Kidney International, Vol. 47 (1995), pp. 1187–1198

TECHNICAL NOTE

Assessing the peritoneal dialysis capacities of individual patients

BÖRJE HARALDSSON

Departments of Nephrology and Physiology, University of Göteborg, Göteborg, Sweden

Assessing the peritoneal dialysis capacities of individual patients. A method for measuring the peritoneal dialysis capacity (PDC) of the individual patient has been developed as an aid to treatment of patients with renal failure and peritoneal dialysis. The patient collects the data him or herself during an almost normal CAPD day using a carefully designed protocol whereby the nursing time is kept to a minimum. The three-pore model is used to describe the PDC with three physiological parameters: (1.) the 'Area' parameter ($A_0/\Delta x$), which determines the diffusion of small solutes and the hydraulic conductance of the membrane (L_pS); (2.) the final reabsorption rate of fluid from the abdominal cavity to blood (Jv_{AR}) when the glucose gradient has dissipated; and (3.) the large pore fluid flux (of plasma, Jv_L), which determines the loss of protein to the PD fluid. In the adult PD population (age 60, $N = 97$) the normal 'Area' parameter was 23,600 cm/1.73 m^2, with an SEM of 650. The Jv_{AR} was 1.49 ml/min/1.73 m^2 and Jv_L was 0.078 ml/min/1.73 m^2. The PDC parameters were reproducible and could adequately predict the concentrations of the test solutes as well as that of β_2-microglobulin. The results in terms of clearance, 'UF volume' and nutritional consequences were presented on easily understandable graphs, whereby patient compliance was improved. These physiological parameters are highly dynamic, as evidenced by the marked increases observed during peritonitis. It seems safe to conclude that PDC is a useful tool to achieve adequate dialysis and to enhance the understanding of PD exchange.

Peritoneal dialysis (PD) is an increasingly popular life-supporting therapy for patients with chronic renal failure. In contrast to the membranes used in hemodialysis, the functional characteristics of the individual PD membrane are unknown. Indeed, it was recognized early that there are large differences in solute and fluid exchange between individual patients treated with continuous ambulatory peritoneal dialysis (CAPD) [1]. Moreover, the consequences of inadequate, or rather insufficient, dialysis appear gradually over a long period of time and include the reappearing uremic symptoms as well as increased morbidity and mortality. The effects appear in patients as the residual renal function declines, a phenomenon often denoted "the end of the honeymoon period." Previously, infections were the major complications of PD. However, the risk of peritonitis has been reduced in the last few years and other problems such as underdialysis are now evident. Against this background, it is not surprising that there is growing interest in methods of measuring PD exchange and providing adequate dialysis.

In 1987, Twardowski et al introduced a simple peritoneal equilibration test (PET) which greatly improved our knowledge of the individual patients and what dialysis treatment to use [2, 3]. Due to the variability of the PET, it has been suggested that predictions should be based on four to five exchanges [4]. In order to reduce the variability, the patient can roll from side to side to achieve better mixing of PD fluid [2, 3]. It is evident, however, that this procedure creates an artificial situation different from the ordinary CAPD day. The exchange is most probably affected by shaking, as has been seen in rats [5, 6], and the procedure has been criticized [4]. There are also reports of exceptionally low variability of PET in selected patients [7]. No doubt, PET can be used to select patients more suitable for automated peritoneal dialysis (APD, the so-called high transporters), or to identify low transporters less suitable for PD Another, perhaps better, way to improve PET is the APEX, where the APEX time is the point where the concentrations of glucose (C_D/C_{D0} = dialysate concentration at time t over initial dialysate concentration) and urea (C_D/C_P = dialysate over plasma concentration ratio) cross [8]. Albeit attractive in their simplicity, the semiquantitative nature of PET and APEX cannot give any details of the physiological properties of the PD membrane. Moreover, whereas some authors find PET to be of clinical value [7, 9], others have reported that PET is incapable of predicting PD exchange [10]. Naturally, the latter objection is also valid for more sophisticated predictions based on PET data [11].

How much is adequate dialysis? This pertinent question is not easily answered. There are guidelines that recommend a weekly Kt/V (= clearance multiplied with time over distribution volume) for urea of 1.7 and a weekly creatinine clearance of 50 liter/week [12] or 55 liter/week [13]. Indeed, clinical studies have suggested that weekly creatinine clearance, creatinine Kt/V or urea Kt/V are useful to assess the effectiveness of PD in the individual patient [14, 15]. Some authors have found statistical correlation to one parameter only [16, 17]. On the other hand, there are studies suggesting that there is a poor correlation between urea kinetic indices and the clinical outcome in CAPD patients [18]. One major problem is to design studies that fully take into account the comorbid conditions since these may confound the analysis. At present, it seems safe to conclude that there is a need for a good noninvasive technique to measure the transperitoneal passage of fluid and solutes under normal PD conditions.

In a previous study, transport was simulated during PD using a small computer to illustrate the importance of various factors in the three-pore model [19]. In the present paper, the peritoneal dialysis membrane characteristics (PDC) of individual patients were assessed using a structured test protocol and a computer program to improve our understanding of PD and to ensure adequate dialysis.

Received for publication June 6, 1994
and in revised form November 8, 1994
Accepted for publication November 14, 1994

Methods

Theoretical background of the three-pore model

Ernest Starling [20] studied the peritoneum one century ago when he formulated the forces behind the transcapillary passage of fluid, and this so-called "Starling balance" seems to be universal for all microvascular beds. Landis and Pappenheimer extended our knowledge of the transcapillary exchange of fluid and solutes and introduced the pore concept using elegant, carefully designed studies [21]. A second pore population (large pores or "leaks" with a radius of 25 nm) was postulated by Grotte [22] based on studies on the lymph composition of dextran fractions with different molecular weights. Moreover, Yudilevich and Alvarez [23] presented evidence for a third water-exclusive pathway in dog hearts in 1967. Thus, the components of the modern "three-pore" theory were already known 25 years ago. More recently, Rippe and Haraldsson [24] showed that the transport of solutes and water across heteroporous membranes could be expressed in explicit terms using irreversible thermodynamics and nonlinear flux equations. Indeed, almost all vascular beds seem to be heteroporous [25, 26]. In addition, proteins have been identified as water-exclusive channels in different cell membranes, for example, CHIP 28 [27].

In a series of articles, Rippe and coworkers have introduced modern theories of capillary physiology to the field of peritoneal dialysis. The three-pore model of fluid and solute transport (or "two-pore" model of solute transport) across the peritoneal membrane has been documented in a series of articles [19, 28–30]. According to this model, the PD membrane can be regarded as a (capillary) membrane with three equivalent (functional) pore populations. The small pore with a Stokes-Einstein radius around 4.7 nm represents the major pathway for small solutes. Macromolecules are transported by convection through a few large pores, SE radius 25 nm. Finally, a third water-exclusive cell pathway is present through which almost 40% of the water passes during an average PD dwell with glucose as osmotic agent. The large pores account for 5% of the hydraulic conductance (L_pS, or UF coefficient), the cell pores 1% of L_pS while more than 90% of L_pS is due to the small pores. The apparent contradiction of the latter two sentences are due to the fact that glucose exerts 100% of its osmotic force across the cell pore pathway and only a few percent across the small pore equivalent.

Patient selection

All patients treated with CAPD at the Department of Nephrology, Sahlgrenska Hospital, Göteborg, Sweden from May 1991 were invited to use the PDC test in order to ascertain adequacy of dialysis and gain insight into the physiological properties of their PD membrane. The test was done at home by the patient in the majority of cases. Apart from their renal insufficiency the patients were healthy, except those patients who were included in the peritonitis group (see below). The study was approved by the ethical committee of the University of Göteborg.

The protocol for PDC determinations

The test was designed to: (i) mimic the ordinary CAPD day, (ii) be performed by the patient with a minimum of nursing time; (iii) yield data from different dwell times and glucose strengths; and (iv) allow calculations of mass balance during a 24 hour period.

Table 1. A representative PDC determination on a male patient

	Glucose conc *g/liter*	Volume of PD fluid *ml*	Time of start of fill	Time of start of drain	Drain volume *ml*	
					Meas	Calc
PD samples	15	2010	10.16 pm	7.53 am	2060	2024
	15	2010	8.10 am	10.24 am	2086	2132
	23	2008	10.56 am	3.04 pm	2518	2438
	15	2012	4.13 pm	7.30 pm	2022	2179
	23	2015	7.55 pm	10.05 pm	2538	2308
	15	1994	10.32 pm	7.57 am	1999	2073

Urea conc *mM*		Creat conc *μM*		Glucose conc *mM*		Albumin conc *g/liter*	
Meas	Calc	Meas	Calc	Meas	Calc	Meas	Calc
30	31.8	762	782	19.1	18.4	0.46	0.49
26	24.5	511	524	41.0	45.8	0.21	0.17
29	28.9	596	657	44.4	41.8	0.26	0.30
28	27.9	562	613	37.0	38.0	0.24	0.21
26	24.1	479	500	52.5	62.9	0.16	0.20
30	31.7	733	776	18.1	19.2	0.49	0.43

	Sodium	Urea	Creatinine	Glucose	Serum albumin
Blood samples	*mM*				*g/liter*
12 Mar 8.02 am	135	31	792	12.7	17
13 Mar 7.40 am	133	33	794	12.7	17

	24-hr urine volume *ml*	Conc of urea *mM*	Conc of creatinine *μM*
Urine samples	135	2.1	7800

The male patient (E.K.), age 62, was diagnosed with diabetes mellitus type I since childhood. He has a height of 160 cm and weight of 64 kg, thus his body surface area of 1.70 m^2 and a BMI of 25 kg/m^2.

