ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 1985, p. 578–582
0066-4804/85/040578-05$02.00/0

Vol. 27, No. 4

Vancomycin Disposition During Continuous Ambulatory Peritoneal Dialysis: a Pharmacokinetic Analysis of Peritoneal Drug Transport

MARK C. ROGGE,[1]†* CURTIS A. JOHNSON,[1] STEPHEN W. ZIMMERMAN,[2] AND PETER G. WELLING[1]‡

School of Pharmacy, University of Wisconsin, Madison, Wisconsin 53706,[1] and Department of Medicine, University Hospitals, Madison, Wisconsin 53705[2]

Received 25 October 1984/Accepted 31 January 1985

Expressions are presented to describe the absorption and also clearance of drugs administered into the peritoneal cavity of patients undergoing continuous ambulatory peritoneal dialysis (CAPD). Application of the expressions to vancomycin kinetics in five male CAPD patients showed that therapeutic levels of vancomycin can readily be achieved and maintained in the systemic circulation by administering the appropriate loading and maintenance doses. The intrinsic peritoneal clearance of vancomycin reported here is higher than the apparent clearances reported previously, averaging 300 to 500 ml/min under the conditions used in this study. The low apparent clearances previously reported are useful clinically although they do not represent the true efficiency of vancomycin removal by CAPD. The degree to which apparent clearance underestimates the true intrinsic clearance is exponentially related to the dwell time of dialysate in the peritoneum. Intraperitoneal administration is a practical alternative to other routes for CAPD patients needing antibiotic or other therapy.

Continuous ambulatory peritoneal dialysis (CAPD) was introduced in 1976 as an alternative to hemodialysis for the maintenance of patients with end-stage renal disease (R. P. Popovich, J. W. Moncrief, J. B. Decherd, J. B. Bomar, and W. K. Pyle, Abstr. Am. Soc. Artif. Intern. Organs 5:64, 1976). Patients on CAPD may receive medication by conventional routes or, in cases of peritonitis, by direct introduction of drug into the peritoneal cavity. Hitherto, movement of solutes across the peritoneal membrane has been poorly defined, and some misleading concepts regarding peritoneal clearance have been generated.

We have developed a pharmacokinetic model for drug disposition during CAPD. The model is applied here to intraperitoneally dosed vancomycin but can be adapted to characterize drug and metabolite disposition and accumulation from any route of administration.

MATERIALS AND METHODS

Theory. For drugs that are not eliminated by extrarenal routes and that are stable in physiological fluids, CAPD in patients with minimal renal function provides a closed system in which drug can equilibrate only between peritoneal dialysate and body fluids and tissues.

The following arguments are based on the assumption that drug transport across the peritoneal membrane is passive and that drug does not preferentially migrate in one direction across the peritoneum. This may not be true for all compounds (13).

Drug introduced on either side of the peritoneal membrane will generally pass through the membrane at a rate determined by the concentration gradient and the intrinsic ability of the drug molecule to penetrate the membrane. Although the peritoneal volume is controlled by the volume of dialysate administered in CAPD, the volume of the physiological compartment is dependent upon the lipophilicity of the drug and its affinity for body tissues and fluids. Thus, the transferable concentration gradient in this closed system and also the amount of drug on either side of the peritoneal membrane are controlled by the relative volumes of the peritoneal and physiological compartments.

When drug is added to dialysate, the transferable concentration from dialysate to the plasma, X, is given by equation 1.

$$X = C_d - \frac{C_{d,o}}{1 + \sigma} = \frac{C_{d,o}}{1 + \sigma} - C_p \quad (1)$$

When drug is given intravenously, the transferable concentration from plasma to dialysate, X', is given by equation 2.

$$X' = \frac{C_{p,o}}{1 + \sigma} - \frac{C_d}{\sigma} = C_p - \frac{C_{p,o}\sigma}{1 + \sigma} \quad (2)$$

In the equations, $C_{d,o}$ and $C_{p,o}$ are initial drug concentrations in dialysate and plasma, respectively, C_d and C_p are dialysate and plasma concentrations at any time t, and σ is the ratio of distribution volume/dialysate volume. The equations assume that drug distribution in the body is instantaneous and homogeneous, and as mentioned earlier, drug transport across the peritoneal membrane is passive and first order in nature.

