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Susceptibility Testing of Bacteria Recovered from Patients with Peritonitis Complicating Continuous Ambulatory Peritoneal Dialysis

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Antagonism of antibiotic activity by peritoneal dialysate has been postulated to be a cause of failure of treatment of peritonitis complicating continuous ambulatory peritoneal dialysis. We evaluated by a case-control study whether unexpected treatment failure could be attributed to such antagonism. Bacteria isolated from 34 patient episodes of peritonitis treated with the same regimen of ciprofloxacin monotherapy were studied. Ciprofloxacin was significantly less active in dialysate than in Iso-Sensitest broth (IB). The median MIC in IB was 0.5 μg/ml, increasing to 2.0 μg/ml for both fresh dialysate (FD) ($P = 0.003$) and pooled dialysis effluent (PDE) ($P = 0.03$); the median MBC in IB was 8.0 μg/ml, increasing to 128.0 μg/ml in FD ($P = 0.0002$) and 64.0 μg/ml in PDE ($P = 0.02$). However, no significant differences were found in the results for patients suffering unexpected treatment failure (relapse of peritonitis) compared with the results for patients whose infection resolved without sequel. In IB the median MICs for relapsers and nonrelapsers were 1.0 and 0.5 μg/ml, respectively ($P = 0.88$); median MBCs were 32.0 and 4.0 μg/ml ($P = 0.19$). In FD median MICs for relapsers and nonrelapses were 2.0 and 1.0 μg/ml ($P = 0.06$); median MBCs were 128.0 μg/ml for both groups ($P = 0.84$). In PDE the median MICs were 2.0 μg/ml for both groups ($P = 0.78$); median MBCs were 256.0 and 64.0 μg/ml ($P = 0.17$). We therefore found no evidence to suggest that antagonism of antibiotic activity by dialysate is a cause of treatment failure or that conventional methods for laboratory susceptibility testing in peritonitis complicating continuous ambulatory peritoneal dialysis should be abandoned in favor of testing in media containing dialysate.

Continuous ambulatory peritoneal dialysis (CAPD) has become an important form of treatment for patients with end-stage renal failure. Peritonitis is the most serious and costly complication of the technique, occurring at a rate of one to two episodes per year of treatment (19).

The difficulty in eradicating an infection in the presence of a foreign body (i.e., the Tenckhoff catheter) is well recognized (11), and it is perhaps surprising that no more than 5 to 10% of episodes of peritonitis fail to respond to intraperitoneal antibiotic therapy (4, 19). Treatment failure has been associated with bacterial colonization of the subcutaneous segment (apparent as a wound infection) (23) or the intra-abdominal segment (clinically inapparent microcolonies or biofilm) (10, 30). Sequestration of bacteria within intraperitoneal phagocytes has also been implicated as a cause of treatment failure (6).

A further postulated cause of treatment failure of bacterial infection is inaccurate in vitro susceptibility testing; the exact clinical relevance of such testing has not been well defined. The variability of these tests and the factors affecting them have been increasingly recognized (13, 16). Selwyn (27) has observed that they are performed with media bearing little similarity to conditions in vivo and has suggested that the susceptibility testing of bacteria recovered in septicemia or soft-tissue infections be performed in excess pooled human serum to more closely represent conditions in blood and tissue fluids than do conventional serum-free media.

Similar reservations concerning the validity of conventional susceptibility testing for bacteria recovered in CAPD-complicating peritonitis have been expressed (7, 36). The activity of antibiotics recommended for the treatment of CAPD-complicating peritonitis against the commonest infecting species has been found to be significantly diminished by both fresh (2, 28) and used (8, 9, 28, 32, 35) dialysate. However, the number of isolates studied has been small, and other workers have failed to confirm these findings (14). The novel quinolone ciprofloxacin has recently been used for the treatment of CAPD-complicating peritonitis (20). The activity of this antibiotic has also been found to be diminished by fresh dialysate (34), used dialysate (15), or both (28), but once again, the number of isolates studied has been small, and others have not reproduced these findings (24, 25).