The patient performed the PDC test himself during an "almost" normal CAPD day following a protocol with five exchanges per 24 hours. The previous overnight dwell was weighed and sampled after mixing (= zero sample). The 'PDC-day' started with a short (2 to 3 hr) PD dwell followed by two intermediate dwells (4 to 6 hr), another short exchange, and finally an overnight dwell (10 to 12 hr). Two different glucose concentrations were alternately used. The well-mixed dialysate samples (50 to 100 ml) and two blood samples (with a 24 hr interval) were analyzed with respect to the concentration of urea, creatinine, glucose, albumin and sodium (in blood only). The exact time of starting each dialysate drain and of starting each fill with fresh fluids was noted, along with the weights of the bags with new or used dialysis fluid. Minimal flushing was used. A 24-hour urine collection was made, the volume measured and the concentrations of urea, creatinine and albumin determined. An example of the PDC protocol is shown in Table 1. Finally, the results of analysis of the blood, dialysate and urine samples together with the protocol data were entered into a computer and the PDC parameters calculated (Table 2).

Laboratory analyses

All dialysate samples were taken by the patient, kept cool (8°C) if possible, and delivered when the second blood sample was taken, that is, within 24 hours. Analyses were performed as routine procedures at the hospital's central laboratory. The

Table 2. Results of the PDC calculations for the patient in Table 1

1. Residual renal function	
Urea clearance	0.25 ml/min/1.73 m^2
Creatinine clearance	0.90 ml/min/1.73 m^2
RRF = GFR	0.60 ml/min/1.73 m^2
Proteinuria	0.3 g/24 hr
2. PDC parameters	
Unrestricted area ($A_{0/\Delta x}$)	33,600 cm/1.73 m^2
Final absorption rate (Jv_{AR})	1.31 ml/min/1.73 m^2
Large pore fluid flux (Jv_L)	0.11 ml/min/1.73 m^2
3. Other parameters calculated	
Hydraulic conductance (L_pS)	0.10 ml/min/mm Hg/1.73 m^2
Estimated lymph flow	0.44 ml/min/1.73 m^2
Hydrostatic capillary pressure	15 mm Hg
Oncotic pressure	17.5 mm Hg
Large pore fraction of L_pS	12%
4. Calculated PD clearance with a PD regime of 4 × 2 liters of 23 g/liter of glucose	

Solute	Molecular wt	Stokes-Einstein radius *nm*	PD clearance *ml/min/ 1.73 m^2*
Urea	60.6	0.26	6.4
Creatinine	113	0.30	6.1
Vitamin B_{12}	1355	0.84	2.9
β_2-microglobulin	9100	1.62	1.0
Albumin	69000	3.55	0.2

Weekly urea Kt/V (PD + urine)	1.88
Total clearance for a solute the size of creatinine	6.7 ml/min/1.73/m^2
Estimated daily fluid removal	1900 ml
Nutritional effects of a PD regime of 4 × 2 liters of 23 g/liter of glucose	
Uptake of glucose from PD	510 kcal/day
Caloric requirements	1600 kcal/day
PD loss of proteins	7.7 g/day
Protein requirements	59 g/day
UGR	408 mmol/24 h
CGR	7.66 mmol/24 h
PNA	2.08 g/kg/day
Calculated LBM	32.5 kg
LBM/W	51%

The average time of drain was 34 min. Abbreviations are in the **Appendix**.

concentration of creatinine (Cr) was automatically corrected for the amount of glucose in the samples

$$[Cr]_{corr} = [Cr] - 0.35 \cdot [Gluc]$$

where the factor (0.35) was dependent on the analytical procedure of the laboratory. The concentration of creatinine is in μmol/liter and glucose mmol/liter.

Calculations of the PDC parameters

The three PDC parameters are:

(1.) The area parameter. The unrestricted pore area available for exchange over the diffusion distance ($A_0/\Delta x$) defines the area parameter. The magnitude of the area parameter is dependent on the assumptions of the present three-pore model (**Discussion**).

(2.) The absorption. The absorption is the final reabsorption rate of fluid from the abdominal cavity to blood (Jv_{AR}). The absorption is rather independent of the theoretical model used,

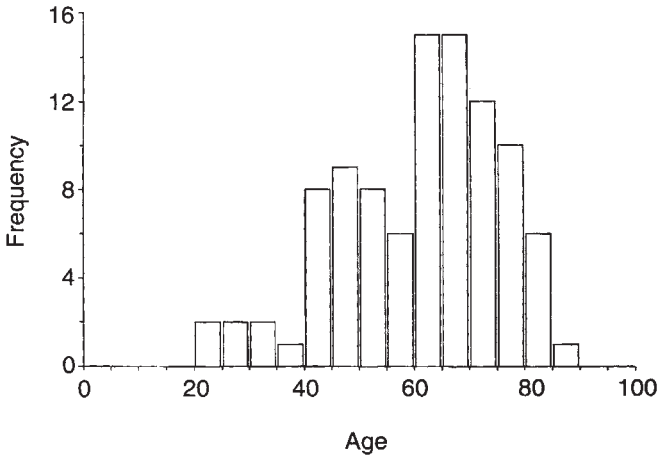

Fig. 1. *The age distribution in the PDC population.*

since it reflects the last phase of the drain volume versus time curve (for details see **Appendix** Eq. 16).

(3.) The large pore flow. The large pore flow is the flux of plasma through the large pores (Jv_L) and is a parameter unique to the three-pore model. Only the larger plasma proteins are subjected to any significant sieving across the large pores. Jv_L does not influence the transport of small solutes or fluid. The Jv_L is quite independent of the assumptions in the model since it is given by the actual 'loss' of plasma proteins (see **Appendix** Eq. 13 for details).

The three PDC parameters are obtained as the best fit between theory and experimental data using non-linear regression and iterative calculations of the three-pore equations of transcapillary exchange analysis [31]. The diffusive capacity of any given solute can be predicted based on its molecular size and the $A_0/\Delta x$, (Eq. 6). The hydraulic conductance (L_pS) is calculated from $A_0/\Delta x$, and there is an uncoupling of L_pS from $A_0/\Delta x$ only if the calculated UF volume deviates more than 10% from that measured, (Eq. 7). The water-exclusive (cell) pathway is assumed to have a constant fraction of L_pS (f_c = 1.0%), while the large pore fraction of L_pS is obtained from the PDC parameter Jv_L and Equation 13. Moreover, the small and large pore radii are assumed to be constant (4.7 and 25 nm, respectively), assumptions that seem valid [25, 32]. In addition, the hydrostatic pressures in the capillaries (P_{capill} = 15 mm Hg) and intraperitoneally (P_{ip} = 6 mm Hg) are constant (**Discussion**).

The PD exchange is less effective during the phases of fluid fill and drain due to the smaller i.p. volumes. This effect is accounted for in the analysis by calculating the time of dialysis from the start of the fill to the start of drain. The residual intraperitoneal volume is considered to be 250 ml for a patient weight of 70 kg, and scaled to the individual patient weight (**Appendix**). The changes of i.p. fluid volume and solute concentration with time are also shown in the **Appendix**. These calculations are repeated for each solute, for every second minute (for the first hour) then every tenth minute during the dwell time and for all exchanges during the day. After adjustment of the PDC parameters, the procedure is repeated another 3 to 10 times until the "best fit" between experimental and calculated data is obtained. If the calculated UF volume is different from the measured UF volume, there is uncoupling of the L_pS (= UF coefficient) from the area parameter (Eq. 7). The

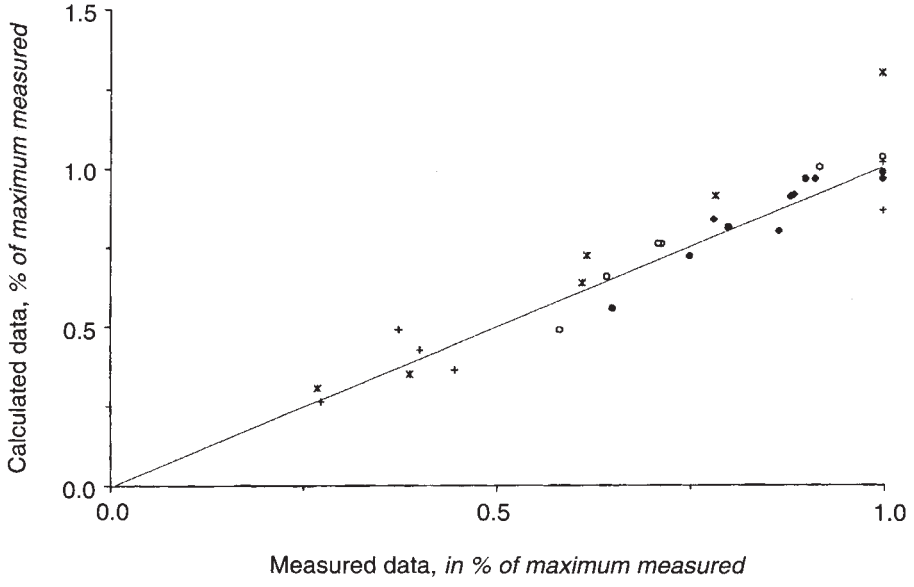

Fig. 2. *A representative example of a PDC measurement in a female CAPD patient, age 66 with interstitial nephritis.* Calculated values are plotted against measured values and the data are expressed in percent of the maximum measured concentration of each solute: urea (●), creatinine (○), glucose (x), albumin (+), or drain volume (◆).

calculation procedure takes approximately four seconds with an average 486DX processor.