When a single drug dose is administered in the dialysate, the dialysate and plasma concentrations are described by equations 3 and 4, where k is the first-order rate constant for transfer of drug from peritoneum to plasma and all other terms are as defined previously.

$$C_d = \frac{C_{d,o}}{1 + \sigma} + \left(\frac{C_{d,o}\sigma}{1 + \sigma}\right)e^{-kt} \quad (3)$$

$$C_p = \frac{C_{d,o}}{1 + \sigma}(1 - e^{-kt}) \quad (4)$$

If sufficient time is allowed for equilibrium to be achieved between dialysate and plasma, then $C_d = C_p = C_{d,o}/(1 + \sigma)$. When a single dose is given intravenously and allowed to

* Corresponding author.
† Present address: School of Pharmacy, University of Michigan, Ann Arbor, MI 48109.
‡ Present address: Warner-Lambert/Parke-Davis Research Division, Ann Arbor, MI 48105.

TABLE 1. Theoretical plasma and dialysate drug concentrations during a 24-h dialysate dwell period after intraperitoneal administration[a]

Time (h)	Dialysate concn (μg/ml)	Plasma concn (μg/ml)
0	100	0
1	61.4	0.79
2	38.1	1.28
5	10.1	1.85
10	2.68	2.00
20	2.02	2.02
24	2.02	2.02

[a] Initial dialysate concentration, 100 μg/ml; distribution volume, 100 liters; transfer constant, 0.5/h; σ, 48.1. Data are generated from equations 3 and 4.

equilibrate with a dialysate compartment, the concentrations of drug in plasma and dialysate are given by equations 5 and 6.

$$C_d = \left(\frac{C_{p,o}\sigma}{1+\sigma}\right)(1 - e^{-kt}) \quad (5)$$

$$C_p = \frac{C_{p,o}\sigma}{1+\sigma} + \left(\frac{C_{p,o}}{1+\sigma}\right)e^{-kt} \quad (6)$$

As $C_{d,o} = C_{p,o} \cdot \sigma$, equations 3, 4, 5, and 6 are identical at equilibrium ($t = \infty$).

Equations 3 and 4 can be expanded to equations 7 and 8, which describe, respectively, dialysate and plasma drug levels at any time after any number of intraperitoneal doses. Equations 7 and 8 differ from equations 3 and 4 by the inclusion of $C_{p,o}$, the plasma concentration immediately preceeding the last intraperitoneal dose.

$$C_d = \left(C_{p,o} + \frac{C_{d,o}}{1+\sigma}\right) + \left(\frac{C_{d,o}\sigma}{1+\sigma} - C_{p,o}\right)e^{-kt} \quad (7)$$

$$C_p = C_{p,o} + \frac{C_{d,o} - C_{p,o}}{1+\sigma}(1 - e^{-kt}) \quad (8)$$

The implications of the above concepts in drug distribution and clearance in CAPD patients are illustrated by the following theoretical example.

Consider an antibiotic that is added to fresh dialysate at an initial concentration of 100 μg/ml. The antibiotic has a distribution volume (V_d) in the body of 100 liters and a peritoneal-plasma transfer constant (k) of 0.5/h. The volume of dialysate is 2.08 liters, resulting in a σ value of 48.1. Plasma and dialysate concentrations during a 24-h dwell period, calculated from equations 3 and 4, are given in Table 1. Owing to the relatively large transfer rate constant, plasma drug levels reach over 90% of equilibrium value by 5 h. At equilibrium approximately 98% of administered drug has migrated from the dialysate into the body distribution volume. If the drug had been administered directly into the systemic circulation, the same equilibrium concentration would eventually be achieved at the same time as after peritoneal dosing, but owing to the high value of σ only 2% of administered drug would transfer from plasma into dialysate.