Thus, doubt surrounds the influence of dialysate on antibiotics used for the treatment of CAPD-complicating peritonitis and the optimal methodology for susceptibility testing of bacteria responsible for these infections. Furthermore, the clinical significance of any such in vitro antagonism of antibiotic activity has never been established. We investigated whether fresh or used dialysate inhibits the bacteriostatic or bacteriocidal activity of ciprofloxacin on bacteria causing CAPD-complicating peritonitis and attempted to establish the clinical relevance of any such antagonism by comparing the results for two groups of isolates derived from patients with CAPD-complicating peritonitis, treated with the same regimen of intraperitoneal ciprofloxacin. Both groups of isolates were considered susceptible on conventional laboratory testing, but isolates in the first group failed to be eradicated from the peritoneal cavity, whereas isolates in the second group were successfully eliminated by this antibiotic.

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TABLE 1. Biochemical composition of growth media

Medium	Amt (mmol/liter) of:				pH	Osmolarity (mosmol/liter)	Amt (g/liter) of protein
	Glucose	Urea	Calcium	Magnesium			
IB	15.5	3.1	0.05	0.05	7.5	215.0	0.15
FD	120.5	0	1.8	0.8	5.6	351.0	0
PDE	53.0	22.0	2.0	1.1	8.2	285.0	1.1

MATERIALS AND METHODS

Bacteria. Thirty-four distinct isolates derived from 34 episodes of CAPD-complicating peritonitis occurring in 21 adult patients were studied. Peritonitis was suspected when patients developed turbid dialysis effluent with or without abdominal discomfort, nausea, or vomiting. Peritonitis was confirmed when semiquantitive microscopy showed that effluent turbidity was due to an elevated polymorphonuclear leukocyte count (22). All isolates were deemed susceptible to ciprofloxacin by the standardized disk diffusion method of Stokes (5), in which the antibiotic susceptibility of an isolate is determined by comparing the size of the zone of inhibition with that of a control organism present on the same plate. All episodes of peritonitis were treated with intraperitoneal ciprofloxacin, alone. At presentation patients received three rapid exchanges to ease peritoneal discomfort and then continued their normal CAPD regimen, 1.5 to 3.0 liters of dialysate (Dianeal 137; Baxter Healthcare Ltd., Thetford, England) according to the patient, exchanged four times daily, with the addition of 50 mg of ciprofloxacin to each liter of dialysate at each exchange, continued for 7 days (20).

The isolates were divided into two groups. The first group consisted of 17 consecutive isolates derived from patients whose infection relapsed after stopping of ciprofloxacin (relapsers), i.e., patients who experienced a recurrence of peritonitis caused by an organism indistinguishable from the original isolate within 28 days of stopping of antibiotic treatment (20). Isolates were characterized by biotype (API Staph, API 20E, and API Strep, as appropriate; API System SA, Balme les Grottes, France) and antibiogram. In addition, staphylococci were phage typed (Staphylococcus Reference Unit, Central Public Health Laboratory, Colindale, England). Typing staphylococci is problematic, but this typing scheme has been found to be highly discriminating (21). The second group (nonrelapsers) was formed by pairing each of the isolates in the first group with an isolate from CAPD-complicating peritonitis, in a different patient, caused by the same species but which resolved without sequel. The isolates studied were *Staphylococcus aureus* (12), *Staphylococcus epidermidis* (14), *Staphylococcus haemolyticus* (2), *Streptococcus sanguis* (2), *Enterococcus faecalis* (2), and *Enterobacter cloacae* (2).

Antibiotic. Ciprofloxacin (Bayer UK Ltd., Newbury, Berkshire, England) was obtained as a pure dry powder. It was dissolved in sterile distilled water, filter sterilized, and stored at −70°C. Doubling dilutions of ciprofloxacin in growth media were prepared from 512.0 to 0.0005 μg of ciprofloxacin per ml.

Growth media. The growth media used in this study were Iso-Sensitest broth (IB) (Oxoid Ltd., Basingstoke, England), fresh dialysate containing 22.7 mg of glucose per ml (FD) (Dianeal 137; Baxter Healthcare Ltd.), and pooled dialysis effluent (PDE) taken from six patients without peritonitis who had not received antibiotics in the preceding month. The pooled dialysate was sterile on culture and lacked antibacterial activity, as judged by failure to inhibit the growth of three test organisms: the Oxford staphylococcus (*S. aureus* NCTC 6571), *Bacillus subtilis* (ATCC 6633), and *Escherichia coli* (NCTC 10418) (22). Antibacterial activity was detected by delivering effluent to a well cut into a blood agar plate previously seeded with the test organism. Plates were examined after overnight incubation at 37°C for any inhibition of growth of the test organisms. Fresh dialysate and pooled dialysis effluent were filtered through a sterile membrane (pore size, 0.45 μm; Millipore Corp., Bedford, Mass.) immediately before use.