PDC during peritonitis

A PDC test was performed on patients who were admitted into the hospital for episodes of peritonitis. Measurements were made during one of the first two days, using the protocol given above.

Results

General

The PDC measurements were performed by 97 stable adult uremic patients treated with peritoneal dialysis, mainly CAPD. The average age was 60 ± 1 years (range 20 to 85; Fig. 1). All patients were able to follow the protocol. The underlying disease of the uremic condition showed the panorama that is common in a dialysis population.

Accuracy of the PDC calculations

A representative example of a PDC measurement is given in Figure 2, expressed as measured data plotted against calculated values (all expressed in percent of the maximal measured value) for drain volume and the concentrations of urea, creatinine, glucose and albumin. Table 1 shows the data from another patient together with the calculated parameters.

In Figure 3 data from all 97 patients are presented as mean calculated (y) versus measured (x) data for drain volume and the concentrations of urea, creatinine, glucose and albumin. Linear regression gives for drain volumes: $y = 0.99x - 60$, $r^2 = 0.99$, $N = 97$; for urea concentrations: $y = 1.02x - 0.55$, $r^2 = 0.96$, $N = 97$; for creatinine concentrations: $y = 0.99x + 39$, $r^2 = 0.97$, $N = 97$; for glucose concentrations: $y = 0.99x + 6.1$, $r^2 = 0.80$, $N = 97$; and, finally, for albumin: $y = 0.83x + 0.12$, $r^2 = 0.88$, $N = 97$. The sixth panel describes β_2-microglobulin as calculated using the measured β_2-microglobulin concentration values in the regression analysis versus not using these measured data: $y = 1.25x + 0.10$, $r^2 = 0.73$. It is evident from the latter 358 measurements that there was a high variability in the data and that actually measuring

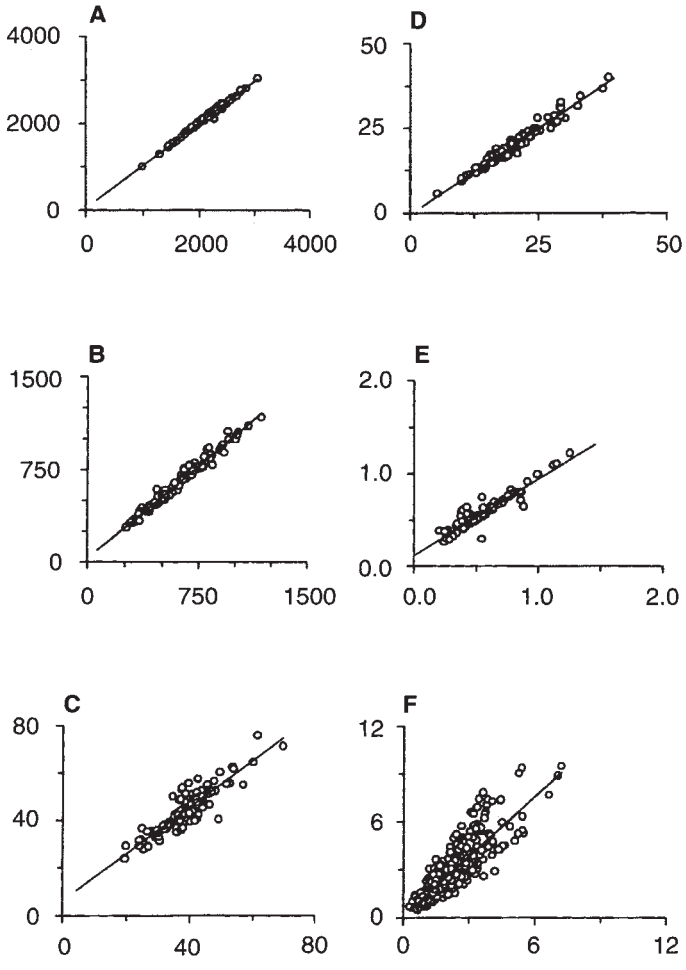

Fig. 3. *Measured (x) against calculated (y) values for drain volumes (ml,* **A***), creatinine concentration (μM,* **B***), glucose (mM,* **C***), urea (mM,* **D***), albumin (g/liter,* **E***).* The mean values are shown for 97 patients. **F** describes the concentration of β_2-microglobulin (mg/liter) calculated using measured data of this solute against estimations made without using the measured β_2-microglobulin values.

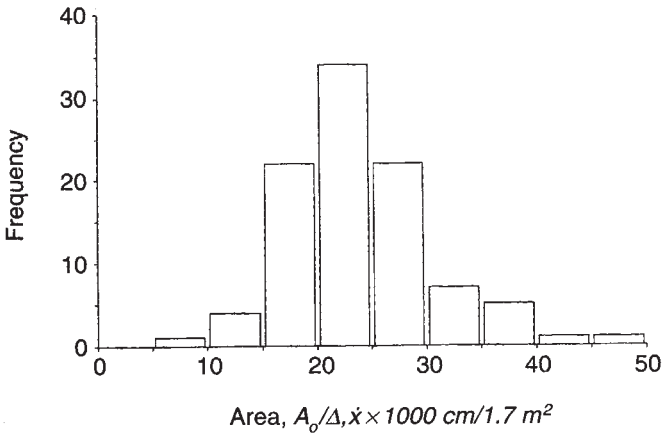

Fig. 4. *The unrestricted pore area over diffusion distance, $A_0/\Delta x$, in a population of 97 patients treated with peritoneal dialysis.*

the β_2-microglobulin concentration did not improve the analysis to any significant degree.

Distribution of the PDC parameters

(1.) The area parameter or the unrestricted pore area over diffusion distance, $A_0/\Delta x$, had a mean value of 23,590 cm/1.73 m^2 with an SEM of 653 (N = 97, range 8,012 to 47,475) and a distribution as shown in Figure 4. The highest $A_0/\Delta x$ (47,475 cm/1.73 m^2) was found in a patient with secondary amyloidosis due to ankylosing spondilitis with no signs of peritonitis. He did, however, have active arthritis and two other measurements within 18 months showed similar values (51,780 and 51,120). The lowest value was obtained in a man (age 42) with chronic glomerulonephritis and no history of intraabdominal infections or previous PD episodes; again, repeated measurements a few months later gave similar results (8,880 and 8,770).

The mean (23,600) ± 1 SD (6,400) data give an opportunity to compare the area parameter to the PET nomenclature. Thus, a patient with a large area parameter ($A_0/\Delta x$ >30,000) would be denoted a 'high transporter' according to PET, 23,600 to 30,000 would be 'high average', 17,200 to 23,600 would be 'low average', and a small Area parameter ($A_0/\Delta x$ <17,200) would be a 'low transporter' (Table 3).

(2.) The final reabsorption rate of fluid from the abdominal cavity, Jv_{AR}, was 1.49 ml/min/1.73 m^2 (SEM = +0.09, −0.08, N = 97), calculated as the geometric mean due to the skew distribution (Fig. 5). The range was 0.13 to 3.77 ml/min/1.73 m^2. Note that this represents the reabsorption rate when there is no crystalloid osmotic pressure difference at all across the peritoneal membrane, (Eq. 16).

(3.) The fluid flux through the large pores, Jv_L, was 0.078 ml/min/1.73 m^2 with an SEM of +0.005, −0.005, N = 97, calculated as the geometric mean due to the skew distribution. The range was 0.008 to 0.284 ml/min/1.73 m^2. Figure 6 gives the distribution profile for Jv_L.

Other calculated parameters

The calculated capillary hydrostatic pressure, P_C, was constant at 15 mm Hg in 89 patients. In 7 patients, the P_C was automatically elevated 5 to 17 mm Hg since the lymph flows must exceed zero.

Table 3. Area parameter conversion to PET

Area parameter, $A_0/\Delta x$, cm per 1.73 m^2	Area % of the normal values in the adult population	PET
> 30,000	> 127	High transport
23,600–30,000	100–127	High average transport
17,200–23,600	73–100	Low average transport
< 17,200	< 73	Low transport

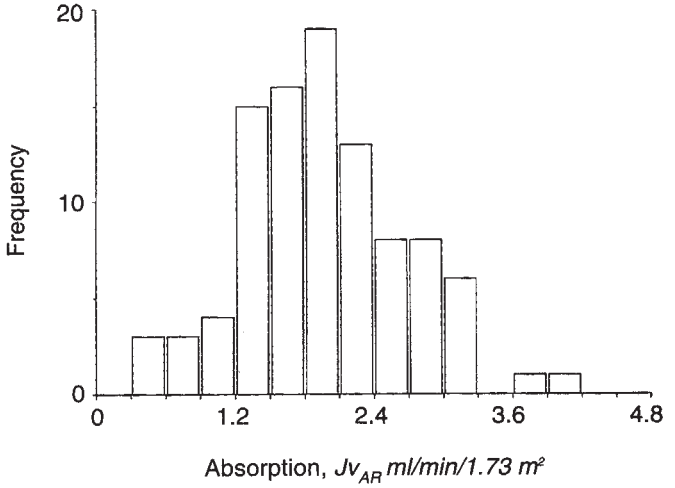

Fig. 5. *The final reabsorption rate of fluid from the abdominal cavity to blood when there is no crystalloid osmotic pressure gradient left, N = 97.*

The hydraulic conductance, L_pS, was strictly coupled to the $A_0/\Delta x$ in roughly one half of the patients. However, the L_pS could be reduced to only 40% or raised to 250% of the value expected from $A_0/\Delta x$ if an uncoupling was needed to adequately describe the 'UF volume' (Eq. 7). The average L_pS was 0.069 ± 0.03 ml/mm Hg/min/1.73 m^2. Several of the patients with low L_pS compared to the area parameter had problems with overhydration and were identified as certain or potential "UF loss" patients.

