PERITONEAL DIALYSIS,

something old, something new.

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The concept that certain biological membranes might function as mediators of solute exchange dates to about 1922 when Putnam characterized "the living peritoneum as a dialyzing membrane" (1). Less than a year later the German physiologist Ganter employed both the pleural and the peritoneal membranes in dialyses of both uremic dogs and human patients (2). Following these initial reports there appeared sporadic descriptions of peritoneal lavage in a variety of settings, but numerous technical difficulties soon resulted in a loss of enthusiasm for such experiments. By 1948, Odel, Ferris and Power were able to collect a total of 101 patients from the literature who had undergone some form of peritoneal dialysis (3). Of 63 patients with acute renal failure, 31 died; of 32 with chronic irreverisble renal failure, 29 died. Within these two groups, peritonitis was the direct cause of death in at least 6 patients. These early therapeutic trials were less than uniform in that technique, method of administration and composition of the lavage fluid varied widely among investigators. Although the importance of fluid composition and tonicity had been demonstrated in animal experiments as early as 1894, clinical insight into these aspects of peritoneal dialysis were slow to develop (4). Accidents due to overhydration with hypotonic fluid (5) and hypotensive shock due to extremely hypertonic fluid (6,7) were not unusual. Most of these early clinical trials in uremic patients were apparently hampered by a lack of understanding as to the quantity of biogenic waste that must be removed in order to achieve a clinical improvement. In many of these early dialyses the total duration of treatment was only 1/2 to 2-1/2 hours (8), or the volume of dialysate was very small (i.e., 6 liters or less) (9). Under such circumstances an insignificant quantity of metabolic waste is removed.

THE PERITONEUM AS MEDIATOR OF EXCHANGE

The peritoneum has a large surface area (approximately 22,000 cm^2) approximating that of the glomerular capillaries, and certainly larger than the surface area of artificial dialyzers (10,11). The functional area involved in dialysis, however, is likely less than 1000 cm^2 (12,13). In comparison to the parietal peritoneum, the larger surface area and richer vascular supply of the visceral peritoneum would suggest that it predominates in exchange processes. Most solutes removed by peritoneal dialysis probably move from peritoneal capillaries into the peritoneal space. There may be some amount of solute exchange involving the peritoneal lymphatics, but this remains an unknown quantity.

Under optimal conditions of dialysis fluid (dialysate) flow, the maximal clearance of urea achieved with peritoneal dialysis is approximately 30 ml/min (14). This is in contrast to the 100-150 ml/min clearance obtained with man-made, hollow-fiber hemodialyzers. It now appears that the primary limitations on peritoneal solute clearance are interstitial resistance and stagnant fluid films around peritoneal capillaries (15). Gas diffusion studies suggest that peritoneal capillary blood flow is two to three times greater than the maximal urea clearance, and therefore poses little or no limitation on the removal of solute (16). In an effort to clarify the effect of stagnant films and pools of fluid on solute exchange, Nolph and

his associates have operated efficient hollow-fiber hemodialyzers in 2 liter pools of dialysate and observed a striking decrease in the clearance of small molecular weight substances. This remained the case even when the dialysate was vigorously agitated, or even when the dialysate was changed each 15 minutes. These workers concluded that "unstirred" or stagnant fluid layers surrounding the dialyzing surface constitute the major barrier to solute clearance in their model, and, most likely, in the peritoneum (16).

The actual pore size of the peritoneal membrane remains unknown. However, several lines of evidence suggest that the average pore diameter is relatively large (40 anstroms or greater) (17). Endothelial intercellular channels may represent effective paths across the capillary wall. These channels are even larger, at 1-2 microns in width (18). Albumin is removed during peritoneal dialysis, suggesting that large molecules may migrate across the capillary wall under conditions of peritoneal lavage. Furthermore, the peritoneal and perhaps the capillary pore size may not be static. Wayland has shown that the topical application of vasodilators such as histamine and sodium nitroprusside to rat mesenteries results in a visual leaking of fluorescent labeled albumin from the microcirculation into the peritoneum. The increase in albumin movement was much larger than could be explained merely as a result of increased blood flow (19). There has been much recent conjecture, based on the observation that at equivalent levels of azotemia, some patients undergoing maintenance peritoneal dialysis may manifest less uremic symptomatology than do patients on maintenance hemodialysis, that the pore size of the peritoneal membrane is more suited to the removal of putative uremic toxins other than urea (20). Indeed, the peritoneum appears to be significantly more permeable to solutes in the so-called "middle-molecule" range (500-5000 daltons), than artificial dialyzing membranes (21).

PERITONEAL KINETICS

A quantitative understanding of solute and solvent (water) transport in the peritoneum is necessary for an appreciation of the clinical benefits and limitations of peritoneal dialysis. Further, such quantitative data allows comparisons among peritoneal and hemodialysis and native renal function.

In physical terms, the peritoneal membrane is a passive, semipermeable barrier to diffusion between the dialysis fluid and body water compartments. To date, no active transport processes have been implicated in the exchange processes occurring during peritoneal dialysis. The Fick equation for passive diffusion states that the number of moles of solute crossing a passive membrane (Δn) with time (t) will be directly proportional to the concentration gradient of that solute (ΔC), the area of the membrane (A) and the permeability (P).

That is: $$\Delta n = \Delta CAPt$$

Rearranging this expression allows the calculation of the permeability coefficient for a given solute:

$$P = \frac{\Delta n}{\Delta CAt}$$

This permeability coefficient carries the units of velocity (distance per unit time). For the majority of physiological solutes, permeability is inversely related to molecular radius. For charged species such as electrolytes, this functional radius should include any hydration shell (i.e., the Stokes-Einstein radius). For the sake of brevity, it can be simply stated that larger molecular species will diffuse more slowly than smaller ones, and will have less membrane permeability. Because the exact area of the peritoneum available for solute exchange (A) is not known, it is not possible to calculate true permeability coefficients (P). Instead, one must rely on expressions such as "clearance" and "dialysance", which are functional expressions of solute transport, and are both dependent on membrane area and permeability.

Clearance: Simply expressed, clearance is that volume of plasma from which a solute is completely removed in a given time. The clinician is most familiar with the expression for renal clearance of a given substance.

$$C = \frac{UV}{Pt}$$

Where "C" equals clearance (ml/min), "U" equals concentration of the solute in the urine, "V" equals the urine volume, "t" equals time, and "P" equals concentration of the solute in plasma. Addis and Van Slyke have adopted this expression to describe the clearance of substances removed by peritoneal lavage (22).

$$C = \frac{dV}{pt}$$

Where "d" equals the concentration of the substance in the effluent dialysis solution, "V" equals volume of the fluid employed, "p" is equal to concentration of the substance in the plasma at the midpoint time of a dialytic exchange. This calculation will allow an estimation of the overall results of a dialysis, but certain limitations become apparent when more sophisticated information is necessary. In one instance, "d" is usually measured on a small aliquot of fluid obtained from the total effluent at the end of a timed fluid exchange. However, no correction is made for the time necessary for fluid inflow, drainage or dwell. Even more important, no correction is made for the change in the plasma to the dialysate concentration ratio of the measured substance which occurs during the dialysis. Nevertheless, the calculation of peritoneal clearance is useful to establish the approximate rate of removal of a given solute.

Dialysance: In 1969, Nolph and Henderson applied the concept of dialysance to peritoneal dialysis in order to obtain a more quantitative estimate of mass transfer (21). Peritoneal dialysance is defined as the rate of solute removal per unit of driving concentration gradient. Mathematically, the relationship is as follows:

$$D = - \frac{V_b V_d}{V_b + V_d} \cdot Ln \left[\frac{1 - \frac{C_d(V_d+V_b)}{C_b V_b}}{t} \right]$$

Where "D" equals peritoneal dialysance, "V_b" equals volume distribution of a solute within the body, "V_d" equals volume of the dialysis fluid returned at the end of an exchange, "C_b" equals solute concentration in plasma at the exchange midpoint, "C_d" equals solute concentration in the effluent dialysate, and "t" is equal to time.

Even such elaborate mathematical treatments, however, contain inherent assumptions which may lead to error. The above expression, for example, assumes that ultrafiltration (removal of solute-free water) does not occur. The expression further assumes that the diffusion of a solute down its concentration gradient proceeds uniformly throughout the time of an exchange. Though in some situations the first condition can be readily met, the second condition is almost never true.

