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A Simple Kinetic Model for Assessing Peritoneal Mass Transfer in Chronic Ambulatory Peritoneal Dialysis

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Changes in the mass transfer characteristics of the human peritoneum could limit the long-term feasibility of chronic ambulatory peritoneal dialysis as a form of renal replacement therapy. Routine assessment of transfer functions is therefore needed, and has been accomplished by clearance measurements of limited accuracy or by rather complex mathematical models. The capacity of the peritoneum to transfer a particular solute is most precisely characterized by a mass transfer-area coefficient (K_{BD}). With the two- and three-pool kinetic models used to determine K_{BD}, tedious computer optimization routines are required to process the measured dialysate and plasma concentrations, and therefore this approach has limited clinical appeal. A simpler model valid for the uremic molecules of greatest interest yields the following algebraic equation:

$$\ln \{V_D(\bar{C}_B - C_D)\} = \ln \{V_D^0(\bar{C}_B - C_D^0)\} - \bar{K}_{BD}\bar{V}_D^{-1} t$$

where V_D is dialysate volume, C is plasma solute concentration in blood (C_B) or dialysate (C_D) and superscript (^{0}) identifies values at zero time or the start of exchange. $\bar{K}_{BD}$ is obtained by solving the equation or from a least squares fit of $\ln \{V_D(\bar{C}_B - C_D)\}$ vs. t data for as few as three data points. The equation has been tested for urea, creatinine and B_{12} using retrospective data from 12 patients. The model appears to be valid for all three solutes, provided diffusion is the dominant solute transfer mechanism. The model requires minimal blood and dialysate sampling and can be readily solved without resort to involved computation. Thus it should be amenable to routine evaluation of a patient's mass transfer capability.

Chronic ambulatory peritoneal dialysis, peritoneal volume, mass transfer characteristics, mathematical model, urea, creatinine, vitamin B_{12}.

CONTINUOUS AMBULATORY peritoneal dialysis (CAPD) is increasingly adopted in certain parts of the world as a first-line therapy for end-stage renal failure. Peritonitis is still the most frequent reason for the discontinuation of CAPD, leading to scepticism in some circles regarding the long-term feasibility of this mode of treatment. However, with decreasing frequency of peritonitis in many centers and better connecting systems, other factors, such as deterioration of the mass transfer properties of the peritoneal membrane, may ultimately limit the successful application of CAPD.

Randerson and Farrell[1] observed a long-term increase in peritoneal resistance in about a fifth of a 15-patient group. Conversely, several workers[2-5] have encountered patients in whom solute transfer was too rapid because of a reduced peritoneal resistance. In these individuals the large quantity of glucose added to the dialysate as an osmotic agent to draw off excess body water appeared to diffuse too quickly out of the peritoneal cavity. Thus water volume control could become a problem leading to abandonment of CAPD or more frequent use of high glucose concentration dialysate.

These observations suggest that routine assessment of peritoneal resistance to solute transfer would be worthwhile. This, however, is not a straightforward proposition in view of the complexity of the transfer process. A solute passing from the blood perfusing the peritoneal lining into the intraperitoneal fluid must negotiate a series of resistances, which include the several structures of the peritoneal membrane as well as stagnant fluid films adhering to both blood and dialysate sides of the membrane. The transfer occurs by simultaneous convection (solvent drag due to water movement into hyperosmotic dialysate) and diffusion (molecular movement down the solute concentration gradient from blood into dialysate). These are passive processes; however, the possibility of active transport has been suggested in the case of electrolyte transfer. In addition, alterations in the hemodynamics of peritoneal perfusion, pharmacologically induced or otherwise, may influence solute transfer and so further complicate the assessment of peritoneal diffusional resistance.

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Two approaches to peritoneal transfer function appear in the literature: Some workers have used clearance data.[6–9] A typical protocol[7–9] involves a 60-minute exchange with the first 10 and the final 20 minutes dedicated to infusion and drainage. However clearance is not a direct measure of peritoneal resistance to solute diffusion since it includes transfer from both diffusion and convection. Also, average clearance values are strongly influenced by the duration of the exchange, since clearance falls off rapidly as equilibrium approaches. Other factors such as differences in the residual dialysate volume before and after the test exchange, changes in osmotic driving force and variation in the infusion and draining times also influence clearance measurement.

