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Physiology of Peritoneal Dialysis

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Peritoneal dialysis is the method of renal replacement therapy used by approximately 100,000 patients worldwide. In particular, since the introduction of continuous ambulatory peritoneal dialysis (CAPD) approximately two decades ago, its popularity has increased greatly, mainly because of its simplicity, convenience, and relatively low cost. Before describing the clinical application of peritoneal dialysis and its potential complications, it is important to have an understanding of the underlying anatomy and physiology on which peritoneal dialysis is based.

I. What is peritoneal dialysis?

In essence, peritoneal dialysis involves the transport of solutes and water across a "membrane" that separates two fluid-containing compartments. These two compartments are (a) the blood in the peritoneal capillaries, which in renal failure contains an excess of urea, creatinine, potassium, and so forth, and (b) the dialysis solution in the peritoneal cavity, which typically contains sodium, chloride, and lactate and is rendered hyperosmolar by the inclusion of a high concentration of glucose. The peritoneal membrane that acts as a "dialyzer" is actually a heteroporous, heterogeneous, semipermeable membrane with a relatively complex anatomy and physiology.

As is explained in detail in Chapter 14, chronic peritoneal dialysis is divided into CAPD and automated peritoneal dialysis (APD). CAPD typically involves four 2.0- to 2.5-L dwells daily, with each lasting 4–8 hours. In APD, anything from 3 to 10 dwells is delivered nightly using an automated cycler. In the daytime, the patient usually carries a dwell, which is drained each night before cycling recommences; this is called continuous cycling peritoneal dialysis (CCPD). Alternatively, the patient is left "dry" during the day, and this is termed nocturnal intermittent peritoneal dialysis (NIPD). Hybrid prescriptions between CAPD and APD, in which APD patients have daytime exchanges or CAPD patients have an extra automated exchange at night, are increasingly being used to augment clearance or fluid removal.

During the course of a peritoneal dialysis dwell, three transport processes occur simultaneously:

A. Diffusion.

Uremic solutes and potassium diffuse from the peritoneal capillary blood down the concentration gradient into the peritoneal dialysis solution, whereas glucose, lactate, and, to a lesser extent, calcium diffuse in the opposite direction.

B. Ultrafiltration.

Simultaneously, the relative hyperosmolarity of the peritoneal dialysis solution leads to ultrafiltration of water and associated solutes across the membrane.

C. Absorption.

Also simultaneously, there is constant absorption of water and solute from the peritoneal cavity both directly and indirectly into the lymphatic system.

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In this chapter, the anatomy of the peritoneal membrane will be considered, as will the physiology of these three transport processes and the net fluid removal and clearances that result from their action.

II. Anatomy

A. Basic anatomy.

The peritoneum is the serosal membrane that lines the peritoneal cavity (Fig. 13-1). It has a surface area that is thought to be approximately equal to body surface area and so typically ranges from 1 to 2 m^2 in an adult. It is divided into two portions:

FIGURE 13-1. Simplified anatomy of the peritoneal cavity showing the visceral and parietal peritoneal membrane. (Adapted from Khanna R, et al, eds. *The essentials of peritoneal dialysis*. Dordrecht: Kluwer, 1993.)

1. The visceral peritoneum, which lines the gut and other viscera, and
2. The parietal peritoneum, which lines the walls of the abdominal cavity.

The visceral peritoneum accounts for about 80% of the total peritoneal surface area and receives its blood supply from the superior mesenteric artery, whereas its venous drainage is via the portal system. In contrast, the parietal peritoneum, which may be more important in peritoneal dialysis, receives blood

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from the lumbar, intercostal, and epigastric arteries and drains into the inferior vena cava. Total peritoneal blood flow cannot be directly measured but has been indirectly estimated at between 50 and 100 mL per minute. The main lymphatic drainage of the peritoneum and of the peritoneal cavity is via stomata in the diaphragmatic peritoneum, which ultimately drain via large collecting ducts into the right lymphatic duct. There is, however, additional drainage via lymphatics in both the visceral and parietal peritoneum.