The theoretical lymph flow calculated in the analysis was 0.41 ml/min/1.73 m^2 BSA (geometrical mean), with an SEM of 0.06 and a range of 0.00 to 2.21.

Reproducibility of PDC

In 15 patients it was possible to repeat the determinations within a few days. Figure 7 shows the area parameters from the first PDC measurement against the second, third and fourth registrations. Standard deviations were calculated for each individual patient. The coefficient of variation (CV% = SD/mean) was used as a measure of the variability. The $A_0/\Delta x$ had a coefficient of variation of 7% with an SEM of 1%; for Jv_{AR} the CV% was 16% with an SEM of 3% and for Jv_L CV% was 20% with an SEM = 4%, N = 15. The $A_0/\Delta x$ showed little variation from time to time, while Jv_L, reflecting protein loss, was less stable as previously noted [33].

PDC during peritonitis

The PDC test was performed in 11 patients with acute peritonitis. Nine patients were infected by *Staphylococci* (aureus or coagulase negative) and one patient had a fungal peritonitis *(Candida Albicans)*. All parameters were higher in the group with

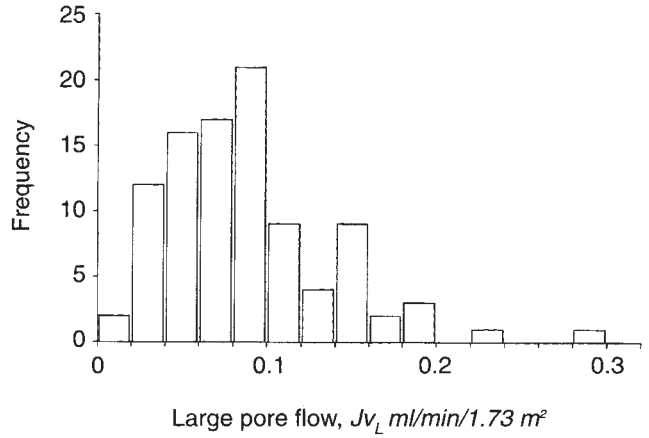

Fig. 6. *The large pore fluid flux, Jv_L, in the PD population of 97 patients.*

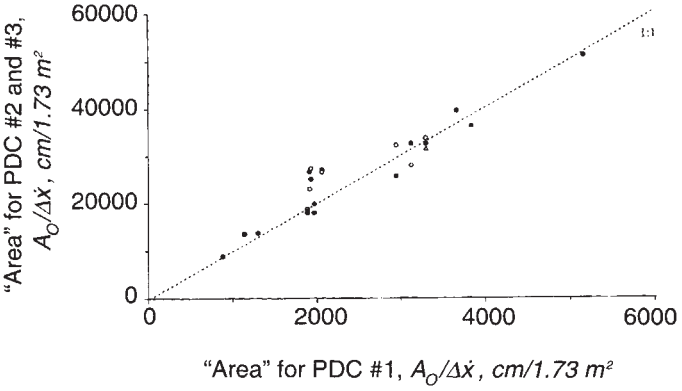

Fig. 7. *The reproducibility of the area parameter is shown by repeated determinations of PDC within a week in the same patient* (N = *15*). The second (●, *N* = 15), the third (O, *N* = 7) and the fourth (Δ, *N* = 1 PDC measurements are plotted against the first. The coefficient of variation for the area parameter is 7% in these 15 patients (±1%).

peritonitis compared to control (Fig. 8). In the early phase of peritonitis $A_0/\Delta x$ was 48,650 cm/1.73 m^2 (geometric mean, SEM = +3370, −3150, range 31,200 to 68,600, *N* = 11), Jv_{AR} was 1.78 ml/min/1.73 m^2 (range 0.91 to 3.64, SEM = +0.27, −0.24) and Jv_L was 0.19 ml/min/1.73 m^2 (range 0.06 to 0.43, SEM = +0.04, −0.03, *N* = 11). In 6 patients PDC had been measured within a six month period prior to the infection. In these patients the peritonitis induced an 81% increase in the area parameter (range 40 to 120%). Two months after the peritonitis, the area returned to previous values or less. In the patient with fungal peritonitis, the area parameter was extremely small two months after the peritonitis, only 8087 cm/1.73 m^2. He had been treated with HD and could not return to PD.

Discussion

This project started with the idea of developing a method of estimating the true PD capacities of individual patients based on current theories of transcapillary exchange. Furthermore, a straightforward experimental protocol should allow the patients to collect the data themselves to mimic the normal PD day. The study is not aimed to validate the three-pore model, but is a

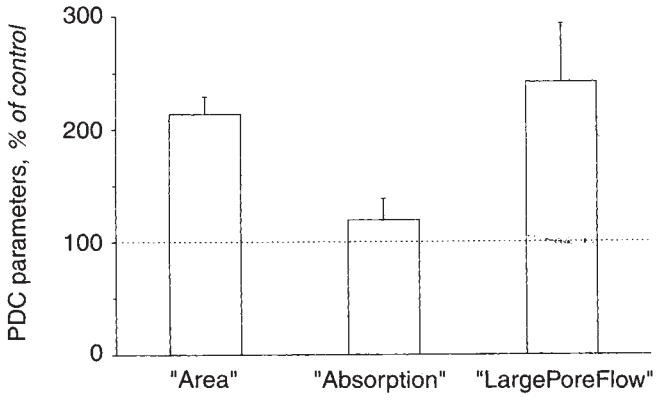

Fig. 8. *Effects of peritonitis on the three PDC parameters.* In accordance with inflammatory reactions in other vascular beds, there are signs of vasodilation, capillary recruitment, opening of large pores giving high protein losses, mean ± SEM, *N* = 11.

pragmatic attempt to make clinical use of basic physiological transport equations. Naturally, the success of such a venture depends on the validity of the underlying mathematical model, as well as the design of the protocol.

The three-pore model

Albeit somewhat simplistic, the three-pore model [19, 28] is probably the best description of the peritoneal membrane to date [34]. One of its major merits is that it seems to be universal for the microvasculature of all organs [25, 32, 35]. Solutes are restricted depending on their molecular size, whereas possible electrical charge interactions are not accounted for in the present analysis. This is mainly due to the ambiguity of data for the peritoneum, cf. [36, 37]. Moreover, the pore dimensions were considered to be constant in all patients, which is most likely close to reality, cf. [25]. The area parameter, $A_0/\Delta x$, was 23,600 cm/1.73 m^2 BSA and for the studied adult population is a value similar to those previously reported [28]. In the present model, the capillary and i.p. hydrostatic pressures were kept constant in all patients, except in seven (7%) where the P_{capill} was automatically raised to give lymph flows above zero. However, P_{capill} is most likely reduced if the patient is hypotensive (for example dehydrated) and increased in case of overhydration. Such alterations in P_{capill} are not accounted for in the present analysis, nor are changes due to body position or alterations in the i.p. pressure. In the literature, there are studies that could allow P_{ip} to change with the intra-abdominal volume [38]. The diffusion of sodium is less than expected from the three-pore model, c.f. [30]. Finally, there may be interstitial concentration gradients or barriers [34, 39] reducing the PS of glucose. It should be emphasized, however, that the model works with remarkable precision for the vast majority of solutes as well as for fluid transport. As an illustration of the potentials of the present model, Figure 9 shows the predicted effects of various osmotic agents on the drain volume plotted against time for a patient with normal PDC parameters. The simulated effects are close to the values published in the literature [40].

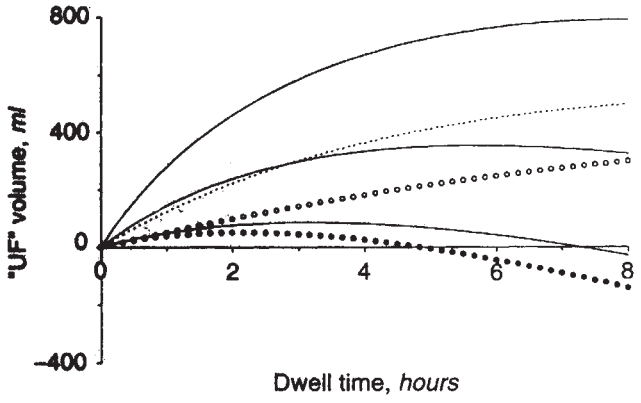

Fig. 9. *The osmotic effects of different osmotic agents are simulated for a patient with an average area = 24,100, slightly high Jv_{AR} = 1.6, Jv_L = 0.14 and L_pS = 0.067.* The osmotic agents are: (solid curves) glucose 15, 25 and 40 g/liter; (solid curve with filled circles) amino acid solution 10 g/liter; (hatched curve) small peptides 40 g/liter, molecular wt = 800, SE radius = 0.64 nm; (open circles) glucose-polymer 75 g/liter + glucose 3.5 g/liter, molecular wt = 18700, SE radius 2.10 nm. The osmotic agents are all assumed to have a reduced PS analogous to i.p. glucose (Eq. 6).