A better parameter to assess peritoneal resistance is the mass transfer-area coefficient, K_{BD}, which arises in kinetic models of the solute mass transfer process. K_{BD} is the inverse of peritoneal diffusion resistance and represents the clearance rate which would be realized in the absence of both ultrafiltration and solute build-up in the dialysate. This approach has been explored by two groups: Randerson and Farrell[2,10–13] and Pyle et al.[14,15] To determine the K_{BD} value for a test exchange during which blood and dialysate solute concentration data have been gathered, a rather tedious computer program is required to solve the systems of equations in the models proposed by these authors. The complexity of the calculations has precluded routine clinical use of this approach and there seems a clear need for a more rapid means of determining K_{BD}. The development and testing of a simplified model for this purpose is reported in this study.

Model Description

The simplified model to be tested is stated mathematically as follows:

$$\ln \{(V_D(\bar{C}_B - C_D)\} = \ln [V_D{}^0(\bar{C}_B - C_D{}^0)\} - \bar{K}_{BD}\bar{V}_D{}^{-1}t$$

This algebraic equation (derivation of which can be found in the Appendix), expresses the change expected in intraperitoneal solute concentration (C_D) as a function of dwell time under the following assumed conditions:

1) The peritoneal membrane is the limiting resistance to solute transfer between blood and dialysate, i.e., the resistance of fluid films on blood and dialysate sides of the membrane is negligible.

2) Solvent water movement is always into the peritoneum (ultrafiltration or Q_u is positive). A corresponding equation can be derived for periods of peritoneal fluid readsorption (equation 9 in appendix).

3) The solute concentration variation in the blood is assumed negligible over the test period of the exchange (blood solute concentration C_B = constant).

4) The K_{BD} parameter, which characterizes the peritoneal membrane diffusion resistance, is assumed to increase in proportion to the intraperitoneal fluid volume (i.e., K_{BD}/V_D = constant). $\bar{K}_{BD}$ is the value corresponding to the mean dialysate volume ($\bar{V}_D$) over the test period. As explained in the appendix, this assumption is primarily one of convenience to obtain the algebraic equation in its simplest computational form.

5) As water is drawn across the peritoneal membrane by osmotic forces (ultrafiltration), solutes tend to be dragged along (solvent drag). However, the solute molecules move at a fraction of the water molecules' velocity. This fraction, known as the sieving coefficient (S), is assumed to be unity for the purpose of obtaining the above simple equation.

6) The total rate of solute transfer across the peritoneum is due to combined convective and diffusive transport. The interdependence between these two transport processes is characterized by a parameter, f, which for the purpose of this model was fixed equal to zero (see the appendix for further explanation of f).

A fuller discussion of the validity and impact of these assumptions on the accuracy of K_{BD} can be found in the appendix. Briefly, the last two (S = 1, f = 0) are the most critical. The error associated with assumptions 5 and 6 approaches zero for very small solute size. The error in K_{BD} estimates due to these assumptions is acceptable for larger solutes as well, as long as solvent drag (convection) plays a minor role in solute transport between blood and dialysate.

Model Verification

The simple model analysis was applied to retrospective data from 12 patients, randomly selected from the 34 patient group investigated by Randerson.[18] Details of the experimental procedure may be found elsewhere.[11,18] Briefly, the test exchange, the second exchange of the day, was conducted with 1.5% glucose dialysate prewarmed to 37 C. During infusion a blood sample was drawn for assay. Immediately after dialysate infusion, 7 ml of peritoneal fluid were withdrawn after in situ mixing. Subsequent samples were drawn at approximately each half-hour point into the exchange. At the 4.5 hour point, a final dialysate sample was obtained, fluid drained back into the dialysate bag, subsampled and volume determined. A final blood sample was taken during drainage. Samples were analyzed by standard techniques for urea, creatinine and tritiated B_{12} concentrations.