Ultrafiltration: Dialysis fluids which contain sufficient solute to be hyperosmolar relative to the plasma will result in a net movement of free water into the peritoneal cavity. The degree of hypertonicity, the time that the fluid is allowed to dwell in the abdomen, and the hydrolic permeability of the peritoneal membrane determine the volume of fluid removed. Clinically, the magnitude of this ultrafiltration is determined by subtracting the volume of fluid instilled in the abdomen from the effluent volume. Fluid mobilized from the interstitial and intracellular space subsequently move into the vascular space. Two lines of evidence indicate that fluid removed by ultrafiltration is lost directly from the intravascular space. The observation that hypotension may occur with the rapid removal of one or two liters of ultrafiltrate, while peripheral edema persists, clinically supports this contention. Further, Aune has shown that the ratio of inulin clearance to urea clearance remains unchanged at about 0.15 over an ultrafiltration range of 0 to 3 ml per minute in rabbits. As urea is distributed in the total body water, and inulin is confined to the extracellular compartment, this ratio would be expected to fall if intracellular water contributed significantly to the formation of ultrafiltrate (23). In 1966 Henderson demonstrated that solute, as well as water, was removed when ultrafiltration occurred (24). In simple terms, frictional forces between solute and solvent obligate that both move across the peritoneal membrane. This convective movement of solute can be expressed mathematically as:

$$J_s = C_b \, (1-\alpha) \, J_w$$

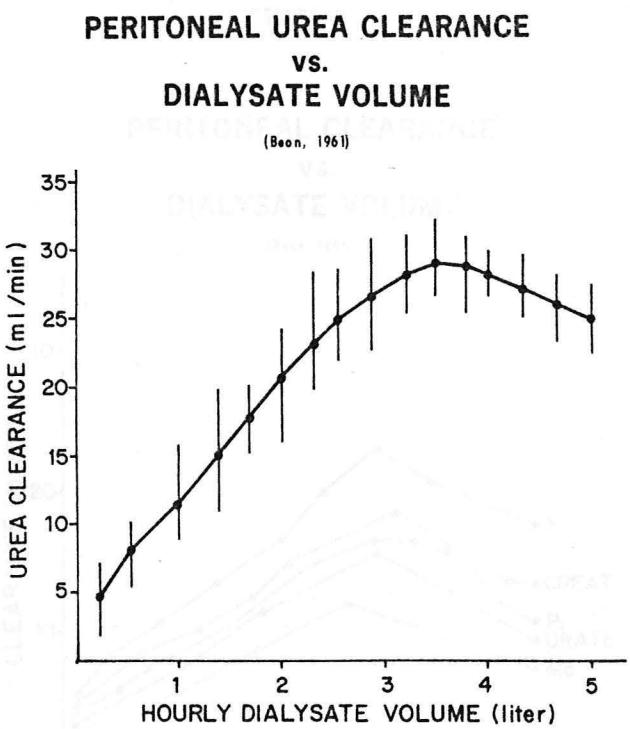
Where "J_s" equals flux rate of solute in question, "C_b" equals concentration of solute in plasma water, "α" equals fraction of the available solute retained by the membrane, and "J_w" equals flux rate of water across

the membrane. The sieving coefficient ($1-\alpha$) is an index of the degree to which the peritoneal membrane permits the passage of the solute in question.

CLINICAL ASPECTS OF PERITONEAL KINETICS

Urea: Of the commonly measured plasma constituents, urea nitrogen is the most efficiently cleared by peritoneal dialysis. The relationship between the rate of peritoneal lavage and urea clearance is shown in Figure 1.

FIGURE 1

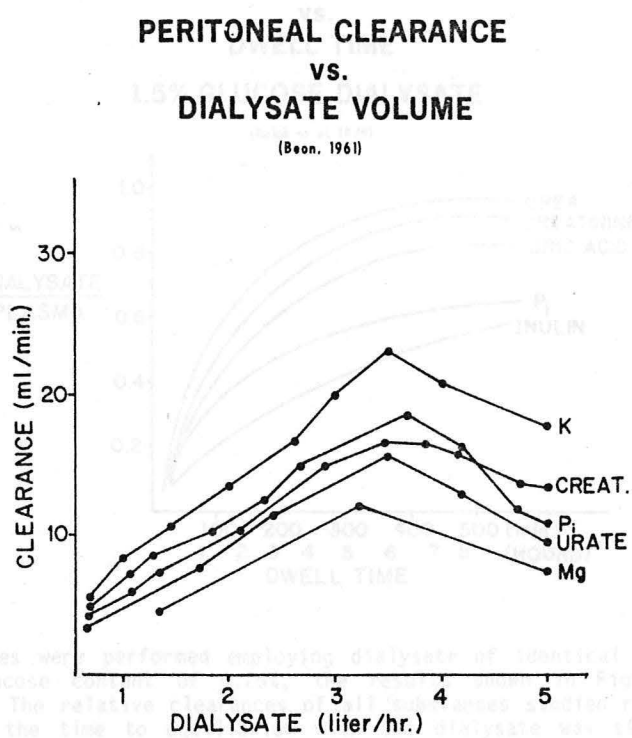


This curve is calculated from 268 clearance studies in 16 patients. Peritoneal urea clearance increases as the flow rate of dialysate increases until a maximum clearance of 28.5 ml/min is reached at a maximum dialysate flow of 3.5 liters/hour. Further increases in the dialysate flow rate result in no further increases and perhaps even a decline in urea clearance (4). This decline in clearance at very high flow rates may be the result of flow through the abdomen so rapidly that no exchange may occur. Employ-

ing a continuous flow method of peritoneal dialysis, Fine et al. have found essentially the same relationship between dialysate flow rate and urea diffusion (6). Assuming that such observations are correct, maintenance of 28.5 ml/min urea clearance would require 84 liters of irrigation fluid per day.

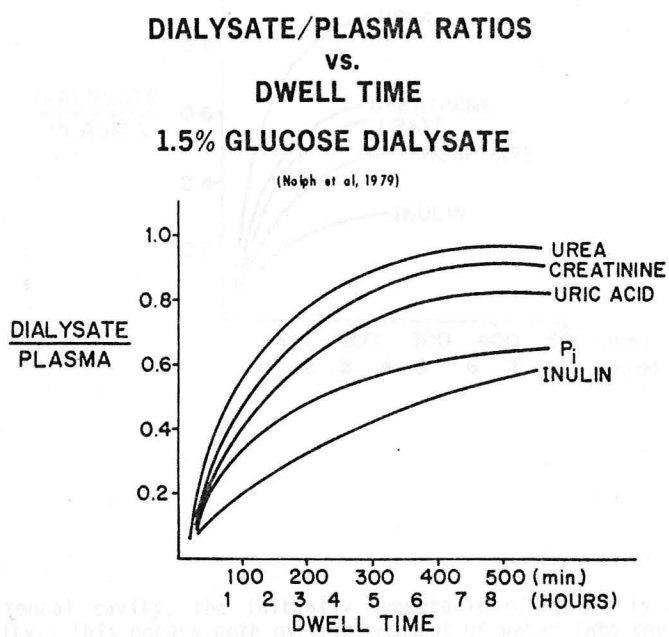
Clearance of other endogenous substances: Figure 2 shows the flow rate to clearance relationships for potassium, creatinine, phosphate, uric acid and magnesium. The peritoneal clearance of potassium is almost as high as urea clearance, at 21 ml/min. This is followed by phosphorus (16 ml/min), creatinine (15 ml/min), uric acid (14 ml/min) and magnesium (11 ml/min). As with urea, the dialysis flow rate at which maximal clearance of these substances occurs is about 3.5 liters/hour.

FIGURE 2



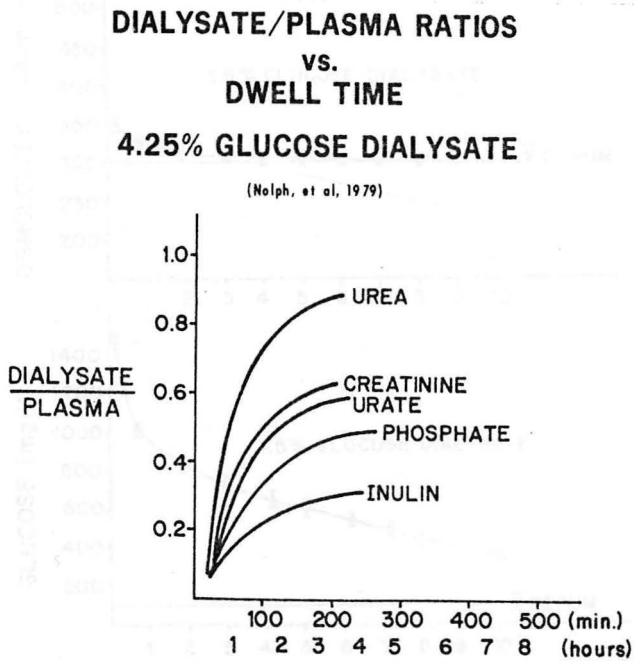
The effect of dwell time on peritoneal clearance: The preceding clearances are based on hourly exchanges of the dialysate. In the late 1970s interest in the use of peritoneal dialysis for long-term management of chronic renal failure spurred interest in longer dwell times, in hopes of decreasing the number of daily exchanges necessary for clinical control of uremic symptoms. Nolph and his associates have investigated the effect of dwell times for up to 8 hours on the removal of various substances. Figure 3 shows the effect of dwell time on the removal of various substances in 5 patients. The fluid employed contained 1.5% glucose. Note that from the time of fluid inflow until about 3 hours of dwell time, the rate of appearance of urea, creatinine, uric acid and phosphorus into the peritoneal fluid was essentially linear with time. The removal of these substances all reached plateau values by about 5 hours of dwell. When the