The peritoneal membrane is lined by a monolayer of mesothelial cells that have microvillae and that produce a thin film of lubricating fluid. Under the mesothelium is the interstitium, which comprises a gel-like matrix containing collagenous and other fibers, and also the peritoneal capillaries and some lymphatics. The interstitium has been described as a two-

phase system in which a colloid-rich, water-poor phase and a water-rich, colloid-poor phase are interspersed.

B. The peritoneal membrane as a "dialyzer."

The peritoneal membrane as a dialyzer can be thought of as comprising six resistances in series. These are:

1. The stagnant capillary fluid film overlying the endothelium of the peritoneal capillaries
2. The capillary endothelium itself
3. The endothelial basement membrane
4. The interstitium
5. The mesothelium
6. The stagnant fluid film that overlies the peritoneal membrane

Newer concepts, such as the three-pore model for peritoneal transport, have been developed in recent years and suggest that the major resistance to peritoneal transport is located in the peritoneal capillary endothelium and its basement membrane. There is also evidence that the interstitium, especially in its colloid-rich phase, offers significant resistance to solute transport. It is now thought that neither the mesothelium nor the stagnant fluid films offer significant resistance to transport.

C. The three-pore model.

This model, which has been well validated by clinical observations, suggests that the peritoneal capillary is the critical barrier to peritoneal transport and that solute and water transport across it is mediated by pores of three different sizes (Fig. 13-2). These are:

FIGURE 13-2. Diagrammatic representation of the three-pore model of peritoneal transport. (Adapted from Flessner MF. *J Am Soc Nephrol* 1991;2:122.)

1. Large pores with a radius of 20–40 nm. Macromolecules, such as protein, are transported by convection through these pores, which likely are large clefts in the endothelium.
2. Small pores with a radius of 4.0–6.0 nm. There are large number of these which also likely correspond to interendothelial clefts; they are responsible for the transport of small solutes, such as urea, creatinine, sodium, and potassium.
3. Ultrapores with a radius of <0.8 nm. These are responsible for the transport of water

only and are thought to correspond to aquaporins, which are known to be present in the peritoneal membrane; these ultrapores, or aquaporins, account for “sieving” by the peritoneal membrane (see below).

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D. Effective peritoneal surface area.

Given the central role of the peritoneal capillaries in peritoneal transport, it should not be surprising that transport is dependent on the surface area of the peritoneal capillaries rather than on the total peritoneal surface area. Furthermore, not all peritoneal capillaries are close enough to the mesothelium to be involved. The distance of each from the mesothelium determines its relative contribution and the cumulative contribution of all of the above capillaries determines the effective surface area and the resistance properties of the membrane. Thus, the concept of “effective peritoneal surface area” has arisen. This corresponds to the area of the peritoneal surface that is sufficiently close to peritoneal capillaries to play a role in transport. Therefore, two patients with the same peritoneal surface area may have markedly different peritoneal vascularity and so also have very different effective peritoneal surface areas. In a given patient, effective peritoneal surface area may vary in different circumstances, increasing, for example, in peritonitis when inflammation increases vascularity. The degree of vascularity of the peritoneum is thus more important than its surface area in determining the transport characteristics of an individual patient.

This concept of the importance of the distribution of capillaries in the peritoneal membrane and of the distance water and solutes have to travel from the capillaries across the interstitium to the mesothelium is termed the “distributed model” of peritoneal

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transport and represents a shift away from viewing the membrane as a discrete “dialyzer” of uniform thickness (Fig. 13-3).

FIGURE 13-3. Distributed model concept showing distribution of peritoneal capillaries in the interstitium and their distances from the mesothelium, represented by the dotted, vertical line. Cp, the solid, curved line, represents the efficiency of transport from a given capillary to the peritoneal space, increasing for capillaries located closest to the mesothelial boundary. (Adapted from Flessner MF. *J Am Soc Nephrol* 1991;2:122.)