The biochemical characteristics of the growth media are listed in Table 1.

Susceptibility testing. The MICs and MBCs of the isolates were established by standard methods (33). Briefly, isolates were incubated in broth (nutrient broth no. 2; Oxoid Ltd.) at 37°C in air in a rotary shaker. After 18 h isolates were added to the doubling dilutions of ciprofloxacin in the growth media to achieve a final concentration of 10^6 CFU/ml. The MICs were read after 18 h of incubation at 37°C in air.

After reading of the MICs a standard loopful (0.001 ml) of fluid was immediately subcultured from all tubes to one quarter of a blood agar plate (Columbia agar base; Oxoid Ltd.) with 6% sterile defibrinated horse blood (Tissue Culture Services Ltd., Botolph, Buckinghamshire, England). The MBCs were read after 18 h of incubation at 37°C in air. The MBC was defined as the lowest concentration of antibiotic which prevented growth and reduced the inoculum by 99.9% (26).

S. aureus NCTC 6571 (ATCC 25923) (ciprofloxacin MIC, 0.25 μg/ml [3]) was used as a control throughout.

Statistical analysis. The statistical significance of any difference in the MICs and MBCs for the 34 isolates when tested in FD and PDE compared with the results when tested in IB was evaluated by the Mann-Whitney U test (29). The same test was applied to evaluate the significance of any difference between the MICs and MBCs of relapsers compared with those of nonrelapsers.

For statistical purposes ciprofloxacin MICs and MBCs were taken to be 1,024 μg/ml for isolates requiring MICs or MBCs greater than 512 μg/ml.

RESULTS

The MICs and MBCs for the isolates in the three test media are listed in Table 2 and represented graphically in Fig. 1, 2, and 3.

Overall results. All organisms were found to require MICs of less than 512.0 μg of ciprofloxacin per ml. Six isolates (from four relapsers and two nonrelapsers) were found to require an MBC of 1,024.0 μg/ml or greater.

The median MICs and MBCs of ciprofloxacin for the 34 isolates were significantly increased when tested in either FD or PDE, by comparison with the result for IB: the median MIC in IB was 0.5 μg/ml, increasing to 2.0 μg/ml for both FD ($P = 0.003$) and PDE ($P = 0.03$); the median MBC

TABLE 2. MICs and MBCs of ciprofloxacin for bacteria causing CAPD-complicating peritonitis

Patients and organism	Concn (μg/ml) in:					
	IB		FD		PDE	
	MIC	MBC	MIC	MBC	MIC	MBC
Relapsers						
S. aureus	0.5	32	0.5	64	1	512
S. aureus	0.5	64	0.5	256	0.5	256
S. aureus	1	128	8	128	1	32
S. aureus	0.5	8	1	64	2	32
S. aureus	2	8	2	128	2	8
S. aureus	1	1	1	64	1	4
S. epidermidis	0.25	1	32	128	4	256
S. epidermidis	1	128	2	≥1,024	2	≥1,024
S. epidermidis	2	512	8	512	2	≥1,024
S. epidermidis	1	512	4	512	16	≥1,024
S. epidermidis	0.5	16	32	128	4	256
S. epidermidis	0.5	128	8	128	0.5	512
S. epidermidis	4	8	4	8	4	8
S. haemolyticus	0.5	1	2	16	0.25	8
S. sanguis	8	256	1	256	1	32
E. faecalis	2	512	32	512	2	≥1,024
E. cloacae	0.06	0.12	2	8	0.03	2
Nonrelapsers						
S. aureus	0.5	4	0.5	512	1	4
S. aureus	0.5	4	2	32	32	64
S. aureus	0.5	4	0.5	32	1	8
S. aureus	2	4	1	64	1	16
S. aureus	2	32	2	32	2	4
S. aureus	4	8	0.5	≥1,024	4	64
S. epidermidis	0.5	8	2	256	2	256
S. epidermidis	0.25	0.5	0.5	64	1	1
S. epidermidis	1	4	1	128	0.5	256
S. epidermidis	0.5	32	8	256	2	256
S. epidermidis	0.5	128	1	256	2	128
S. epidermidis	0.5	2	1	128	1	256
S. epidermidis	2	256	8	≥1,024	4	≥1,024
S. haemolyticus	0.5	2	0.5	64	1	4
S. sanguis	2	128	2	128	4	16
E. faecalis	8	64	4	128	2	256
E. cloacae	0.12	1	2	4	0.06	0.5

