign material bearing small numbers of bacteria results in sepsis far more readily than the implantation of bacteria alone (James & McLeod, 1961); the manufacture of implants from materials to which bacteria adhere poorly in the native state is therefore important. However, implanted materials adsorb molecules such as tissue proteins which may modify the nature of the surface available for microbial adhesion. Therefore when a micro-organism colonizes an implanted device, it is likely that the nature of the interaction with the substrate differs from that occurring with an unimplanted device and it is of importance to investigate adhesion to materials in the post-implantation states. An understanding of the nature of the bacterial surface structures mediating attachment is also relevant since this may provide information governing the eventual choice of implant materials with low potential for colonization.

The following study has investigated the relative propensity to infection of a number of cannula materials with a variety of bacteria. Six commonly used materials have been exposed to bacteria which are commonly (staphylococci) or uncommonly (*Escherichia coli*, *Klebsiella aerogenes* and *Pseudomonas aeruginosa*) involved in cannula infections. The effects on adhesion of treatment with pronase, which cleaves a wide range of peptide bonds, and a mixed glycosidase containing a number of glycosidic enzymes have provided information on adhesive mechanisms.

MATERIALS AND METHODS

Substrates. The following substrates were obtained in the form of intravascular cannulae.

(1) Fluorinated ethylene propylene copolymer (FEP-Teflon, FEP) containing $BaSO_4$ for radio-opacity, as 'Wallace IV Cannula' (H. G. Wallace & Co., Colchester, Essex).

(2) Polyethylene (PE) as 'Surcath' (Vygon, Unit 'E', Eskdale Road, Uxbridge, Middlesex).

(3) Polypropylene (PP) as 'Medicut' (Sherwood Medical Industries Ltd., County Oak, Crawley, West Sussex).

(4) Polytetrafluoroethylene (PTFE-Teflon, PTFE) as 'Venflon' (Viggo AB., Helsingborg, Sweden).

(5) Polyvinylchloride (PVC) as 'Drum Cartridge Catheter' (Abbott Laboratories).

(6) Silicone rubber containing $BaSO_4$ (SIL) used in 'Piggy Back' cannulae (H. G. Wallace & Co.).

The internal and external diameters of each type of cannula were measured using a microscope graticule, and from this were calculated the relative lengths required to provide equal surface areas. Before use each cannula was bisected longitudinally to ensure adequate washing.

Strains of bacteria. Strains of *Staphylococcus aureus*, *S. epidermidis*, *Klebsiella aerogenes* and *Pseudomonas aeruginosa* isolated from infections of intravascular devices were used in the experiments, the *Klebsiella* and *Pseudomonas* species were kindly provided by Dr S. Eykyn, Department of Clinical Microbiology, St Thomas's Hospital, London, SE1 7EH. Strains of *Escherichia coli* from cannula infections were unobtainable and those used had been isolated from urinary tract infections.

Adhesion experiments involving enzyme treatments. The methods used have been described previously (Barrett, 1985). Bacteria were grown overnight at 37 °C on nutrient agar containing D-[1-^{3}H]glucose at a concentration of 370 Bq/ml. The micro-organisms were harvested into phosphate-buffered saline (PBS, Oxoid BR14a) and washed twice by centrifugation and were resuspended to E_{560}0·1. To each of three 10 ml suspensions of each micro-organism was added 10 ml of one of the following; PBS, pronase (BDH) 200 μg/ml in 0·05 M Tris adjusted to pH 8·0 with acetic acid, mixed glycosidase containing at least 12 glycosidic enzymes (Miles laboratories) 2 mg/ml in 0·05 M sodium acetate buffer pH 5·5. The suspensions of bacteria were then left at room temperature for 1 h and centrifuged twice before resuspending to E_{560}0·1 in PBS. Viable counts of the micro-organisms subjected to these treatments were made. 1 ml of each suspension was added to a 7 ml capped plastic tube containing the measured amount of one of the plastic cannula substrates. The tubes were tumbled for 1 h at room temperature. Each strain was examined in duplicate. At the end of the hour, the bacterial suspension was decanted from the tube and the cannula material inside was washed three times with PBS, a procedure which had previously been found to remove loosely adherent organisms; the cannula materials were then left to dry.