III. Physiology of peritoneal transport.

As mentioned above, peritoneal transport comprises three processes that take place simultaneously. These are (a) diffusion, (b) ultrafiltration, and (c) fluid absorption. For simplicity, these will be considered separately.

A. Diffusion.

This process is critical for removal of uremic solutes in peritoneal dialysis. Diffusion

typically occurs down the concentration gradient from peritoneal capillary blood to dialysis solution. Peritoneal diffusion depends on the following factors:

1. **The concentration gradient.** For a substance such as urea, this is maximal at the start of a peritoneal dialysis dwell, when the concentration in the dialysis solution is zero. It gradually decreases during the course of the dwell. This effect can be counteracted by the performance of more frequent exchanges, as is typically done in APD, or by increasing dwell volumes, which allows the gradient to remain greater for a longer time.

2. **Effective peritoneal surface area.** As already stated, this depends not only on the total peritoneal surface area but also on the degree of vascularity, which may vary between patients and within a given patient under different conditions (e.g., peritonitis). It can also be increased by using larger fill volumes, which recruit more peritoneal membrane, but this effect is limited in most individuals once volumes reach 2.5–3 L.
3. **Intrinsic peritoneal membrane resistance.** This parameter is not well characterized but may reflect differences in the number of pores per unit surface area of capillary available for peritoneal transport and the distance across the interstitium of these capillaries from the mesothelium.
4. **Molecular weight of the solute concerned.** Substances with lower molecular weight, such as urea (MW 60), are more easily transported than those with higher molecular weights, such as creatinine (MW 113) or albumin (MW 69,000).
    a. **Mass transfer area coefficient.** The combined effects of factors 2–4 are sometimes measured by an index called the mass transfer area coefficient (MTAC). For a given solute, the MTAC is equivalent to the diffusive clearance of that solute per unit time in a given patient if dialysate flow is infinitely high, so that the gradient is always maximal if ultrafiltration has not occurred. Typical MTAC values for urea and creatinine are 17 and 10 mL per minute, respectively. The MTAC is mainly a research tool and is generally not used in clinical practice.
    b. **Peritoneal blood flow.** It is important to note that diffusion does not generally depend on peritoneal blood flow because 50–100 mL per minute is already more than adequate relative to MTAC values for even the smallest solutes. Thus, in contrast to the situation in hemodialysis, diffusion in peritoneal dialysis is dependent on dialysate rather than blood flow. The ability of vasoactive agents to influence peritoneal transport is not related to their ability to increase peritoneal blood flow per se but rather to the associated recruitment of larger numbers of peritoneal capillaries that increase effective peritoneal surface area. The same effect is seen in peritonitis where inflammation increases peritoneal vascularity, and there is a consequent increase in peritoneal diffusion. It should be noted that the proportion of peritoneal blood flow involved in peritoneal dialysis is unknown, and it is

possible that in some areas of the peritoneum blood flow may limit diffusion.

B. Ultrafiltration.

This occurs as a consequence of the osmotic gradient between the relatively hypertonic dialysis solution and the relatively hypotonic peritoneal capillary blood. It is usually due to the presence of high concentrations of glucose in dialysate and depends on the following:

1. **Concentration gradient for the osmotic agent (i.e., glucose).** Again, this is typically maximal at the beginning of a peritoneal dialysis dwell and decreases with time due to dilution of the glucose by ultrafiltrate and due to diffusion of the glucose itself from the dialysis solution into the blood (Fig. 13-4). The gradient is also less in the presence of marked hyperglycemia. The gradient can be maximized by

using more hypertonic solutions of dextrose or by doing more frequent exchanges, as is done with APD.

FIGURE 13-4. Dialysate glucose level after instillation of a 4.25% dextrose (3.86% glucose) exchange into the peritoneal cavity. The initial level is close to 3,860 mg per dL.

