Peritoneal Dialysis

Ploumis S. Pasadakis and Dimitrios G. Oreopoulos

Introduction

Although several attempts were made to use the peritoneal cavity for dialysis in the late nineteenth century, its use in the management of patients in end-stage renal disease (ESRD) was accepted as a long-term therapy only after Tenckhoff's development of the indwelling silicon-rubber catheter (1963) and the introduction of continuous ambulatory peritoneal dialysis (CAPD) in 1976.

The concept of CAPD was based on mathematical calculations of the peritoneal-membrane kinetics and the requirements to achieve adequate removal of uremic waste products to sustain life. Popovich et al. suggested a scheme of five 2 L exchanges daily, 7 days a week to achieve an adequate control [1]. The main advantages of the new technique were good steady-state biochemical control, more liberal dietary and fluid intakes than with hemodialysis, improvement of anemia and increased well-being of patients, who were able to undertake more physical and social activities away from the hospital.

The need to disconnect the peritoneal catheter from peritoneal dialysis (PD) system to perform each new exchange remains the major source of contamination and of subsequent peritonitis. Several devices have been developed to minimize the risk of contamination, and many attempts have been made to enhance the efficiency of PD by increasing fluid flow, exchange volume, and by optimizing dwell time.

The first continuous cyclic peritoneal dialysis (CCPD), which retains the physiological advantages of CAPD while eliminating daytime exchanges, used a dialysis cycler with a timer; it allowed a programmed delivery of three or more 2 L nocturnal exchanges while a fourth exchange was left to dwell throughout the day [2]. This system, which provides a convenient, continuous therapy and a higher dose of dialysis, has caused a recent resurgence of interest in automated PD. Combinations of CAPD and CCPD have recently been utilized, particularly in large patients with no residual renal function.

Most countries now offer PD in their chronic dialysis programs and many patients have chronic support by this modality in their end stage renal failure. According to the recently reported data of United States Renal Data System (USRDS), CAPD/CCPD modalities accounted for 14.7% of dialysis therapies [3].

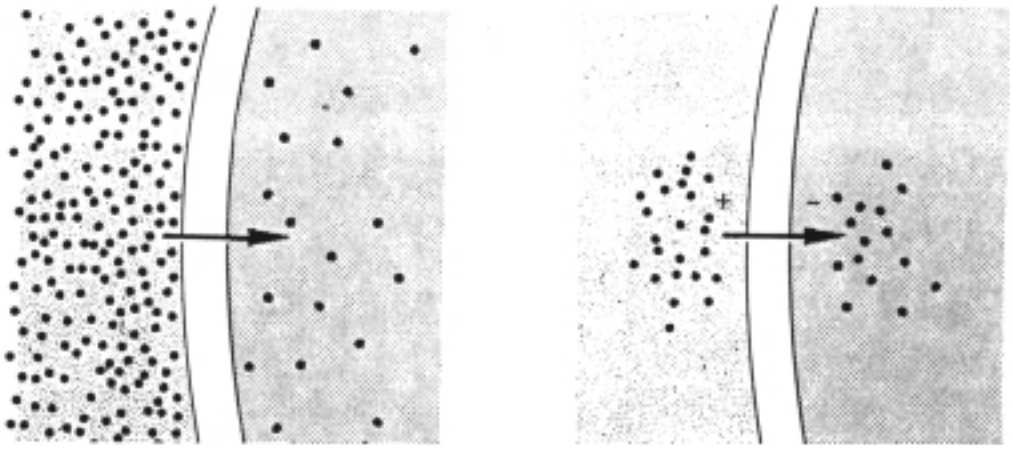

Figure 1. The semipermeable peritoneal membrane. Small solutes are moving through pores by the effect of concenration (left) and electrical (right) difference.

The Physiology of PD

Solutes that accumulate in the blood of patients with ESRD such as urea, creatinine, phosphate, potassium and hydrogen diffuse through the peritoneal membrane into the dialysis solution that has been infused into the peritoneal cavity. Addition of lactate to the solution helps to correct the acidosis when it diffuses into the circulation and is changed by hepatic metabolism to bicarbonate.

Dialysis represents an exchange between the blood in the interstitial capillaries of the peritoneum (blood compartment) and the infused solution (solution compartment) across the peritoneal membrane. The latter, acting as a semipermeable membrane, allows water and small molecules to pass through faster than larger molecules. The driving force by which the various solutes move from the higher (blood and body tissues) to lower concentration compartment (dialysis solution) is the concentration gradient of solutes between plasma and dialysis solution (Figure 1.). In the same way, the driving force for water transport is the pressure gradient generated from differences in hydrostatic, osmotic and oncotic pressures across the peritoneal membrane. A crystalloid osmotic pressure gradient is achieved by the addition of glucose (dextrose) in various concentrations to the solution while colloid osmosis can be induced by adding large molecules such as glucose polymers (icodextrin).

In addition to the phenomena of diffusion and ultrafiltration, there is also considerable absorption from the peritoneal cavity. Such absorption occurs during the equilibrium period either directly into the peritoneal capillary microcirculation or via peritoneal lymphatics.

Peritoneal Circulation-lymphatics

The peritoneal cavity is lined by a continuous serous membrane consisting of a layer of squamous mesothelial cells resting on a thin submesothelial basement membrane and the peritoneal interstitium. Venous flow from the parietal peritoneum drains into the inferior vena cava and systematic circulation while venous drainage from visceral peritoneum

flows into the portal system. This is important because, during their first circulatory pass, intraperitoneally administered drugs will be handled partly by the liver.

Approximately 25% of the cardiac output is directed to the splanchnic vascular bed and the subsequent abdominal splanchnic blood flow usually exceeds 1200 mL/min at rest; however, gas diffusion techniques have shown that the "effective peritoneal capillary blood flow" available for PD is approximately 68 – 82 mL/min.

Lymph drains from the peritoneal cavity mainly through specialized lymph stomata located in the subdiaphragmatic peritoneum; these passages open and close with inspiratory and expiratory diaphragmatic movements. From the diaphragm and through the subdiaphragmatic lymph nodes, almost 80% of the lymph drain to the venous circulation via the right lymph duct. Thus lymphatics draining returns excess intraperitoneal fluid and protein from the peritoneal cavity to the systematic circulation while they provide the only pathways for absorption of intraperitoneal biologically inert particles, colloids and cells.

Solute and Water Transport Across the Peritoneum

The principal determinants of the rate of diffusive solute transport for PD are the concentration gradient between blood and dialysate ($C_p - C_d$), the molecular weight of the solute, and the peritoneal membrane resistance. By changing the peritoneal solution as frequently as possible, we can keep the concentration gradient > 0 and thus maintain a continuous solute removal (Figure 2). However peritoneal clearances of urea cannot exceed a maximum of 40 mL/min even with the more rapid exchanges of dialysate, which

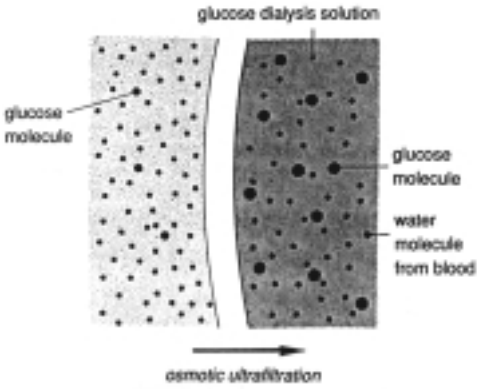

Figure 2. Osmotic ultrafiltration across the peritoneal membrane. Glucose molecules in the dialysis solution generate the driving force for water removal from the peritoneal capillaries to peritoneal cavity.

achieve a flow rate of 4 – 6 L/hour (Figure 3) [4]. Regarding molecular size, smaller molecules diffuse more rapidly than larger ones and the peritoneal membrane does not impede the passage of solutes up to the size of inulin (5200 daltons). On the contrary the transport of larger solutes such as β2-microglobulin (β_2M), myoglobin and albumin, appears to be clearly restricted. Such large substances create oncotic pressure across the membrane, which acts in the same way as hydrostatic pressure, causing bulk flow of water through the pores. During this convective flow, the concentration of solutes, such as sodium and potassium, per L ultrafiltrate usually is far below their respective concentrations in the extracellular fluid, because of the sieving effect of the peritoneal membrane.

Ultrafiltration in PD

The presence of glucose in the peritoneal solution generates an osmotic pressure that induces osmotic ultrafiltration, the main mechanism whereby fluid is drawn from blood into the dialysate. This bulk movement

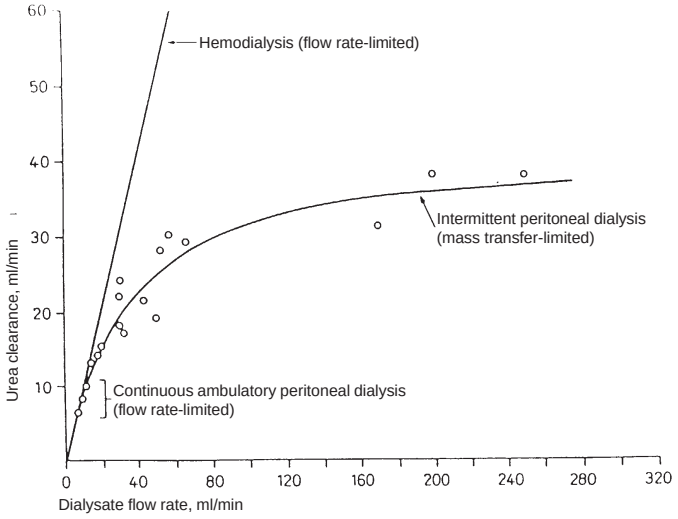

Figure 3. Clearance of small solutes (urea clearance) as a function of dialysate flow rate in HD and PD treatment.