Randerson did not measure fluid volume directly but instead estimated the time course of V_D from the infused ($V_D{}^i$) and drained dialysate volume ($V_D{}^d$) according to the following empirical equation:

$$V_D = V_D{}^d - (V_D{}^d - V_D{}^i) \exp(-t/\beta) \qquad (10)$$

where β is a time constant associated with intraperitoneal volume expansion. Randerson arbitrarily assumed that

90% of the volume change occurred within the first 120 minutes, which leads to $\beta = 52.1$ min. The mean value of V_{BD} required for the simplified model was obtained by integration of equation 10 using the same β value.

Pre/post blood concentrations were averaged to obtain $\bar{C}_B$.

Results and Discussion

Table 1 lists the K_{BD} values calculated using the simplified model as well as those attained by Randerson from the same patient data. The gaps in the table reflect rejection of experimental data for a variety of reasons, including net negative ultrafiltration (infused volume exceeding drained volume) and some solute data which were suggestive of sample mix-up. The last column of Table 1 lists correlation coefficients of linear fit for the simplified model.

The Randerson model shares most of the assumptions made for the simplified model. The assumption of a constant C_B which is the only difference between the two models, should introduce negligible error. One would therefore expect little difference between the K_{BD} values obtained from the Randerson and simplified models. In fact the agreement between the two models is close. However there are significant differences for some patients (e.g., urea K_{BD} for patient 1 is 11% less using the simpler model) because of differences in the numerical techniques associated with each model. Randerson's model seeks the K_{BD} value which results in the "best" agreement (minimum least squares error) between the experimental values of C_D and those predicted by the model. With the simpler model the best fit is sought for values of $\ln\{V_D(\bar{C}_B - C_D)\}$. In addition, the Golden Section numerical search routine utilized by Randerson may not result in the absolute best value of K_{BD} in certain situations.

An additional error may arise with Randerson's general model in that the numerical integration starts at the C_D and C_B values of $t = 0$. If either of these is in error, it will influence the K_{BD} value obtained. This appears to be the case for patient 3. The deviation from linearity, evidenced by the low correlation coefficients for urea and creatinine, $R = 0.950$ and 0.901, respectively, is mostly due to the $t = 0$ points falling well above the best fit line through the remaining points. The general model is forced to go through this point, resulting in an even poorer fit of the experimental data; whereas for the simpler model, the $t = 0$ intercept is a parameter of best fit obtained from the linear correlation.

Table 1 suggests that the simpler linear model provides equally reliable and, in some instances, better estimates of K_{BD} than those arrived at with the tedious computations utilized by Randerson. However, this concordance does not validate the major assumptions of $f = 0$, $S = 1$ adopted in both the Randerson and simplified models. Some justification of these assumptions can be taken from the linear fit achieved from the plot of $\ln\{V_D(\bar{C}_B - C_D)\}$ data vs. t as predicted by the simple model equation. The correlation coefficients of linear fit (R) listed in Table 1 exceed 0.98 in all cases save one instance for each solute. Figure 1 shows the straight line fit typical of most of the patient/solute pairs listed.

The error associated with the assumptions $f = 0$, $S = 1$ approach zero for small solutes and small Peclet numbers. Consequently, the linear fit for urea and creatinine is more limited by random error in the experimental data than by these two assumptions. Indeed the data point