2. **Effective peritoneal surface area** (as described above).
3. **Hydraulic conductance of the peritoneal membrane.** This differs from patient to patient and perhaps reflects the density of small pores and ultrapores in the peritoneal capillaries, as well as the distribution of distances of capillaries from the mesothelium.
4. **Reflection coefficient for the osmotic agent (i.e., glucose).** This measures how effectively the osmotic agent diffuses out of the dialysis solution into the peritoneal capillaries. It is between 0 and 1; the lower the value, the faster the osmotic gradient is lost and the less sustained ultrafiltration is. For glucose, this coefficient is typically low (approximately 0.03). Newer polyglucose preparations have values close to 1.
5. **Hydrostatic pressure gradient.** Normally, the capillary pressure (around 20 mm Hg) is higher than the intraperitoneal pressure (around 7 mm Hg), which should favor ultrafiltration. This effect is greater in an overhydrated and lower in a dehydrated patient. Rises in intraperitoneal pressure tend to oppose ultrafiltration, and this may occur when larger dwell volumes are used. This picture is complicated by the fact that interstitial pressure is less than both capillary and intraperitoneal pressures; therefore, hydrostatic pressure gradients alone do not explain ultrafiltration.

6. **Oncotic pressure gradient.** This tends to oppose ultrafiltration but operates to a

lesser degree in a hypoalbuminemic patient.

a. **Sieving.** As is the case in hemodialysis, ultrafiltration in peritoneal dialysis involves not just water transport but also convective solute transport. However, during ultrafiltration, in contrast to the situation in hemodialysis, solute does not move across the membrane in direct proportion to its concentration in blood. This is because “sieving” of solute occurs at the peritoneal membrane. Sieving coefficients for the various solutes differ with molecular weight, charge, and so forth, as well as between patients. Values vary between 0 and 1, and the higher the sieving coefficient, the greater the convective transport for that solute. This sieving effect is accounted for by the ultrapores, which are responsible for about half of total ultrafiltration and which transport only solute-free water. Sieving makes ultrafiltration a less effective form of convective solute transport. However, without sieving, glucose-induced ultrafiltration itself could not occur as the membrane would not be “semipermeable.”

b. **Alternative osmotic agents.** For many years, efforts have been made to develop alternative osmotic agents that may induce more effective ultrafiltration than glucose. The ideal osmotic agent would be safe, inexpensive, and would have a high reflection coefficient (i.e., would not diffuse out of the peritoneal cavity into the blood to dissipate the osmotic gradient). The recent development of a polyglucose molecule called “icodextrin” is of some promise in this regard. Icodextrin is a large molecule with a high reflection coefficient, and so ultrafiltration is sustained at a relatively steady level throughout even a long-duration dwell.

C. Fluid absorption.

This occurs via the lymphatics at a relatively constant rate and with little or no sieving, so that its net effect is to counteract both solute and fluid removal. It has been increasingly recognized that only a small proportion of this absorption occurs directly into the lymphatics. The majority is absorbed across the parietal peritoneum into the tissues of the abdominal wall, from where it is subsequently taken up by the lymphatics and perhaps even by peritoneal capillaries. Typical values for peritoneal fluid absorption are 1.0–2.0 mL per minute, of which 0.2–0.4 mL per minute go directly into the lymphatics. The determinants of this process are:

1. **Intraperitoneal hydrostatic pressure.** The higher this is, the greater the amount of fluid that is absorbed; intraperitoneal hydrostatic pressure is raised by increasing intraperitoneal volume as a result of more effective ultrafiltration or the use of larger infusion volumes. It is also higher when patients are sitting than when they are standing, and it is lower when they are supine (Fig. 13-5).