Animal models. Under sterile conditions, measured bisected lengths of each cannula material were tied together with surgical sutures. The scapular regions of six anaesthetized New Zealand White rabbits were shaved and one type of each cannula material was implanted subcutaneously into each rabbit. Following sacrifice of the animals 7 days later the cannula materials were removed. They were washed twice in PBS and then placed in 7 ml plastic tubes as above.

Measurement of adhesion. Adhesion was measured by immersing the segments of cannulae which had been exposed to bacteria in scintillation vials containing 'Scintillator 299' (United Technologies, Packard). These were counted in a liquid scintillation counter (LKB Rackbeta 1217). In order to allow for the different quenching of β-activity by the various plastics, 40 μl of a suspension of radiolabelled micro-organisms were dried on to each type of cannula material; the ratio of the number of β-counts in this to that in the same volume of suspension in the absence of cannula material was then used to correct adherent count values. Adhesion was expressed as the percentage of inoculated counts recovered from the cannula material.

Statistical methods. Adhesion values were transformed to $\log_{10}$ and analysis of variance ratios was made using the 'Nanostat' package (© Professor M. J. R. Healey, Department of Statistics, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT).

Table 1. *Mean (and standard deviation) percentage adhesion of bacteria to cannula materials after 1 h incubation at room temperature*

	FEP		PE		PP		PTFE		PVC		SIL	
	C	R	C	R	C	R	C	R	C	R	C	R
S. epidermidis	5·2 (3·0)	58·4 (32·8)	6·6 (5·7)	30·4 (30·1)	21·3 (13·6)	33·1 (18·6)	13·7 (7·4)	20·9 (18·3)	8·2 (4·9)	21·1 (14·1)	39·7 (22·2)	19·0 (8·3)
S. aureus	1·9 (1·3)	27·7 (6·4)	4·9 (1·4)	33·4 (12·5)	7·4 (1·4)	17·0 (8·9)	5·8 (1·4)	33·1 (11·3)	4·4 (1·8)	27·1 (7·3)	19·2 (3·1)	24·6 (4·5)
E. coli	0·8 (0·2)	25·0 (16·8)	2·0 (1·4)	15·4 (14·8)	0·4 (0·1)	19·6 (24·9)	0·5 (0·6)	37·8 (31·3)	1·2 (0·4)	7·6 (4·1)	1·1 (0·4)	16·0 (11·4)
K. aerogenes	3·6 (3·9)	17·4 (11·3)	8·3 (8·1)	16·3 (9·9)	2·7 (3·2)	16·8 (12·6)	2·8 (2·8)	19·0 (12·7)	10·8 (7·8)	23·5 (19·3)	9·6 (8·1)	14·0 (7·8)
Ps. aeruginosa	11·5 (6·9)	18·3 (5·5)	22·3 (11·3)	9·9 (3·5)	7·5 (3·7)	9·9 (3·5)	5·5 (3·9)	27·9 (10·4)	9·9 (5·0)	8·9 (4·5)	27·5 (12·7)	18·9 (5·6)

C, control materials (8 cannula segments). R, materials removed from rabbits after 1 week's implantation (4 cannula segments).
Four strains of each species were examined. Observations were made on two replicates for control materials, singly for implanted materials.
FEP, fluorinated ethylene propylene copolymer; PE, polyethylene; PP, polypropylene; PTFE, polytetrafluoroethylene; PVC, polyvinylchloride; SIL, silicone rubber.

RESULTS

Inter-species differences in adhesion to control and rabbit-implanted materials. Values for bacterial adhesion to materials removed from rabbits, along with control material examined at the same time, are shown in Table 1. There were no significant differences in the adhesion of the various species to materials removed from rabbits ($F = 1{\cdot}07$). In the case of unimplanted materials however, the observed rank order of adhesion was highly significant ($F = 13{\cdot}0$ corrected for strain-species interaction, $P < 0{\cdot}0005$), i.e. *S. epidermidis* > *Ps. aeruginosa* > *S. aureus* ≫ *K. aerogenes* > *E. coli*.