The time taken for 95% equilibration between plasma and dialysate to be achieved, whatever the dosage route, is approximately 4.5 transfer half-lives, or 4.5 (0.693/k). Thus, for equilibrium to be achieved during a normal dialysis dwell time of 6 h, the transfer constant k must be equal to or greater than 0.5/h. It will be shown in this report that vancomycin does not meet this criterion.

If drug is administered with each fresh dialysate exchange, accumulation will occur in the body, as indicated by equations 7 and 8. As drug accumulates the initial transferable concentration with each subsequent exchange will diminish, and the rate of drug transfer will therefore decrease (Table 2). Under the specified conditions an initial administered dialysate concentration of 50 μg/ml gave rise to a plasma drug level of 2.36 μg/ml. With identical subsequent dialysate doses the rate of increase in plasma levels continued to decrease and was only 1.7 μg/ml during the 6-h duration of the eighth exchange. The k value of 0.77/h in this example permitted 99% equilibration to occur during a 6-h dwell period. With subsequent exchanges, the rate of drug transfer would progressively decrease as the concentration gradient between dialysate and plasma decreased. Thus, although 99% equilibration is achieved during each exchange, it would take 38 6-h exchanges, or 10 days, for plasma concentrations to equal 90% of the initial administered dialysate concentration of 50 μg/ml. This is due to the decreasing transferable concentration with each dialysate exchange.

Thus, although equilibration between dialysate and plasma may be approached during a single dwell period, depending on the transfer rate constant k, a considerable time may be required, involving repeated dialysate doses, to achieve plasma levels of drug that are similar to those in the administered dialysate.

To achieve the same plasma level as that in the repeated dialysate doses quickly, a loading dose is required. Provided equilibrium between dialysate and plasma is approached within a single dwell period, the magnitude of the loading dose concentration can readily be calculated by multiplying the quantity of drug in maintenance dialysate doses by the factor 1 + σ. For the example in Table 2 an initial dialysate concentration of 21 × 50 μg/ml = 1,050 μg/ml would achieve a plasma level of 50 μg/ml during the initial dialysis, and this could be maintained by adding drug to a concentration of 50 μg/ml in subsequent dialysates. If on the other hand k is too small for equilibrium between dialysate and plasma to occur within a single dwell period, then the loading dose can be calculated by means of equation 9.

$$\text{Loading dialysate concentration} = \frac{C_p(1+\sigma)}{(1 - e^{-kt})} \quad (9)$$

Clearance. Removal of substances from plasma by CAPD

TABLE 2. Theoretical plasma and dialysate drug concentrations after repeated intraperitoneal drug doses[a]

Dose	Concn at end of dwell (μg/ml)		Relative change[b]	
	Plasma	Dialysate	Plasma	Dialysate
1	2.36	2.85		
2	4.61	5.19	2.25	2.36
3	6.75	7.41	2.14	2.24
4	8.79	9.53	2.04	2.14
5	10.7	11.6	1.91	2.03
6	12.6	13.4	1.90	1.90
7	14.4	15.32	1.80	1.90
8	16.1	17.11	1.70	1.80

[a] Transfer constant, 0.77/h; initial dialysate concentration for each exchange, 50 μg/ml; σ, 20; dwell time, 6 h. Data are generated from equations 7 and 8.

[b] Relative to concentration at end of previous dwell time.

is best described in terms of clearance. CAPD clearance has traditionally been calculated by similar methods to those used for renal clearance (2–5, 7–10, 13). However, owing to the non-sink nature of the CAPD system, the small volume of dialysate relative to body distribution volume, and the arbitrary use of a 6- to 8-h dwell period in most CAPD treatments, calculated CAPD clearances are variable and generally grossly underestimate true clearance of substances from the plasma into the dialysate.