How to interpret the PDC parameters

What is the morphological counterpart to the physiological expression $A_0/\Delta x$ or the area parameter? The area represents the unrestricted area (A_0) of the pores in all capillaries perfused at a given time normalized with respect to the diffusion distance (Δx). The functional term 'pore' is probably equivalent to the interendothelial junction at the microscopical level [41] and shows little variation in its size or number. In most other organs, and most likely the peritoneum, there is heterogeneity of perfusion, with interrupted flow in some capillaries and high flows in others changing with time [42], with only one out of four to six of the capillaries being adequately perfused at any given time, cf. [43]. Hence, a large capillary reserve exists whereby the area parameter can be increased several-fold, for example, during an inflammatory reaction. Moreover, drugs and other conditions that affect the recruitment of capillaries may affect the area parameter. Such conditions include over/underhydration with subsequent involvement of the sympathetic nerves, as well as certain vasodilators [44]. The instillation of acidic, lactate-containing hyperosmolar solutions may also induce (short-lasting) recruitment of capillaries and hence increase the area parameter.

The second PDC parameter, Jv_{AR}, represents the sum of the lymphatic flow and the transcapillary Starling forces (Eq. 16). The latter also include the hydraulic conductance, L_pS, which is calculated from the area parameter for most patients. The L_pS can be uncoupled from $A_0/\Delta x$ if needed to get an acceptable description of the UF volumes (Eq. 7). Note that Jv_{AR} *per se* is not dependent on any assumption of the underlying transport route. The Jv_{AR} only reflects the last part of the drain volume versus time curve. High rates of Jv_{AR} were seen in the patients with large area parameters, due to a more rapid dissipation of glucose, but could also be seen in patients with a normal area parameters.

The large pore fluid flux (Jv_L) determines the loss of proteins from blood to the abdominal cavity. It is almost pure plasma that flows through the large pore system with size discrimination for the larger proteins only. The Jv_L is dependent on the hydrostatic pressure gradient and the L_pS is accounted for by the large pores (Eq. 13). There is no strict coupling of L_pS since an increase in L_pS will be counterbalanced by an apparent reduction in the number of large pores. An increased number of large pores represents a true increase in the (capillary) permeability since it affects the selectivity of the (PD) membrane. Indeed, inflammatory reactions increase the number of large pores.

Comparison between the area parameter and PET

Most PD clinics are familiar with the PET terminology, where the patient population is divided into four groups: high, high-average, low and low-average transporters. The PET classification is not corrected for the influence of the UF rate, but for most of the cases it is possible to express the PETs in terms of the area parameter according to Table 3. The term 'permeability' is sometimes used to interpret PET instead of 'transporters,' but it is not adequate in this situation, since 'high permeability' implies altered membrane selectivity which has not occurred. It is therefore recommended that the use of (high/low) permeability should be avoided.

Inflammatory reactions

The typical inflammatory reaction is characterized by vasodilatation, capillary recruitment, opening of large pores (or 'leaks') with a higher protein loss, increased lymph flow and pain. The reactions observed in the acute phase of peritonitis are in accordance with such an inflammatory reaction (Fig. 8). In some patients the inflammatory reaction was rather weak, while in others there were marked changes.

Nutritional aspects

As is shown in Table 2, the computer calculates the amounts of calories and protein required for the particular patient during almost resting conditions (Eq. 24). Moreover, the PD uptake of calories with a given regimen is calculated together with the estimated loss of proteins. The urea and creatinine generation rates (UGR, CGR) are those obtained on the day of measurement and are valid if that was a representative day, that is, normal food intake, no infection, etc. This also applies to the protein equivalent of nitrogen appearance rate, PNA [45] (previously denoted protein catabolic rate, PCR), and to the estimation of lean body mass, LBM. The PNA is calculated from UGR and from the losses of protein in urine and PD fluid (Eq. 21). Note that falsely high values of LBM can be obtained if the food contains a significant amount of creatinine (that is, meat), an error that has been calculated to be small [46] but probably significant (**Note added in proof**).

Adequacy of dialysis

The calculated PD membrane characteristics can be used to simulate any PD treatment. The results are presented as easily understandable graphs showing the estimated values for clearance (PD alone and PD + renal), the resulting removal of fluid (PD and PD + renal) and the nutritional consequences (see above). An example of the results in terms of clearance and 'UF-volume' is shown in Figure 10. The clearance of the renal replacement therapy is calculated for a solute the size of creatinine and is suggested to be at least 5.5 ml/min/1.73 m^2, corresponding to a weekly creatinine clearance (PD + GFR, not PD + renal creatinine clearance) of 55 liters [13]. There is considerable

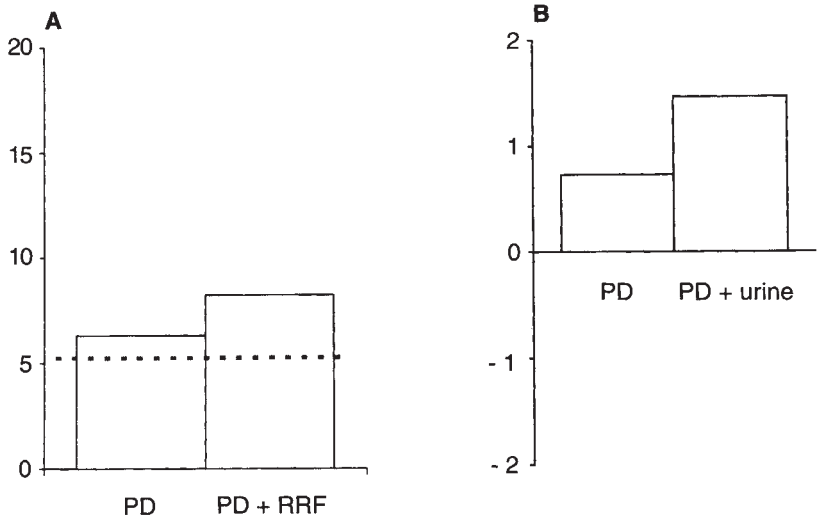

Fig. 10. *The results in terms of clearance for a solute the size of creatinine* **A** *and fluid removal* **B** *are presented graphically.* RRF is residual renal function. The hatched line represents the minimal clearance level of 5.5 ml/min/1.73 m^2 BSA.

experience of measuring the glomerular filtration rate of nondialysis patients with renal insufficiency [47], and many centers recommend that dialysis should be started at a renal residual function (RRF) of 5 ml/min or more to prevent the loss of important body functions [48]. It therefore seems logical to ascertain that the dialysis clearance reaches the minimal level of 5.5 ml/min at least for creatinine, since the clearance of larger solutes will be lower with PD than the renal clearance (higher values will be seen for urea). The computer can easily calculate the predicted clearance of any solute based on its molecular size and several other solutes are presented on the screen on demand. The resulting Kt/V value for urea is also calculated, using V = 58% of the body weight.

Pedagogical aspects

A subjective experience of PDC is that both physicians and nurses have gained insight into the physiological properties of the PD membrane and how PD works. Several patients have also taken an active part in the interpretation of the PDC results, giving an improved patient motivation, knowledge and compliance although these effects have not been quantified. The issue of patient compliance is often neglected. However, recent studies have suggested that almost one fourth of the patients use a lower dose of dialysis than prescribed, and the total dialysis dose is approximately three fourths of that expected [49, 50]. Therefore, it is essential to optimize the patient motivation and hence patient compliance in order to ensure adequate dialysis. The PDC program seems to be useful in this respect as well.

Urea kinetic modeling

There have been attempts to use urea kinetic modeling based on the Pyle, Moncrief and Popovich model [51] as a prescription aid in PD [11]. This widely used model has important drawbacks: (i) The membrane is considered to be extremely permeable to small solutes, allowing almost free diffusion. (ii) On the other hand, the membrane is highly selective with respect to osmosis, showing high 'apparent' reflection coefficients for small solutes, for example, 0.5 for glucose. Note that these two properties are incompatible. (iii) Using current irreversible thermodynamics to calculate pore radii [52], the apparent pore radius in that model seems to increase with increasing solute size. (iv) Finally, larger solutes are not more effective osmotic agents than glucose according to the model [53], but actual measurements show that they are more effective [54]. In contrast, the three-pore model gives predictions close to those observed *in vivo* (Fig. 9). Naturally, there are limitations with the present three-pore model, but it is internally more consistent and offers a universal description of the fluxes of fluids and solutes across microvasculature in almost all organs [26]. More studies are required, however, to improve the analysis further. Hopefully, the PDC method can stimulate such efforts and be used to better quantify the effects of various drugs, osmotic agents, etc.

Economical aspects

The nursing time required for PDC include giving adequate instructions, handing over a standardized PDC kit, taking two blood samples, sending the samples to the laboratory and entering the data into the computer. The patients perform the PDC test themselves, which makes the nursing time less than with traditional PET. A total of six PD samples (5 during the PDC day + the start sample), one urine sample and two blood samples are collected. The cost of the chemical analyses varies between laboratories and therefore it seems suitable to make a relative comparison. Thus, in Göteborg the cost of the PDC test is less than half of a renal clearance measurement (Cr-EDTA), 10% more than the cost of PD fluids during one day, 50% more than the cost of a chest X-ray, or about the same as one injection of erythropoetin (5400 units).