Inter-materials differences in adhesion to control and rabbit-implanted materials. The rank order of affinity for bacteria shown by implanted materials (PTFE > FEP > PP/SIL > PE > PVC) just achieved significance at the 5% level ($F = 2{\cdot}7$). Differences in affinity displayed by control materials (SIL > PE > PVC > PP > FEP > PTFE) were significant at the 0·05% level ($F = 14{\cdot}2$ corrected for species-substrate interactions). The mean adhesion values for the six materials fell into two groups; FEP and PTFE displaying significantly lower ($P < 0{\cdot}001$) overall affinity for bacteria (mean percentage adhesion values 4·0 and 4·6) than did the other substrates (mean percentage adhesion values 9·8–21·1).

Adhesion of individual species to different unimplanted materials. Table 2 shows the mean and standard deviation of percentage adhesion values for each micro-organism to the untreated plastic materials. Since the experiments on all organisms could not be performed simultaneously, the values in this table cannot be compared directly between species. Viable counts confirmed that the organisms had survived enzyme treatments. Although strains of individual species sometimes differed in their order of preference for the plastics, and in the nature of their response to the enzyme treatments, analysis of variance ratios within each species revealed that significant differences in adhesion were attributable both to the type of plastic and to the type of enzyme studied. For each species analysis was made of the variance of bacterial adhesion to the six plastic substrates within each enzyme group; the mean adhesion to each individual substrate was compared with the mean of the other five and divided by the standard error, based on the value of enzyme-strain interactions, in order to produce a t-value. For all species a uniform preference for the silicone polymer in comparison with other materials ($P < 0{\cdot}0005$) was found. However, in contrast to Table 1 where FEP and PTFE could be shown to be least attractive overall for bacteria, no single material showed a consistent lowest affinity for every species. The analysis for material preferences was repeated within the two enzyme groups; for the glycosidase-treated group the findings were essentially the same as for untreated organisms, in the pronase-treated group *S. epidermidis* and *E. coli* showed no material preferences of outstanding significance and those shown by the other organisms varied between species.

Influence of enzyme treatments on adhesion to unimplanted materials. Differences in mean adhesion values following enzyme treatments were compared with standard errors derived from enzyme-strain interactions and the level of significance was calculated from the resulting t-value; the significance of the

Table 2. *Mean (and standard deviation) percentage adhesion values for five bacterial species to intravascular cannula materials*