FIGURE 13-5. Intra-abdominal pressure after infusing various volumes of dialysis

solution. (Modified from Diaz-Buxo JA. Continuous cycling peritoneal dialysis. In Nolph KD, ed. *Peritoneal dialysis*. Hingham: Martinus Nijhoff, 1985.)

2. **Effectiveness of lymphatics.** The effectiveness of lymphatics absorbing fluid from the peritoneal cavity may differ markedly from person to person, but this is not well understood.

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IV. Clinical assessment and implications of peritoneal transport

A. Peritoneal equilibration test (PET).

In clinical practice, indices such as the MTAC and hydraulic conductance of the peritoneal membrane are too complex for routine measurement and peritoneal transport is assessed using equilibration ratios between dialysate and plasma for urea (D/P urea), creatinine (D/P Cr), sodium (D/P Na), and so forth (Fig. 13-6). Equilibration ratios measure the combined effect of diffusion and ultrafiltration rather than either in isolation. However, they correlate well with MTAC values for the corresponding solutes, suggesting diffusion as their primary determinant. They thus are greatly influenced by the molecular weight of the solute

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concerned as well as by the membrane permeability and effective surface area. Interestingly, body size tends to have little relation to equilibration ratios despite its supposed equivalence to peritoneal surface area, presumably indicating that actual and effective peritoneal surface areas correlate poorly.

FIGURE 13-6. Rate of entry of urea, creatinine, and vitamin B_{12} into peritoneal dialysis solution that has been left in the abdomen. Results are expressed as the ratio of the level in dialysate (D) to the level in plasma (P). Typical D/P ratios for urea at time points of 40 minutes, 2 hours, and 4 hours are indicated.

Conventionally, equilibration ratios are measured in a standardized PET that involves a 2-L 2.5% dextrose dwell with dialysate samples taken at 0, 2, and 4 hours and a plasma sample at 2 hours. A PET is also used to measure net fluid removal and the ratio of dialysate glucose at 4 hours to dialysate glucose at time zero (D/D_0 G). Patients are classified principally on the basis of their 4-hour D/P Cr into one of four categories: high, high-average, low-average, and low transporters (Fig. 13-7). The protocol for performing a PET and its use in the evaluation of ultrafiltration failure is further discussed in Chapter 18, whereas its role in peritoneal dialysis prescription is described in Chapter 17.

FIGURE 13-7. Standard peritoneal equilibration curves for urea, creatinine, and sodium, as well as glucose absorption showing ranges of values for high, high-average, low-average, and low transporters. (Modified from Twardowski et al. Peritoneal equilibration test. *Perit Dial Bull* 1987;7:138.)

1. **High transporters** achieve the most rapid and complete equilibration for creatinine and urea, presumably because they have a relatively large effective peritoneal surface area or high intrinsic membrane permeability (i.e., low membrane resistance). However, high transporters rapidly lose their osmotic gradient for ultrafiltration because the dialysate glucose diffuses

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into the blood through the highly “permeable” membrane. Thus, high transporters have the highest D/P Cr, D/P Ur, and D/P Na values but have low net ultrafiltration and D/D_0 G values. They also have higher dialysate protein losses and so tend to have lower serum albumin values.

2. **Low transporters**, in contrast, have slower and less complete equilibration for urea and creatinine, reflecting low membrane permeability or small effective peritoneal surface area. They thus have low D/P Ur, D/P Cr, and D/P Na and high D/D_0 G with good net ultrafiltration. Dialysate protein losses are lower, and serum albumin values tend to be higher.

3. **High-average and low-average transporters** have intermediate values for these ratios and for ultrafiltration and protein losses.

   In practice, high transporters tend to dialyze relatively well but to ultrafiltrate poorly, whereas low transporters ultrafiltrate well but dialyze poorly, although these issues are often masked while residual renal function is still substantial. Thus, high transporters tend to do best on peritoneal dialysis regimens that involve frequent short-duration dwells (e.g., APD), so that ultrafiltration is maximized. Low transporters, in contrast, tend to do best on regimens based on long-duration, high-volume dwells, so that diffusion is maximized. Average transporters can do well on any of a variety of peritoneal dialysis regimens.