Conclusion

Basic physiology can be utilized for the description of the PD exchange in individual patients. The patient can perform the PDC measurements himself during an almost normal CAPD day thus requiring a minimum of nursing time. The resulting peritoneal dialysis capacities are reproducible and can be used to ascertain adequate dialysis and to predict the effects of any dialysis treatment. Hence, PDC seems to be useful in the management of the PD patients. Moreover, the dramatic microvascular changes induced by peritonitis are in total agreement with the inflammatory reaction observed in other vascular beds. With a tool that

interprets the intricate processes of PD in physiologically appropriate parameters, there may not be a need for guessing or using semiquantitative tests.

Acknowledgments

Part of this work was presented at ASN in Baltimore [55] and at a symposium on adequacy of dialysis in Berlin in March 1994. The study was supported by the Swedish Medical Research Council grant no. 9898 and the Medical faculty of Göteborg, LUA no. 721986. I am particularly grateful to the patients taking part in the study and the devoted staff of the Department of Nephrology, Sahlgrenska Hospital under its head, Prof. Mattias Aurell. The helpful advice of my former teacher in research, Prof. Bengt Rippe, Lund, Sweden is warmly acknowledged. The PDC computer software is distributed by Gambro AB, Lund, Sweden.

Reprint requests to Börje Haraldsson, Department of Nephrology, Blå stråket 5, University of Göteborg, Sahlgrenska Hospital, S-413 45 Göteborg, Sweden.

Appendix

List of abbreviations

The terminology is based on the recommendations of the International Physiological Society [56].

W	Weight (kg)
L	Height (m)
BSA	The body surface area (in m^2)
P_{capill}	Capillary hydrostatic pressure (15 mm Hg)
P_{ip}	Intraperitoneal hydrostatic pressure (6 mm Hg)
$\pi_{subsript}$	Osmotic pressure (mm Hg) where the subscript denotes protein (prot), glucose (gluc), urea, sodium (Na) or anions
a_e	Stokes-Einstein radius (nm)
r_p	Pore radius (nm)
α	The ratio of solute to pore radii (a_e/r_p)
$r_{p,s}$	Small pore radius (4.7 nm)
$r_{p,L}$	Large pore radius (25.0 nm)
V_{Res}	Residual volume (ml)
V_{DF}	Volume of the dialysis fluid prior to instillation
C_p, C_D	Concentrations in plasma and dialysate
Cl or K	Clearance (in ml/min/1.73 m^2 BSA)
R	The universal gas constant
T	The absolute temperature
N	Avogadro's number
η	The viscosity of water
L_pS	The hydraulic conductance or the UF coefficient (ml/min/mm Hg/1.73 m^2 BSA)
$A_0/\Delta x$	Unrestricted pore area over diffusion distance (the area PDC parameter, cm/1.73 m^2 BSA)
A_m/A_0	The fractional area available for diffusion of a solute m
σ_m	The reflection coefficient for a solute m
D_m	The free diffusion coefficient for a solute m (cm^2/s)
Jv	Fluid flux (ml/min)
Jv_{AR}	The final reabsorption rate of fluid from the abdominal cavity to blood ("absorption", ml/min/1.73 m^2 BSA)
Jv_L	Large pore fluid flux ("large pore flow," ml/min/1.73 m^2)
Jv_{Lymph}	Lymph flow (ml/min/1.73 m^2)
Js	The flux of solute (mmol/min or g/min)
UGR	Urea generation rate (mmol/day)
PNA	Protein equivalent of nitrogen appearance rate (g/kg/day)
CGR	Creatinine generation rate (mmol/day)
LBM	Lean body mass (kg)
Subscripts:	
c,s,L	the cell, small or large pore pathway
m	a solute m

Basic capillary exchange parameters

There are several estimations of the body surface area from a person's height (L, in m) and weight (W, in kg) including the one below [57]:

$$BSA = 0.02350 \cdot (100 \cdot L)^{0.4226} \cdot W^{0.51456} \quad \text{(Eq. 1)}$$

The body mass index (BMI in kg/m^2) is given by:

$$BMI = \frac{W}{(L)^2} \quad \text{(Eq. 2)}$$

The free diffusion coefficient is related to the Stokes Einstein radius of a solute:

$$D_{37^\circ} = \frac{R \cdot T}{6 \cdot \pi \cdot \eta \cdot N \cdot \alpha_e} = \frac{3.27656 \cdot 10^{-6}}{\alpha_e} \quad \text{(Eq. 3)}$$

In the literature there are several equations describing the fractional pore area available for diffusion of a solute m, but the expression covering most solute sizes was presented by Mason, Wendt and Bresier [52]:

$$\frac{A_m}{A_0} = \frac{(1-\alpha)^{9/12}}{1 - 0.3956 \cdot \alpha + 1.0616 \cdot \alpha^2} \quad \text{(Eq. 4)}$$

and for calculations of the solute reflection coefficient [52]:

$$\sigma_m = 1 - \frac{(1-\alpha)^2 \cdot [2-(1-\alpha)^2] \cdot \left(1 - \frac{\alpha}{3}\right)}{1 - \frac{\alpha}{3} + \frac{2\alpha^2}{3}} \quad \text{(Eq. 5)}$$

where α is the ratio of the solute m Stokes Einstein radius over the pore radius.

The diffusion capacity, or permeability surface area (PS), of a solute m is given by:

$$PS_m = \frac{A_0}{\Delta x} \cdot D_m \cdot \frac{A_m}{A_0} \quad \text{(Eq. 6)}$$

Urea is, however, more soluble in oil than are, for example, glucose and creatinine, as reflected by a three- to fivefold higher octanol/water partition coefficient [58]. As a result the PS_{urea} is increased by a factor of 1.2, allowing for some transport through the lipid membranes. On the other hand, the $PS_{glucose}$ is less than predicted from the $A_0/\Delta x$ [28], which may be due to properties in the interstitium, such as interstitial concentration gradients or interstitial restriction of diffusion, serial barriers, etc. [34]. Therefore $PS_{glucose}$ was reduced by a factor of 0.8. Moreover, the PS for sodium is only 6 ml/min/1.73 m^2 [30], while PS for most other hydrophilic solutes seem to be well predicted from equation 6. Initially, there seem to be a vasodilatation and recruitment of

capillaries that transiently increased PS of all solutes with a factor of $1 + e^{-0.04t}$, t is in minutes.

The hydraulic conductance, L_pS, or the UF coefficient, is normally close to 0.070 ml/min/mm Hg/1.73 m^2 [28]. Therefore, L_pS was calculated from the $A_0/\Delta x$ as:

$$L_pS = \frac{0.070 \cdot \frac{A_0}{\Delta x}}{23000} \quad \text{(Eq. 7)}$$

No more than a 5% deviation of "UF volume" is accepted, otherwise there is uncoupling of L_pS from the $A_0/\Delta x$. This deviation is calculated as $(\Delta V_{UF}/V_{DF})$, where ΔV_{UF} is the difference between measured and calculated UF volume and V_{DF} the infused volume of dialysis fluid. Plasma proteins exert a colloid osmotic pressure which can be calculated [21] as:

$$\pi = 2.1 \cdot + 0.16\left(\frac{C_{prot}}{10}\right)^2 + 0.009\left(\frac{C_{prot}}{10}\right)^3 \quad \text{(Eq. 8)}$$

where C_{prot} is the total protein concentration in g/liter. Several laboratories do not analyze total protein in serum (S_{prot}) and approximate S_{prot} concentrations can be calculated from measured S_{alb} values: $C_{prot} = C_{alb}/0.4783$, based on 78 patients. The ratio of the two calculated osmotic pressures (prot/alb) is 1.000 ± 0.0195 ($N = 78$).

Each solute exerts a crystalloid osmotic pressure (in mm Hg) according to van't Hoffs law:

$$\pi = R \cdot T \cdot \Delta C = 19.33 \cdot \Delta C \quad \text{(Eq. 9)}$$

where ΔC is given in mmol/liter.

According to the three-pore concept, the reflection coefficient for the membrane as a whole is the result of the characteristics of three independent pore populations. Thus, the weighted average reflection coefficient for solute m ($\overline{\sigma_m}$) is:

$$\overline{\sigma_m} = \frac{L_pS_c}{L_pS_{tot}} \cdot \sigma_{c,m} + \frac{L_pS_s}{L_pS_{tot}} \cdot \sigma_{s,m} + \frac{L_pS_L}{L_pS_{tot}} \cdot \sigma_{L,m} \quad \text{(Eq. 10)}$$

where L_pS_{tot} is the hydraulic conductance of the entire membrane.

The fluid flux through the cell pathway is:

$$Jv_c = L_pS_c \cdot (P_{capill} - \pi_{prot} - P_{ip} - \pi_{gluc} - \pi_{urea} - \pi_{Na} - \pi_{anions}) \quad \text{(Eq. 11)}$$

where L_pS_c is 1.0% of total hydraulic conductance (L_pS_{tot}) of the membrane.

The fluid flux through the small pores are given by:

$$\text{reset}Jv_s = L_pS_s \cdot (P_{capill} - \sigma_s\pi_{prot} - P_{ip} - \sigma_s\pi_{gluc} - \sigma_s\pi_{urea} - \sigma_s\pi_{Na} - \sigma_s\pi_{anions}) \quad \text{(Eq. 12)}$$

Finally, the fluid flux through the large pores is:

$$Jv_L = L_pS_L \cdot (P_{capill} - P_{ip}) \quad \text{(Eq. 13)}$$

since no significant osmotic gradients can be maintained across these pores.