in IB was 8.0 μg/ml, increasing to 128.0 μg/ml in FD (P = 0.0002) and 64.0 μg/ml in PDE (P = 0.02).

Comparative results. The MICs for all organisms in IB were ≤8.0 μg/ml. The median MICs for relapsers and nonrelapsers were similar, 1.0 and 0.5 μg/ml, respectively, and the rankings of these two sets of data were not significantly different (P = 0.88), as expected from the results of disk sensitivity testing. Although the median MBCs in this medium were higher for relapsers than for nonrelapsers (32.0 and 4.0 μg/ml, respectively), the two sets of data were not significantly different (P = 0.19).

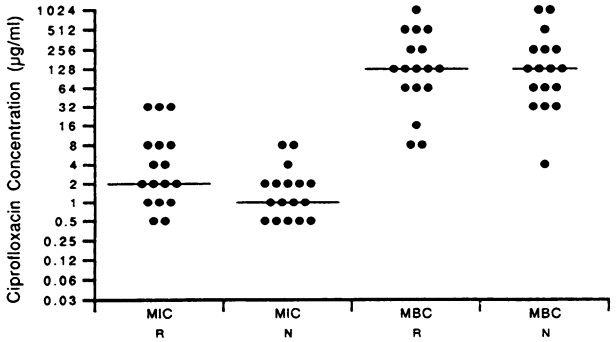

FIG. 2. MICs and MBCs for bacteria in FD. R, relapsers; N, nonrelapsers. The horizontal bars represent median values.

In FD the median MICs for relapsers and nonrelapsers were 2.0 and 1.0 μg/ml, respectively, and the rankings were not significantly different (P = 0.06). The median MBCs were 128.0 μg/ml for both groups, and the rankings were not significantly different (P = 0.84).

In PDE the median MICs were 2.0 μg/ml for both groups, and the rankings were not significantly different (P = 0.78). Median MBCs were 256.0 and 64.0 μg/ml for relapsers and nonrelapsers, respectively, and the rankings were not significantly different (P = 0.17).

DISCUSSION

Our results support the contention that the antibacterial activity of ciprofloxacin is reduced when tested in dialysis fluid; we have found that both the bacteriostatic and bacteriocidal activities of ciprofloxacin against bacteria recovered in CAPD-complicating peritonitis are significantly diminished by both FD and PDE, by comparison with the results of conventional sensitivity testing. For the MICs the effect was modest, the median values increasing from 0.5 μg/ml in IB to 2.0 μg/ml for both FD and PDE. However, the effect for the median MBCs was more dramatic, increasing from 8.0 μg/ml in IB to 128.0 μg/ml for FD and 64.0 μg/ml in PDE.

We cannot, however, support the contention that this reduced in vitro activity must result in reduced clinical efficacy in the treatment of CAPD-complicating peritonitis, a

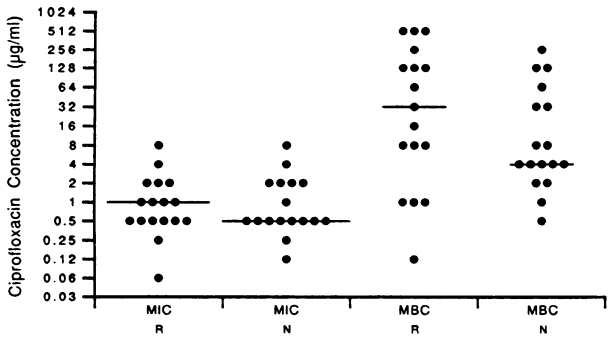

FIG. 1. MICs and MBCs for bacteria in IB. R, relapsers; N, nonrelapsers. The horizontal bars represent median values.