   Therefore, the PET is useful because it guides prescription of peritoneal dialysis and because it helps to predict the particular complications that a given patient will be prone to develop.

B. Net fluid removal.

As already stated, net fluid removal in peritoneal dialysis depends on the balance between peritoneal ultrafiltration and peritoneal absorption and thus on the determinants of these two processes. As lymphatic flow and the transport qualities of the membrane are not

amenable to alteration, fluid removal in peritoneal dialysis can, in clinical practice, be enhanced by:

1. Maximizing the osmotic gradient
    a. Higher tonicity dwells (e.g., 4.25% dextrose)
    b. Shorter duration dwells (e.g., APD)
    c. Higher dwell volumes
2. An osmotic agent with a higher reflection coefficient (e.g., polyglucose)
3. Increasing urine output (e.g., with diuretics)

As is shown in Fig. 13-8, the net fluid removal with a 1.5% 2-L dextrose dwell is maximal in the first hour and intraperitoneal volume is greatest after 90 minutes. After this time, the volume being ultrafiltered is less than that being resorbed, and by 6–10 hours, the intraperitoneal volume falls below 2 L, and the patient is achieving net fluid gain. If the more hypertonic 4.25% dextrose dialysis solution is used, initial fluid removal is greater and more sustained, and intraperitoneal volume is greatest after about 3 hours and will not fall below 2 L until after many hours.

FIGURE 13-8. Ultrafiltration volume (volume drained minus volume instilled) as a function of time after infusion of dialysis solution containing 1.5% dextrose (1.35% glucose, ***open circles***) **or 4.25% dextrose (3.86% glucose**, *closed circles*). **(Modified from Diaz-Buxo JA. Intermittent, continuous ambulatory and continuous cycling peritoneal dialysis. In: Nissenson AR, et al, eds**. ***Clinical dialysis***. **Norwalk, CT: Appleton-Century-Crofts, 1984.)**

The effect of larger dwell volumes on net fluid removal is complex. On the one hand, fluid removal increases because the

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osmotic gradient persists longer due to the greater quantity of glucose in the peritoneal cavity and because the effective surface area over which water is transported is likely increased. On the other hand, fluid removal decreases because intraperitoneal pressure rises (Fig. 13-5), thereby decreasing the hydrostatic gradient that favors ultrafiltration and promoting peritoneal fluid absorption into the tissues and lymphatics. The net effect of these forces varies and is difficult to predict.

C. Peritoneal clearance.

Clearance for a given solute is defined as the volume of plasma cleared of that solute per unit time. It is thus equal to the quantity of solute removed in a given time divided by the plasma concentration of that solute during that time. It is typically measured in milliliters per minute or, in peritoneal dialysis, as liters per week. In peritoneal dialysis, clearance of a given solute is the net result of the effects of diffusion plus ultrafiltration minus fluid

absorption.

In hemodialysis, clearance for a small solute, such as urea, is relatively constant during the treatment; however, with peritoneal dialysis, it changes, being maximal at the start of a dwell, when both diffusion and ultrafiltration are greatest, and being less as the dwell proceeds and both ultrafiltration and diffusion decline due to loss of the urea concentration gradient and the glucose osmotic gradient, respectively. In practice, however, peritoneal clearance is measured per day or per week rather than per

minute or per hour, and peritoneal dialysis is best described as a modality in which a low level of clearance is delivered continuously, as compared with hemodialysis where a high level of clearance is delivered intermittently.