The transport of different solutes across the membrane are easily obtained once the partial fluid fluxes through the pores are known, using the following non-linear flux equation. Thus, clearance of a solute m through the small pores is:

$$Cl_{s,m} = \frac{Jv_s \cdot (1 - \sigma_{s,m}) \cdot \left[1 - \frac{C_D}{C_P} e^{-Pe}\right]}{1 - e^{-Pe}} \quad \text{(Eq. 14)}$$

where the modified Peclet number is:

$$Pe = \frac{Jv_s \cdot (1 - \sigma_{s,m})}{PS_{s,m}} \quad \text{(Eq. 15)}$$

The concentration ratio (C_D/C_p) in equation 14 is inverted if the concentration in the dialysate exceeds that of plasma, which normally is the case solely for glucose. Similar calculations are made for the clearance of solutes through the large pores. The total clearance is merely the sum of the small and the large pore clearances.

The final reabsorption rate of fluid from the abdominal cavity occurs when the crystalloid osmotic gradients have dissipated and is thus given by:

$$Jv_{AR} = -L_pS[P_{capill} - P_{ip} - \sigma_{prot}(\pi_p - \pi_{ip})] + Jv_{lymph} \quad \text{(Eq. 16)}$$

Note that lymph flow is only one (minor) component of Jv_{AR}.

Changes of intraperitoneal volume and solute concentrations with time

The following equations are used to estimate the initial solute concentration i.p. at the start of the PD cycle:

$$C_D(0) = \frac{V_{DF} \cdot C_{DF} + V_{Res} \cdot C_{Res}}{V_{DF} + V_{Res}} \quad \text{(Eq. 17)}$$

where C_{DF} stands for the concentration of solutes in the dialysis fluid prior to instillation. The residual volume is scaled to the body weight as: $V_{Res} = \frac{250 \cdot W}{70}$, that is, 250 ml for a 70 kg human. C_{Res} is the concentration in the residual volume, which is unknown at the start of the PDC protocol but thereafter is given by the previously drained fluid. As reasonable estimates of C_{Res} at the start of the protocol the following expression was used: $C_{Res} = k \cdot C_P$; where k is 1 for glucose and sodium, k is 0.8 for urea and creatinine and k is 0.05 for albumin. Note that this approximation is needed only for the start of the PDC protocol, not the subsequent 4 or 5 exchanges.

Numerical integration was used to obtain the changes of volume and concentration with time, using two minute steps for the first hour followed by steps of 10 minutes. Thus, the i.p. volume after a short time interval is:

$$V(t + \Delta t) = V(t) + \Delta t \cdot (Jv_c + Jv_s + Jv_L - Jv_{Lymph}) \quad \text{(Eq. 18)}$$

The concentration of a solute m after a short time interval is:

$$C_{D,m}(t + \Delta t) = \frac{C_{D,m}(t) \cdot V(t) + Cl_{(s+L),m} \cdot \Delta t \cdot C_{p,m}(t)}{V(t + \Delta t)} \quad \text{(Eq. 19)}$$

The residual renal function (RRF) can be estimated from the mean of the clearances of urea and creatinine with reasonable accuracy if RRF is less than 15 ml/min [47]. The clearance for urea or creatinine (in ml/min/1.73 m^2 BSA) is given by:

$$Cl = \frac{C_U \cdot V_U \cdot 1.73}{C_P \cdot 24 \cdot 60 \cdot BSA} \quad \text{(Eq. 20)}$$

where C_U and C_P are the concentrations in urine and plasma and V_U is the 24-hour urine volume.

$$RRF = \frac{Cl_{urea} + Cl_{creat}}{2} \quad \text{(Eq. 21)}$$

The generation rates of urea and creatinine are calculated applying the principles of conservation of mass. Thus, two blood samples are taken with a 24 hour interval and the total losses through urine and dialysate are measured. The blood concentrations are also allowed to change. From the urea generation rate (UGR) the protein equivalent of the nitrogen appearance rate (PNA, previously called the protein catabolic rate, PCR) can be calculated according to the relation observed in stable patients on CAPD [45]:

$$PNA = \frac{19 + 0.272 \cdot UGR + ProtLoss}{W} \quad \text{(Eq. 22)}$$

where ProtLoss is the sum of protein losses in dialysate and urine. The creatinine generation rate, CGR can be used to estimate lean body mass [46]:

$$LBM = 7.38 + (3.278 \cdot CGR) \quad \text{(Eq. 23)}$$

Note, however, that the calculations of LBM from CGR neglects the food intake of creatinine [46], which must be controlled if LBM is to be used to follow patients over time (**Note added in proof**).

The basal metabolic rate during slight activity can be estimated as:

$$bmr = k \cdot W \quad \text{(Eq. 24)}$$

where k is 33 kcal/kg/day for the ages 30 to 70, 10% more in the age group 16 to 30 and 10% less above 70 years of age. For children k is 84 kcal/kg/day if the weight is less than 10 kg, 66 kcal/kg/day for W = 10 to 15 kg, 54 kcal/kg/day for weights 15 to 25 kg, 48 kcal/kg/day for W = 25 to 35, 42 kcal/kg/day for weights 35 to 60 kg, and k is 36 kcal/kg/day for higher weights. The protein requirements are estimated as 0.8 g/kg/day for adults (above 15 years of age) and 1.5 g/kg/day for children. The presented values for protein and caloric requirements are adjusted (±10%) in case of over/underweight, where underweight is equivalent to a BMI less than 20 for men and less than 18.5 for women, while overweight means a BMI >25 for men and >24 for women.

Note that the aqueous solute concentrations [59] were used whereby the space in serum occupied by lipids and proteins are accounted for. Thus, serum aqueous concentrations C′ for a neutral solute with the serum concentration C is:

$$C' = \frac{C}{(1 - 0.016 - 0.000718 \cdot C_{prot})} \quad \text{(Eq. 25)}$$

where 0.016 is the lipid factor and C_{prot} is the concentration of proteins or $S_{alb}/0.40$.

Note added in proof

Creatinine kinetics cannot be used due to variabilities in meat intake. HARALDSSON B, JOHANSSON A-C, ATTMAN P-O: Creatinine generation rate—A blunt tool for assessments of lean body mass. (abstract) *J Am Soc Nephrol* 5:492, 1994

References

1. SMEBY LC, WIDERÖE TE, JÖRSTAD S: Individual differences in water transport during continuous peritoneal dialysis. *ASAIO Trans* 4:17–27, 1981
2. TWARDOWSKI ZJ, NOLPH KD, KHANNA RA, PROWANT BF, RYAN LP, MOORE HL, NIELSEN MP: Peritoneal equilibration test. *Perit Dial Bull* 7:138–147, 1987
3. TWARDOWSKI ZJ: Clinical value of standardized equilibration tests in CAPD patients. *Blood Purif* 7:95–108, 1989
4. GOTCH F: The Peritoneal Equilibration test (PET) is not a realistic measure of peritoneal clearance. *J Am Soc Nephrol* 2:361–361, 1991
5. RUBIN J, JONES Q, PLANCH A, LOCKARD V, BOWER J: Enhancement of peritoneal transport in rats by disrupting stagnant fluid films. *Am J Med Sci* 295:108–113, 1989
6. LEVITT MD, KNEIP JM, OVERDAHL MC: Influence of shaking on peritoneal transfer in rats. *Kidney Int* 35:1145–1150, 1989
7. LO W-K, BRENDOLAN A, PROWANT BF, MOORE HL, KHANNA R, TWARDOWSKI ZJ, NOLPH KD: Changes in the peritoneal equilibration test in selected chronic peritoneal dialysis patients. *J Am Soc Nephrol* 4:1466–1474, 1994
8. VERGER C, LARPENT L, VENIEZ G, BRUNETOT N, CORVAISIER B: L'APEX. . . . description et utilisation. *Bull Dial Perit* 1:36–40, 1991
9. DAVIES SJ, BROWN B, BRYAN J, RUSSELL GI: Clinical evaluation of the peritoneal equilibration test: A population-based study. *Nephrol Dial Transplant* 8:64–70, 1993
10. BURKART JM, JORDAN JR, ROCCO MV: Assessment of dialysis dose by measured clearance versus extrapolated data. *Perit Dial Int* 13:184–188, 1993
11. VONESH EF, LYSAGHT MJ, MORAN J, FARRELL P: Kinetic modeling as a prescription aid in peritoneal dialysis. (see comments) *Blood Purif* 9:246–270, 1991
12. KESHAVIAH PR, NOLPH KD, PROWANT B, MOORE H, PONFERRADA L, VAN STONE J, TWARDOWSKI ZJ, KHANNA R: Defining adequacy of CAPD with urea kinetics. *Adv Perit Dial* 6:173–177, 1990
13. TZAMALOUKAS AH, MURATA GH, SENA P: Assessing the adequacy of peritoneal dialysis. *Perit Dial Int* 13:236–238, 1993
14. TEEHAN BP, SCHLEIFER CR, BROWN JM, SIGLER MH, RAIMONDO J: Urea kinetic analysis and clinical outcome on CAPD. A five year longitudinal study. *Adv Perit Dial* 6:181–185, 1990
15. TATTERSALL JE, DOYLE S, GREENWOOD RN, FARRINGTON K: Kinetic modelling and underdialysis in CAPD patients. *Nephrol Dial Transplant* 8:535–538, 1993
16. BLAKE PG, BALASKAS EV, IZATT S, OREOPOULOS DG: Is total creatinine clearance a good predictor of clinical outcomes in continuous ambulatory peritoneal dialysis? (see comments). *Perit Dial Int* 12:353–358, 1992
17. SELGAS R, BAJO MA, FERNANDEZ-REYES MJ, BOSQUE E, LOPEZ-REVUELTA K, JIMENEZ C, BORREGO F, DE ALVARO F: An analysis of adequacy of dialysis in a selected population on CAPD for over 3 years: The influence of urea and creatinine kinetics. *Nephrol Dial Transplant* 8:1244–1253, 1993
18. BLAKE PG, SOMBOLOS K, ABRAHAM G, WEISSGARTEN J, PEMBERTON R, CHU GL, OREOPOULOS DG: Lack of correlation between urea kinetic indices and clinical outcomes in CAPD patients (erratum in *Kidney Int* 40:388, 1991) *Kidney Int* 39:700–706, 1991
19. RIPPE B, STELIN G, HARALDSSON B: Computer simulations of peritoneal fluid transport in CAPD. *Kidney Int* 40:315–325, 1991
20. STARLING EH: On the absorption of fluids from the connective tissue spaces. *J Physiol (Lond)* 19:312–326, 1896
21. LANDIS EM, PAPPENHEIMER JR: Exchange of substances through the capillary walls, in *Handbook of Physiology. Circulation*, edited by HAMILTON WF, DOW P, Washington D.C., Am Physiol Soc, 1963, vol 2, pp 961–1034
22. GROTTE G: Passage of dextran molecules across the blood-lymph barrier. *Acta Chir Scand* (Suppl) 211:1–84, 1956