TABLE 1. *Model Test Results*

Patient Number	Solute	K_{BD} Estimates (ml/min) Randerson Model	K_{BD} Estimates (ml/min) Simple Model	Simple Model Correl. Coeff. R
1	Urea	21.2	18.8	.994
	Creat	8.8	7.4	.986
	B_{12}	2.4	2.0	.966
2	B_{12}	8.8	8.0	.997
3	Urea	19.7	11.4	.950
	Creat	4.2	2.6	.901
4	Urea	18.3	17.5	.996
	Creat	7.6	7.2	.993
	B_{12}	3.5	3.3	.980
5	Urea	28.3	25.4	.994
	Creat	22.8	21.4	.995
	B_{12}	9.3	8.5	.989
6	Urea	14.4	15.5	.997
	Creat	4.2	4.6	.995
7	Urea	16.0	16.8	.987
	Creat	6.3	6.4	.990
	B_{12}	2.1	1.9	.994
8	Urea	18.1	18.8	.999
	Creat	8.3	7.5	.997
	B_{12}	3.1	2.9	.989
9	Urea	15.7	19.2	.997
10	Urea	20.4	16.3	.993
	Creat	17.1	14.3	.995
	B_{12}	7.7	6.6	.992
11	Urea	18.6	16.4	.995
	Creat	14.0	12.6	.995
	B_{12}	5.2	4.7	.998
12	Urea	18.6	18.7	.996
	Creat	11.7	11.6	.998
	B_{12}	2.9	2.9	.985
Mean values	Urea	19 ± 4	18 ± 4	0.99 ± 0.01
	Creat	11 ± 6	10 ± 6	0.98 ± 0.03
	B_{12}	5 ± 3	5 ± 3	0.99 ± 0.01