Clearance in peritoneal dialysis is influenced by all of the factors that determine diffusion, ultrafiltration, and absorption. In clinical practice, peritoneal clearance can be increased by:

1. Maximizing time on peritoneal dialysis (i.e., no “dry time”)
2. Maximizing concentration gradient (i.e., more frequent exchanges as in APD and larger dwell volumes)
3. Maximizing effective peritoneal surface area (i.e., larger dwell volumes)
4. Maximizing peritoneal fluid removal (as described above)

The mechanism by which increasing dwell volumes augment clearance is sometimes confusing. Larger dwell volumes enhance urea and creatinine diffusion from blood to dialysate because the greater volume makes the gradient stay higher for longer. However, the corollary of this is that D/P ratios tend to be a little lower with larger dwell volumes. Effective peritoneal surface area may also increase because of recruitment of more membrane by the greater fluid volume, and consequently MTAC values may rise. This effect tends to be modest or absent once volumes exceed 2.5 L in adults, presumably because all of the available membrane has been recruited. These two effects increase diffusive clearance even though D/P ratios may be lower. An additional effect is that, as already described, the larger dwell volume may in some patients diminish ultrafiltration slightly. Thus, a switch from 2.0- to 2.5-L dwells represents a 25% increase in infused volume but might, for example, be associated with a decrease in D/P ratios by 3% and of ultrafiltration by 5%, leading to a net increase of about 20% in clearance.

It should also be noted that changes in the peritoneal dialysis prescription alter urea and creatinine clearances to different degrees because the latter is more time-dependent than the former. Thus, a switch from CAPD to NIPD may lead to a much more marked decrease in creatinine than in urea clearance, whereas a switch from NIPD to CCPD will cause a disproportionately greater enhancement in creatinine clearance. These effects are especially marked in low transporters whose creatinine clearance is particularly time-dependent, as reflected by the flat shape of the creatinine equilibration curve.

1. **Measurement of clearance.** Peritoneal clearance per day in peritoneal dialysis is easily measured and corresponds to the total daily dialysate drain volume multiplied by the solute concentration in that dialysate and divided by the simultaneous plasma concentration of the same solute. Stated more simply, clearance equals the drain volume multiplied by the D/P ratio for the solute concerned.

   In CAPD, it is presumed (quite reasonably) that the plasma urea does not alter significantly during the day because dialysis is continuous. Thus, the plasma sample can be taken at any convenient time during the day concerned. In APD, there is significantly more intense dialysis at night than in the daytime; therefore, a constant plasma urea cannot be assumed. It is recommended

   that the plasma sample be taken in the middle of the noncycling period (usually midafternoon) when the urea is about halfway between its lowest level (in the morning after cycling) and its highest level (at night before cycling).

   Clearance is measured per day but expressed per week. It is conventional to normalize urea clearance to total-body water (*V*), which is typically estimated using the Watson nomogram (see Table 17-4). Creatinine clearance is normalized to 1.73 m^2 surface area, which is estimated using the formula of DuBois (see Table 17-4).

2. **Examples of peritoneal clearance calculations.** See Table 17-4.

D. Sodium removal.

In peritoneal dialysis, it is helpful to consider sodium removal separately from water removal. As already mentioned, ultrafiltration in peritoneal dialysis involves sodium sieving, so that water losses are proportionately greater than sodium losses. At the end of a 4-hour dwell, dialysate sodium levels will have fallen from the initial 132 mEq per L to about 120–125 mEq per L (Fig. 13-7). In the early part of a dwell, dialysate sodium falls rapidly because it is diluted by ultrafiltrate containing only about 80 mEq sodium per L. This effect is partly counteracted by diffusion, which becomes more significant as the concentration gradient for sodium widens. Thus, late in the dwell, when ultrafiltration is much lower, diffusion raises the dialysate sodium back up to about 125 mEq per L. Overall, net sodium removal with a 4-hour, 1.5% dextrose, 2-L exchange is minimal, although with a 4-hour, 4.25% dextrose, 2-L dwell, it is typically in excess of 70 mEq. Thus, in an anuric patient, sodium removal requires the use of more hypertonic solutions. Lowering the sodium concentration in the dialysis solution would increase diffusive sodium removal but would require greater concentrations of glucose to achieve the same osmotic effect. Such solutions can be made up but are not commercially available.