FIGURE 3



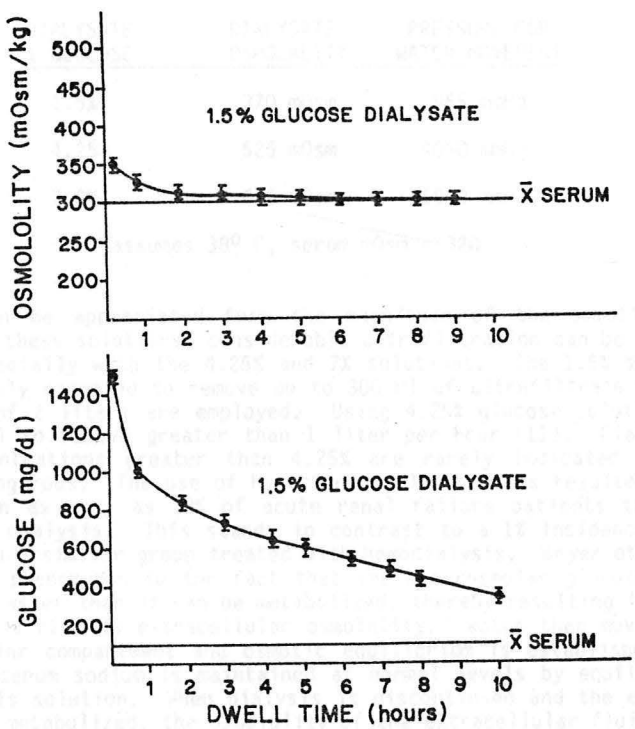
same studies were performed employing dialysate of identical composition except glucose content of 4.25%, the results shown in Figure 4 were obtained. The relative clearances of all substances studied remained the same, but the time to equilibrium with the dialysate was significantly reduced. Employing this glucose concentration, the rate of movement of the substances from the plasma to the dialysate reached plateau levels in less than 3 hours. At the same time that endogenous substances are moving into

FIGURE 4



the peritoneal cavity, the initially hypertonic dialysate is approaching isotonicity. This occurs both by the movement of water into the peritoneal cavity (ultrafiltration), and the absorption of dialysate glucose. Figure 5 shows the relationship of dialysate dwell time and glucose content (lower panel), and osmolarity versus dwell time (upper panel). By 4 hours of dwell, tonicity of the dialysate is essentially equal to that of the plasma. The glucose concentration of the dialysate, initially 1500 mg% (1.5%), decreases to approximately half of that value.

FIGURE 5



Water movement: When the dialysate is made hypertonic to plasma by the addition of glucose, water moves into the peritoneal cavity. Commercial dialysis fluids are available with 1.5% glucose (372 mosmoles/liter), or 4.25% glucose (525 mosmoles/liter). A dialysate containing 7% glucose (678 mosmoles/liter) was previously available, but has now been withdrawn from most markets. Of course, glucose may be added to commercial solutions to achieve almost any desired osmolality. Because most chronically uremic patients have a serum osmolality greater than 300 mosmoles/liter, 1.5% glucose dialysate is considered essentially isotonic to such plasma and relatively little ultrafiltration is expected. This may not, however, be the case in patients with acute renal failure and considerable ultrafiltration may occur with 1.5% glucose solutions. As one increases the glucose concentration of any given dialysate, ultrafiltration will increase proportionately. Table I shows the osmolality of dialysate fluids containing 1.5%, 4.25% and 7% glucose, and the osmotic pressure each solution exerts on the peritoneum in a chronic renal failure patient with a serum osmolality of 320 mosmoles/liter.

TABLE I

OSMOTIC DRIVING FORCE FOR WATER MOVEMENT

DIALYSATE % GLUCOSE	DIALYSATE OSMOLALITY	PRESSURE FOR WATER MOVEMENT
1.5%	370 mOsm	965 mmHg
4.25%	525 mOsm	4050 mmHg
7.0%	678 mOsm	6950 mmHg

*assumes 38° C, serum mOsm = 320

As can be appreciated from the magnitude of the osmotic pressure exerted by these solutions, considerable ultrafiltration can be expected to occur, especially with the 4.25% and 7% solutions. The 1.5% solution can be reasonably expected to remove up to 300 ml of ultrafiltrate when hourly exchanges of 2 liters are employed. Using 4.25% glucose solutions, it is not unusual to remove greater than 1 liter per hour (11). Dialysate glucose concentrations greater than 4.25% are rarely indicated and may be frankly dangerous. The use of hypertonic solutions has resulted in hypernatremia in as many as 13% of acute renal failure patients treated with peritoneal dialysis. This stands in contrast to a 1% incidence of hypernatremia in a similar group treated with hemodialysis. Boyer et al. attributes this phenomenon to the fact that the hyperosmolar glucose may enter the blood faster than it can be metabolized, thereby resulting in hyperglycemia, and a rise in extracellular osmolality. Water then moves from the intracellular compartment and osmotic equilibrium is established. During this time serum sodium is maintained at normal levels by equilibrium with the dialysis solution. When dialysis is discontinued and the excess serum glucose is metabolized, the osmolality of the extracellular fluid falls and water moves back into the intercellular space resulting in a rise in serum sodium (25).

PHARMACOLOGIC ENHANCEMENT OF PERITONEAL CLEARANCES

As previously cited, under normal conditions peritoneal clearance of most solutes is not limited by peritoneal blood flow. However, in the presence of blood volume depletion, intense vasospasm, decreased cardiac output, or microcirculatory disease involving platelet thrombi, peritoneal blood flow may be sufficiently disrupted as to reduce peritoneal solute clearance. Under such circumstances repletion of blood volume, treatment of vasospasm with antihypertensive drugs, or the administration of antiplatelet-aggregating agents such as dipyridamole given systemically may improve clearance (26).

The administration of drugs, hormones or prostaglandins that vasodilate can accelerate peritoneal mass transport rate even if the peritoneal blood flow has not previously been reduced. Studies indicate that clearances will increase only if the compound selectively dilates the splanchnic vasculature or is applied locally by intraperitoneal instillation.

Nitroprusside and isoproterenol increase clearances to more than 150% of control values when given intraperitoneally (27). This increase in peritoneal transport is not accompanied by evidence of nonspecific inflammation such as increased leucocytes in the dialysate. Note that the use of intravenous agents which caused widespread vasodilitation may actually decrease peritoneal clearance as a result of generalized hypotension. When given intravenously, dopamine increases splanchnic blood flow and peritoneal transport rates by virtue of adrenergic receptor-mediated somatic vasoconstriction raising perfusion pressure and dopaminergic receptor-mediated splanchnic vasodilitation (28).

Because of the inhibition of transport by membrane charge, drugs that affect membrane charge may increase solute transport. Accordingly, increases in sodium removal occur when furosemide is added intraperitoneally during hypertonic peritoneal dialysis, and increased mass transport of urea and inulin result when protamine sulfate is added to the peritoneal dialysis solution (29,30).

Peritoneal capillary permeability may be increased directly by the local application of a number of drugs which have been eluded to in previous sections of this review. Histamine, and dioctyl sodium succinate are examples of such agents (31).

Augmentation of the transport of specific solutes may be achieved by the addition of appropriate drugs. For example, the intraperitoneal instillation of albumin or Tris buffer can enhance barbiturate removal and lipid promotes glutethimide transport. Certain chelators such as EDTA can augment removal of certain heavy metals, such as lead (32).

COMPOSITION OF THE DIALYSATE

Table II shows the composition of commercially available solutions for peritoneal dialysis (Dianeal®, Travenol Laboratories, Inc., Morton Grove, Ill.). In simplest terms, dialysis fluids are designed to permit maximal removal of endogenous waste products and toxins, to correct acid-base disturbances, and to prevent significant absorption of the fluid from the peritoneal cavity. The electrolyte composition is such as to mimic the ideal composition of potassium-free extracellular fluid. In this way, any electrolyte abnormality will tend to be corrected by movement of the involved ions along their concentration gradients. Potassium is omitted from most available dialysis fluids except Dianeal K® (4.0 mEq/L), because hyperkalemia is a frequent concomitant of situations in which dialysis is required.

TABLE II

COMPOSITION OF COMMERCIALLY AVAILABLE PERITONEAL DIALYSATES

	PREPACKAGED SOLUTIONS	PROPORTIONING SYSTEMS
Sodium (mEq/L)	141	129-137
Potassium	0 or 4.0	0
Chloride	101 or 105	96-102
Calcium	3.5	3.4-3.6
Magnesium	1.5	0.5
Lactate (mM/L)	45	37-39
Glucose (gms/L)	15-70	5-35
Osmolality (mOsm)	372-678	300-450

The sodium and chloride concentrations (141 and 101, respectively) are generally acceptable and result in normal serum concentrations of these ions at the end of dialysis. The occurence of hypernatremia has been addressed in the preceding section. Maxwell, however, has observed that the use of dialysate with sodium concentrations of 120 to 130 mEq/L reduced the incidence of hypernatremia and may result in a net removal of significant amounts of sodium (33).