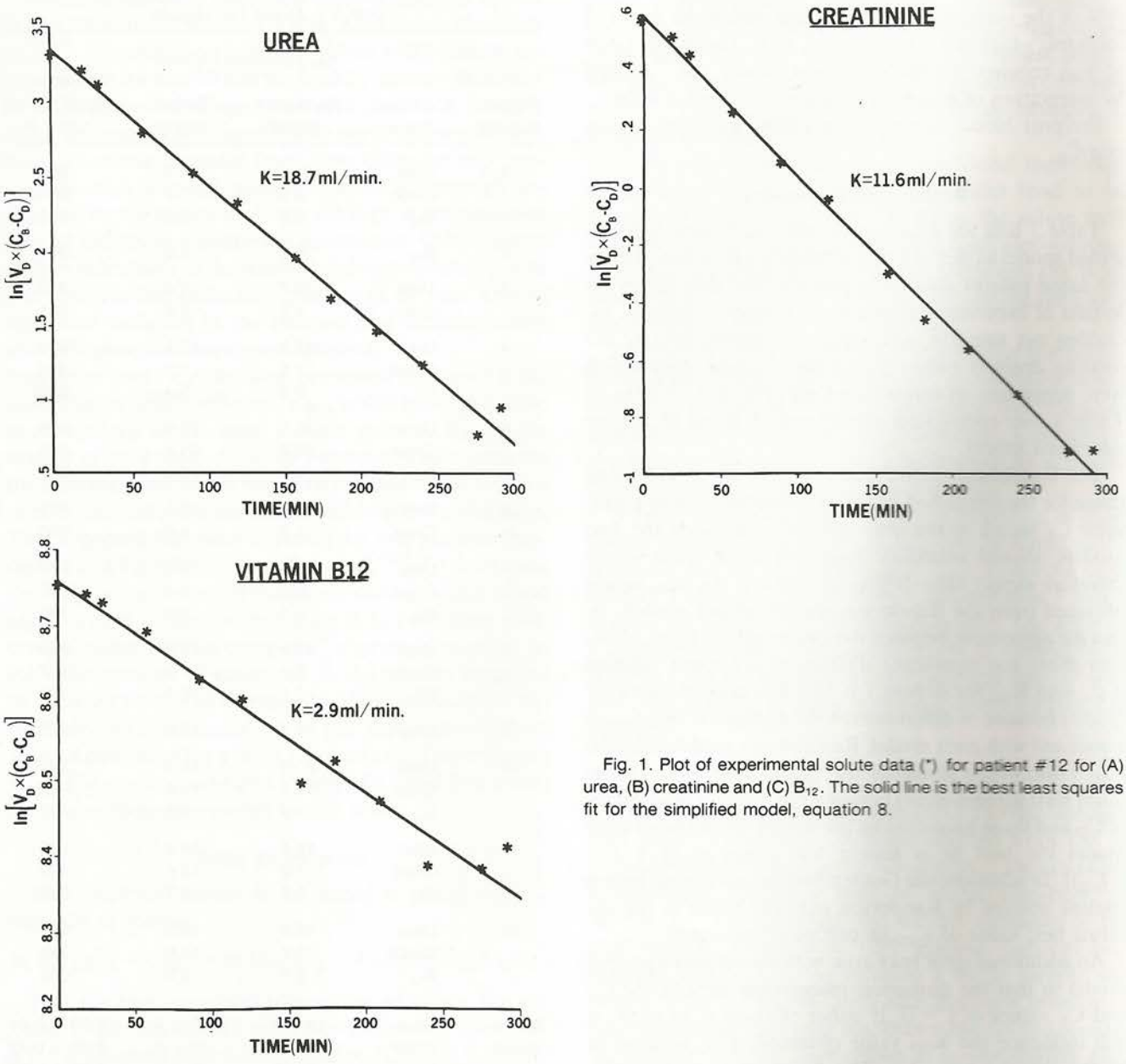

Fig. 1. Plot of experimental solute data (*) for patient #12 for (A) urea, (B) creatinine and (C) B_{12}. The solid line is the best least squares fit for the simplified model, equation 8.

scatter about the line of best fit is random, as illustrated in Fig. 1. The validity of the simple model should decrease with increasing solute size, as K_{BD} values fall off, convective transfer becomes more important, and the likelihood of solute rejection at the peritoneal membrane (i.e., $S < 1$) increases. For these reasons, we expected a less satisfactory linear fit for vitamin B_{12} (1355 Daltons molecular weight). Yet Table 1 demonstrates a linear fit for B_{12} entries comparable to those for urea and creatinine. This is because for all B_{12} entries in Table 1, diffusive transfer is the major mode of transport, accounting for more than 85% of total B_{12} appearance in dialysate (except 59% for patient 7). Thus, although the assumption of negligible reflection of B_{12} at the peritoneal membrane is probably incorrect, little error in K_{BD} results. Since convective transport plays a minor role for all patient-solute entries in Table 1, the K_{BD} values listed are insensitive to the choice of parameter β, used in the determination of dialysate volume and ultrafiltration rate profiles.

The three B_{12} tests excluded from Table 1 as unreliable were all associated with large fluid shifts across the peritoneum (net ultrafiltration was negative in one of these cases). It would appear, therefore, that the simple model remains applicable for larger solutes if the contribution of ultrafiltration to solute transfer is small.

The good correlation coefficients cannot be taken as an absolute indicator of model precision. For a few patient-solute combinations the plotted data did not fall randomly about a straight line but rather appeared to follow a smooth curve, consistent with a gradual fall off in K_{BD} over the dwell period. For example, the K_{BD} value for urea in patient 10 is listed in Table 1 as 16.3 ml/min for the simple model linear plot with R = 0.993. However, the four data points over the first 50 minutes of this exchange fall on a straight line suggesting a K_{BD} value of ~25 ml/minute while the final five data points (for the 140- to 270-minute period) also follow a straight line but indicate a K_{BD} of ~13 ml/minute. It is not clear whether an actual physiological change occurred during this exchange or this is an artifact introduced by other factors, such as the model assumptions, or errors in the experimental and empirical data used. If K_{BD} does change during an exchange, it is easily observed from the linear plot proposed here; whereas, it remains concealed in the curve fitting routines used in the more general models.

Further work is required on several fronts in pursuit of the goal of assessing peritoneal membrane permeability on a routine clinical basis. It will be necessary to establish the ranges of S, K_{BD} and ultrafiltration volume shift within which the accuracy of the simplified model is adequate. In addition, for long-term changes in peritoneal resistance to be documented with any confidence, the ability to achieve reproducible K_{BD} evaluations will have to be demonstrated. Farrell and Randerson[12,13] have shown consistent K_{BD} values for evaluations repeated over three consecutive days and for three or four periodic evaluations over a period of several months. Routine assessment is only practicable with a minimum of patient blood and dialysate sampling. Therefore, it will be necessary to evaluate prospectively several simple protocols to establish the best compromise between simplicity and accuracy of the test. Our current recommendation is to take three dialysate samples 10–15 minutes apart during the first hour of dialysis with a blood sample taken mid-way through the study period. Without a marker of volume change, the peritoneal content must be collected at the end of the sampling period in order to provide an estimate of V_D. The dialysate used should contain a minimal amount of glucose (0.5% glucose, if available, if not, 1.5%) to minimize ultrafiltration errors.