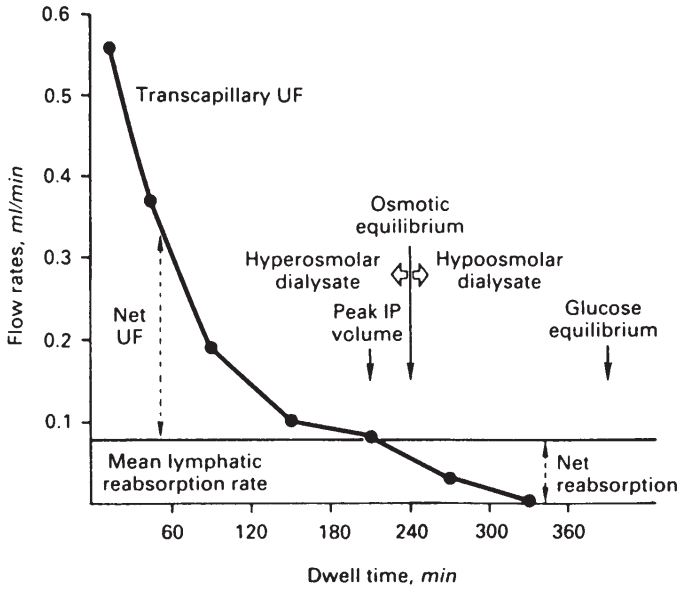

Figure 4. Effect of dwell time on mean transcapillary ultrafiltration. The peak intraperitoneal volume occurs when transcapillary ultrafiltration rate equals the lymphatic absorption rate.

is responsible for a substantial percentage of solute removal (convective transport), which is increased (up to 20% of total removal) for substances with a large molecular weight.

Net ultrafiltration rate, a balance between osmotic ultrafiltration removing water and solutes into peritoneal cavity and lymphatic absorption from the peritoneal fluid, is maximal at the beginning of an exchange when the glucose concentration is at its maximum. Then there is an exponential decrease because of a decline in the glucose concentration gradient due to glucose absorption and dilution by ultrafiltrate, and of lymphatic absorption of peritoneal fluid at a rate of about 0.5 to 1.5 mL/min (Figure 4). Peak intraperitoneal vol-

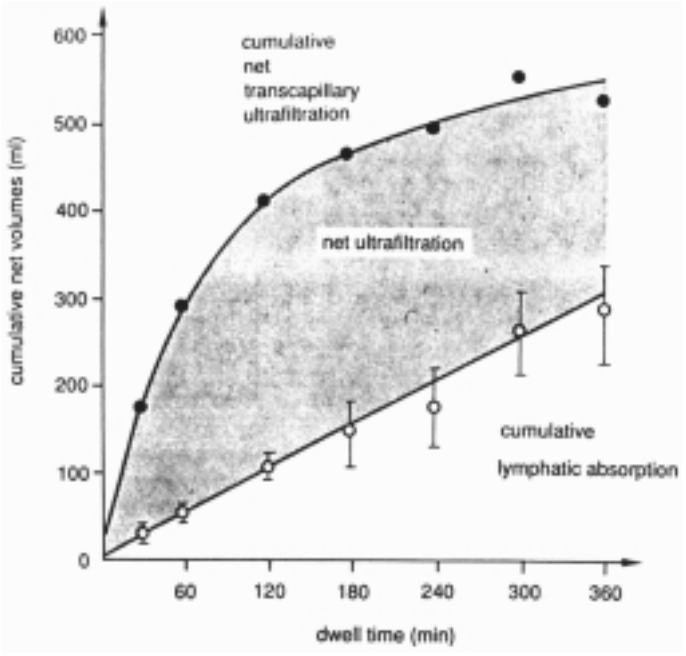

Figure 5. Cumulative net ultrafiltration during PD exchange.

ume occurs at about 120 – 180 min of dwell when ultrafiltration rate equals absorption rate (Figure 5). The maximal transcapillary ultrafiltration induced by 3.86% glucose dialysis solution in the supine position averages 15 mL/min.

standing the peritoneal transport characteristics during the various forms of PD help the operator to choose the most efficient form for the individual patient. Also knowledge of peritoneal membrane characteristics is important to adequate dialysis and to the manipulation and management of some of the common clinical difficulties during PD.

Assessing Peritoneal Ultrafiltration and Solute Transport

The total volume of water and solutes removal from the body during an exchange depends on the degree of equilibrium established during the dwell period, across the peritoneal membrane, between the peritoneal capillary blood and the infused solution. Under-

Clinical Evaluation of Peritoneal Ultrafiltration and Solute Transport – Peritoneal Equilibration Test (PET)

Of the several methods developed for the assessment of peritoneal membrane function, the most commonly used is the PET (Table 1). The reproducibility of this test was demonstrated in systematic studies of CAPD patients, which showed differences in water and solute removal rates during 4 hours dwell time

Table 1. Peritoneal Equilibration Test

1. Pretest exchange fluid is drained completely over 20 min in the sitting position, after an overnight exchange dwell for 8 – 12 hours.

2. A warmed 2 L of 2.5% glucose dialysis solution is weighted (V1) and infused at a rate 200 mL/min;the patient should roll from side to side for better solution mixing after each 400 mL infusion.

3. At the completion of infusion (time 0), 200 mL of peritoneal fluid is drained into the bag, mixed well, a 10 mL sample is taken (S0) and the remaining 190 mL is reinfused

4. The patient is ambulatory during dwell time.

5. After 2 hours dwell*, another dialysate sample (S2) and a blood sample are taken.

6. After 4 hours dwell, the dialysis solution is drained out completely in sitting position, the bag with dialysate is again weighted (V2) and a new sample is taken (S4). Assuming a specific gravity of 1.0, ultrafiltrate is measured by the subtraction V2 – V1.

7. Concentration of creatinine and glucose are measured in solution and blood samples+.

8. Measurement of a) dialysate to plasma ratios (D/P) of creatinine in the samples S2,S4 and b) the ratio D/D0 of the solution glucose concentrations (D) in S2,S4 and the concentration at the beginning (S0).

* Time is measured from the end of infusion
** Because glucose interferes with the Jaffe reagent for creatinine, to avoid overestimation of the creatinine in the dialysis bag, a correction factor must be multiplied.

in 2 L exchange using 2.5% glucose [5]. The differences are graphically presented in equilibration curves. Using this test, the patients were classified into groups according to dialysate to plasma ratios (D/P) of solutes, and glucose absorption (Figure 6):

– The mean D/P values for a 4-hour, 2.5% glucose exchange is 0.65 for creatinine; lower values, i.e. < 0.50, characterize patients who have low permeability transport properties.
– Glucose absorption is more rapid early in the dwell and in patients with high peritoneal permeability, this produces a severe decrease in the osmotic gradient that is responsible for ultrafiltration. Thus, after a 4-hour 2.5% glucose exchange, such patients have lower drainage fluid glucose levels (< 500 mg/dL compared to normal levels of 720 mg/dl).

Using these results, patients can be divided into 4 groups:

– Low transporters who show: a) low D/P of creatinine (< 0.50), and b) low rate of glucose absorption inducing peak ultrafiltration late in the exchange.
– High transporters who show: a) high D/P of small solutes and peritoneal clearances that are close to unity in 4-hour exchange, and b) rapid absorption of glucose inducing peak ultrafiltration early in an exchange. Ultrafiltrates volumes are minimal in 4-hour exchange due to fluid absorption.
– Low average and high average transporters who present with intermediate equilibration rates.

A recent PET study found that these groups, were distributed between CAPD patients as follows: high average (53.1%), low average (30.9%), high (10.4%) and low (5.6%) [6].

In a 4-hr exchange of 2 L (2050 mL) of 2.5% glucose, the net ultrafiltrate is approximately 320 mL (2370 mL drainage volume-2050 mL instilled volume). Because net ultrafiltration rate is a balance between osmotic ultrafiltration removing water into peritoneal cavity and the lymphatic absorption of peritoneal fluid, a decrease in ultrafiltrate represents either a decrease in osmotic ultrafiltration or an increase in lymphatic absorption.

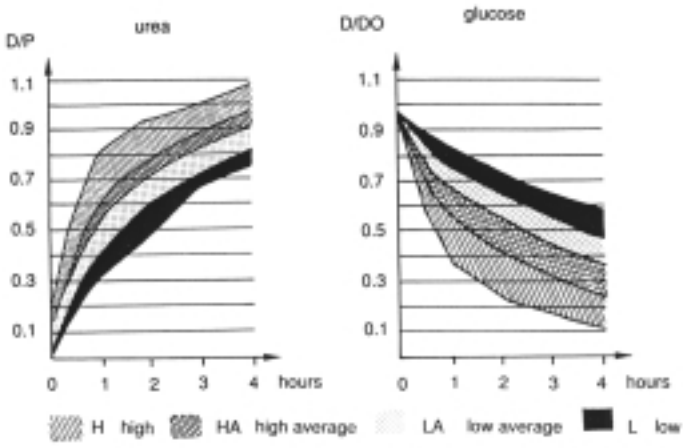

Figure 6. The equilibration test for urea and glucose absorption. Area shaded in different patterns portray results representing high (H), high average (HA), low average (LA) and low (L) peritoneal equilibration rates, in patients on CAPD.