As noted earlier, potassium is cleared by peritoneal dialysis at a rate similar to that of urea. Work by Brown et al. has shown that potassium in the dialysate equilibrates with the extracellular rather than the intracellular fluid (34). Thus, the use of potassium-free dialysate to treat hyperkalemia does not result in a rapid loss of potassium from body stores. Given a patient with a serum potassium of 8 mEq/L and hourly 2 liter exchanges of dialysate, one could expect to remove a maximum of 8 to 12 mEq of potassium per hour. A normal 80 kg adult must lose 200 to 300 mEq of potassium in order to lower the serum concentration by 1 mEq/L (22). If hyperkalemia is not present, one may select a dialysate potassium concentration which reflects the desired serum concentration. However, the clinician must be aware of factors which affect potassium movement between the intracellular and the extracellular space and the possible interaction with drugs, notably cardiac glycosides. The amount of potassium added to the dialysate is a decision involving many factors, some of which are listed in Table III. The correction of acidosis and the tissue uptake of

TABLE III

FACTORS INFLUENCING THE SERUM POTASSIUM
IN DIALYSIS PATIENTS

1) Acid-base status

2) Carbohydrate metabolism

   a) Uremia
   b) Glucose loads
   c) Diabetes

3) Extensive trauma - tissue destruction

4) Hypercatabolic states

5) Digitalis

of dialysate glucose will tend to lower the serum potassium. Extensive trauma, especially if accompanied by large areas of devitalized tissues, and patients who are severely catabolic, can be expected to release large amounts of potassium and, thus, should be closely monitored for electrocardiographic manifestations of potassium toxicity. On the other hand, hypokalemia must be avoided if the patient is receiving digitalis. Maher and Schreiner have reported a high incidence of arrhythmias, some of which proved fatal, in patients undergoing dialysis (35). When dialysis is indicated in a patient taking digitalis preparations, the serum potassium should be maintained in a range of 4.0 to 5.0 mEq/L.

The calcium concentration of available solutions is generally 3.5 mEq/L. This concentration is equal to or slightly greater than the ionized concentration in the serum of most patients. Therefore, calcium is usually absorbed by the patient. This situation may aggravate digitalis toxicity, and if serum phosphorus is markedly elevated, may contribute to soft tissue calcification. The magnesium concentration of available dialysate is 1.5 mEq/L. Most uremic patients do not have elevated serum magnesium levels and this concentration is acceptable. It should be noted that Burnell has suggested that the use of low magnesium (0.5 mEq/L) dialysate may improve the metabolic bone disease of uremia (36). This is presumably a result of the impaired end-organ sensitivity to parathyroid hormone in states of relative magnesium deficiency. However, the efficacy and safety of low magnesium dialysate solutions remains to be determined.

In most situations, bicarbonate cannot be added to dialysate solutions because of the simultaneous presence of calcium. Therefore, all available solutions contain lactate or acetate. Early studies by Dixon et al. have shown that essentially all the lactate present in dialysate fluids (45 mEq/L) is absorbed in 80-90 minutes (37). In patients with normal hepatic function, lactate is rapidly converted to bicarbonate and plasma lactate concentrations never exceed the normal range. This rapid metabolism of

lactate to bicarbonate maintains the high dialysate to plasma lactate gradient necessary for continued absorption. Acetate, which is metabolized largely by peripheral tissues, has replaced lactate in hemodialysis systems. Similar to lactate, acetate is rapidly converted to bicarbonate. Several years ago, Borchardt and Richardson showed that acetate was modestly bacteriostatic in vitro and suggested that its use in peritoneal dialysate might reduce the frequency of peritonitis (38). However, later work showed that the addition of small amounts of plasma protein, such as occurs in the abdomen, completely eliminated any bacteriostatic effect (39,40).

The use of glucose as an osmotic agent in peritoneal dialysate has been discussed above. Figure 5 shows the rate of disappearance of glucose from the dialysate as a function of dwell time. In the case of both 1.5% and 4.25% glucose dialysate, glucose is rapidly absorbed from the peritoneum. In 4 nondiabetic patients studied by Boen and his associates, employing 1.5% glucose dialysate and 2.5 liter/hour exchanges, each patient absorbed between 300 and 720 g of glucose/day (4). The amount of insulin secreted as a result of the glucose absorbed is variable. As a result, the prediction of blood sugar concentrations is difficult at best, especially when one considers the carbohydrate intolerance of uremic patients (41). In nondiabetic patients, however, it is unusual to observe blood glucose levels greater than 500 mg/dl, even when 4.25% glucose is employed (42). Nolph has reported a range of 207 to 727 mg/dl for 9 patients treated with three consecutive exchanges containing 7% glucose (42). Certainly, hyperglycemia has been noted when hypertonic glucose is employed in the dialysate (43-45) and hyperosmolar coma, usually in a diabetic patient, can occur (46).

Sorbitol has been suggested as an alternative to glucose in dialysis solutions. Sorbitol is less permeable than glucose, but when absorbed is metabolized to fructose in the liver, presumably making the problem of hyperosmolar coma less likely. It should be noted, however, that at least one death has resulted from such dialysate (47). Further, Sorbitol has been implicated in peripheral neuropathies and the formation of cataracts (48).

Fructose has also been employed in peritoneal dialysates. The absorption of this hexose is similar to glucose, although it has been reported that the subsequent rise in total blood reducing substance (sugars, glucose and fructose) is significantly less than that which occurs with similar dialysate concentrations of glucose alone (49). This is attributed to the rapid uptake and metabolism of fructose by the liver. Though the use of fructose in peritoneal dialysis appears safe, several factors should be borne in mind. First, the use of intravenous fructose has resulted in lactic acidosis in patients with diabetic ketoacidosis or hypotension (50). Secondly, impaired liver function will prevent the metabolism of fructose with potentially disasterous consequences. Like Sorbitol, the blood concentration of fructose cannot be lowered by insulin. Therefore, glucose may be preferable to fructose if for no other reason than hyperglycemia can be effectively controlled with insulin.

Other additives: There are essentially no prospective studies to confirm or refute the value of routinely adding heparin to peritoneal dialysate solutions. It is common practice to add 500-1000 units of heparin to each liter of dialysate in order to prevent fibrin clot formation in the peritoneal catheter. This small amount of anticoagulant is likely harmless, but is also probably unnecessary after the first 3 to 4 exchanges, at which time the initial bleeding resulting from abdominal puncture should have ceased.

Antibiotics: There is no data to indicate that the routine use of antibiotics in peritoneal dialysate reduces the instance of infection. In the past, chloramphenicol has been advocated for such purposes, principally because of its low rate of absorption from the peritoneum (51). This practice has not been continued, as it is now apparent that efforts to avoid contamination are significantly more effective in preventing peritonitis than is the prophylactic use of any antibiotic. The addition of antibiotics to peritoneal dialysate may be indicated in a variety of conditions, the most common of which is peritonitis. Frequently a patient undergoing peritoneal dialysis will require antibiotic treatment for an associated illness. Under these circumstances it is necessary that the clinician know if the antibiotic of choice is removed by the dialysis process. Such is the case for cephalosporins, aminoglycosides and numerous other agents. Under these circumstances it is frequently advisable to add the antibiotic to the dialysate at the desired serum concentration. Tables IV-VI are a compilation of data regarding the absorption and removal of antimicrobial agents in patients undergoing peritoneal dialysis.

TABLE IV

THE USE OF ANTIBIOTICS IN PERITONEAL DIALYSIS PATIENTS

DRUG	ABSORPTION FROM DIALYSATE	REMOVAL FROM BLOOD	DOSE ADJUSTMENT	REF
Penicillin G	yes	no	<4 MU/D	52
Ampicillin	yes	no	none	53
Methicillin	yes	no	none	54
Isoxazolyl penicillins	yes	no	none	53
Carbenicillin	yes	yes	2 g Q 6-12 h	55
Cephalothin	yes	yes	none	56
Cephalexin	yes	yes	none	56
Cephamandole	----------no data available----------			
Cephoxitin	----------no data available----------			
Clindamycin	? (no)	no	none	57
Chloramphenicol	slight	no	none	56
Erythromycin	? (no)	? (no)	none	56
Tetracyclines	-----should be avoided in renal failure----			
Gentamicin, Tobramycin, Amikacin	yes	yes	Load parenterally-maintenance via dialysate*	58-60
Vancomycin	no	no	gm/week	61

*Add drug to dialysate at the desired concentration

TABLE V

THE USE OF ANTITUBERCULOUS DRUGS IN PERITONEAL DIALYSIS PATIENTS

DRUG	ABSORPTION FROM DIALYSATE	REMOVAL FROM BLOOD	DOSE ADJUSTMENT	REF
Ethambutol	?	yes	*10-12 mg/kg/d	62
Rifampin	? (no)	? (no)	none	63
Isoniazid	? (no)	slight	none	64
Ethionamide	?	? (no)	none	65
Para-amino-salicylic acid	?	?	**decrease	65
Streptomycin	yes	yes	0.5 g QD	60

*lower than the nationally recommended dose; may prevent optic neuritis
**PAS-is usually not recommended in renal failure patients

TABLE VI

THE USE OF ANTIFUNGAL AGENTS IN PERITONEAL DIALYSIS PATIENTS

DRUG	ABSORPTION FROM DIALYSATE	REMOVAL FROM BLOOD	DOSE ADJUSTMENT	REF
Amphotericin B	?	? (no)	none	67
5-Fluorocytosine	? (yes)	yes	25-50 mg/kg each 48-72 h*	68
Miconazole	no	no	none	69