		FEP	PE	PP	PTFE	PVC	SIL	Mean
S. epidermidis	N	2·8 (2·6)	2·6 (3·1)	3·8 (4·1)	1·2 (1·3)	1·0 (0·6)	12·1 (10·5)	3·9
	G	3·8 (3·0)	6·7 (5·8)	3·7 (2·3)	2·5 (2·4)	2·9 (2·4)	11·6 (4·0)	5·2
	P	0·8 (1·0)	0·6 (0·2)	0·3 (0·2)	0·3 (0·3)	0·3 (0·1)	3·6 (4·8)	1·0
S. aureus	N	1·3 (0·9)	1·5 (0·7)	0·9 (0·6)	0·5 (0·3)	0·6 (0·2)	2·3 (1·7)	1·2
	G	1·3 (0·4)	3·2 (1·5)	1·9 (0·9)	0·8 (0·3)	1·6 (0·6)	4·3 (1·4)	2·2
	P	0·2 (0·1)	0·5 (0·1)	0·2 (0)	0·1 (0·1)	0·5 (0·2)	0·5 (0·1)	0·3
E. coli	N	1·2 (0·9)	2·4 (1·6)	2·1 (2·0)	1·1 (0·6)	1·9 (1·1)	3·4 (2·9)	2·0
	G	0·7 (0·5)	1·7 (1·1)	1·9 (0·7)	1·3 (1·3)	0·9 (0·4)	2·4 (1·4)	1·2
	P	0·7 (0·3)	2·1 (1·5)	0·7 (0·3)	0·7 (0·3)	1·3 (0·7)	1·7 (0·9)	1·0
K. aerogenes	N	0·4 (0·2)	0·6 (0·3)	0·2 (0·1)	0·4 (0·1)	0·6 (0·2)	0·6 (0·2)	0·4
	G	0·7 (0·2)	1·1 (0·6)	0·5 (0·2)	0·7 (0·3)	1·3 (1·1)	2·1 (1·5)	0·9
	P	0·6 (0·3)	1·0 (0·4)	0·4 (0·2)	0·5 (0·1)	1·2 (1·0)	0·9 (0·5)	0·7
Ps. aeruginosa	N	4·4 (3·7)	21·2 (15·2)	10·1 (9·1)	16·1 (20·0)	15·5 (9·7)	30·4 (27·4)	16·4
	G	10·5 (9·7)	38·5 (29·7)	25·1 (20·1)	30·4 (27·2)	23·2 (18·2)	58·6 (36·4)	31·0
	P	10·1 (11·1)	40·3 (29·7)	19·8 (19·7)	20·7 (18·1)	37·2 (32·0)	49·2 (32·3)	29·6

N, untreated bacteria; G, glycosidase treated; P, pronase treated; FEP, fluorinated ethylene propylene copolymer; PE, polyethylene; PP, polypropylene; PTFE, polytetrafluoroethylene; PVC, polyvinylchloride; SIL, silicone rubber.

Each mean is taken from duplicate observations of six strains (five for *S. aureus*). Adhesion values cannot be compared directly between organisms as the experiments were performed separately.

effects produced by the enzymes is shown in Table 3. In the case of the two Gram-positive species, pronase and glycosidase treatments consistently resulted in respective decreases and increases in the measured levels of adhesion; only one strain of *S. epidermidis* differed in yielding decreased adhesion values after treatment with glycosidase. The effects of enzyme treatments on individual strains of the Gram-negative species were less consistent; overall *E. coli* adhered less well after treatment with either enzyme whereas the adhesion of *K. aerogenes* was increased. However, both *E. coli* and *K. aerogenes* adhered relatively poorly in all circumstances. The variation in adhesion amongst strains of *Ps. aeruginosa* was large regardless of enzyme treatment and consistent trends were not observed.

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Table 3. *Influence of enzyme treatments on bacterial adhesion to intravascular cannula material (irrespective of material type)*

Organism	Influence of enzyme treatment on adhesion compared with untreated control	
	Pronase	Glycosidase
S. epidermidis	↓ ($P < 0{\cdot}0025$)	↑ ($P < 0{\cdot}025$)
S. aureus	↓ ($P < 0{\cdot}0005$)	↑ ($P < 0{\cdot}0025$)
E. coli	↓ ($P < 0{\cdot}05$)	↓ ($P < 0{\cdot}025$)
K. aerogenes	↑ ($P < 0{\cdot}005$)	↑ ($P < 0{\cdot}0005$)
Ps. aeruginosa	↑ ($P < 0{\cdot}05$)	↑ ($P < 0{\cdot}05$)

↑, Increased adhesion; ↓, decreased adhesion.

DISCUSSION

In vitro studies have shown that plasma adsorbed to synthetic materials usually reduces the ability of bacteria to adhere (Barrett, 1983; Hogt *et al.* 1985). *In vivo* however, materials are in a position to adsorb a variety of tissue proteins and organized thrombus formation occurs (Gott *et al.* 1961). The interaction of a micro-organism with an organized surface of this type may differ from that with a simple plasma coating, and this is likely to explain the results shown in Table 1 where rabbit-implanted cannulae, which presumably presented a complex surface rather than simple adsorbed proteins, displayed a greater affinity for bacteria than unimplanted materials.