Appendix–Model Theory

The mass balance for a solute, migrating into or out of the peritoneal fluid, is related to the rate of solute accumulation in dialysate. This, in turn, is given by the sum of the rate of solute diffusion from blood into dialysate and rate of solute convection from blood into dialysate.

There is some evidence[16] for an additional term to account for peritoneal drainage via the lymphatics. For macromolecules such as those used as peritoneal volume markers, lymphatic drainage appears to be the principal route of transfer out of the peritoneum.[16] However, for most solutes of interest this is an insignificant transport pathway and will not be considered further in this derivation.

Solute accumulation in the peritoneal fluid is given by

$$\frac{d}{dt}(V_D\bar{C}_D)$$

where V_D is peritoneal fluid volume, $\bar{C}_D$ is the spatially averaged solute concentration in the peritoneal fluid. The bar on C_D may be dropped if the peritoneal contents can be considered homogeneous. This will be assumed the case.

Solute diffusion and convection across the peritoneal membrane, separating the vascular and peritoneal compartments, is a simultaneous, coupled process. Its division into two independent terms, as suggested above, is artificial and arbitrary. For transfer across a homogeneous membrane and close to steady-state it is convenient to separate the transfer rate into the following two terms[17]:

$$K_{BD}(C_{BM} - C_{DM}) + SQ_u\bar{C}$$

The first term is the diffusional transfer rate which would occur in the absence of ultrafiltration. C_{BM} and C_{DM} represent the concentrations of solute at the blood membrane and the dialysate membrane interfaces, respectively, while K_{BD} is the mass transfer-area coefficient referred to in the introduction. K_{BD} is a direct (inverse) measure of total membrane resistance to diffusive transfer, reflecting both membrane area available for diffusion and the specific resistance of the membrane to solute diffusion. Q_u is the ultrafiltration rate into the peritoneum while S is the solute sieving coefficient reflecting membrane selectivity. $\bar{C}$ is a mean concentration defined as follows:

$$\bar{C} = (1 - f)C_{BM} + fC_{DM}$$

where

$$f = \frac{1}{Pe} + \frac{1}{[\exp(Pe) - 1]}$$

$$Pe = \frac{SQ_u}{K_{BD}}, \text{ a modified Peclet number.}$$

When the Peclet number is large as in the case of a large solute (small K_{BD} value) and a large ultrafiltration rate, f approaches 0 and $\bar{C}$ approaches C_{BM}. As the Peclet number falls off with decreasing solute size, diffusion becomes the principle mode of transport and f rises towards a limiting value of 0.5 as Pe approaches 0.

Two major simplifications are required to arrive at the simplified model. The first of these is arbitrarily to set f = 0. This was seen above to be the correct value for large Pe values; however, the associated error is also small for very low Pe values since the convective term involving f becomes increasingly small in comparison to the diffusive term. It can be shown that with this assumption K_{BD} will be underestimated by a fractional amount equal to Pe × f. For Pe < .20, this assumption will result in K_{BD} estimates within 10% of the correct value. The Peclet number for urea transfer into 1.5% dextrose dialysate in most instances would exceed 0.20 only during the initial minutes of the exchange when Q_u is highest.