*dose recommendation for hemodialysis patients

TECHNICAL ASPECTS AND CLINICAL APPLICATIONS

A number of varying techniques now allow the use of the peritoneum for both temporary dialytic therapy and the management of chronic renal failure. In the case of acute renal failure, when dialysis will be required for only a limited period of time, peritoneal dialysis is accomplished by the placement of a temporary catheter, 4-8 cm below the umbilicus. It is necessary that the abdomen be prepared as if for surgery, but the catheter may usually be inserted by an experienced internist at the patient's bedside. Following the placement of such a catheter, dialysis is undertaken with commercially available solutions, as described in the previous section. In general, each exchange consists of 2 liters of fluid warmed to body temperature prior to instillation. Warming the dialysate not only avoids unnecessary discomfort and loss of body heat, but also increases the

clearance of most putative uremic toxins. Fluid is instilled in the abdomen as rapidly as it will run. With the administration sets available at Parkland, this will require a minimum of 10 minutes. Dwell times will, vary but generally should not exceed 30 minutes. Thereafter, the fluid is drained by gravity as rapidly as possible. The total time for each exchange should not exceed 1 hour. A technical mistake that unnecessarily prolongs many dialyses is the attempt to recover the instilled volume in its entirety despite unduly slow outflow. It is far better to proceed to the next exchange whenever drainage converts from a steady stream to a drip. Positive fluid balance cannot proceed indefinitely, but a positive reservoir of 1 or even 2 liters often allows the outflow volume to again equal the inflow volume yet with rapid drainage. Hourly exchanges should continue for no more than 48 hours. The risk of peritonitis increases strikingly after that time. As previously mentioned, antibiotics should not be routinely added to the dialysate, but samples of the effluent dialysate should be checked for cell count and bacterial growth each 24 hours. Table VII outlines the common problems encountered with acute peritoneal dialysis. These data were obtained from 184 dialyses performed on 107 patients (70).

TABLE VII

TECHNICAL PROBLEMS OCCURRING WITH ACUTE PERITONEAL DIALYSIS

Pain (73%)	
Minimal	18 %
Moderate (required analgesic)	52
Severe (dialysis terminated)	2.4
Hemorrhage (32%)	
Minimal (pink drainage after 4 h)	21
Moderate (frankly bloody drainage)	10
Severe (required transfusion)	1
Inadequate Drainage (37.5%)	
Loss of siphon	24.4
Catheter occlusion	11.0
Preperitoneal catheter placement	1.6
Peritoneal loculation	0.5
Leakage (36%)	
Minimal	15
Moderate (frequent dressing changes)	13
Severe	8
Other (8.2%)	

From: Vaamonde, 1977

Indications for acute peritoneal dialysis: Certainly the most frequent and important indication for peritoneal dialysis is acute renal failure. There are no absolute contraindications to peritoneal dialysis. Rather, in most cases of drug overdoses, renal failure complicated by hypermetabolism, the presence of extensive abdominal adhesions, or the presence of a synthetic abdominal aortic graft, hemodialysis is likely the treatment of choice. In addition, a number of other abdominal conditions, such as hernia, undiagnosed abdominal disease, markedly distended bowel, abdominal wall infection, tense asites, or very large polycystic kidneys may represent relative contraindications to peritoneal dialysis.

Peritoneal dialysis is preferred to hemodialysis in a number of situations: 1) infants; 2) when active bleeding is present or the risk of anticoagulation is great; 3) when vascular access cannot be obtained; 4) when the patient is hypotensive or when severe heart disease is present; 5) when peritonitis complicates acute renal failure; and 6) when massive diuretic resistant fluid overload is the only reason for dialysis.

Complications of acute peritoneal dialysis: Although generally assumed to be a safe procedure, the morbidity and mortality with peritoneal dialysis can be considerable. In one series involving two teaching hospitals where patients underwent peritoneal dialysis on general medical wards, only 1/3 of the dialyses were accompanied by no or minor complications (70). The mechanical (technical) complications have been outlined in Table VII. Table VIII shows the complications which occurred during these 184 peritoneal dialyses. It should be noted, however, that the majority of these complications did not require the termination of dialysis.

TABLE VIII

MEDICAL COMPLICATIONS OF ACUTE PERITONEAL DIALYSIS

	(%)
Cardiovascular (15%)	
Pulmonary edema	1.6
CHF	0.5
Anasarca	3.3
Pulmonary (22%)	
Atelectasis	7.6
Aspiration	1.6
Pneumonia	7.1
Pleural Effusion	5.4
Respiratory Arrest	0.5
Metabolic (45%)	
Hyperglycemia (300-1100 mg/dl)	8.6
Hyperkalemia (>5 mEq/L)	6.0
Hypokalemia (<3 mEq/L)	10.3
Hypernatremia (>150 mEq/L)	8.2
Hyponatremia (<130 mEq/L)	2.2
Metabolic alkalosis (>30 mEq/L)	6.5
Other	3.2

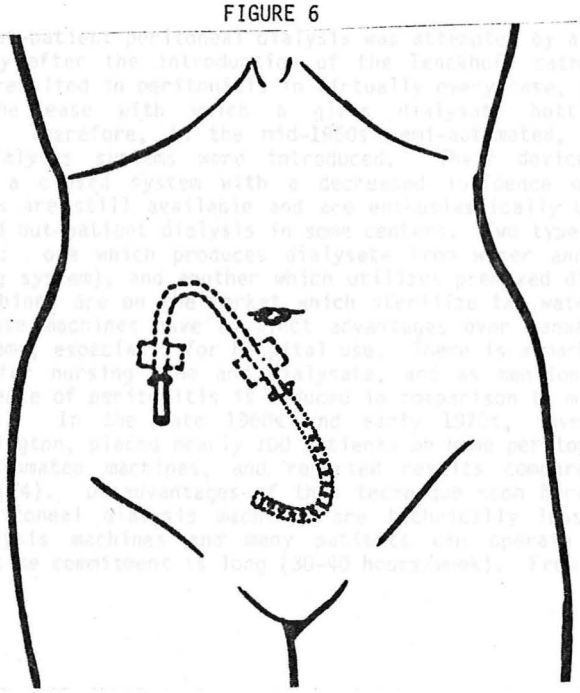
From: Vaamonde et al., 1975

Intra-abdominal trauma is a special consideration for any physician who is called upon to perform a peritoneal dialysis. Perforations of the bowel are most likely to occur in unconscious or cachectic patients or those who have had previous abdominal surgery or peritonitis. Though some authors suggest that pain is a marker of bowel perforation, many series (Table VII) indicate that pain with peritoneal dialysis is very common but bowel perforation is relatively uncommon. Perforation is suggested by failure of a dialysate to return from the abdomen, watery diarrhea, cloudy, malodorous or feculent effluent dialysate. If a bowel puncture is small and the catheter is promptly removed, the perforation will usually seal within 12 hours. Generalized peritonitis rarely develops, but localized signs of peritonitis are common. Under such circumstances, one should continue dialysis and administer antibiotics both systemically and intraperitoneally (71). A few simple precautions will usually reduce the risk of intra-abdominal trauma. The urinary bladder should be emptied prior to dialysis catheter insertion, and 1 to 2 liters of dialysate should be infused into the peritoneal cavity through a long, large-bore needle. This will provide a cushion for catheter insertion. Using these precautions, Vaamonde and his associates reported no cases of intra-abdominal trauma in greater than 175 consecutive peritoneal dialyses (72).

CHRONIC PERITONEAL DIALYSIS

Approximately 10 years ago two technical advances, the development of a bacteriologically safe peritoneal catheter and automated dialysate delivery system, generated the first interest in peritoneal dialysis as a chronic treatment for end-stage renal disease. The silastic Tenckhoff catheter (Figure 6) has made repeated peritoneal puncture unnecessary and permits

FIGURE 6



almost infection-free long-term access to the peritoneal cavity (72). With the aid of a trocar, the catheter is inserted under a local anesthetic. One of two dacron felt cuffs rests in the subcutaneous tissue above the peritoneum. The catheter is placed in an arcuate subcutaneous position. The distal dacron cuff is left just below the skin. These two cuffs allow connective tissue ingrowth, which serves both to anchor the catheter and also as a barrier to infection. After about 6 weeks, the patient may bathe and even swim without fear of infection. These catheters remain remarkably free of infection. However, an occasional superficial infection occurs at the catheter exit site. These are almost always due to Staphylococcus, and may be treated conservatively with antibiotics. However, if the infection involves the dacron cuff, it may be suppressed but cannot be irradicated with antibiotics, and elective replacement is in order (74).

A second problem unique to this type of catheter is erosion of the dacron cuff through the abdominal wall. This is always the result of a subcutaneous tunnel made too short at the time of implantation. The subsequent cuff erosion is a result of pressure necrosis. Infection is not usually a factor in cuff erosion, but may occur if the catheter is not electively repositioned. The Tenckhoff catheter has undergone a number of minor modifications, including the attachment of an inflatable saline-filled balloon to the intraperitoneal portion of the catheter which allegedly keeps the tip of the catheter in the pelvis (75). Another recent modification has been the placement of several plastic disks around the intraperitoneal portion of the catheter to prevent outflow occlusion of the drainage holes by the omentum (76).