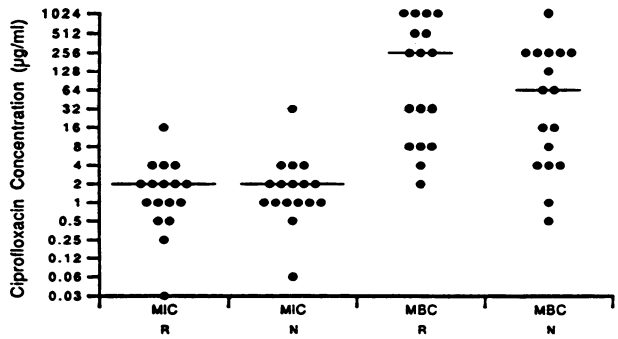

FIG. 3. MICs and MBCs for bacteria in PDE. R, relapsers; N, nonrelapsers. The horizontal bars represent median values.

view advanced not only for quinolones such as ciprofloxacin (34) but also for cephalosporins (2). We found no significant difference in the reduction in the activity of ciprofloxacin between isolates from cases responding to treatment and those with treatment failure. This finding is in line with in vivo evidence of efficacy; both ciprofloxacin and cephalosporins such as ceftazidime have performed well in clinical trials of the treatment of CAPD peritonitis (12, 20). Nor do our findings support the contention that the current methodology of laboratory susceptibility testing is a poor predictor of treatment outcome (7, 8). For ciprofloxacin at least, our data do not indicate that any change from the usual methods for susceptibility testing (i.e., disk testing and MIC evaluation in conventional media) is necessary.

Venditti et al. (31) found only 1 of 22 clinical strains of coaglulase-negative staphylococci to be tolerant to ciprofloxacin (MBC ≥32-fold higher than MIC in conventional laboratory media). By contrast, in the present study 8 of the 14 strains of coagulase-negative staphylococci (and six strains of other bacteria) were tolerant to ciprofloxacin. However, there is no evidence that such tolerance accounted for unexpected treatment failure in the present study, as nonrelapsers were also infected with these strains.

The finding that four patients whose infection resolved without relapse were infected with bacteria which would not be killed by the therapeutic regimen (MBCs of 64.0 μg/ml or greater in IB) suggests that a contribution from the host immune response to the elimination of peritoneal infection may be important, and there is good evidence from other studies that this is indeed the case. Although both cellular and humoral peritoneal immunity are compromised by CAPD, immune function is at least partially restored during infection. Verbrugh et al. (32) have reported that the concentration of phagocytic leukocytes in dialysis effluent from uninfected patients will not inhibit bacterial growth in vitro but that during peritonitis leukocyte concentrations are sufficient to represent an adequate phagocytic challenge to the microbe. Although the opsonic activity of dialysis effluent is also very low in the absence of peritonitis, Keane and Peterson (17) have demonstrated that the extent of residual opsonic activity varies between patients and that the incidence of peritonitis caused by *S. epidermidis* (the commonest infecting organism) in those with the lowest opsonic activity was seven times greater than the rate for patients with the highest opsonic activity. Lamperi and Carozzi (18) achieved a long-term increase in effluent opsonic activity in CAPD patients with intraperitoneal infusions of immunoglobulin. Patients with comparatively low levels of antistaphylococcal opsonic activity and high rates of coagulase-negative staphylococcal peritonitis treated with their corrective regimen showed a remarkable eightfold decrease in peritonitis caused by these organisms. Thus, there is evidence to suggest that the host immune response is an independent variable influencing the outcome of CAPD peritonitis. We have reported the outcome of relapsing peritonitis in 12 patients treated with intraperitoneal ciprofloxacin (20, 21) which also supports this view. Seven of these patients received an alternative antibiotic, and five were cured; five patients received a further course of ciprofloxacin (in the same dosage regimen that had previously failed to eradicate the infection), and three were cured. This unexpectedly successful outcome of treatment of the relapses may have been due to an enhanced host immune response, and this possibility merits further study. The cause for failure of retreatment in the remaining cases may have been provided by Anwar and colleagues (1), who have found that bacteria present as biofilms on foreign bodies (such as the CAPD Tenckhoff catheter) are considerably less sensitive to antibiotics than conventional laboratory testing suggests, and this phenomenon also merits investigation.