The sieving coefficient, S, is a function of solute size and characteristics of the membrane. For low molecular weight solutes the sieving coefficient rises towards unity. Setting S = 1 represents the second of the two major assumptions. A clear

consensus does not emerge from the literature on solute sieving coefficients for the peritoneal membrane. Pyle and Popovich[14] have computed K_{BD} and S values using a complex patient model which retains the exact function for f. Their results suggest S > .7 for solutes of molecular weight less than 200 Daltons with S = .8 a representative value for urea. Randerson and Farrell[11] argue the sieving coefficient should be close to 1 for small solutes and adopt this as well as the f = 0 assumption. In addition, both groups assume that the peritoneal membrane is the limiting resistance; thus $C_{BM} \rightarrow C_B$ and $C_{DM} \rightarrow C_D$. Together, these assumptions yield the following equation for the variable-volume dialysate pool

$$\frac{d}{dt}(C_D V_D) = K_{BD}(C_B - C_D) + Q_u C_B \quad (1)$$

In arriving at this equation convective movement of solvent water has been assumed to be from blood into dialysate ($Q_u > 0$). During the latter state of a long-term dwell, there may be a reabsorption of peritoneal fluid. During such periods of reverse ultrafiltration ($Q_u < 0$), the appropriate simplification is f = 1 (the limiting value of f for large negative values of Pe) and $\bar{C} = C_{DM} = C_D$. This gives, for $Q_u < 0$,

$$\frac{d}{dt}(C_D V_D) = K_{BD}(C_B - C_D) + Q_u C_D \quad (2)$$

To describe the changes occurring in C_B, an additional differential equation must be written for the body pool which accounts for solute generation and renal excretion. For larger solutes, such as B_{12}, the body pool must be further divided into extra- and intracellular compartments. The resulting CAPD model is a set of two or three nonlinear differential equations. To obtain a value of K_{BD} from serial dialysate solute concentrations spanning a test exchange, Randerson[18] used the following approach. With an initial estimate of K_{BD}, the set of differential equations were solved on a main frame computer by Runge–Kutta integration to obtain predicted dialysate concentrations corresponding to the sample times. This process was repeated 15 times. An optimal estimate of K_{BD} was reached by decreasing the deviation between the predicted and experimental dialysate concentrations at each computation. This approach requires sophisticated software development and too much computer time to be practicable for routine evaluation of peritoneal properties. This is even more the case in the technique adopted by Pyle[19] which required computer optimization of two parameters, S and K_{BD}. A simplified CAPD model, which obviates the need for complex computation will be described next.

Ultrafiltration into the peritoneum results in an expanding intraperitoneal volume. This is expressed mathematically as

$$Q_u = \frac{dV_D}{dt}$$

This is applied to the last term in equation 1

$$Q_u C_B = \left\{\frac{dV_D}{dt}\right\} C_B = \frac{d}{dt}\{V_D C_B\} - V_D \frac{dC_B}{dt} \quad (3)$$

Substituting the last expression from equation 3 into 1 and rearrangement of terms gives

$$\frac{d}{dt}\{V_D C_D\} - \frac{d}{dt}\{V_D C_B\} = K_{BD}(C_B - C_D) - V_D \frac{dC_B}{dt}$$

Gathering the two terms on the left-hand side of the equation and multiplying through by $-dt/\{V_D(C_B - C_D)\}$ results in equation 4.

$$\frac{d[V_D(C_B - C_D)]}{V_D(C_B - C_D)} = -\frac{K_{BD}}{V_D} dt + \frac{dC_B}{C_B - C_D} \quad (4)$$

The differential equation is now in a form which can be integrated analytically; however, there is some uncertainty as to the variation of the K_{BD}/V_D term with time. Two assumptions are available.[20] A constant surface area assumption would imply that for peritoneal fluid volumes exceeding some threshold value required for complete wetting of the membrane, the value of K_{BD} is constant. Conversely, one might argue that K_{BD} should increase in proportion to the peritoneal fluid volume, in which case K_{BD}/V_D would be a constant. Which assumption is more appropriate is not clear from the literature. Randerson[18] did not find a statistical difference in K_{BD} values between 1L exchange patients and 2L exchange patients. Nor was there a significant difference between adult K_{BD} values and those of two pediatric subjects. In contrast, Popovich et al[21] found K_{BD} measurements in a premature infant were proportional to adult values.