E. Protein losses.

Obligatory dialysate protein losses are a feature of peritoneal dialysis and typically average 5–10 g daily of which half is accounted for by albumin. These losses are probably the major cause of the lower serum albumin levels seen in peritoneal dialysis, as compared with hemodialysis patients. Losses are greatest and serum albumin is lowest in high

transporters. The losses or clearances of large molecular weight proteins such as albumin are relatively constant during the course of a dwell, but low molecular weight proteins such as lysozyme behave more like small solutes such as creatinine in that their clearance falls markedly as the dwell proceeds.

As already mentioned, protein losses are believed to occur via a relatively small number of large pores that correspond to interendothelial clefts. Peritoneal absorption of fluid is a form of “bulk flow” and so involves protein, as well as other solutes. It thus acts to decrease net peritoneal protein losses.

During peritonitis, protein losses increase markedly for a number of days, presumably due to an increase in effective peritoneal surface area consequent to increased vascularity. This effect is in part mediated by prostaglandins. Protein losses on intermittent peritoneal dialysis regimens appear to be no less per day than

those on continuous regimens, presumably because the losses continue even during the “dry” interdialytic periods.

V. Residual renal function.

There is evidence that residual renal function persists longer and at a higher level in chronic peritoneal dialysis patients than those on hemodialysis and that this plays an important part in the success of peritoneal dialysis. Residual function contributes to salt and water removal and to clearance of both small and medium-size molecular weight solutes. Creatinine clearance is disproportionately high with residual renal function as tubular secretion contributes to the overall clearance to a greater extent. The opposite is the case with urea clearances where tubular resorption is significant. There is evidence that the mean of urea and creatinine clearance is a reasonable estimate of true glomerular filtration rate in the failing kidney; this estimate is used when calculating the renal contribution to total creatinine clearance in patients on peritoneal dialysis. Residual renal function has been shown to be predictive of patient outcome in peritoneal dialysis, perhaps because it is associated with better preserved renal endocrine and metabolic function and superior volume homeostasis, as well as greater small- and large-molecule clearance.

SELECTED READINGS

Flessner MF. Peritoneal transport physiology: insights from basic research. *J Am Soc Nephrol* 1991;2:122–135.

Flessner MF, et al. Blood flow does not limit peritoneal transport. *Perit Dial Int* 1999;19(Suppl 2):S208.

Heimburger O, et al. A quantitative description of solute and fluid transport during peritoneal dialysis. *Kidney Int* 1992;41:1320–1332.

Keshaviah P, et al. Relationship between body size, fill volume and mass transfer area coefficient in peritoneal dialysis. *J Am Soc Nephrol* 1994;4:1820–1826.

Krediet RT, et al. Icodextrin's effect on peritoneal transport. *Perit Dial Int* 1997;17:35–41.

Krediet RT. The peritoneal membrane in chronic peritoneal dialysis. *Kidney Int* 1999;55:341–356.

Mactier RA, et al. Influence of dwell time, osmolality, and volume of exchanges on solute mass transfer and ultrafiltration in peritoneal dialysis. *Semin Dial* 1988;1:40.

Rippe B, et al. Computer simulations of peritoneal transport in CAPD. *Kidney Int* 1991;40:315–325.

Rippe B, et al. A three-pore model of peritoneal transport. *Perit Dial Int* 1993;13(Suppl 2):S35–S38.

Rippe B, et al. Role of transcellular water channels in peritoneal dialysis. *Perit Dial Int* 1999;19(Suppl 2):S95–S101.

Ronco C. The “nearest capillary” hypothesis: a novel approach to peritoneal transport physiology. *Perit Dial Int* 1996;16:121–125.

Twardowski ZJ, et al. Peritoneal equilibration test. *Perit Dial Bull* 1987;7:138.