In assessing baseline peritoneal membrane permeability, one must make PET measurements 3 – 4 weeks after the initiation of PD. The results should not be used as a precise measure of dialysis adequacy, but rather as a general guide to the prescription of the more suitable mode of dialysis for the patient's peritoneal membrane characteristics. In general, average transporters do better on continuous PD schedules (long dwell) while high transporters do better on intermittent dialysis (short dwell). The standard continuous and intermittent PD regimens include:

– CAPD with the continuous presence of dialysate in the peritoneal cavity, drained and reinstilled 4 – 5 times/24 hours,
– CCPD which uses a dialysis machine with a timer to provide a programmed replacement of dialysate in 3 to 5 two liter (2 L) nocturnal exchanges; in the morning, the patient disconnects the cycler and leaves a fresh 2 L solution to dwell throughout the day, and
– nocturnal intermittent peritoneal dialysis (NIPD, dry PD) that is similar to CCPD but differs in that the abdomen is left empty during the daytime, while the nocturnal exchanges are increased to 5 – 8 exchanges.

Peritoneal Solute Clearances (K_p)

K_p expresses the volume of plasma cleared of the solute by the peritoneal membrane per unit time. This can be measured using the equation

$$K_p = (V_t / t) \times (D/P)$$

where V_t is the volume of dialysate drained at the end of the exchange, t is the duration of the exchange and D/P is the dialysate-to-plasma ratio for solute concentrations in that exchange. By changing the equation to

$$K_p \times t = V_t \times (D/P),$$

it can be shown that the clearance-time product (solute removal) is equal to the volume of dialysate drained times the D/P ratio.

In patients with low peritoneal transport rates, the equilibration of solutes (D/P) and therefore the peritoneal clearance per exchange increase almost linearly during the exchange and consequently long-dwell exchanges are critical for solute removal. On the contrary, in high transporters the rapid increase in D/P allows one to perform short-dwell exchanges to maintain better ultrafiltration rates.

In CAPD the product ($K_p \times t$) can be calculated for a 24-hour period by pooling the drained volumes of all exchanges (V_d) during that period, measuring the D/P and multiplying the $V_d \times$ (D/P). Similar calculations are performed for a patient on NIPD, in whom the V_d represents the total drained volume of all nightly exchanges. The serum samples can be obtained from CAPD patients at any time, while in CCPD patients, they are taken at the midpoint of the long daily dwell. In NIPD an average of pre- and postdialysis concentrations may be more suitable because the plasma solute concentration (P) may change over the session.

Table 2. Composition of PD Solutions

	Commercial Solution	Usual plasma level in dialysis patient
Sodium (mmol/L)	132 – 134	135 – 142
Potassium (mmol/L)	0 – 2	4 – 6
Calcium (mmol/L)	1.25 – 1.75	1.15 – 1.29
Magnesium (mmol/L)	0.25 – 0.75	0.65 – 0.70
Chloride (mmol/L)	95 – 106	95 – 100
Lactate (mmol/L)	35 – 40	1 – 2
Glucose (gr/dL)	1.5 – 4.25	70 – 120
pH	5.5	7.2

PD Apparatus and Devices

Dialysis Solutions

Dialysis solutions for CAPD are available in sterilized collapsible plastic containers in several volumes and various concentrations of the osmotic agent glucose. Solutions with 1.5, 2.5, 3.5, or 4.25% dextrose contain 1.36, 2.27, 3.17 and 3.86 gr. of D-monohydrate glucose, respectively. The listed and the true glucose concentrations differ because the molecular weight of D-glucose monohydrate is 10% greater than that of anhydrous glucose. The clear underfilled plastic bags contain 0.25, 0.5, 0.75, 1.0, 2.0, 2.5 and 3.0 L; the potential volume of the container exceeds by about 50% the volume of the contents to accommodate any ultrafiltrate. There are also 5.0 L plastic containers for cycling machines.

The composition of PD solution is tailored to correct the electrolyte and acid-base imbalances by restoring the normal composition of the body fluids (Table 2).

Electrolyte Homeostasis

In the uremic syndrome the accumulated sodium, potassium and magnesium ions have to be removed and the associated hypocalcemia and acidosis have to be corrected. Depending on the concentration gradients, PD removes only small amounts of sodium and chloride while it removes large amounts of potassium and magnesium.

Because of the peritoneal membrane's sieving effect, the net removal of sodium per L ultrafiltrate (70 mmol/L) is significantly lower than the plasma sodium concentration. This hyponatremic ultrafiltrate further dilutes the dialysate and with short dwell exchanges, the greater removal of water tends to produce hypernatremia. Clinical studies have reported no specific side effects with the use of standard CAPD solutions of 132 – 134 mmol/L of sodium, while the use of lower sodium concentrations can accelerated the diffusive loss of sodium. Variations in the net daily removal of sodium can be attributed to differences in dietary intake, in residual renal function or to

intrinsic autoregulatory mechanisms for the adjustment of removal rates [7]. Experimentally, various sodium concentrations have been used, as higher sodium concentrations (137 mmol/L) to correct orthostatic hypotension, and ultra low sodium (98 mmol/L) to avoid fluid overload in patients with insufficient ultrafiltration.

Potassium should equilibrate slightly faster than sodium because of its lower nuclear charge and its smaller hydration radius; with four 2 L exchanges per day about 30 mmol of potassium are removed with dialysate. Because this value is lower than the usual daily intake (70 – 80 mmol), enhanced intestinal potassium excretion is essential to maintain normal serum potassium values. The hypokalemia found in 10 – 36% of CAPD patients had been attributed to their anabolic state, malnutrition and the use of large doses of diuretics [8].

Although minor changes in serum magnesium are difficult to interpret, hypermagnesemia is common in dialysis patients. By lowering magnesium in the dialysis solution, one can treat hyperphosphatemia with magnesium salts as an additional aluminum-free phosphate binder [9].

Since standard CAPD solutions contain 1.75 mmol of calcium – a concentration that is higher than normal serum diffusible calcium levels (1.15 – 1.29 mmol) calcium is absorbed from the dialysate when such solutions are used. Convective transport counteracts diffusive uptake and during dialysis with a 4.25% glucose solution, ultrafiltration may cause a decrease in total calcium uptake. Despite the otherwise favorable effect of calcium absorption because of uremic hypocalcemia, in the presence of normal serum calcium levels, this absorption may be associated with hypercalcemia and soft-tissue calcification when using calcium-containing phosphate binders. To avoid such side effect, low calcium solutions have been introduced. A major risk of these new solutions is the progression of hyperparathyroidism, which may be enhanced in patients undergoing two or more 4.25% exchanges per day. Such patients require a frequent monitoring of calcium and PTH levels.

Acid-base Balance

Two of the major achievements of PD are the correction of metabolic acidosis and the maintenance of satisfactory acid-base status. Standard solutions contain lactate (L- or D-racemic forms) as a bicarbonate-generating agent because of the technical difficulties in preparing, sterilizing and storing solutions containing mixtures of bicarbonate, calcium, magnesium and glucose. The absorption of lactate is maximal during the first few minutes of dwell, which permits an adequate buffer transfer even with rapid exchanges, while long dwell exchanges enable an almost complete buffer transfer independent of the initial lactate concentration. During dwell, bicarbonate diffuses back into the dialysate at a rate determined by blood bicarbonate concentration, while ultrafiltration enhances this loss. Organic anions, which play the role of effective alkaline equivalents also are drawn into the dialysate.

Although lactate is a powerful peripheral vasodilator that also effects myocardial contractility, there is no clear evidence that these actions have clinical relevance during dialysis with a lactate buffer. Patients with hepatic disease may have a lower metabolic rate with a consequent increase in serum lactate levels.

Generally the low pH of dialysis solution (≈ 5.5) is well tolerated, however, during inflow some patients may complain of pain, which may be relieved by neutralizing the solution pH with alkali before instillation.

Other Osmotic Agents

Several low-molecular-weight agents – glycerol, sorbitol, xylitol, fructose and amino acids have been used to generate a high osmotic gradient in peritoneal transport, but glucose appears to be the safest, most effective and most easily metabolized agent for this purpose. Amino acid solutions have been introduced to achieve the dual goals of glucose substitution and nutritional improvement of malnourished CAPD patients [10]. Despite their significance in nutritional efficacy, one must consider associated increases in blood urea nitrogen (BUN) levels, the tendency to metabolic acidosis and increased cost.

Larger molecules of less absorbable substances – (glucose polymers, gelatin, dextrans, polycations, and polypeptides) have been studied, in an attempt to slow the dissipation of the osmotic gradient and, at the same time, to reduce the calorie load. Recently Krediet et al. have shown that icodextrin, a glucose polymer consisting mainly of α-1,4 linkages between glucose molecules, is superior to glucose in the induction of net ultrafiltration during long dwells – a feature that may be important during peritonitis episodes and in patients with ultrafiltration failure [11].

Peritoneal Catheters

For acute PD the rigid peritoneal catheter provides a quick, easily accessible route into the intraperitoneal cavity at the bedside. Once inserted, it can be used safely for a maximum of 72 hours beyond which there is an increasing risk of peritonitis. Thus when one anticipates that the patient will need PD for more than one week, a permanent catheter should be installed. Furthermore their use is accompanied by a high rate of complications.

The permanent catheter has a number of advantages:

- safe implantation without major surgery,
- adequate dialysate inflow and outflow, and
- maintenance of its position for long periods without intra-abdominal migrations.

The most widely used device for chronic PD is the Tenckhoff catheter and its modifications, all of them being straight or slightly curved with several side holes at their intra-abdominal part. They are made of silicon rubber or polyurethane with one or two cuffs of Dacron velour. Profuse collagen tissue ingrowth between the fibers provides a strong bond with the surrounding tissues. This fibrous tissue fixes the cuff in position and prevents the passage of bacteria into the subcutaneous channel. Experienced surgeons or nephrologists should implant these catheters in the operating room or at the bedside, using a guidewire and dilators, or peritoneoscopy.

