Principles of Peritoneal Dialysis

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Peritoneal dialysis is a technique whereby infusion of dialysis solution into the peritoneal cavity is followed by a variable dwell time and subsequent drainage. Continuous ambulatory peritoneal dialysis (CAPD) is a continuous treatment consisting of four to five 2-L dialysis exchanges per day (Fig. 4-1A). Diurnal exchanges last 4 to 6 hours, and the nocturnal exchange remains in the peritoneal cavity for 6 to 8 hours. Continuous cyclic peritoneal dialysis, in reality, is a continuous treatment carried out with an automated cycler machine (Fig. 4-1B). Multiple short-dwell exchanges are performed at night with the aid of an automated cycler machine. Other peritoneal dialysis treatments consist of intermittent regimens (Fig. 4-2A-C).

During peritoneal dialysis, solutes and fluids are exchanged between the capillary blood and the intraperitoneal fluid through a biologic membrane, the peritoneum. The three-layered peritoneal membrane consists of 1) the mesothelium, a continuous monolayer of flat cells, and their basement membranes; 2) a very compliant interstitium; and 3) the capillary wall, consisting of a continuous layer of mainly non-fenestrated endothelial cells, supported by a basement membrane. The mesothelial layer is considered to be less of a transport barrier to fluid and solutes, including macromolecules, than is the endothelial layer [1]. The capillary endothelial cell membrane is permeable to water through aquaporins (radius of approximately 0.2 to 0.4 nm) [2]. In addition, small solutes and water are transported through ubiquitous small pores (radius of approximately 0.4 to 0.55 nm). Sparsely populated large pores (radius of approximately 0.25 nm, perhaps mainly venular) transport macromolecules passively. Diffusion and convection move small molecules through the interstitium with its gel and sol phases, which are restrictive owing to the phenomenon of exclusion [3,4]. The splanchnic blood flow in the normal adult ranges from 1.0 to 2.4 L/min, arising from celiac and mesenteric arteries [5]. The lymphatic vessels located primarily in the subdiaphragmatic region drain fluid and solutes from the peritoneal cavity through bulk transport.
Dialysis as Treatment of End-Stage Renal Disease

The extent of lymph drainage from the peritoneal cavity is a subject of controversy owing to the lack of a direct method to measure lymph flow.

Dialysis solution contains electrolytes in physiologic concentrations to facilitate correction of acid-base and electrolyte abnormalities. High concentrations of glucose in the dialysis solution generate ultrafiltration in proportion to the overall osmotic gradient, the reflection coefficients of small solutes relative to the peritoneum, and the peritoneal membrane hydraulic permeability. Removal of solutes such as urea, creatinine, phosphate, and other metabolic end products from the body depends on the development of concentration gradients between blood and intraperitoneal fluid, and the transport is driven by the process of diffusion. The amount of solute removal is a function of the degree of its concentration gradient, the molecular size, membrane permeability and surface area, duration of dialysis, and charge. Ultrafiltration adds a convective component proportionately more important as the molecular size of the solute increases.

The peritoneal equilibration test is a clinical tool used to characterize the peritoneal membrane transport properties [6]. Solute transport rates are assessed by the rates of their equilibration between the peritoneal capillary blood and dialysate (see Fig. 4-8). The ratio of solute concentrations in dialysate and plasma at specific times during the dwell signifies the extent of solute transport. The fraction of glucose absorbed from the dialysate at specific times can be determined by the ratio of dialysate glucose concentrations at specific times to the initial level in the dialysis solution. Tests are standardized for the following: duration of the preceding exchange before the test; inflow volume; positions during inflow, drain, and dwell; durations of inflow and drain; sampling methods and processing; and laboratory assays [7].

Creatinine and urea clearance rates are the most commonly used indices of dialysis adequacy in clinical settings. Contributions of residual renal clearances are significant in determining the adequacy of dialysis. The mass-transfer area coefficient (MTAC) represents the clearance rate by diffusion in the absence of ultrafiltration and when the rate of solute accumulation in the dialysis solution is zero. Peritoneal clearance is influenced by both blood and dialysate flow rates and by the MTAC [8]. Therefore, the maximum clearance rate can never be higher than any of these parameters. At infinite blood and dialysate flow rates, the clearance rate is equal to the MTAC and is mass-transfer–limited. Large molecular weight solutes are mass-transfer–limited; therefore, their clearance rates do not increase significantly with high dialysate flow rates [9]. In CAPD, blood flow and MTAC rates are higher than is the maximum achievable urea clearance rate. However, the urea clearance rate approximately matches the dialysate flow rate, suggesting that the dialysate flow rate limits CAPD clearances.

Peritoneal Dialysis Regimens

**FIGURE 4-1**
Continuous peritoneal dialysis regimens. **A**, Continuous ambulatory peritoneal dialysis (CAPD); **B**, continuous cyclic peritoneal dialysis (CCPD) is shown. Multiple sequential exchanges are performed during the day and night so that dialysis occurs 24 hours a day, 7 days a week.
FIGURE 4-2
Intermittent peritoneal dialysis regimens. Peritoneal dialysis is performed every day but only during certain hours. A, In daytime ambulatory peritoneal dialysis (DAPD), multiple manual exchanges are performed during the waking hours. B, Nightly peritoneal dialysis (NPD) is also performed while patients are asleep using an automated cycler machine. One or two additional daytime manual exchanges are added to enhance solute clearances.