To more accurately describe intrinsic clearance or the amount of drug transferred from plasma to dialysate during CAPD, we modified the fundamental clearance equation 10, where dX'/dt is the rate of solute removal and C_p is the plasma concentration, to account for transferable concentration, as in equation 11.

$$\mathrm{CL_{CAPD}} = \frac{(dX'/dt)V_d}{C_p} \tag{10}$$

$$\mathrm{CL_{CAPD}} = \frac{d\left(C_p - \frac{C_{p,o}\sigma}{1+\sigma}\right)V_d/dt}{C_p} \tag{11}$$

This replaces an absolute concentration gradient that does not exist in CAPD. The parenthetical term in equations 10 and 11 is the transferable concentration of solute from plasma to dialysate, and V_d is the distribution volume. By substitution and integration, equation 11 can be expressed in the form of equation 12.

$$\mathrm{CL_{CAPD}} = k \cdot V_d \tag{12}$$

Equations 10 to 12 describe the intrinsic CAPD clearance, which is unaffected by dialysate volume or dwell time.

Patients and methods. Five male patients receiving CAPD treatment participated in the study. Demographic data are given in Table 3. None of the patients had experienced peritonitis during 4 months before the study, and none was receiving antibiotic therapy during or for 1 month before the study. All subjects gave written, informed consent to participate. The study was conducted in the peritoneal dialysis unit, University Hospital, Madison, Wis. All subjects were receiving CAPD before, during, and after the study.

Vancomycin (Vancomycin hydrochloride; Eli Lilly & Co., Indianapolis, Inc.) was administered intraperitoneally as a 1-g loading dose in the initial dialysate, followed by three 50-mg maintenance doses with subsequent exchanges. All doses were administered in 2.08 liters of fresh dialysate (Dianeal peritoneal dialysate; Travenol Laboratories, Inc., Deerfield, Ill.) via a Tenckhoff catheter. Each dwell period was 6 h, including ca. 10 min each for instillation and drainage. Dialysate samples (5 ml) were obtained serially from three subjects via a three-way stopcock. Dialysate in the peritoneum was mixed by pumping ca. 50-ml volumes of dialysate in and out of the peritoneal cavity several times before sampling. Blood samples (7 ml) were obtained from all five subjects via a forearm catheter which was kept patent by heparin. Plasma was obtained by centrifugation. Plasma and dialysis samples were stored at −20°C until assayed, within 2 weeks.

TABLE 3. Subject demographic data

Subject[a]	Age (yr)	Weight (kg)	Comments	Time since last peritonitis episode (months)
1	49	119.7	Obese	24
2	32	98.0		24
3	53	78.5	Diabetic	None experienced
4	54	78.8	Diabetic	6
5	63	64.0	Diabetic, double amputee	11

[a] All subjects were males.

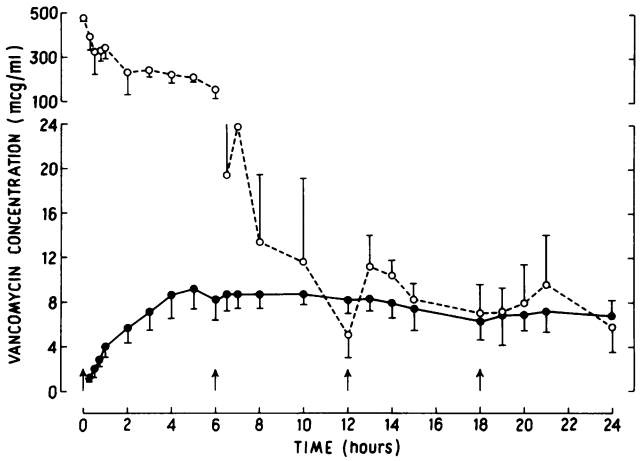

FIG. 1. Mean plasma (●) and dialysate (○) vancomycin levels in five subjects who received an initial intraperitoneal 1-g dose and three subsequent intraperitoneal 50-mg doses of vancomycin at 6-h intervals. Error bars indicate one standard deviation. Vertical arrows indicate dialysate bag exchanges.