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REFERENCES

1. **Anwar, H., M. K. Dasgupta, and J. W. Costerton.** 1990. Testing the susceptibility of bacteria in biofilms to antibacterial agents. Antimicrob. Agents Chemother. **34**:2043–2046.
2. **Appleby, D. H., and J. F. John.** 1982. Effect of peritoneal dialysis solution on the antimicrobial activity of cephalosporins. Nephron **30**:341–344.
3. **Bayer UK Ltd.** 1990. Bayer ciprofloxacin manual. Bayer UK Ltd., Newbury, Berkshire, England.
4. **Bint, A. J., R. G. Finch, R. Gokal, H. J. Goldsmith, B. Junor, and D. Oliver.** 1987. Diagnosis and management of peritonitis in continuous ambulatory peritoneal dialysis. Lancet **i**:845–849.
5. **Brown, D., and R. Blowers.** 1978. Disc methods of sensitivity testing and other semiquantitative methods, p. 8–30. *In* D. S. Reeves, I. Phillips, J. D. Williams, and R. Wise (ed.), Laboratory methods in antimicrobial chemotherapy. Churchill Livingstone, Ltd., Edinburgh.
6. **Buggy, B. P., D. R. Schaberg, and R. D. Swartz.** 1984. Intraleucocytic sequestration as a cause of persistent *Staphylococcus aureus* peritonitis in continuous ambulatory peritoneal dialysis. Am. J. Med. **76**:1035–1040.
7. **Craddock, C. F.** 1987. CAPD peritonitis. Lancet **i**:1320–1321.
8. **Craddock, C. F., R. Edwards, and R. G. Finch.** 1987. Pseudomonas peritonitis in continuous ambulatory peritoneal dialysis: laboratory predictors of treatment failure. J. Hosp. Infect. **10**:179–186.
9. **Edwards, R., R. C. F. Thompson, and R. G. Finch.** 1987. Antibiotic susceptibility of staphylococci from CAPD peritonitis in children. J. Antimicrob. Chemother. **20**:138–139.
10. **Evans, R. C., and C. J. Holmes.** 1987. Effect of vancomycin hydrochloride on *Staphylococcus epidermidis* biofilm associated with silicone elastomer. Antimicrob. Agents Chemother. **31**:889–894.
11. **Eykyn, S. J.** 1988. Staphylococcal sepsis, the changing pattern of disease and therapy. Lancet **i**:100–104.
12. **Gray, H. H., S. Goulding, and S. J. Eykyn.** 1985. Intraperitoneal vancomycin and ceftazidime in the treatment of CAPD peritonitis. Clin. Nephrol. **23**:81–84.
13. **Greenwood, D.** 1976. Unrealistic nature of the 'MIC.' J. Antimicrob. Chemother. **2**:312–313.
14. **Grise, G., J. F. Lemeland, and J. P. Fillastre.** 1985. Étude de la stabilité de huit céphalosporines de deuxième et troisième générations dans le liquide de dialyse péritonéale. Pathol. Biol. **33**:335–339.
15. **Guay, D., R. Klicker, T. Pence, and P. Peterson.** 1986. In vitro antistaphylococcal activity of teicoplanin and ciprofloxacin in peritoneal dialysis effluent. Eur. J. Clin. Microbiol. **5**:661–663.
16. **Hamilton-Miller, J. M. T.** 1977. Towards greater uniformity in sensitivity testing. J. Antimicrob. Chemother. **3**:395–392.
17. **Keane, W. F., and P. K. Peterson.** 1984. Host defence mechanisms of the peritoneal cavity and continuous peritoneal dialysis. Perit. Dial. Bull. **4**:122–127.
18. **Lamperi, S., and S. Carozzi.** 1989. Immunological defenses in CAPD. Blood Purif. **7**:126–143.
19. **Ludlam, H. A.** 1991. Infectious consequences of continuous ambulatory peritoneal dialysis. J. Hosp. Infect. **18**(Suppl. A): 341–345.
20. **Ludlam, H. A., I. Barton, L. White, C. McMullin, A. King, and I. Phillips.** 1990. Intraperitoneal ciprofloxacin for the treatment of peritonitis in patients receiving continuous ambulatory peritoneal dialysis (CAPD). J. Antimicrob. Chemother. **25**:843–851.
21. **Ludlam, H. A., W. C. Noble, R. R. Marples, and I. Phillips.** 1989. The evaluation of a typing scheme for coagulase-negative