If equation 4 is integrated assuming K_{BD} is proportional to V_D, equation 5 results

$$\ln\{V_D(C_B - C_D)\} = \ln\{V_D^0(C_B^0 - C_D^0)\} - \frac{K_{BD}}{V_D} t + \int_{C_B^0}^{C_B} \frac{dC_B}{C_B - C_D} \quad (5)$$

where t refers to time elapsed after some reference time, such as the beginning of infusion or initial sample time. The superscript (^{0}) refers to variable values at the reference time. For K_{BD} constant the corresponding integration yields equation 5a

$$\ln\{V_D(C_B - C_D)\} = \ln\{V_D^0(C_B^0 - C_D^0)\} - K_{BD}\int_0^t \frac{dt}{V_D} + \int_{C_B^0}^{C_B} \frac{dC_B}{C_B - C_D} \quad (5a)$$

While the assumption of a constant K_{BD} seems intuitively the more likely assumption, equation 5 has been chosen for testing in this paper on the basis of its simpler form. Since K_{BD} varies linearly with V_D, K_{BD} values must either be averaged over the V_D values encountered in the exchange or referenced to some arbitrary V_D value. The former approach will be taken.

Equation 5 (or 5a) may be used directly to calculate K_{BD} from serial blood and dialysate concentrations or the C_B values may be calculated with a single blood sample via a mass balance, assuming a single body pool

$$C_B = \frac{V_B^0}{V_B} C_B^0 + \frac{V_D^0}{V_B} C_D^0 - \frac{V_D}{V_B} C_D + \frac{Gt}{V_B} - \frac{K_R}{V_B}\int_0^t C_B dt \quad (6)$$

where V_B represents solute distribution volume, K_R is renal clearance and G is generation rate for the solute. If the solute distribution volume, V_B, includes the body water pool from which the increase in dialysate volume is being drawn then

$$V_B = V_B^0 + V_D^0 - V_D \quad (7)$$

Alternatively, a constant volume body pool assumption, that is $V_B = V_B^0$ constant, will introduce only a small error. The equations 5–7 are an exact equivalent of the equations solved

by Randerson.[18] However in this format the solution for best K_{BD} value is relatively straightforward. Equations 6 and 7 are solved for the C_B values corresponding to the serial C_D values. The integral in equation 5 (last term) may be evaluated at each of the serial data points by numerical integration. Values for the first minus the last term in equation 5 may then be determined and plotted vs. t. A linear fit should result with a constant slope equal to $-K_{BD}/V_D$. The average value for K_{BD} over the test period is obtained as $\bar{K}_{BD} = \bar{V}_D \times (-\text{slope})$. This approach offers a considerable simplification over the tedious computer optimization technique used by Randerson[18]; nevertheless, a further approximation leads to an even simpler analysis.

One of the chief benefits of CAPD is it is essentially a continuous treatment mode, eliminating the large swings in solute concentrations which occur with intermittent therapies. During a typical CAPD exchange there will be an initial fall in C_B; however, as dialysate equilibration is approached there will be a levelling off and subsequent rise in C_B as rate of solute removal falls below the generation rate, G. The maximum C_B variation, however, is small and it is reasonable to approximate C_B as a constant over an exchange period. This assumption results in the following equation after elimination of the integral term from equation 5.

$$\ln \{V_D(\bar{C}_B - C_D)\} = \ln \{V_D^0(\bar{C}_B - C_D^0)\} - \bar{K}_{BD}\bar{V}_D^{-1}t \quad (8)$$

where $\bar{C}_B$ now represents mean blood concentration. This simplified model can be solved directly for $\bar{K}_{BD}$ with two data points or for multiple data $\bar{K}_{BD}$ can be obtained from a least squares fit performed on a microcomputer or calculator or from a direct plot of the data.

Applying the same assumptions to equation 2, one arrives at an analogous equation for periods of negative ultrafiltration

$$\ln (\bar{C}_B - C_D) = \ln (\bar{C}_B - C_D') - \bar{K}_{BD}\bar{V}_D^{-1}t' \quad (9)$$

where the superscript (′) refers to concentration values at some reference time point during the negative ultrafiltration period.

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