Vancomycin concentrations were determined by cup-plate microbiological assay with Difco no. 11 agar (Difco Laboratories, Detroit, Mich.) as growth medium and *Bacillus subtilis* ATCC 6633 as test organism. Standard solutions were prepared with pooled human plasma and drug-free drained dialysate. All samples were assayed in triplicate. Assay precision was less than 10% in the vancomycin concentration range of 0.5 to 100 μg/ml in both plasma and dialysate.

The vancomycin distribution volume V_d was determined in each subject by dividing the quantity of vancomycin absorbed from the peritoneum at 6 h (the end of the first dwell period) by the plasma concentration at 6 h. Distribution volumes at later times were similarly calculated by dividing the cumulative amount of vancomycin absorbed by the plasma concentration. It was assumed that negligible drug decomposition occurred in the body (6, 11, 12).

The value of the vancomycin transfer constant (k) was obtained by two methods. In the first method, k was obtained by simultaneously fitting dialysate and plasma data to equations 7 and 8 by using the nonlinear regression program NREG (1). In the second method, k was obtained by means of a Sigma Minus plot of drug remaining to be absorbed during the initial 6-h dwell period (14) by means of equation 13.

$$\%\ \text{Unabsorbed} = 100 - \frac{C_p(1+\sigma)100}{C_{d,o}} \tag{13}$$

RESULTS

Mean plasma and dialysate vancomycin levels in the five subjects during the four dialysate dwell periods are shown in Figure 1.

During the first dwell period, the mean concentration of vancomycin in plasma steadily increased to 9.1 μg/ml at 5 h

TABLE 4. Mean vancomycin body distribution volume and transfer constant values

Exchange	Parameter (± SD)				
	V_d (liters)	k (per h)[a]	k (per h)[b]	σ[c]	CL_{CAPD} (ml/min)[d]
1	83 ± 26	0.238 ± 0.11	0.210 ± 0.03	38 ± 10	314 ± 117
2	95 ± 15	—[e]	—	—	357 ± 91
3	134 ± 55	—	—	—	508 ± 241
4	128 ± 40	—	—	—	491 ± 201

[a] Obtained from simultaneous nonlinear fitting of dialysis and plasma data.
[b] Obtained from Sigma Minus plots of dialysis data.
[c] Ratio of V_d to dialysis volume. Data for the two subjects in which vancomycin was not determined in dialysate were based on estimated bioavailability of 71% based on the other three subjects.
[d] Obtained for three subjects.
[e] —, Not calculated.

but decreased slightly to 8.2 μg/ml at 6 h. During the entire 6-h period the mean concentration in dialysate decreased from an initial value of 474.3 to 153.3 μg/ml. Both the increase in individual plasma levels and the decrease in dialysate levels were apparently first order in nature. The percentage of drug absorbed in this period was 65.3, 65.2, and 83.5% for the three subjects whose dialysis concentrations were determined, yielding a mean percentage absorption of 73.1 ± 10.5% (standard deviation).

During subsequent dwell periods mean plasma levels of vancomycin were reasonably constant, fluctuating between 6.3 and 8.7 μg/ml. Plasma levels tended to fall somewhat during the third dwell period but remained constant during the final period. Dialysis levels of vancomycin were higher during the second dwell period than during subsequent periods, possibly due to contamination from residual dialysate remaining in the peritoneum from the first exchange. During the third and fourth periods dialysate levels were similar to concurrently obtained plasma levels.

The body distribution volumes for vancomycin, calculated for three subjects after each dialysate exchange, and the k values, calculated from the first dwell period by two methods for all subjects, are summarized in Table 4.

After the first exchange the mean apparent distribution volume of vancomycin was 83 liters, or 1.2 liters/kg. This value is similar to previously reported values (3, 5). The volume increased during the second and third exchanges but was constant at ca. 130 liters, or 1.8 liters/kg, between the third and fourth exchanges.