In the case of adhesion to cannulae removed from rabbits, there were no major differences between the species of bacteria studied, and the differences between types of cannula material were far less than for unimplanted materials. This suggests that the nature of the adherent thrombus may be similar irrespective of the type of underlying polymer. It is therefore unlikely that the nature of the material from which a cannula is made influences the rates of infection which arise following implantation. Only in the study of Sheth *et al.* (1983*a*) has a difference in infection rates been related to the type of implanted cannula material and, in contrast to the implications of Table 1, PVC cannulae were infected more frequently than those made from FEP; however, since FEP cannulae accounted for only 10% of these authors' samples, they may have represented a selected group of patients. Alternatively the differences found by Sheth *et al.* may indicate that the infections were initiated before the cannulae became coated with proteins, i.e. before implantation, and therefore reflect the different affinities of bacteria for the unimplanted materials.

In contrast to implanted cannulae, highly significant differences were found in the degrees of adhesiveness to unimplanted materials shown by different bacteria. *S. epidermidis* showed the greatest adhesion of the species investigated, a finding also noted by Sheth *et al.* (1983*b*) who compared adhesion of this organism with that of *E. coli* – the least adhesive of bacteria in Table 1. It is therefore likely that the recovery of *S. epidermidis* as the most common species from removed intravascular devices results not only from its prominence amongst the skin flora,

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but also from its particular affinity for cannula materials. Conversely, it has been noted (Eykyn, 1984) that *E. coli* is absent from cannula infections, and this is reflected in Table 1 where it showed poor adhesion to unimplanted (but not implanted materials). The association of the incidence of cannula infection with the degree of bacterial adhesion to unimplanted, rather than implanted, materials suggests that most cannula infections are likely to be initiated at the time of implantation rather than later.

Other workers who have examined the adhesion of bacteria to unimplanted materials, have generally obtained results similar to the findings in Table 2. For example Botta, Costa & Pugliese (1984) found polyethylene endoscope material more attractive to bacteria than PTFE (although there were differences between types of PTFE), and Fricker (1984) made the same observations with campylobacter-like organisms. The adhesion of micro-organisms in the specific case of intravascular cannulae has also been examined by workers such as Ashkanazai (1984) who compared the adhesion of bacteria to polyethylene and 'Teflon' (presumably PTFE) and noted the greater attractiveness of the former polymer, likewise Rotrosen, Gibson & Edwards (1983) found that *Candida* species adhered better to PVC cannulae that to Teflon. Sheth *et al.* (1983*b*) working with PVC and FEP found significantly less adhesion of *S. epidermidis* to the latter material. The overall adhesion values for unimplanted materials shown in Tables 1 and 2 support the view that the Teflon polymers (FEP and PTFE) have the lowest affinity for bacteria amongst the materials examined.

Ludwicka *et al.* (1984) have also examined the ability of *S. epidermidis* to adhere to a number of materials used for medical purposes and found adhesion greatest to the most hydrophobic polymers, silicone being the most hydrophobic of those they examined. Similarly, Hogt *et al.* (1983) considered the adhesion of coagulase-negative staphylococci to FEP to be mainly due to hydrophobic interactions, although the adhesion of encapsulated strains has not been found to correlate with hydrophobicity (Hogt, Dankaert & Feijen, 1985). In Table 2 the silicone-based polymer was the most attractive material not only for *S. epidermidis*, but for all five bacterial species examined.

Protein-mediated adhesion to synthetic polymers has been noted by Hogt *et al.* (1983) who found the adhesion of coagulase-negative staphylococci to FEP to be due to protease-sensitive factors, possibly as a result of a reduction in hydrophobicity, and Barrett (1985) found the adhesion of *S. aureus* to silicone rubber sensitive to trypsin. In the present study, the adhesion of both staphylococcal species was reduced by proteolytic enzymes, and this was found to be the case not only for the materials examined by earlier workers, but for all materials investigated.