23. YUDILEVICH DL, ALVAREZ OA: Water sodium and thiourea transcapillary diffusion in the dog heart. *Am J Physiol* 213:308–314, 1967
24. RIPPE B, HARALDSSON B: Fluid and protein fluxes across the microvasculature. Application of two-pore equations. *Acta Physiol Scand* 131:411–428, 1987
25. TAYLOR AE, GRANGER DN: Exchange of macromolecules across the microcirculation, in *Handbook of Physiology. The Cardiovascular System. Microcirculation*, edited by RENKIN EM, MICHEL CC, Bethesda, Am Physiol Soc, 1984, vol 4, pp 467–520
26. RIPPE B, HARALDSSON B: Transport of macromolecules across microvascular walls: The two-pore theory. *Physiol Rev* 74:163–219, 1994
27. DEMPSTER JA, VAN HOEK AN, VAN OSS CH: The quest for water channels. *News Physiol Sci* 7:172–176, 1992
28. RIPPE B, STELIN G: Simulations of peritoneal solute transport during CAPD. Application of two-pore formalism. *Kidney Int* 35:1234–1244, 1989
29. ZAKARIA ER, RIPPE B: Osmotic barrier properties of the rat peritoneal membrane. *Acta Physiol Scand* 149:355–364, 1993
30. VONESH EF, RIPPE B: Net fluid absorption under membrane transport models of peritoneal dialysis. *Blood Purif* 10:209–226, 1992
31. BOOTH GW, PETERSON TI: Non-linear estimation, in *Mathematics and Application Reports*, (vol 3) IBM, New York, 1960
32. RIPPE B, HARALDSSON B: Transport of macromolecules across microvascular walls. The two-pore theory. *Physiol Rev* 74:163–219, 1994
33. ZEMEL D, KREDIET RT, KOOMEN GC, STRUIJK DG, ARISZ L: Day-to-day variability of protein transport used as a method for analyzing peritoneal permeability in CAPD. *Perit Dial Int* 11:217–223, 1991
34. FLESSNER MF: Peritoneal transport physiology: Insights from basic research. *J Am Soc Nephrol* 2:122–135, 1991
35. RENKIN EM: Capillary transport of macromolecules: Pores and other endothelial pathways. *J Appl Physiol* 58:315–325, 1985
36. LEYPOLDT JK, HENDERSON LW: Molecular charge influences transperitoneal macromolecule transport. *Kidney Int* 43:837–844, 1993
37. HARALDSSON B: The peritoneal membrane acts as a negatively charged barrier restricting anionic proteins. *J Am Soc Nephrol* 4:407, 1993
38. TWARDOWSKI ZJ, KHANNA R, NOLPH KD, SCALAMOGNA A, METZLER MH, SCHNEIDER TW, PROWANT BF, RYAN LP: Intraabdominal pressures during natural activities in patients treated with continuous ambulatory peritoneal dialysis. *Nephron* 44:129–135, 1986
39. FLESSNER MF, FENSTERMACHER JD, DEDRICK RL, BLASBERG RG: A distributed model of peritoneal-plasma transport: Tissue concentration gradients. *Am J Physiol* 248:F425–F435, 1985
40. MISTRY CD, GOKAL R: Glucose polymer as an osmotic agent in CAPD. *Adv Exp Med Biol* 260:149–156, 1989
41. BUNDGAARD M: The three-dimensional organization of tight junctions in a capillary endothelium revealed by serial-section electron microscopy. *J Ultrastruct Res* 88:1–17, 1984
42. RENKIN EM: Control of microcirculation and blood - tissue exchange, in *Handbook of Physiology. The Cardiovascular System. Microcirculation* (vol 4), edited by RENKIN EM, MICHEL CC, Bethesda, Am Physiol Soc, 1984, pp 627–687
43. FOLKOW B, HALICKA HD: A comparison between 'red' and 'white' muscle with respect to blood supply capillary surface area and oxygen uptake in rest and exercise. *Microvasc Res* 1:1–14, 1968
44. FAVAZZA A, MOTANARO D, MESSA P, ANTONUCCI F, GROPUZZO M, MIONI G: Peritoneal clearances in hypertensive CAPD patients after oral administration of clonidine, enalapril, and nifedipine. *Perit Dial Int* 12:287–291, 1992
45. BERGSTRÖM J, FÜRST P, ALVESTRAND A, LINDHOLM B: Protein and energy intake, nitrogen balance and nitrogen losses in patients treated with continuous ambulatory peritoneal dialysis. *Kidney Int* 44:1048–1057, 1993
46. KESHAVIAH PR, NOLPH KD, MOORE HL, PROWANT B, EMERSON PF, MEYER M, TWARDOWSKI ZJ, KHANNA R, PONFERRADA L, COLLINS A: Lean Body mass estimations by creatinine kinetics. *J Am Soc Nephrol* 4:1475–1485, 1994
47. LEVEY AS, MADAIO MP, PERRONE RD: Laboratory assessment of renal disease: Clearance, urinalysis, and renal biopsy, in *The Kidney,* edited by BRENNER BM, RECTOR FC, Philadelphia, W.B. Saunders Company, 1991, pp 919–968
48. MITCH WE, WALSER M: Nutrional therapy of the uremic patient, in *The Kidney* (vol 2), edited by BRENNER BM, RECTOR FC, Philadelphia, W.B. Saunders Co., 1991, pp 2186–2222
49. KEEN M, LIPPS B, GOTCH F: The measured creatinine generation rate in CAPD suggests only 78% of prescribed dialysis is delivered. *Adv Perit Dial* 3:73–75, 1993
50. WARREN PJ, BRANDES JC: Compliance with the peritoneal dialysis prescription is poor. *J Am Soc Nephrol* 4:1627–1629, 1994
51. PYLE WK, MONCRIEF JW, POPOVICH RP: Peritoneal evaluation in CAPD, in *Proceedings of the 2nd International Symposium on CAPD,* edited by MONCRIEF JW, POPOVICH RP, New York, Masson, 1981, pp 35–52
52. MASON EA, WENDT RP, BRESLER EH: Similarity relations (dimensional analysis) for membrane transport. *J Membr Sci* 6:283–298, 1980
53. RIPPE B: A three-pore model of peritoneal transport. *Perit Dial Int* 13 (Suppl 2):S35–S38, 1993
54. MISTRY CD, GOKAL R: Single daily overnight (12-h dwell) use of 7.5% glucose polymer (Mw 18700; Mn 7300) +0.35% glucose solution: A 3-month study. *Nephrol Dial Transplant* 8:443–447, 1993
55. HARALDSSON B: Quantitative measurements of the peritoneal dialysis capacities (PDC) of individual patients. (abstract) *J Am Soc Nephrol* 2:361, 1991
56. BASSINGTHWAIGHTE JB, CHINARD FP, CRONE C, GORESKY CAL, RENEMAN RS, ZIERLER KL: Terminology for mass transport and exchange. *Am J Physiol* 250:H539–H545, 1986
57. GEHAN EA, GEORGE SL: Estimations of human body surface area from height and weight. *Cancer Chemother Rep* 54:225–235, 1970
58. FENSTERMACHER JD, RAPOPORT SI: Blood brain barrier, in *Handbook of Physiology,* Bethesda, Am Physiol Soc, 1984, pp 969–1000
59. WANIEWSKI J, HEIMBÜRGER O, WERYNSKI A, LINDHOLM B: Aqueous solute concentrations and evaluation of mass transport coefficients in peritoneal dialysis. *Nephrol Dial Transplant* 7:50–56, 1992