The mean σ value, which is the ratio of the vancomycin apparent distribution volume in the body to the dialysate volume, was 38 ± 10 (standard deviation). This value suggests that to achieve plasma levels equal to the maintenance dialysate levels rapidly, the loading dialysate dose should be 38-fold higher than the maintenance dose. The actual loading dose of 1 g was 20-fold greater than the maintenance dose, and steady-state equilibrium between dialysate and plasma was approached in the third exchange. A higher loading dose would have achieved equilibrium more quickly.

The mean transfer constant was 0.24 and 0.21/h, calculated by curve fitting by nonlinear regression and Sigma Minus plots, respectively. These values are statistically indistinguishable. The mean transfer half-life, calculated from 0.693/k, was ca. 3 h. This value indicates that a 13-h dwell would be required for plasma and dialysate levels of vancomycin to reach 95% equilibrium. That equilibrium was not achieved during the initial 6-h dwell period in this study is clear from Fig. 1. The mean coefficients of determination indicating closeness of fit in nonlinear regression analysis of dialysate and plasma data to equations 7 and 8 were, respectively, 0.94 ± 0.05, and 0.93 ± 0.04, indicating satisfactory description of the data by the equations.

The mean intrinsic CAPD clearances for each exchange, calculated from equation 11, are also given in Table 4. As the transfer constant k was calculated only from the first exchange, the clearance increased in proportion to apparent increases in V_d, from an initial value of 314 ml/min to 500 ml/min during the later exchanges.

DISCUSSION

CAPD is now accepted as a practical alternative to hemodialysis for maintenance of functionally anephric or severely uremic patients.

The objectives of the work described in this communication were twofold. The first was to examine drug disposition and clearance during CAPD by application of simple kinetic principles. The second was to determine the feasibility of peritoneal administration as an alternative to oral or parenteral drug administration. This is particularly important for treatment of peritonitis, with or without systemic involvement, a common complication associated with CAPD.

The theoretical arguments presented here show that drug disposition and clearance in CAPD is uniquely influenced by the closed and intermittent nature of the system. The closed nature of the body distribution and dialysate volumes requires consideration of a transferable drug concentration, and the intermittent and variable dwell time results in variable CAPD apparent clearance values.

We have shown, consistent with previous observations (4, 8), that vancomycin is efficiently and rapidly absorbed into the general circulation after intraperitoneal administration. The transfer half-life is approximately 3 h so that 75% equilibration is achieved during a single 6-h dialysis period. However, owing to the large dilution effect associated with the relative values of vancomycin distribution volume in the body and dialysate volume, many exchanges are required before plasma drug levels equal those administered in the dialysate. Thus, to achieve equilibrium rapidly, a loading dose is required. The ratio of loading dose to maintenance is proportional to the body and dialysate volumes. In the case of vancomycin an ideal loading dose is approximately 38-fold greater than the maintenance dose. For drugs with smaller distribution volumes, for example some cephalosporins and aminoglycosides, the ratio would be reduced accordingly.

Under the conditions used in the present study, the apparent distribution volume of vancomycin progressively increased to reach steady-state values of ca. 130 liters, or 1.8 liters/kg, during the third and fourth dialysate exchanges. This suggests that complete tissue penetration may take up to 12 h and also that previous estimates of vancomycin distribution volume based on single-dose data may be low (2, 4).

Both the theoretical and clinical data show that conventional methods of calculating apparent peritoneal clearance, used clinically, grossly underestimate the true intrinsic clearance. Previously reported clearances of 2.4 to 2.5 ml/min (4, 8) were calculated based on arbitrary dialysate dwell times and markedly underestimate the intrinsic peritoneal clearance of 300 to 500 ml/min. The intrinsic clearance is constant for a particular drug and is independent of dwell time. If exchanges were performed every hour instead of every 6 hours, the "apparent" clearance would have increased dramatically.

For vancomycin and other drugs that do not bind significantly to plasma proteins it is not necessary to consider binding when calculating clearance. For drugs that are extensively bound, however, it is necessary, as when calculating any clearance value, to differentiate between the unbound fraction and total drug. As plasma albumin and other macromolecules do not readily cross biological membranes, true CAPD clearance for highly protein-bound drugs should be based on free drug in plasma and dialysate.