HOME DIALYSIS

Manual out-patient peritoneal dialysis was attempted by a few investigators shortly after the introduction of the Tenckhoff catheter. These early trials resulted in peritonitis in virtually every case, probably as a result of the ease with which a glass dialysate bottle could be contaminated. Therefore, in the mid-1960s semi-automated, fully closed peritoneal dialysis systems were introduced. These devices offer the advantage of a closed system with a decreased incidence of infection. These machines are still available and are enthusiastically used for both in-patient and out-patient dialysis in some centers. Two types of machines are available: one which produces dialysate from water and concentrate (proportioning system), and another which utilizes premixed dialysate. At least two machines are on the market which sterilize tap water by reverse osmosis. These machines have distinct advantages over manual peritoneal dialysis systems, especially for hospital use. There is a marked reduction in the cost for nursing time and dialysate, and as mentioned above the overall incidence of peritonitis is reduced in comparison to manual peritoneal dialysis. In the late 1960s and early 1970s, investigators in Seattle, Washington, placed nearly 100 patients on home peritoneal dialysis using semi-automated machines, and reported results comparable to home hemodialysis (74). Disadvantages of this technique soon became apparent. Automated peritoneal dialysis machines are technically less complicated than hemodialysis machines and many patients can operate them alone; however, the time commitment is long (30-40 hours/week). From the point of

view of most patients, automated home peritoneal dialysis offers no clear-cut advantage over hemodialysis. The patient and his movements are still restricted by his machine. Further, the cost of automated peritoneal dialysis was equal to and in most cases greater than home hemodialysis.

In 1976 Popovich, Moncrief et al. described the technique of continuous ambulatory peritoneal dialysis (CAPD) (77). As with other forms of chronic peritoneal dialysis, a Tenckhoff catheter was employed, but this new method used the continuous presence of dialysate (24 hour/day, 7 days/week) in the peritoneal cavity. Exchanges were performed five times each 24-hour period. Dwell time averaged 4 hours during waking hours and 8 hours overnight. Two years later these same authors published the results of CAPD in 9 patients for a total of 136 patient weeks (77). Their results were, to say the least, encouraging. In virtually every case, serum chemistries remained at levels maintained by hemodialysis or to some extent improved. The hematocrits of these patients improved from 24 $\pm$ 5% to 32 $\pm$ 5% after 18 weeks of CAPD. Protein loss in the peritoneal effluent was significant, averaging about 2.0 g with each 4-hour exchange and over 5 g with 8-hour (overnight) exchanges. Nevertheless, these patients were able to maintain a mean serum albumin concentration of 3.8 $\pm$ 0.2 g/dl after 11 weeks and in one patient after 22 weeks of CAPD the serum albumin was 3.5 mg/dl. The protein loss in these patients was no doubt offset by an increased protein intake of 1 g/kg/day. Table IX compares the clearances of urea and vitamin B-12 (a middle molecule marker) achieved with CAPD to intermittent peritoneal dialysis, hemodialysis and normal renal function. As this table demonstrates, the clearance of small molecular weight substances such as urea was less with CAPD than with hemodialysis, but greater than with ordinary intermittent peritoneal dialysis. However, substances of the size generally held as middle molecules, such as vitamin B-12, were cleared better by CAPD than by either IPD or hemodialysis.

TABLE IX

CLEARANCES BY VARIOUS DIALYSIS TECHNICS AND NORMAL KIDNEYS (LITERS/WEEK)

SOLUTE	2 NORMAL KIDNEYS	HEMODIALYSIS 15 HR/WK	INTERMITTENT P.D. 40 HR/WK	CAPD
Urea	604	135	60	85
B_{12}	1008	30	16	50

From: Popovich et al., 1978

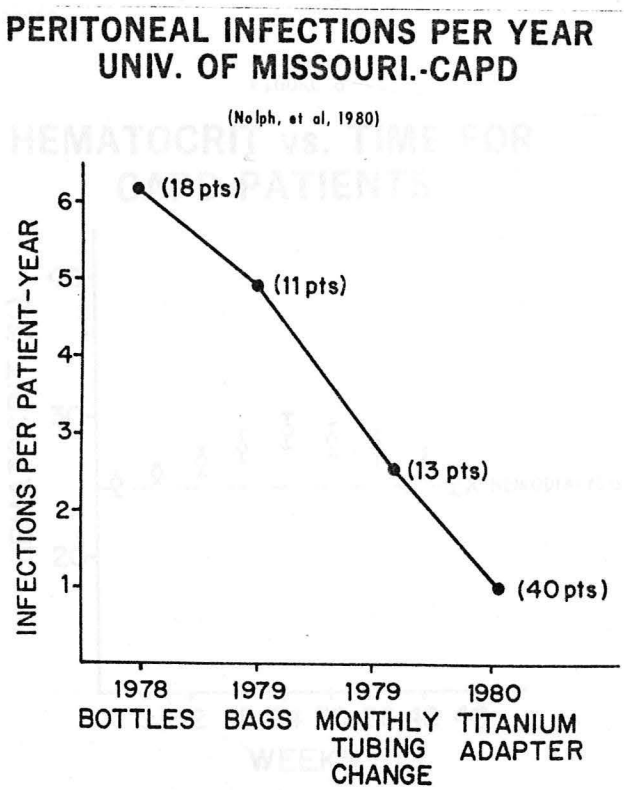
Perhaps the most striking result of this early study was the tremendous enthusiasm for the technique expressed by the patients. Virtually all patients reported an increased sense of well being, increased appetite and energy. Most patients increased their daily activities above the level at which they had performed for years. However, this new technique which promised so much was not without problems. There were 13 episodes of bacterial peritonitis during the 136 patient weeks. One patient, apparently unable to master the skills necessary to change his fluid containers in an aseptic manner, developed peritonitis four times in 11 weeks and was subsequently restarted on maintenance hemodialysis. Nevertheless, the authors felt that this rather high rate of peritonitis was primarily a technical problem that could be overcome.

Rubin and his associates followed 18 patients on CAPD for a period of 24 months or 136 patient weeks, and reported 97 episodes of infective peritonitis. This represents 37 episodes per patient year. In 54 of these episodes hospitalization was required. In the remaining 43 cases, therapy was initiated and completed at home. Sixteen of the 97 episodes occurred while the patient was hospitalized for reasons other than peritonitis. Of the 97 episodes of peritonitis, 55% were due to gram-positive organisms of which 31% were due to Staph. epidermidis, 10% to S. aureus, and 11% to Streptococcal species. Gram-negative organisms accounted for only 15% of all cases of peritonitis, principally Enterobacter, Pseudomonas and Acinetobacter species. There were two episodes of peritonitis due to Candida and one due to Nocardia. In no case did the peritonitis appear to be the result of more than one organism. It is of interest that there were no infections due to anaerobic organisms. Other investigators have noted that anaerobic peritonitis in patients undergoing peritoneal dialysis is most unusual. This may be at least partly the result of the relatively high oxygen tension maintained in the peritoneal dialysate. Even after 8 hours dwell time, dialysate usually has a pO_2 greater than 15 mm of mercury (79).

In 1978 Oreopoluos and his colleagues described the use of plastic bag dialysate containers in CAPD (80). This single innovation has probably been the single most important practical advance in peritoneal dialysis since the introduction of the Tenckhoff catheter. The use of collapsible plastic bags allows the patient to infuse the dialysate and then, without disconnecting the container from the tubing, roll up the plastic bag and carry it within his clothing during the allotted dwell time. After the dwell time, the bag is unrolled and the effluent allowed to drain by gravity. Following this, a new bag of dialysate is attached and the procedures are repeated. Such a system obviously reduces the frequency of obligatory breaks in the system by 50% (80). Since that time a second innovation has improved the integrity of the system even further. A titanium luer-type catheter-to-tubing adaptor introduced by Nolph and his associates (81) has been shown superior to the previously employed plastic connector with regard to maintenance of the necessary connection and its ability to withstand repeated scrubs with antibiotic solutions. Employing these innovations, the incidence of peritonitis has been drastically reduced. The University of Missouri group has most recently reported a

peritonitis incidence of one to two infections per patient year. Furthermore, 80% of these episodes were successfully treated on an out-patient basis (82). The incidence of peritonitis in the Missouri CAPD population is shown as a function of technical changes in the CAPD system in Figure 7. The reduction of the incidence of peritonitis to an "acceptable" level has been the primary factor responsible for the recent enthusiasm for CAPD as a viable treatment modality for end-stage renal disease.