The role in adhesion attributed to bacterial surface carbohydrates in the present work differs somewhat from that noted in related fields. McCourtie & Douglas (1981) found that the adherence of *Candida* species to dental 'acrylic' was postively related to growth of the organism in the presence of certain oligosaccharides. Carbohydrate-mediated adhesion to polystyrene by certain Gram-negative bacilli has also been suggested by the work of McEldowney & Fletcher (1986), and the blocking of adhesion by D-mannosamine suggested an involvement of surface carbohydrates in the adhesion of *S. epidermidis* to PVC

(Franson *et al.* 1984). The finding of increased staphylococcal adhesion following glycosidase treatment has not been noted previously, and this is perhaps at variance with the concept of a carbohydrate-based 'slime' mediating the adhesion of *S. epidermidis* to intravascular cannulae (Christensen *et al.* 1982). The strains of *S. epidermidis* studied in the present work were not examined for slime production, and the increased adhesion following glycosidase treatment may imply the presence of a carbohydrate-based microcapsule hiding more adhesive structures within the bacterial surface. The role of slime in adhesion has, in any case, been questioned by later work (Ishak *et al.* 1985). The increased adhesion of *Ps. aeruginosa* and *K. aerogenes* produced by both pronase and glycosidase may indicate that more adhesive structures are masked in a more complex fashion within the Gram-negative species.

The findings of this study have provided supporting evidence of the importance of infection of implants at the pre-implantation stage since the differing affinities of bacteria for cannula materials in the unimplanted state is reflected in their degree of involvement in cannula infection. This study has also shown important differences in the affinity of materials used in the manufacture of intravenous cannulae for bacteria. Although it is not possible to generalize from the study of a single cannula type, it would appear that on bacteriological grounds silicone-based polymers, which are widely used in the manufacture of long-term central venous access devices, are a poor choice since this type of material displays the greatest affinity for all bacteria investigated. In contrast the Teflon grades (FEP and PTFE) showed the lowest overall affinity for bacteria and may therefore be more suitable.

There have been attempts to reduce the surface reactivity of implanted materials by coatings such as heparin (Friedman *et al.* 1970) and hydromer (Kristinsson & Spencer, 1986), and the selection of a material with low affinity for bacterial surface proteins should reduce infection at the pre-implantation stage. In the case of infection arising after implantation, the present study suggests a different approach is required; the impregnation of plastic materials with antiseptic substances as has been reported by Kingston, Seal & Hill (1986) appears a likely solution.

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REFERENCES

Ashkenazai, S. (1984). Bacterial adherence to plastics. *Lancet* i, 1075–1076.

Barrett, S. (1983). Staphylococcal infection of plastic inserts; a method to measure staphylococcal adhesion. *British Journal of Clinical Practice* suppl. no. 25, 81–85.

Barrett, S. P. (1985). Protein-mediated adhesion of *Staphylococcus aureus* to silicone implant polymer. *Journal of Medical Microbiology* **20**, 249–253.

Botta, G. A., Costa, A. G. M. A. & Pugliese, V. (1984). Bacterial adherence to plastics: a role in endoscope-transmitted infections. *Lancet* i, 398–399.

Christensen, G. D., Simpson, W. A., Bisno, A. L. & Beachey, E. H. (1982). Adherence of slime-producing strains of *Staphylococcus epidermidis* to smooth surfaces. *Infection and Immunity* **37**, 318–326.

Downes, E. M. (1977). Late infections after total hip replacement. *Journal of Bone and Joint Surgery* **59B**, 42–44.

EYKYN, S. J. (1984). Infection and intravenous catheters. *Journal of Antimicrobial Chemotherapy* **14**, 203–205.

FRANSON, T. R., SHETH, N. K., ROSE, H. D. & SOHNLE, P. G. (1984). Quantitative adherence *in vitro* of coagulase-negative staphylococci to intravascular catheters: inhibition with D-mannosamine. *Journal of Infectious Diseases* **149**, 116.

FRICKER, C. R. (1984). Adherence of bacteria associated with active chronic gastritis to plastics used in the manufacture of fibreoptic endoscopes. *Lancet* i, 800.