"Connectology": Transfer Sets and Dialysis Systems

The dialysis solution is infused into the peritoneal cavity via a plastic tubing transfer set that connects the plastic bag and the peritoneal catheter. Commonly the transfer set is connected to the catheter via an on-line plastic connector, which screws onto a special titanium Luer-Lock connector. The other end is connected to the solution bag; this is an important connection because approximately two-thirds of all episodes of peritonitis can be attributed to touch contamination of this connection [12]. Many connection systems have been developed to avoid touch contamination; these are based on individual exchange procedures – manual, mechanical, sterilized, anti-

septic, and disposable. The term "connectology" refers to these different equipment and methods of connections.

A straight or Y-shaped transfer set is connected to the solution bag via connection techniques that can be categorized as one of 3 types:

– the spike and port method,
– the Luer-lock method, or
– the mechanical assist.

The standard spike and port connection is the simplest of these; one pushes a plastic spike at one end of the transfer set into a small rubber port on the dialysate bag. A connection shield that contains a sponge soaked with povidone-iodine gives added protection at the spike-outlet port site. The sponge, which remains in place during the dwell period, is removed at the time of the next exchange.

The halves of the Luer-lock connectors are closed with a twisting action that seems to be easier to perform and prevents touch contamination without the need for fine hand control. The Luer system comes with a protective, povidone-iodine clamshell or a cap containing antiseptic.

The mechanical assist devices designed to reduce peritonitis are portable, convenient and easy to use. In most of them, a lever-assisted exchange system helps patients, particularly those with visual and manual impairment, to insert the transfer set spike into the port of the dialysis bag. Some of these devices also include a system that sterilizes the connection site before the infusion. The ultraviolet (UV) light device (UV-Flash) has a mechanical system to assist the patients in spiking the transfer set, and an UV light system that irradiates and sterilizes the spike and port before connection.

In the simplest dialysis system fresh dialysis fluid is infused from a bag that, once empty, is rolled up and stored in a little pouch on the patient's body, keeping the tubing clamp closed. At the end of the dwell, the bag is unrolled and placed on the floor, the clamp is opened and the effluent is drained into the bag. Then the spike of the transfer set is removed from the used bag and inserted into a new one. This transfer set is changed once every 6 months by a dialysis nurse. This system, though inexpensive, is used only infrequently because newer systems provide a lower peritonitis rate.

The Y-shaped transfer sets consisting of a stem and two limbs, one for infusion of the dialysis solution and the other for its drainage. The concept behind the Y systems is that before connection with the bag, the patient runs a small volume of fresh dialysate (30 – 100 mL) into the drain bag (flush), which carries with it any contaminating bacteria. Similarly after connection with the catheter, the patient drains out fluid from the abdomen before he infuses fresh dialysate, thus washing out any contaminating bacteria (flush after connect). With its "flush before fill" procedure, the Y set gives significantly lower peritonitis rates than straight sets; also, because of the disconnection there is less mechanical stress on the exit site and tunnel and hence fewer episodes of minor trauma and consequently of exit-site infection.

Some Y-sets come attached to an empty sterile drain bag, which the patient connects to his catheter and to the appropriate fresh dialysis bag. To minimize the connections (to the peritoneal catheter), sterile sets are available which include the empty and the full dialysate bag (twin or double bag systems). At the end of the exchange, the bags, the lines and the transfer set are disconnected and disposed. Also reuseable Y-sets are available which combine the flush-before-fill advantages with a disinfectant that is injected into the Y-set lumen immediately after an exchange. This system, called O-set, because of the O shape

Table 3. Characteristics of the Main Regimens of PD

Feature	CAPD	CCPD	NIPD
Number of exchanges /week	28	28	49 – 56
Daytime exchanges /week	21	7	0
Daytime dwell (hour/week)	84	98 – 112	0
Nocturnal exchanges/week	7	21	49 – 56
Nocturnal dwell (hour/week)	56 – 70	45 – 60	28 – 42
Dialysis time (hours/week)	168	168	56 – 70
Cycler time (hours/week)	0	56	56 – 70
Dialysate volume (L/week)	56	56	98 – 112
Number of "connections"/week	28	14	7
Peritoneal Clearances C_{Cr} (L/week)			
Urea / creatinine	57/47	57/47	62/39
Ultrafiltration L/D	1.3 – 2.0	0.7 – 1.7	1.5 – 2.0

formed by the two joined limbs. At the time of the next exchange, the antiseptic is drained out and the dialysate effluent rinses the stem. O-Sets have not gained wide acceptance because of the frequent, accidental instillation of antiseptic into the peritoneal cavity.

PD Machines

These machines deliver predetermined volumes of solution into the peritoneal cavity, and drain it out after a programmed dwell time. A heater warms the solution to body temperature, and the force of gravity directs the fluid through lines that are clamped (on or off) to permit flow in or out of the peritoneal cavity. Dialysis solutions of different glucose concentrations can be attached simultaneously usually with the spike-and-port method into a multipronged manifold, which can hold several dialysis containers (up to 5 – 8 containers of 3 – 5 L each), provide an efficient solution volume for nightly exchanges. Because the machine always controls the inflow volume, it is not essential to have an accurate volume in each container.

Technique of PD – Choice of Treatment Modality

Prescription of a PD technique includes:

- the method of dialysis – manual or automated,
- the regimen – intermittent or continuous,
- the infusion volumes and the type of solutions to be used per exchange, and
- the volume of solution to be infused over a specified time period – dose of dialysis.

Table 3 shows some characteristics of the main regimens.

Intermittent Regimens

These regimens are especially suitable for patients who maintain some residual renal function and/or high peritoneal transport rates. There are 3 schedules:

Intermittent Peritoneal Dialysis (IPD)

Here, a 16 – 20 hour treatment is given 2 – 3 times a week, using a cycler machine. The usual dose is about 40 – 60 L per session (80 – 120 L/week). This regimen is most suitable for high and high-average transporters who maintain renal residual function.

Nocturnal Intermittent Peritoneal Dialysis (NIPD)

Treatment is given every night while the patient sleeps using a cycler to perform 7 – 8 exchanges over 8 – 10 hours. The daytime is free of exchanges. The usual volume per session is 14 – 16 L (98 – 112 L/week). This method is particularly useful in high transporters who have a decreased ultrafiltration with 4 – 6 hours dwell; in these patients this method gives a clearance of small solutes equivalent to that of CAPD. Also NIPD is helpful to patients with hernias, pericatheter leaks and back pain because it operates at a lower intraperitoneal pressure because the patient is supine during dialysis. The alleged increase of peritoneal fluid leukocyte and higher gamma globulin concentration during the long dwell time may contribute to the lower incidence of peritonitis in these patients. The major disadvantage of this technique is its reduced removal of solutes, particularly the larger molecules. Daytime IPD may be useful as a hospital-based therapy in bedridden, severely handicapped patients, who cannot sustain hemodialysis.

Daytime Ambulatory Peritoneal Dialysis (DAPD)

DAPD is treatment for 12 – 16 hours is given only during the day when the patient is ambulatory, in several short exchanges with 3 – 4 hours dwell time. The short time of equilibrium in this modality can be used only by patients who maintain residual renal function and/or high peritoneal transport rates – characteristics that allow small solutes to reach their peak clearances and the ultrafiltration volume to balance the intake of fluids. The dose per session is 8 L (56 L/week).

Continuous Regimens

The standard CAPD and CCPD usually provide adequate dialysis in patients with average peritoneal transport rates.

Continuous Ambulatory Peritoneal Dialysis (CAPD)

This – the most common prescribed dialysis throughout the world – uses three or four 2L daytime exchanges during the day and another before bedtime; dialysis solution is continuously present in the abdomen. This continuity provides a more “physiological” steady state and confers some advantages in body fluid control, in control of hypertension, while it is easier to achieve normal blood sugar levels in diabetics with the intraperitoneal administration of insulin in each exchange.

The volumes and the glucose concentration of the solutions are selected according to pa-

tient's needs and peritoneal transport characteristics. Usually the overnight exchange with 8 – 10 hours dwell time is of 2.25%, or in the presence of low ultrafiltration, a 4.25% solution is used to maintain the osmotic gradient and avoid fluid absorption. The standard daily dose of 8 L (56 L/week) can be increased by increasing the volumes per exchange (to 2.5 or 3.0 L/exchange), or by increasing the number of exchanges (5 exchanges/day).

As a treatment CAPD is suitable for patients with average, low or high peritoneal transport rates.

Continuous Cyclic Peritoneal Dialysis (CCPD)

This technique retains the physiological advantages of CAPD but eliminates diurnal exchanges; using a dialysis cycler, three 2 L exchanges are given at night, while a fourth 2 L exchange is left to dwell throughout the day over 14 – 16 hours. This method provides the same dose as CAPD and is more suitable for patients who need a partner to help them with the dialysis. Also this method is attractive for active individuals who otherwise would be inconvenienced by the daily interruptions required by CAPD. The lower incidence of hernias and pericatheter leaks associated with this modality may be due to reduced mean intraperitoneal pressure during the hours of activity. The dose can be increased by increasing the nightly treatment time (8 – 10 hours), the volume of each exchange, or by performing more daily exchanges.

Alternate PD Regimens

The standard regimens can be modified to provide adequate dose of PD, particularly in anuric patients, or in those with large body size and low or even low-average transport kinetics. When needed, performing 2 exchanges during the long dwell, (enhanced CCPD) provides extra dialysis and, at the same time minimizes the disadvantages of CAPD and CCPD, namely increased glucose absorption and decreased ultrafiltration. Also, CAPD patients who require a fifth exchange can perform it during the night with a minicycler (Quantum – Baxter).

Alternate regimens are easier to perform with the dialysis modalities that use cyclers, because it is impractical to perform more than 5 manual daily exchanges when one needs a higher dose or longer treatment time. On the contrary, patients seem to accept more readily an increase of nocturnal treatment time to 10 – 12 hours/day if it is carried out mainly during the hours of sleep.