FIGURE 7

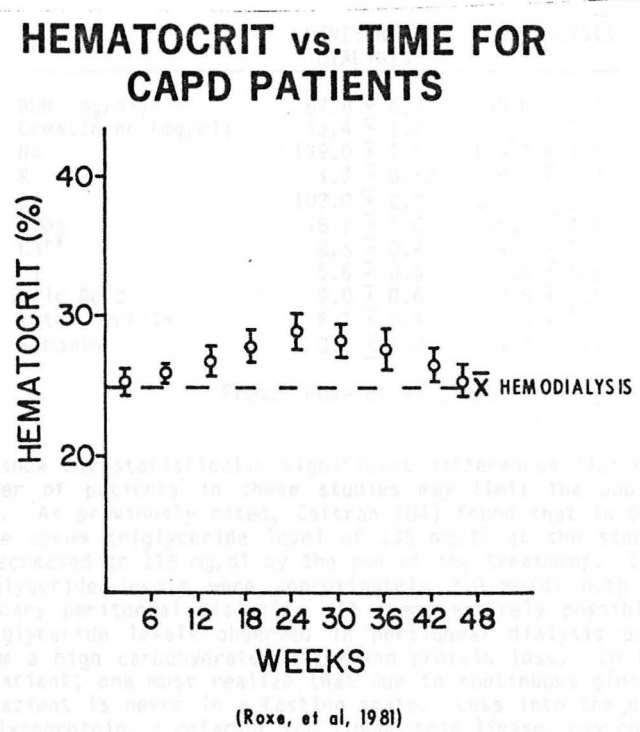


THE CONSEQUENCES OF LONG-TERM PERITONEAL DIALYSIS

Hematological: It has been widely reported that peritoneal dialysis, when compared to hemodialysis, results in a significant increase in the hemoglobin and hematocrits of patients so treated. However, Roxe and his associates have recently reported on patients followed for as long as 3

years and as shown in Figure 8, have observed that though there is an initial rise in the hematocrit (up to 6 months), there is an equally significant decline thereafter, with values returning to a level similar to hemodialysis patients by 48 months (83). These data were collected on 16 peritoneal and 16 hemodialysis patients. Previous explanations for the rise in the hemoglobin associated with peritoneal dialysis have included 1) elimination of the chronic blood loss associated with hemodialysis; or 2) more effective removal of an unknown toxin. However, neither explanation can account for the failure of this hematocrit increase to persist. Further studies will clearly be necessary to explain the occurrence of this biphasic response.

FIGURE 8



(Roxe, et al, 1981)

Extracellular chemistries: Table X displays the serum chemistries of patients treated by either hemodialysis or peritoneal dialysis. Notice that the levels of azotemia (BUN and creatinine) are comparable. However, significant differences between potassium, bicarbonate, calcium and serum albumin. In general, these differences appear to be minor and may have

little or no biological significance. A matter of much greater concern, however, is the lipid metabolism of these patients. Both hemodialysis and peritoneal dialysis have been associated with hypertriglyceridemia (84,85), and some investigators have noted that the rise in serum triglycerides accompanying peritoneal dialysis is greater than that occuring with hemodialysis (84). Furthermore, dialysis (hemo- or peritoneal) has been associated with the decrease in HDL (86). When Roxe et al. compared the lipid profiles of 7 hemodialysis and 7 peritoneal dialysis patients, they were

TABLE X

BIOCHEMICAL COMPARISON OF PATIENTS ON HEMODIALYSIS AND PERITONEAL DIALYSIS

	PERITONEAL DIALYSIS	HEMODIALYSIS	P
BUN (mg/dl)	87.8 ± 6.7	90.0 ± 6.4	N.S.
Creatinine (mg/dl)	13.4 ± 1.2	14.6 ± 1.1	N.S.
Na	139.0 ± 1.5	139.0 ± 1.3	N.S.
K	4.7 ± 0.12	5.4 ± 0.33	<0.001
Cl	102.0 ± 2.2	100.0 ± 1.2	N.S.
HCO_3	18.2 ± 1.0	16.0 ± 1.5	<0.01
Ca^{++}	8.5 ± 0.4	9.0 ± 0.3	N.S.
Pi	5.6 ± 0.5	5.2 ± 0.5	N.S.
Uric Acid	9.0 ± 0.6	8.8 ± 0.5	N.S.
Total protein	6.1 ± 0.4	7.0 ± 0.3	<0.001
Albumin	3.2 ± 0.2	3.9 ± 0.1	<0.001

From: Roxe et al., 1981

unable to show any statistically significant differences (Table XI). The small number of patients in these studies may limit the application of these data. As previously cited, Cattran (84) found that in 64 patients, the average serum triglyceride level of 195 mg/dl at the start of hemodialysis decreased to 118 mg/dl by the end of the treatment. In contrast, serum triglyceride levels were approximately 310 mg/dl both before and after ordinary peritoneal dialysis. It seems entirely possible that the higher triglyceride levels observed in pertioneal dialysis patients may result from a high carbohydrate intake and protein loss. In the case of the CAPD patient, one must realize that due to continuous glucose absorption the patient is never in a fasting state. Loss into the dialysate of α-1-acid glycoprotein, a cofactor for lipoprotein lipase, may contribute to the impaired clearance of triglycerides (87). At this time it can only be said that one should expect rather marked lipid abnormalities in patients undergoing chronic peritoneal dialysis. These changes are generally in the same direction as those seen in hemodialysis patients, although their relative magnitude is yet unsettled.

TABLE XI

LIPID PROFILES OF HEMODIALYSIS AND PERITONEAL DIALYSIS PATIENTS

	CONTROL (N = 20)	PERITONEAL DIALYSIS (N = 7)	HEMODIALYSIS (N = 7)
Cholesterol (mg/dl)	206 ± 7.8	183 ± 14.4	160 ± 13.58
Triglycerides	90 ± 8.9	173 ± 32.3*	158 ± 29.1*
HDL	50 ± 1.8	40 ± 3.0	33 ± 3.8*
LDL	128 ± 2.9	108 ± 10.2	93 ± 9.4*
VLDL	20 ± 2.0	33 ± 7.6*	34 ± 5.7*
Free fatty acids	684 ± 57.5	510 ± 84.2	492 ± 43.3

*$p < 0.05$, comparison with controls

From: Roxe et al., 1981

Protein and amino acid loss: Early on, the obligatory loss of protein and amino acids into the dialysate were thought to be sufficient to rule out chronic peritoneal dialysis as a viable treatment for chronic renal failure (88,89). In patients undergoing intermittent peritoneal dialysis (each 4-10 days for 36 hours) protein losses have averaged 1.0-2.2 g/L of fluid with a total protein loss of 20-200 g/dialysis (90). Most of the protein lost was albumin, although significant amounts (up to 20 g) of immunoglobulins have been reported lost after a single dialysis (91). These figures, however, have recently been disputed by Blumenkrantz, who reports the protein losses for intermittent peritoneal dialysis, CAPD and acute PD, as shown in Table XII. He believes that the older data, indicating much higher protein losses in the dialysate were influenced by low-

TABLE XII

AVERAGE PROTEIN LOSSES DURING PERITONEAL DIALYSIS

	INTERMITTENT PD (10 hr)	CAPD (24 hr)	"ACUTE" PD (36 hr)
Total protein (g)	13.2	9.4	18.8
Albumin	9.1	6.2	11.3
IgG	1.3	1.2	2.5
IgA	0.19	0.17	0.41
Transferrin	0.13	0.36	--

From: Blumenkrantz et al., 1980

grade peritonitis and the peritoneal irritation of repeated catheter insertion. Protein losses increase slightly when hypertonic dialysate is employed, but peritonitis results in marked increases in protein losses. Loss of amino acids also occur with peritoneal dialysis. The quantity of amino acids lost in patients undergoing acute peritoneal dialysis has been reported to be about the same (4-6 g) as is lost during hemodialysis (92). Preliminary information indicates that amino acid loss increases with peritonitis (90).

Nutrient requirements: Protein losses during peritoneal dialysis obviously increase the need for dietary protein. Truly adequate balance studies have not been performed, but most authorities agree that protein restriction is not advisable for the patients undergoing chronic peritoneal dialysis and most prescribe 1.0-1.5 g/kg body weight/day. At this level of protein intake most patients will achieve positive nitrogen balance (93,94). If there is evidence of severe protein depletion, at least 1.5 g/kg/day should be given and the frequency of the dialytic exchanges increased. Protein supplements such as eggs, milk drinks or calcium casinate may be needed. Claims have been made that peritoneal dialysis patients can maintain a positive nitrogen balance on as little as 0.6 g/kg/day of protein as long as it is given with an otherwise high caloric diet (50 Kcal/kg) (95,96). This claim, however, has yet to be confirmed by other laboratories.

It should be noted that a high protein diet usually is high in both potassium and phosphorus. The increased potassium intake (usually around 75 mEq/day) is usually not a problem, and actually avoids the necessity of adding potassium to the dialysate. The increase in phosphorus may or may not result in an increase in serum phosphate. As with any renal failure patient, phosphorus binding antacids should be given to keep the serum phosphate less than 5.0 mg/dl.