FRIEDMAN, L. I., LIEM, H., GRABOWKI, E. F., LEONARD, E. F. & MCCORD, C. W. (1970). Inconsequentiality of surface properties for initial platelet adhesion. *Transactions of the American Society for Artificial Internal Organs* **16**, 63–73.

GOTT, V. L., KOEPKE, D. E., DAGGETT, R. L., ZARNSTORFF, W. & YOUNG, W. P. (1961). The coating of intravascular plastic prostheses with colloidal graphite. *Surgery* **50**, 382–389.

HOGT, A. H., DANKERT, J., DE VRIES, J. A. & FEIJEN, J. (1983). Adhesion of coagulase-negative staphylococci to biomaterials. *Journal of General Microbiology* **129**, 2959–2968.

HOGT, A. H., DANKERT, J. & FEIJEN, J. (1985). The adhesion of *Staphylococcus epidermidis* and *Staphylococcus saprophyticus* to a hydrophobic biomaterial. *Journal of General Microbiology* **131**, 2485–2491.

ISHAK, M. A., GRÖSCHEL, H. M., MANDELL, G. L. & WENZEL, R. P. (1985). Association of slime with pathogenicity of coagulase-negative staphylococci causing nosocomial septicaemia. *Journal of Clinical Microbiology* **22**, 1025–1029.

JAMES, R. C. & MCCLEOD, C. M. (1961). Induction of staphylococcal infection in mice with small inocula introduced on sutures. *British Journal of Experimental Pathology* **42**, 266–277.

KINGSTON, D., SEAL, D. V. & HILL, I. D. (1986). Self-disinfecting plastics for intravenous catheters and prosthetic inserts. *Journal of Hygiene* **96**, 185–198.

KRISTINSSON, K. G. & SPENCER, R. C. (1986). Adherence of staphylococci to three synthetic i.v. catheters. *Presented at meeting of Pathological Society of Great Britain, 2 July.*

LIDWELL, O. M., LOWBURY, O. J. L., WHYTE, W., BLOWERS, R., STANLEY, S. J. & LOWE, D. (1982). Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. *British Medical Journal* **2**, 10–14.

LIÑARES. J., SITGES-SERRA, A., GARAU, J., PÉRES, J. L. & MARTIN, R. (1985). Pathogenesis of catheter sepsis: a prospective study with quantitative and semiquantitative cultures of catheter hub and segments. *Journal of Clinical Microbiology* **21**, 357–360.

LUDWICKA, A., JANSEN, B., WADSTRÖM, T. & PULVERER, G. (1984). Attachment of staphylococci to various synthetic polymers. *Zentralblatt für Bakteriologie und Hygiene* **A256**, 479–489.

MCCOURTIE, J. & DOUGLAS, J. (1981). Relationship of cell surface composition of *Candida albicans* and adherence to acrylic after growth on different carbon sources. *Infection and Immunity* **32**, 1234–1241.

MCELDOWNEY, S. & FLETCHER, M. (1986). The effect of growth conditions and surface characteristics of aquatic bacteria on their attachment to solid surfaces. *Journal of General Microbiology* **132**, 513–523.

ROTROSEN, D., GIBSON, T. R. & EDWARDS, J. E. JR (1983). Adherence of *Candida* species to intravenous catheters. *Journal of Infectious Diseases* **147**, 594.

SHETH, N. K., FRANSON, T. R., ROSE, H. D., BUCKMIRE, F. L. A., COOPER, J. A. & SOHNLE, P. G. (1983*a*). Colonisation of bacteria on polyvinyl chloride and teflon intravascular catheters in hospitalised patients. *Journal of Clinial Microbiology* **18**, 1061–1063.

SHETH, N. K., ROSE, H. D., FRANSON, T. R., BUCKMIRE, F. L. A. & SOHNLE, P. G. (1983*b*). *In vitro* quantitative adherence of bacteria to intravascular catheters. *Journal of Surgical Research* **34**, 213–218.