This study has shown that effective concentrations of vancomycin can be achieved in the systemic circulation by administering a suitable loading dose, followed by lower maintenance doses, into the peritoneal cavity. In this study a plasma vancomycin concentration greater than 8 μg/ml was achieved in the first exchange. This is above the MIC for most susceptible organisms, although some strains of staphylococci may require higher concentrations. Higher drug concentrations can be achieved by adding more drug to the dialysate. If high plasma levels are required more rapidly, then either a parenteral bolus dose may be given or a higher dose may be administered in the initial dialysate with a shorter dwell time. For example, a 3.6-g intraperitoneal dose of vancomycin would achieve a plasma level of ca. 25 μg/ml within 3 h, after which time fresh dialysate containing the appropriate maintenance dose could be instilled.

ACKNOWLEDGMENTS

The work was supported in part by a grant from Eli Lilly & Co.

We also thank the peritoneal dialysis nursing staff at the University of Wisconsin Hospitals for their considerable assistance.

LITERATURE CITED

1. **Academic Computer Center.** 1972. MACC nonlinear regression routines. Academic Computer Center, University of Wisconsin, Madison.
2. **Blevins, R. D., C. E. Halstenson, N. G. Salem, and G. R. Matzke.** 1984. Pharmacokinetics of vancomycin in patients undergoing continuous ambulatory peritoneal dialysis. Antimicrob. Agents Chemother. **25**:603–606.
3. **Brown, S. T., D. J. Ahearn, and K. D. Nolph.** 1973. Reduced peritoneal clearances in scleroderma increased by intraperitoneal isoproterenol. Ann. Intern. Med. **78**:891–894.
4. **Bunke, C. M., G. R. Aronoff, M. E. Brier, R. S. Sloan, and F. C. Luft.** 1983. Vancomycin kinetics during continuous ambulatory peritoneal dialysis. Clin. Pharmacol. Ther. **34**:631–637.
5. **Dunham, C. B., L. J. Hak, J. H. Hull, and A. M. Mattocks.** 1981. Enhancement of peritoneal dialysis clearance with docusate sodium. Kidney Int. **20**:563–568.
6. **Glew, R. H., and R. A. Pavuk.** 1981. Stability of vancomycin and aminoglycoside antibiotics in peritoneal dialysis concen trate. Nephron **28**:241–243.
7. **Nolph, K. D., R. P. Popovich, A. J. Ghods, and Z. Twardowski.** 1978. Determinants of low clearances of small solutes during peritoneal dialysis. Kidney Int. **13**:117–123.
8. **Pancorbo, S., and C. Compty.** 1982. Peritoneal transport of vancomycin in 4 patients undergoing continuous ambulatory peritoneal dialysis. Nephron **31**:37–39.
9. **Pancorbo, S., and C. Compty.** 1983. Pharmacokinetics of cefamandole in patients undergoing CAPD. Periton. Dial. Bull. **3**:135–137.
10. **Pierratos, A.** 1984. Peritoneal dialysis glossary. Periton. Dial. Bull. **4**:2–3.
11. **Rubin, J., J. Humphries, G. Smith, and J. Bower.** 1983. Antibiotic activity in peritoneal dialysate. Am. J. Kidney Dis. **3**:205–208.
12. **Sewell, D. L., and T. A. Golper.** 1982. Stability of antimicrobial agents in peritoneal dialysate. Antimicrob. Agents Chemother. **21**:528–529.
13. **Somani, P., R. S. Shapiro, H. Stockard, and J. T. Higgins.** 1982. Unidirectional absorption of gentamicin from the peritoneum during continuous ambulatory peritoneal dialysis. Clin. Pharmacol. Ther. **32**:113–121.
14. **Wagner, J. G.** 1975. Fundamentals of clinical pharmacokinetics, p. 77–80. Drug Intelligence Publications, Inc., Hamilton, Ill.