Bone disease and neuropathy: Claims that peritoneal dialysis patients have less bone or nerve disease than those treated with hemodialysis are very difficult to substantiate. Patients on CAPD are generally in negative calcium balance when the dialysate calcium is less than 3 mEq/L. Despite this, serum calcium remains essentially unchanged, indicating that the compensatory mechanisms are effective, either by increasing calcium absorption from the gut, or increasing bone mobilization, or both. In contrast to early reports suggesting that parathyroid hormone levels decreased in peritoneal dialysis patients (97), Dalmez et al. showed that while peritoneal dialysis removed some PTH fractions, it does not decrease the plasma level of the active hormone. PTH decreased only when its secretion was suppressed by an increase in serum calcium (98). In a study of 28 CAPD patients followed for three years, the Toronto group was unable to demonstrate improvement or reduced rate of progression of bone disease as judged by serial evaluations of bone mineral mass, bone density, or cortical thickness. Radiographic evidence of subperiosteal resorption progressed in almost all patients and appeared for the first time in several patients after starting CAPD. These changes occurred despite treatment with vitamin D_3 or 1,25-dihydroxy-D_3 and calcium. The experience of other investigators seems to be similar (99).

Uremic neuropathy is a difficult entity to quantitate. Classical approaches to the evaluation of this problem have involved semi-quantitative approaches to the complaints voiced by patients, physical examinations, and the measurement of peripheral nerve conduction velocities. Obvious problems with the scientific evaluation of data obtained by the first two of these methods have led to the extensive utilization of nerve conduction velocity measurements to characterize uremic neuropathy. There is at least one major difficulty associated with this approach. The expected daily variation in nerve conduction velocity, both in normal and in uremic subjects, is about 17% (100). When other neurological techniques have been employed to evaluate both the central and peripheral nervous system of uremic patients, the data obtained have confirmed that there are indeed differences between normals and uremics but have failed to confirm any significant differences among patients managed by varying methods of dialysis. At least one study has indicated by the use of serial EEGs and measurements of evoked potentials in patients maintained on peritoneal and hemodialysis that the two treatments may affect the central nervous system differently. Both treatment groups have increased slow wave activity on EEG as compared to controls. These changes seem to correlate better with the blood urea nitrogen in patients treated by peritoneal dialysis than in those treated by hemodialysis. Furthermore, hemodialysis patients appeared to have more changes in the background EEG and photic-driving responses, whereas peritoneal patients showed changes mainly in the visual-evoked potentials (83). Certainly such findings are interesting, but at this time are of limited clinical significance.

Transport characteristics of the peritoneal membrane after long-term peritoneal dialysis: When peritoneal dialysis and especially continuous ambulatory peritoneal dialysis is employed in the treatment of end-stage renal disease, the peritoneum is continuously exposed to dialysate, the composition of which is clearly not the same as normal extracellular fluid which bathes the peritoneum. Further, recurrent bouts of peritonitis could theoretically alter the transport properties of the membrane. Such a situation is of obvious concern to both the physician and the patient who approach a program of chronic peritoneal dialysis. To study this question, Rubin and his associates assessed the clearances of urea, creatinine, inulin, and dialysate protein content in 12 patients at the time that CAPD was initiated and again after 6 months and 1 year of continuous amubulatory peritoneal dialysis. In spite of the fact that 11 patients had at least one episode of peritonitis, and that 2 patients experienced 11 such episodes during the investigational period, no patient experienced a decrement in the clearance properties of the peritoneum, or an increase in peritoneal protein loss for longer than 2-3 weeks following an episode of acute peritonitis (101). It would appear, therefore, that CAPD, at least up to one year, has no adverse effect on the ability of the peritoneum to act as a dialyzing membrane. Episodes of peritonitis acutely alter clearance properties and protein excretion but there is no evidence that these changes persist following the resolution of the acute illness.

The economics of chronic peritoneal dialysis: The yearly cost of maintenance hemodialysis in this country is staggering, and shows no immediate signs of decreasing. For the past seven years the Federal government has borne the cost of essentially all chronic dialysis, and has therefore become a vocal advocate of alternate and less costly treatment programs. The treatment alternatives available to end-stage renal disease patients today are: 1) renal transplantation; 2) in-center hemodialysis; 3) home hemodialysis; 4) home intermittent peritoneal dialysis; and 5) chronic ambulatory peritoneal dialysis. Clearly, the most cost-effective and satisfactory treatment is transplantation. Though a favorable result is less than assured in all cases, a successful transplantation costs only a few thousand dollars and may result in complete and permanent rehabilitation of the patient. For a variety of reasons, however, transplantation is available to only a small portion of the dialysis population. The current yearly cost for in-center, 3 times per week hemodialysis, is between $20-30,000/patient, depending on the location. This figure does not include the costs of drugs, intercurrent hospitalization, nor the cost of transportation to and from the dialysis unit. Home hemodialysis costs are roughly 1/4 to 1/3 this amount. Home hemodialysis and intermittent peritoneal dialysis require an initial expenditure for necessary equipment. This equipment consists of the dialysis machines, and the necessary plumbing and water purification systems. These one-time initial expenditures may cost as much as $5,000. Continuous ambulatory peritoneal dialysis, however, involves essentially no "start-up" cost and is, therefore, much less expensive in the first year. Thereafter, its cost will be similar to that of other home dialysis methods. Virtually the entire cost of chronic ambulatory peritoneal dialysis is accounted for by dialysate, antiseptic prep kits and bandages. Currently the anticipated cost for one year of chronic ambulatory peritoneal dialysis is $6,000-8,000. However, when considering the economic aspects of the end-stage renal disease patient, one must examine the rehabilitative capacity of any form of treatment. In this regard CAPD is rivaled only by renal transplantation. The CAPD patient is not "tied to a machine" and therefore has substantially greater potential for rehabilitation than do other dialysis patients. Only time and a large number of patients will show if this potential is indeed recognized.

Advantages and indications for chronic peritoneal dialysis: With the technical advances previously described, peritoneal dialysis has become a viable and attractive alternative to hemodialysis. Intermittent, automated peritoneal dialysis may be undertaken at home and requires considerably less skill than home hemodialysis. Further, a help-mate is not essential. However, this technique has been available for several years and has enjoyed only limited popularity with both patients and physicians. The failure of home dialysis, both peritoneal and hemodialysis, to gain widespread acceptance among patients and physicians may be largely due to the widespread availability of in-center hemodialysis, and the lack of incentive for patients to accept responsibility for their own treatment. In the perception of many patients, home dialysis has offered little or no advantage over in-center dialysis. On the other hand, patient enthusiasm for CAPD is uniformly striking. The advantage to the patient is very clear - freedom. Though the daily time investment in CAPD is significant (30-40 minutes, 4-5 times per day), the procedures may be carried out anywhere there are facilities for handwashing. Patients may now travel unencumbered

by dialysis schedules or the need to sacrifice vacation time in dialysis units. Road trips require only the availability of clean restrooms three to four times per day. Fulltime employment is eminently feasible.

CAPD offers many equally important, though less obvious, advantages as opposed to home hemodialysis: 1) CAPD requires a training period of two weeks or less, as opposed to six or more weeks required for home hemodialysis; 2) CAPD is technically a much less complicated procedure; 3) CAPD requires no partner - the requirement for a partner has excluded many patients from home hemodialysis treatment; 4) Patients admitted to home hemodialysis programs must have permanent, preferably owned, residences. This is necessary for the installation of the plumbing and water purification equipment. CAPD carries no such requirement. Given the advantages offered to the patient, the economic advantage offered to those who pay the bill, and the growing patient enthusiasm, CAPD promises to be a treatment modality with wide appeal. There seem to be few, if any, disadvantages for the patient who prefers CAPD over in-center or home hemodialysis. However, this is not to imply that all patients with end-stage renal disease are candidates for CAPD. Relatively few, but important, characteristics should be possessed by the potential CAPD patient in order to maximize the chance for favorable results. Patients enrolled in CAPD programs must be reliable, motivated, compliant and able to master the minimal skills involved in performing the bag and tubing changes in an aseptic manner. The patient must have adequate vision and manual dexterity to accomplish the tasks. The presence of extensive abdominal disease, hernia, or lumbar spinal disease may exclude certain patients from continuous ambulatory peritoneal dialysis. Understanding of and compliance with strict aseptic techniques necessary for the proper performance of CAPD cannot be overstressed. Just as the problem hemodialysis patient is he who is repeatedly volume overloaded and hyperkalemic, the problem CAPD patient will be he who experiences repeated bouts of peritonitis.

SUMMARY

The peritoneum has been used as a dialyzing membrane for over 80 years. During most of that time the technique was a medical curiosity or an experiment in physiology. Over the past 30 years peritoneal dialysis has come to be recognized as a reliable and safe management therapy for acute renal failure. Over the past 15-20 years, interest in alternative treatments for chronic renal failure have led to the development of automated peritoneal dialysis systems. These methods, however, have enjoyed little success, largely due to the lack of patient enthusiasm. A little over five years ago, the technique of continuous ambulatory peritoneal dialysis was born. The successful application of this simple technique was made possible by the advent of a bacteriologically secure peritoneal catheter and collapsible plastic dialysis bags. These innovations, coupled with the remarkable freedom offered patients by the technique, have produced a treatment system which is likely to enjoy explosive growth in the

years to come. Clearly, peritoneal dialysis and specifically CAPD is not without problems. Peritonitis, plasma lipid abnormalities, and perhaps even changes in peritoneal transport characteristics with prolonged dialysis are areas for concern which may determine the future for CAPD. Nevertheless, safety, simplicity, cost, and the rehabilitative potential of patients on CAPD, seem to offer promise for this old but revitalized technique.

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