Tidal Peritoneal Dialysis (NTPD)

In this method the cycler infuses a fixed volume (1.2 – 1.5 L) with rapid exchanges (4 – 6 min dwell time, 20 min total exchange time) during a dialysis session that lasts 8 – 10 hours. The infusion volume is added to a constant "tidal" volume of 1.2 – 1.5 L of solution that is maintained in the peritoneal cavity throughout the session. This tidal volume is achieved after an initial filling with a large (3 L) volume of solution; during the drain phase, only one-half of this volume escapes from the abdomen. The next fill and drain volumes are equal to the tidal volume and only at the end of the session is the peritoneal cavity drained completely; it remains empty until the next treatment. The usual dose is 26 – 30 L/session. This form of NIPD avoids waste dwell time during the initial fill and the end of drain when the peritoneal cavity is empty and no dialysis takes place.

Adequacy of PD

The primary goal of PD as renal replacement therapy is to maintain the uremic patient in the best physical and clinical condition and prevent the complications of ESRD. Assessing PD adequacy not only helps to establish the minimum dose compatible with short-term well-being and absence of uremic symptoms, but also helps define the optimum dialysis dose, i.e. the dose that provides favorable long-term outcomes to survival, rehabilitation and quality of life.

Although some uremic symptoms such as pericarditis, nausea, vomiting, and a rising BUN and serum creatinine concentration are the result of insufficient clearance of uremic toxins, there are no symptoms or biochemical findings that clearly defines PD adequacy. It is considered that such clinical criteria as a feeling of well-being in the absence of uremic symptoms, such as anorexia, nausea, and insomnia are associated with good fluid balance, normal blood pressure and biochemical status of decreased BUN < 100 mg/dL and of serum creatinine concentration < 18 mg/dL, are indices of adequate PD. Stable lean body mass, stable nerve conduction velocities, and a hematocrit (HCT) > 25% without recombinant human erythropoietin (rHu-EPO) or anabolic steroids also have been proposed as indices of adequacy.

Recently more specific methods using urea and creatinine kinetics have been described to assess the adequacy of PD, in which the dose of dialysis is determined by weekly measurements of creatinine and urea clearances.

Normalized Weekly Clearances

Weekly clearances are normalized to reflect the patient's size so as to individualize the dose of dialysis. Creatinine clearance (C_{Cr}) is normalized to body surface area (BSA) standardized for a BSA of 1.73 m^2, while the volume of body water (*V*) in which urea is distributed has been used to normalize the weekly urea clearance. The latter approach produces the parameter *Kt/V* that governs urea kinetics during hemodialysis; this symbol represents the volume of plasma cleared of urea (*K*) over a certain time (*t*) divided by the urea distribution volume (*V*), which is roughly equal to the total body water – 60% of lean body weight (BW) in men, 55% in women. In large patients, to assume fixed percentage of BW for the volume of distribution (*V*) may introduce errors and thus the Watson method [13] is used to provide reasonable approximation of the actual *V*.

Men *V* (L) = 2.447 + 0.3362 × BW(kg) + 0.1074 × Ht (cm) – 0.09516 × Age (yrs)

Women *V* (L) = –2.097 + 0.2466 × BW(kg) + 0.1069 × Ht (cm)

This formula was derived by comparing total body water measurements to simple anthropometric measurements (weight. height, age) in subjects without edema, volume deficit or ESRD.

According to the urea kinetic model, weekly *Kt/V* for urea (Kt/V_{urea}) provides an objective index of adequacy; originally adequate dialysis was defined as a weekly urea *Kt/V* > 1.9 – 2.0, while values between 1.7 to 1.9 were considered marginal. Patients in the latter range should be observed closely for signs and symptoms of inadequate dialysis. Inadequate dialysis may due to inadequate clearance of solutes, a hypercatabolic state

and/or failure to adhere to the dialysis prescription. For intermittent therapies such as NIPD, a weekly Kt/V_{urea} of 2.2 is recommended; this figure is based mainly upon extrapolation from hemodialysis and urea kinetics.

Also, several workers have proposed that adequate dialysis requires a total weekly creatinine clearance (C_{Cr}) of at least 60 L per 1.73 m^2 BSA [14 – 16]. Weekly creatinine clearance may be better than Kt/V_{urea} to assess dialysis adequacy, as a good correlation between urea kinetic analysis and clinical outcomes in patients on CAPD has not been shown [17], but this remains in debate. Until we have this confirmation, one should use both weekly values of 1.9 for urea (Kt/V_{urea}) and 60 L for creatinine clearance (C_{Cr}) as reasonable goals for continuous therapies such as CAPD or CCPD. In patients with residual renal function, weekly Kt/V_{urea} of 2.0 corresponds to 60.5 – 67.6 L/week/1.73m^2 of C_{Cr}; in the anuric patient, the equivalent is a creatinine clearance of 52.1 L/week/1.73m^2 [18, 19]. This means that, in absence of residual renal function (RRF), the theoretical adequate target for Kt/V_{urea} should be increased between 2.0 and 2.25.

Residual Renal Function (RRF)

Although RRF in hemodialysis, may be significant only for clearance of middle molecular weight and larger solutes, in PD residual renal solute clearances contribute significantly to total solute and water removal. Preservation of RRF may be particularly important to the effectiveness of long-term PD; therefore reports that PD provides better preservation of RRF than does hemodialysis are of great interest [20, 21].

To assess RRF, residual clearances (C_r) of creatinine (C_{rCr}) and urea (C_{rUr}) have to be measured. The use of both measurements instead of creatinine clearance alone provides a more accurate estimate of glomerular filtration rate (GFR) as the arithmetic mean of urea and creatinine clearances [$GFR = (C_{rCr} + C_{rUr}) / 2$], (Table 4). This is due to the different tubular mechanisms of secretion of creatinine and reabsorption of urea, and to the fact that as GFR declines the contribution of residual renal creatinine clearance to the total creatinine clearance rises disproportionally. Therefore measurement of sole residual renal creatinine clearance would lead to overestimation of GFR.

The corrected value of GFR is then added to peritoneal creatinine clearance (K_{pCr}) and normalized to 1.73 m^2 to calculate the total creatinine clearance (C_{Cr}). A residual GFR of 1 mL/min is equivalent to 10 L (1ml × 60 × 24 × 7); that may be a significant proportion of the total of C_{Cr}. Failures to account for the loss of RRF over time can lead to underdialysis even though dialysis efficiency has not been declined. The corresponding value of 1 mL/min of renal urea clearance to weekly Kt/V_{urea} is 0.25 L.

Middle-molecular-weight Toxins and the Peak Concentration Hypothesis

Early attempts to quantify PD noted that PD patients appeared to be in “comparable good health” relative to hemodialysis patients despite much lower small solute clearances. This difference was ascribed to more efficient peritoneal clearance of middle molecule weight toxins, a conclusion that seems to fit with recent knowledge that CAPD patients do as well clinically as those undergoing hemodialysis despite the lower weekly urea clearance (Kt/V) [17, 22]. In fact, the minimum recommended Kt/V for each hemodialysis is 1.2 – a

Table 4. Calculations of Weekly Creatinine Clearance C_{Cr}, Weekly Kt/V_{urea} and PCR

A)	Collection of 24-hour volumes of dialysate (V_d) and urine (V_u) and measurements of creatinine and urea nitrogen concentrations in dialysate (Dcr, Dur) and urine (Ucr, Uur) respectively.
B)	Measurement of the plasma creatinine (Pcr) and urea nitrogen concentrations (Pur) in a sample taken on the day of collection at any time in CAPD. In CCPD and NIPD the sample may be drawn in midpoint of the session (NIPD) and the daily long dwell exchange (CCPD).
C)	Calculate daily residual renal clearances (L/day) of creatinine (C_{rCrr}) and urea (C_{rUr}) as: C_{rCr} (L/day) = (Vu × Ucr) / Pcr and C_{rUr} (L/day) = (Vu × Uur) / Pur The average of the 2 measurements estimates GFR (GFR mL/min = [(C_{rCr} + C_{rUr}) /2] x1000/1440)
D)	Calculate peritoneal creatinine clearance (K_{pCr}) as: K_{pCr} (L/day) = (V_d) × (Dcr / Pcr) Calculate peritoneal urea clearance (K_{pUr}) as: K_{pUr} (L/day) = (V_d) × (Dur / Pur)
E)	Estimate patient's body surface area (BSA) to use normalize creatinine clearance: $(BSA)^2$ = Ht (cm) × BW (Kg) /3600 Estimate the volume of urea distribution in the body water (*V*) by Watson equation: Men *V* (L) = 2.447 + 0.3362 × BW(kg) + 0.1074 × Ht (cm) – 0.09516 × Age (yrs) Women *V* (L) = -2.097 + 0.2466 × BW(kg) + 0.1069 × Ht (cm)
F)	Calculate weekly creatinine clearance C_{Cr} = 7 × (C_{rCr} + K_{pCr}) and then normalized for BSA=1.73m^2.
G)	Calculate weekly urea clearance K_{prt} = 7 × (C_{rUr} + K_{pUr}) and then normalized for volume of urea distribution to give Kt/V_{urea}
H)	Calculate PCR (g/day) = 10.76 × (UGR + 1.46) = 6.49 UNA + 0.294 V Calculate PNA (g/day) = 10.76 × ((UNA/1.44) + 1.46) where UGR (urea generation rate, mg/min) = ((Uur (mg) + Dur (mg)) / 1440 and UNA (urea nitrogen appearance, g/day) = (Uur (g) + Dur (g) and V = the total body water (L).
I)	Calculate normalized PCR (nPCR) = PCR / (V/0.58) Where V/0.58 is equivalent to standard weight based on V

figure that represents a weekly *Kt/V* of 3.6, well above the minimum weekly Kt/V_{urea} of 1.9 – 2.0 in CAPD patients. Keshaviah has called this observation the "peak concentration hypothesis" [23]. This hypothesis postulates that uremic toxicity and the likelihood of developing early uremic symptoms is related more to the peak plasma levels of urea and other small uremic toxins rather than to the average value of these elements. According to this, clearances must be time averaged because CAPD is a continuous while hemodia-

lysis (HD) is an intermittent therapy. Therefore HD requires a higher *Kt/V* to reduce the peak interdialysis concentration of urea to the steady state level of CAPD. For similar reasons, patients undergoing intermittent PD require a Kt/V_{urea} of at least 2.2 because urea nitrogen concentrations peak between dialyses [24].