staphylococci suitable for epidemiological studies. J. Med. Microbiol. **30**:161–165.
22. **Ludlam, H. A., T. N. C. Price, A. J. Berry, and I. Phillips.** 1988. Laboratory diagnosis of peritonitis in patients on continuous ambulatory peritoneal dialysis. J. Clin. Microbiol. **26**:1757–1762.
23. **Ludlam, H. A., A. E. Young, A. J. Berry, and I. Phillips.** 1989. The prevention of infection with *Staphylococcus aureus* in continuous ambulatory peritoneal dialysis. J. Hosp. Infect. **14**:293–301.
24. **McCormick, E. M., and R. M. Echols.** 1987. Effect of peritoneal dialysis fluid and pH on bactericidal activity of ciprofloxacin. Antimicrob. Agents Chemother. **31**:657–659.
25. **Quentin, C., J. L. Bouchet, I. Gaillard, and C. Bebear.** 1990. Stability of fosfomycin and quinolones in peritoneal dialysis solutions. J. Antimicrob. Chemother. **25**:878–880.
26. **Schoenknecht, F. D., L. D. Sabath, and C. Thornsberry.** 1985. Susceptibility tests: special tests, p. 1000–1008. *In* E. H. Lennette, A. Balows, W. J. Hausler, Jr., and H. J. Shadomy (ed.), Manual of clinical microbiology, 4th ed. American Society for Microbiology, Washington, D.C.
27. **Selwyn, S.** 1976. Unrealistic nature of the 'MIC.' J. Antimicrob. Chemother. **2**:221–222.
28. **Shalit, I., D. F. Welch, V. H. San Joaquin, and M. I. Marks.** 1985. In vitro antibacterial activities of antibiotics against *Pseudomonas aeruginosa* in peritoneal dialysis fluid. Antimicrob. Agents Chemother. **27**:908–911.
29. **Snedecor, G. W., and W. G. Cochran.** 1980. Statistical methods, p. 144–145. Iowa State University Press, Ames.
30. **Spencer, R. C.** 1988. Infections in continuous ambulatory peritoneal dialysis. J. Med. Microbiol. **27**:1–9.
31. **Venditti, M., C. Santini, P. Serra, A. Micozzi, G. Gentile, and P. Martino.** 1989. Comparative in vitro activities of new fluorinated quinolones and other antibiotics against coagulase-negative *Staphylococcus* blood isolates from neutropenic patients, and relationship between susceptibility and slime production. Antimicrob. Agents Chemother. **33**:209–211.
32. **Verbrugh, H. A., W. F. Keane, W. E. Conroy, and P. K. Peterson.** 1984. Bacterial growth and killing in chronic ambulatory peritoneal dialysis fluids. J. Clin. Microbiol. **20**:199–203.
33. **Waterworth, P. M.** 1978. Quantitative methods for bacterial sensitivity testing, p. 31–40. *In* D. S. Reeves, I. Phillips, J. D. Williams, and R. Wise (ed.), Laboratory methods in antimicrobial chemotherapy. Churchill Livingstone, Ltd., Edinburgh.
34. **Weissauer-Codon, C., I. Engels, and F. D. Daschner.** 1987. In vitro activity of four new quinolones in Mueller-Hinton broth and peritoneal dialysis fluid. Eur. J. Clin. Microbiol. **6**:324–326.
35. **Wilcox, M. H., R. Edwards, and R. G. Finch.** 1985. Laboratory studies on coagulase-negative staphylococci from CAPD-associated peritonitis. J. Antimicrob. Chemother. **15**:297–303.
36. **Wilcox, M. H., and R. G. Finch.** 1990. Ciprofloxacin and CAPD peritonitis. J. Antimicrob. Chemother. **26**:447–448.