PD Adequacy and Nutritional Status

The correlation between Kt/V_{urea} and the protein equivalent of nitrogen appearance (PNA), also expressed as the protein catabolic rate (PCR) [25 – 27] provides indirect evidence of a link between PD adequacy and nutritional status. On the other hand, low Kt/V_{urea} values often are associated with hypoalbuminemia – a marker for malnutrition, and PCR levels < 0.9 g/kg/day are an index of decreased dietary protein intake (DPI) [13, 27]. These findings indicate that an increase in the dialysis dose (*Kt/V*) may increase DPI by increasing appetite, and may prolong the patients' survival on dialysis.

PCR can be measured from a 24-hour dialysate and urine collection (Table 4). Measurements of PCR from renal urea-nitrogen kinetics will provide an estimate of DPI. This calculation assumes that the patient is in a steady state; if so, PCR can be normalized to weight by dividing by the factor *V*/0.58 assuming as equivalent to standard weight (nPCR) [26]. PD patients with nPCR levels > 0.9 g/kg/day are in neutral nitrogen balance.

The serum albumin level is not a sensitive marker of nutritional status but it has been used as a predictor of outcome, because low serum albumin levels have been associated with an increased risk of morbidity and death in the PD population [28, 29].

PD Adequacy and Clinical Outcome

Recently a multicenter prospective cohort study (CANUSA) evaluated the effect of therapy dose and nutritional status on clinical outcome, using statistical techniques [15]. In this study decreased values of Kt/V_{urea} and weekly C_{cr} were associated with an increased relative risk of death. More specifically, a decrease in Kt/V_{urea} of 0.1 and in weekly C_{cr} of 5 L/1.73 m^2 BSA produced 5% and 7% increases, respectively, in the relative risk of death.

However, both a Kt/V_{urea} of 2.1 and a weekly C_{Cr} of 70 L/1.73 m^2 BSA were associated with a 78% expected 2-year survival rate. It has also been reported that underdialysis increases mortality in PD patients with ischemic cardiac disease or left ventricular dysfunction [22, 29]. Although we await clinical validation of these observations, they indicate the close relationship between PD adequacy and clinical outcome.

Acute and Chronic PD Prescription

Acute PD may be performed in patients with acute renal failure (ARF) when recovery of renal function is anticipated or in some predialysis patients with temporary exacerbation of renal failure.

Acute PD Prescription

After insertion of an acute, or more often, a chronic peritoneal catheter (Tenkchoff), the

dialysis prescription must be individualized to the patient and to his/her clinical situation. Acutely ill patients with unstable hemodynamic signs will need frequent re-evaluation and modifications in the composition of the therapeutic solutions.

The common duration of an acute PD session lasts from 24 – 72 hours with hourly exchanges of usually 2 L peritoneal solution.

Although many adult patients can tolerate 2 L of fluid, infusion volumes must be adjusted not only to the patients peritoneal cavity size but also to any respiratory disease and/or abdominal or inguinal hernias. However because larger infusion volumes increase water and solute removal rates, calculation of the most appropriate volume depends on the severity of the uremic syndrome. In some instances, one should arrange a gradual increase in volume every 10 exchanges from 0.5 – 2.5 L to avoid early fluid leakage.

Careful evaluation of the time required for first exchanges and the drainage volumes obtained enable one to avoid such common errors as abdominal distension due to incomplete drainage or slow filling because of kinking of the catheter.

Glucose (Dextrose) Concentration

Exchanges of 2 L dialysis solution hourly (inflow 10 min, dwell 30 min, outflow 20 min) with 1.5% glucose solutions usually gives an ultrafiltration rate of 50 – 150 mL/hour, which yields 1200 – 3600 mL/24 hours. Using a higher glucose concentration of 2.5 – 4.25%, one can remove larger volumes (200 – 400 mL/hour). In patients with pulmonary edema, 2 or 3 consecutive exchanges (without dwell time) of 4.25% glucose solution may remove up to 1000 mL/hour.

Dwell Time

Decreasing the standard dwell time (30 min) to 15 min and performing two 2 L exchanges/hour will increase the dialysate flow rate to about 4 L/hour (66 mL/min) and will give more efficient dialysis. These higher values are close to the maximum achievable urea clearance of approximately 35 mL/min with a dialysis flow rate of 70 – 80 mL/min. Most patients do not need high flow rates; however they may be used for short periods in hypercatabolic and hyperkalemic patients.

Complications of Acute PD

In addition to infection and acute catheter complications, acute PD may be associated with other more or less serious medical complications.

One may encounter hypervolemia, due to poor ultrafiltration rates, or hypovolemia and hypotension due to excess water removal. Often hypotension is seen with rapid hypertonic exchanges and, when it is severe, it may require temporary discontinuation of dialysis session and infusions of intravenous (IV) saline. Close evaluation of the patient's dialysis regimen, with special attention to the frequency, osmotic strength and volume per exchange can help to avoid this serious complication. Frequent (every 6 hour) blood samples may be required for early correction of electrolyte (hypokalemia) and glucose (hyperglycemia) disorders, which may accompany rapid exchanges. Potassium should be added to the dialysis solution (2 – 4 mEq/L) especially in normokalemic patients with metabolic acidosis and those who receive digitalis to prevent potentially fatal arrhythmias. IV administration of 5% dextrose in water may be required to correct hypernatremia that occurs

with hypertonic dialysis due to excess water removal because of peritoneal membrane's sieving effect.

Patients on acute PD may develop acid – base imbalance in the presence of simultaneous IV administration of bicarbonate solution because of a rapid correction of metabolic acidosis leading to paradoxical acidosis of cerebrospinal fluid (CSF), hyperventilation, and finally alkalosis. Patients with hepatic failure and slow lactate metabolism may also present with elevated plasma lactate levels.

Diabetic patients usually require additional doses of regular insulin intraperitoneally to cover the glucose absorbed during dialysis, as follows: 3 – 4 U/L for 1.5%, 5 – 6 U/L for 2.5% and 7 – 10 U/L for 4.25%. To avoid rebound hypoglycemia one should not administer insulin with the last 3 – 4 exchanges of each dialysis session. Also to compensate for dialysate protein losses (8 – 20 g/24 hours), another noticeable feature of acute PD, oral or IV protein supplementation may be required.

Chronic PD Prescription

In chronic PD, the dose of dialysis must be individualized according to the patient's BSA, RRF, peritoneal-membrane transport characteristics, nutritional status, disease-specific requirements and special clinical circumstances. Chronic dialysis prescription should specify the exchange volume, the dwell time, the number of daily or nightly exchanges, and the composition of the peritoneal fluid in order to provide the most beneficial dose. Adequate dialysis will improve the patient's outcome and the success of long-term PD therapy.

Dialysis Dose

Recent schedules recommend the targets of 1.9 – 2.0 for Kt/V_{urea}, or 60 – 70 L per 1.73 m^2 BSA weekly C_{cr} for continuous PD in patients with RRF [6]. However, with intermittent dialysis or in the absence of residual function, the adequacy indices must be increased to the range of 2.0 and 2.2 for Kt/V_{urea}, and 70 – 80 L per 1.73 m^2 C_{Cr}. It is recommended to provide the maximum dialysis that can be delivered to the individual patient, within the social and clinical circumstances, quality of life, lifestyle and cost considerations.

Initial PD Prescription

One can determine the initial PD regimen by estimating the volumes of fluid that the patient needs in order to achieve the minimal target of solute clearance. As a rule, one should use the highest tolerable volume, based on the patient's discomfort. Assuming that the patient has average peritoneal transport characteristics ($D/P_{creat} = 0.70$), the major determinants are the patient's BSA value and the RRF. Large patients often require large instillation volumes at the beginning of PD unless they have significant RRF. Accordingly, the standard prescription of four 2L exchanges may be modified (Table 5) while further clinical validation is often required [30]. However, Nolph and coworkers [31] have pointed out that a dose of four times 2 liters daily is inadequate for functionally anephric patients weighing > 65 kg. Actually, this weight is near the average of patients starting ESRD therapy.

One determines the total dialysis dose (by dialysis and residual urine) from the 24-hour dialysate and urine collection and the PET 3 – 4 weeks after initiation of dialysis. Then the dose is re-evaluated every 6 – 12 months

Table 5. Possible Initial Dialysis Regimens (Life-Style Choice: CAPD – CCPD)

	GFR (corrected C_{Cr}) > 2 mL/min	GFR (corrected C_{Cr}) 0 – 2 mL/min
CAPD		
BSA 1.7m^2	4 × 2 L/D	4 × 2.5 L/D
BSA 1.7 – 2.0m^2	4 × 2.5 L/D	4 × 3.0 L/D
BSA > 2.0 m^2	4 × 3.0 L/D	4 × 3.0 L/D nightly exchange device
CCPD		
BSA 1.7m^2	4 × 2.0 L/D (9 h/night) + 2.0 L/day	4 × 2.5 L/D (9 h/night) + 2.0 L/day
BSA 1.7 – 2.0m^2	4 × 2.5 L/D (9 h/night) + 2.0 L/day	4 × 3.0 L/D (9 h/night) + 2.5 L/day
BSA > 2.0 m^2	4 × 3.0 L/D (9 h/night) + 3.0 L/day	4 × 3.0 L/D (10 h/night) + 2X2.5 L/day

Assumptions: 70-kg male, anuric, BSA = 1.73 m^2, 4-hour D/P = 0.65, UF = 2 L. From [30].

to compensate for any decrease in residual urine by an increase in the dialysis dose. RRF is monitored at least every 3 months because the decline in RRF is unpredictable and may proceed at different rates in different patients. During the first 2 – 3 years of therapy the most likely change in total solute clearance is a change in the RRF.

Optimizing Instilled Volume and Dwell Time

Usually, to increase solute clearances, it is better to increase the volume per exchange, maintaining the dwell and diffusion time, rather than to increase the number of exchanges with shorter dwell time, unless the patient has high peritoneal transport characteristics. An exchange volume of 2.5 L allows almost all patients to reach C_{cr} and *Kt/V* targets even when they become anuric (Table 5) [30]. A fill volume of 2.5 L seems to give an average-sized individual maximal peritoneal transport, and a volume of 3.0 L suits patients with BSA > 2.0 m^2 [32]. However, one must balance the benefits of increasing clearance by increasing volumes with the risks associated with larger volumes such as

– an increase in hernias due to increased intra-abdominal pressure with larger volumes, and
– an increased peritoneal glucose absorption.

Drain time must also be evaluated because extended drainage may decrease dwell and diffusion times leading to a decrease in clearance. Volume adjustments can be made more easily with cycler-assisted CCPD and NIPD where one merely dials in the new value on the cyclers. Often the patient tolerates larger exchange volumes better on these modalities than on CAPD because most of the exchanges take place with the patient in supine position. However, most of these patients will need "wet" days, i.e. dialysate in the abdomen during the day, especially when they become anuric. Also, increased fill volumes of 2.5 L should be used to improve C_{Cr} in patients on automated PD (APD) (Table 6) [30].

Table 6. Impact of Larger CAPD and APD Fill Volumes

Method	CAPD			APD		
No of exchanges	4	5	4	6	5	4
No of exchanges (day/night)	3/1	4/1	3/1	0/6	1/5	1/4
Exchange volume (mL)	2000	2000	2500	2000	2000	2500
Volume day/night (L)	6/2	8/2	7.5/2.5	0/12	2/10	2/10
Dwell time/day (min)	270	156	270	0	720	720
Dwell time/night (min)	510	510	510	60	78	105
Total C_{Cr} (L/1.73m^2)	56.7	58.9	66.1	31	38	52

Assumptions: 70-kg male, anuric, BSA = 1.73 m^2, 4-hour D/P = 0.65, UF = 2 L. From [31].

According to recent data, changes between treatment modalities with different dwell times may affect the weekly delivered dose because with long cycle therapies such as CAPD, the ratio of weekly C_{Cr} to weekly Kt/V_{urea} is higher in a given patient than with short cycle techniques, such as NIPD. Therefore, if one changes a patient from CAPD to NIPD and the C_{Cr} is kept constant, the weekly Kt/V_{urea} will increase. In contrast, if patients change from CAPD to NIPD and keep the same weekly Kt/V_{urea}, the C_{Cr} will decrease [18].

Dialysis Solution Composition

The composition of PD solution is tailored to correct the electrolyte and acid-base imbalances and restore the normal composition of the body fluids. Most CAPD, CCPD, and NIPD solutions contain similar concentration of Na (132 – 134 mEq/L), Cl (95 – 106 mEq/L), Mg (0.25 – 0.75 mEq/L) and lactate (35 – 40 mEq/L) while Ca concentrations may range from "low" (1.15 – 1.29 mEq/L) to high levels (1.25 – 1.75 mEq/L). Higher dextrose concentrations are used to increase the daily ultrafiltration rate, depending on the patient's transport rates and clinical situation. Table 7 shows typical ultrafiltrate volumes in different PD regimens.

Clinical and Laboratory Monitoring in Chronic PD Therapy

Frequent clinical and laboratory evaluations are required after dialysis is initiated to recognize early and manage effectively any water and electrolytic disorders. Careful evaluations of cardiovascular status, clinical examinations for evidence of early peritoneal complications and accurate records regarding the medical situation and the components of the PD treatment are essential.

By the end of training period (12 – 14 days), routine clinical and laboratory examinations may be instituted (Table 8).

Medications

With the initiation of dialysis, phosphate-binding agents and water-soluble vitamins may be continued at the same doses; usually diuretics and antihypertensive agents need adjustment during the early phases of training.

Table 7. Ultrafiltrate Volumes in Various PD Regimens with 2 L Exchanges

	Exchanges			mL/exchange	Total daily UF (mL)
CAPD					
8 L/D	3 daytime	×	1.5%	3 × 200 = 600	1000
	1 nightly	×	4.25%	1 × 500 = 500	
8 L/D	3 daytime	×	2.5%	3 × 300 = 900	1400
	1 nightly	×	4.25%	1 × 500 = 500	
CCPD					
10 L/D	4 nightly	×	1.5%	1000	800
	1 daytime (14-hour)	×	4.25%	– 200	
10 L/D	4 nightly	×	2.5%	2000	1800
	1 daytime (14-hour)	×	4.25%	– 200	
NIPD (8 – 10 hour)					
15 L/D	7 nightly	×	1.5%		1500
15 L/D	7 nightly	×	2.5%		2000
15 L/D	7 nightly	×	4.25%		2500

Table 8. Laboratory Monitoring of Chronic PD Patients

Every month	Every 3 – 6 months	Every 6 months	Yearly
BUN	RRF	Nerve conduction velocity	Chest X-ray
Creatinine	24-hour urine collection	Bone mineral density	
Sodium	D/P	PTH	
Potassium	PET	EKG	
CO_2	Dialysate protein		
Ca	Weekly C_{Cr}, Kt/V_{urea}		
Mg	NPCR		
Total Protein			
Albumin			
Alk. Phospatase			
Bilirubin			
SGOT			
HCT			
Hemoglobin			

Large doses of loop diuretics (120 – 500 mg of furosemide) may increase diuresis even when urine output has fallen to 100 – 200 mL/day. Commonly diabetic patients need an adjusted dose of intraperitoneal insulin to balance the increased load of glucose.

Complications Other than Peritonitis and Exit-site Care

These complications relate to the peritoneal catheter and the presence of dialysate in the peritoneal cavity, or represent uremic organ dysfunction that develops during PD. This section will discuss the former.

Catheter-related Complications

Surgical wound infection due to contamination is a rare complication. This complication may be prevented by strict adherence to sterile surgical precautions and the prophylactic use of antibiotics against the most frequent causative organisms, *Staphylococcus aureus* and *Pseudomonas species.*

Marked *pain on inflow* of dialysis solution may due to the solution's low pH, its low temperature, to the "jet flow" from the catheter tip or to distension of the tissue around the catheter. This pain my be relieved by alkalization of the dialysis solution with sodium bicarbonate (5 – 25 mEq/L), warming the solution and a choice of lower infusion rates. Usually local abdominal pain around the incision or pelvic pain (urinary bladder) are of minor importance. However, pain that is severe, diffuse or persistent may require clinical and radiographic revaluation. *Localized outflow pain* associated with drainage usually indicates that the omentum or other tissues trap the catheter. Reflex ileus may develop after catheter insertion but usually this only lasts about 24 – 36 hours.

Visceral perforations of bowel, bladder or aorta are major complications that are associated with the blind catheter insertion method.

Bloody dialysate, which is seen frequently after catheter insertion, usually, is due to the lysis of peritoneal adhesions from previous abdominal surgery, or to peritoneal irritation. The presence of bleeding disorders predisposes to this complication. Addition of heparin to the dialysis solution (500 U/L) may prevent fibrin clot formation and possible catheter obstruction.

Dialysate Leakage (Early and Late)

Early pericatheter leakage occurs in about 7 – 29% of midline catheter implantations and in 6.5% after the commonly used paramedian insertion. Predisposing factors for this complication are age > 60 years, obesity, diabetes mellitus, chronic use of steroids, multiparity and a previous abdominal operation. It appears as either a discharge of clear dialysate around the catheter at the exit-site, as localized swelling of the subcutaneous tissue of the anterior abdominal wall or as a genital swelling due to dialysis solution infiltration. Computed tomography (CT) scan after filling the peritoneal cavity with 2 L of dialysate containing 100 mL of the radiocontrast agent diatrizoate meglumine, may help determine the source of the leak. One may stop this leak by using lower fill volumes or by temporary discontinuation of PD for 10 – 14 days. However *leakage that develops late* during dialysis is difficult to correct with conservative measures and may require surgical repair.

Catheter Malfunction (Early and Late)

During the break-in period, in about 15 – 20% of the implanted catheters the peritoneal solution will not flow out – *outflow or one-way obstruction*, or will not flow in either

direction – *two-way or complete obstruction*. Common causes of two-way obstruction are blood or fibrin clots, tissue debris or kinking of the catheter's intramural segment.

Catheter malfunction late in the course of PD can be due either to clot or fibrin debris following episodes of peritonitis or more commonly to catheter dislodgment secondary to constipation, distention of the sigmoid colon, omentum wrapping, and intra-abdominal adhesions. Clinical examination, abdominal X-rays and catheterography may reveal the cause and indicate the correct management. Conservative management includes bowel stimulation by enema and the injection of heparin either to the dialysis bag applying manual pressure, or as an aseptic "flush" of the catheter's lumen with a syringe containing 500 – 1000 U heparin in 20 mL of normal saline. Also one may infuse fibrinolytic agents (streptokinase or urokinase) into the lumen. If these measures fail, the catheter has to be replaced.

Complications Related to Dialysate in the Peritoneal Cavity

The presence of dialysate in the peritoneal cavity increases the intra-abdominal pressure from 0.5 – 1.5 cm H_2O (when it is empty) to 2 – 10 cm H_2O (after filling), and predisposes to the following complications:

– *Hernias.* The constant increase in intra-abdominal pressure may overwhelm the structurally weak abdominal sites and induce several types of hernias – *inguinal, umbilical, incisional, or epigastric;* these have been observed in between 10 – 25% of CAPD population. Except for the patient's degree of physical activity, other predisposing factors are old age, obesity, female gender, multiparity and early pericatheter leak. Because of the risk of bowel incarceration and strangulation, particularly in small hernias, they should be repaired. After hernioplasty, intermittent dialysis with small volumes or hemodialysis is instituted for 2 – 4 weeks before returning to continuous therapy.

– *Abdominal wall and genital edema.* This complication, which develops in about 10% of CAPD patients has been attributed to peritoneal defects at the site of insertion. One should suspect abdominal-wall edema when there is a sudden decrease in effluent volume, and increased abdominal girth and body weight in the absence of edema elsewhere; diagnosis can be confirmed by CT scan using 2L solution with contrast medium. If the edema is refractory to conservative measures, surgical repair of the underlying defect is required.

– *Hemoperitoneum.* This usually self-limited benign complication may appear infrequently at any time during PD therapy. In women it has been related to retrograde menses, ovulation or endometriosis, but many other intra-abdominal events may be responsible for this type of bleeding.

– *Hydrothorax.* Its clinical presentation varies from asymptomatic pleural effusion discovered on routine chest X-ray to life-threatening respiratory failure. Ninety percent of these cases are on the right side, indicating the presence of a diaphragmatic defect – pleuro-peritoneal communication. The diagnosis can be made by intraperitoneal infusion of 2 L dialysate with Tc^{99m} macroaggregated albumin and subsequent detection of thoracic radioactivity. Interruption of CAPD or pleurodesis with talc, tetracycline, or autologous blood or surgical repair have been tried with varying results.

– *Back pain.* This infrequent feature is due to spinal lordosis due to the presence of PD solution, which aggravates pre-exisiting back strain. These patients do well with night dialysis technique.

Ultrafiltration Failure

The most common type of ultrafiltration failure during CAPD therapy is associated with high solute transport and early dissipation of osmotic *gradient (type I ultrafiltration failure:* D/P > 0.8, glucose dialysate levels < 500mg/dL). Frequently it is observed during episodes of peritonitis because of an increased peritoneal membrane permeability that is usually abates as the inflammation resolves. However, ultrafiltration failure may occur in association with decreased peritoneal transport rates of small solutes as a consequence of adhesions and a decrease in peritoneal surface area (*type II ultrafiltration failure:* D/P < 0.5, glucose dialysate levels > 720 mg/dL). This complication has been attributed to severe or recurrent episodes of peritonitis and extensive adhesion formation while, in a few cases, the underlying cause may be the syndrome of sclerosing peritonitis.

The patient's ultrafiltation capacity can be diminished by leakage of the dialysate through the abdominal wall, by patient overhydration and by increased lymphatic absorption of dialysate. For diagnosis, patients with apparent ultrafiltration failure requires measurements of ultrafiltration volume and a PET study.

Although type I ultrafiltration failure can be managed by temporary cessation of PD, lowers fill volumes and a reduction of long dwell, type II ultrafiltration is refractory to conservative measures.

References

[1] *Popovich RP, Moncrief JW, Dechered JF, Bomar JB, Pyle WK* 1976 The definition of a novel portable / wearable equilibrium dialysis technique. Abstract. Trans Am Soc Artif Int Organs *5:* 64

[2] *Diaz-Buxo JA, Walker PJ, Chandler JT, Farmer CD, Holt KL, Cox P* 1981 Continuous cyclic peritoneal dialysis. Excerpta Medica, Amsterdam pp 126-130

[3] United States Renal Data System. USRDS 1998 Annual Data Report National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases. Bethesda, MD, April 1998

[4] *Nolph KD, Twardowski JZ* 1985 The Peritoneal dialysis system. In: Nolph KD: Peritoneal Dialysis. Martinus Nijhoff Publishers, Boston pp 24-44

[5] *Twardowski ZJ* 1990 PET-A simpler approach to determining prescriptions for adequate dialysis therapy. Advances in Peritoneal Dialysis *6:* 186-191

[6] *Blake P, Burkart MJ, Churhill ND et al* 1996 Recommended clinical practices for maximizing peritoneal dialysis clearances. Perit Dial Int *16:* 448-456

[7] *Nolph KD, Sorkin MI, Moore H* 1980 Autoregulation of sodium and potassium removal during continuous ambulatory peritoneal dialysis. Trans Am Soc Artif Inter Organs *26:* 334-337

[8] *Schilling H, Wu G, Petit J et al* 1985 Nutritional status of patients on long term PD. Perit Dial Bull *5:* 12-18

[9] *Hutchinson AJ, Gokal R* 1992 Improved solutions for peritoneal dialysis: physiological calcium solutions, osmotic agents and buffers. Kidney Int *42 (Suppl 38):* S153-159

[10] *Oreopoulos DG, Crasweller P, Katirtzoglou A et al* 1980 Amino acids as an osmotic agent (instead of gucose) in continuous ambulatory peritoneal dialysis. In: Legrain M (ed.): Continuous Ambulatory Peritoneal Dialysis. Amsterdam: Exerpta Medica 335-340

[11] *Krediet TR, Marja M, Ho-dac-Pannekeet et al* 1997 Icodextrin's effect on peritoneal transport. Perit Dial Int *17:* 35-41

[12] *Vas SI* 1984 Etiology and treatment of peritonitis. Trans Am Soc Artif Intern Organs *30:* 682-4

[13] *Watson PE, Watson ID, Batt RD* 1980 Total body water volumes for adult males and females estimated from simple anthropometric measurements. Am J Clin Nutr *33:* 27-39

[14] *Keshaviah P* 1993 Urea kinetic and middle molecule approaches to assessing the adequacy of hemodialysis and peritoneal dialysis. Kidney Int Suppl *40:* S28

[15] Canada-USA (CANUSA) 1996 Peritoneal Dialysis Study Group. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: Association with clinical outcomes. J Am Soc Nephrol *7:* 198

[16] *Brandes JC, Piering WF, Beres JA et al* 1992 Clinical outcome of continuous peritoneal dialysis predicted by urea and creatinine kinetics. J Am Soc Nephrol *2:* 1430

[17] *Blake PG, Sombolos K, Abraham G* 1991 Lack of correlation between urea kinetic studies and clinical outcomes in PD patients. Kidney Int *39:* 700

[18] *Nolph KD, Twardowski ZJ, Keshavian PR* 1992 Weekly clearances of urea and creatinine on PD and NIPD. Perit Dial Int *12:* 298-303

[19] *Tzamaloukas AH, Murata GH, Malhotra D et al* 1996 Creatinine clearance in continuous ambulatory peritoneal dialysis: dialysis dose required for a minimal acceptable level. Perit Dial Int *16:* 41-47

[20] *Rottembourg J, Issad B, Gallego JL* 1982 Evolution of residual renal function in patients undergoing maintenance hemodialysis or continuous ambulatory peritoneal dialysis, Proc Eur Dial Transplant Assoc *19:* 397-401

[21] *Cancarini GC, Brunori G, Camerini C, Brassa S, Manili L, Majorca R* 1986 Renal function recovery and maintenance of residual diuresis in PD and hemodialysis. Perit Dial Bul *6:* 77-79

[22] *Davies SJ, Bryan J, Phillips L, Russel GI* 1996 The predictive value of KT/V and peritoneal solute transport in PD patients is dependent on the type of comorbidity present. Perit Dial Int *16:* S158-S162

[23] *Keshaviah P, Nolph K* 1989 The peak concentration hypothesis: a urea kinetic approach to comparing the adequacy of continuous ambulatory peritoneal dialysis (PD) and hemodialysis. Perit Dial Int *9:* 257-260

[24] *Nolph KD* 1992 What's new in peritoneal dialysis-an overview. Kidney Int Suppl *38:* S148

[25] *Lindsay RM, Spanner E* 1989 A hypothesis: the protein catabolic rate is depended upon the type and amount of treatment in dialysed uremic patients. Am J Kidney Dis *13:* 382-389

[26] *Nolph KD, Moore HL, Prowant B et al* 1993 Cross sectional assesment of weekly urea and creatinine clearances and indices of nutrition in continuous ambulatory peritoneal dialysis patients. Perit Dial Int *13:* 178-183

[27] *Lutes R, Holley Jl, Perlmutter J, Piraino B* 1993 Correlation of normalized protein catabolic rate to weekly creatinine clearance and KT/V in patients on peritoneal dialysis. Adv Perit Dial *9:* 97-100

[28] *Teehan BP, Schleifer CR, Brown J* 1994 Adequacy of continuous ambulatory peritoneal dialysis: Morbidity and mortality in chronic peritoneal dialysis. Am J Kidney Dis *24:* 990

[29] *Churchill DN, Taylor DW, Keshaviah PR* 1996 Adequacy of dialysis and nutrition in continuous ambulatory peritoneal dialysis: association with clinical outcomes. J Am Soc Nephrol *7:* 198-207

[30] *Burkart MJ, Schreiber M, Korbet MS et al* 1996 Solute clearance approach to adequacy of peritoneal dialysis. Perit Dial Int *16:* 457-470

[31] *Nolph KD, Jensen RA, Khanna R, Twardowski ZJ* 1994 Weight limitations for weekly urea clearances using various exchange volumes in continuous ambulatory peritoneal dialysis. Perit Dial Int *14:* 261-264

[32] *Nolph KD* 1996 Has peritoneal dialysis peaked? The impact of the CANUSA study. ASAIO Trans *42:* 136-138