Solute Removal

FIGURE 4-3
Solute removal. Solute concentration gradients are at maximum at the beginning of dialysis and diminish gradually as dialysis progresses. As the gradients diminish, the solute removal rates decrease. Solute removal can be enhanced by increasing the dialysate flow rate by either increasing the intraperitoneal dialysate volume per exchange or increasing the frequency of exchange. By convection or enhanced diffusion, solutes are able to accompany the bulk flow of water. (From Nolph and coworkers [10]; with permission.)
Solute removal. The rates of change of solute concentrations are similar for 1.5% dextrose dialysis solutions (panel A) and 4.25% dextrose dialysis solutions (panel B). Hypertonic exchanges enhance solute removal owing to larger drain volumes. Net solute diffusion ceases at equilibration when the dialysate to plasma solute ratio (D/P) is near 1.0. Smaller size solutes (i.e., urea and creatinine) diffuse across the membrane faster, equilibrate sooner, and are influenced more by exchange frequency as compared with larger size solutes (i.e., uric acid, phosphates, inulin, and proteins). (From Nolph and coworkers [10]; with permission.)

FIGURE 4-5
Solute removal. In a highly permeable membrane, smaller molecules (i.e., urea and creatinine) are transported at a faster rate from the blood to dialysate than are larger molecules, enhancing solute removal. Similarly, glucose (a small solute used in the peritoneal dialysis solution to generate osmotic force for ultrafiltration across the peritoneal membrane) is also transported faster, but in the opposite direction. The high transporter dissipates the osmotic force more rapidly than does the low transporter. Both osmotic and glucose equilibriums are attained eventually in both groups, but sooner in the high transporter group. Intraperitoneal volume peaks and begins to diminish earlier in the high transporter group. When the membrane is less permeable, solute removal is lower, ultrafiltration volume is larger at 2 hours or more, and glucose equilibriums are attained later. Consequently, intraperitoneal volume peaks later. Ultrafiltration in a low transporter peaks late during dwell time. Therefore, a low transporter continues to generate ultrafiltration even after 8 to 10 hours of dwell. The solute creatinine dialysate to plasma ratio (D/P) increases linearly during the dwell time. Patients with average solute transfer rates have ultrafiltration and mass transfer patterns between those of high and low transporters. NIPD—nightly intermittent peritoneal dialysis; NTPD—nighttime tidal peritoneal dialysis; DAPD—daytime ambulatory peritoneal dialysis; NIPD (NE)—continuous cyclic peritoneal dialysis (night exchange); CCPD (DE)—continuous cyclic peritoneal dialysis (day exchange). (From Twardowski [11]; with permission.)
Principles of Peritoneal Dialysis

Solute sieving. **A**, Dialysate sodium concentration is initially reduced and tends to return to baseline later during a long dwell exchange of 6 to 8 hours. **B**, Dialysate sodium concentration decreases, particularly when using 4.25% dextrose dialysis solution, because of the sieving phenomenon. Removal of water during ultrafiltration unaccompanied by sodium, in proportion to its extracellular concentration, is called sodium sieving [7,12]. The peritoneum offers greater resistance to the movement of solutes than does water. This probably relates to approximately half the ultrafiltrate being generated by solute-free water movement through aquaporin channels. Therefore, ultrafiltrate is hypotonic compared with plasma. Dialysate chloride is also reduced below simple Gibbs-Donnan equilibrium, particularly during hypertonic exchanges. Patients with a low peritoneal membrane transport type tend to reduce dialysate sodium concentration more than do other patients. Therefore, during a short dwell exchange of 2 to 4 hours, net electrolyte removal per liter of ultrafiltrate is well below the extracellular fluid concentration. As a result, severe hypernatremia, excessive thirst, and hypertension may develop. This hindrance can be overcome by lowering the dialysate sodium concentration to 132 mEq/L. In patients who use cyclers with short dwell exchanges and who generate large ultrafiltration volumes, lower sodium concentrations may need to be used (such as 118 mEq/L for 2.5% glucose solutions or 109 mEq/L for 4.25% solutions). In continuous ambulatory peritoneal dialysis with long dwell exchanges of 6 to 8 hours, significant sieving usually does not occur, whereas in automated peritoneal dialysis with short dwell exchanges, sieving may occur. Sieving predisposes patients to thirst and less than optimum blood pressure control, especially in those who have low-normal serum sodium levels, those with low peritoneal membrane transporter rates, or both. (From Nolph and coworkers [10]; with permission.)

Fluid removal by ultrafiltration. During peritoneal dialysis, hyperosmolar glucose solution generates ultrafiltration by the process of osmosis. Water movement across the peritoneal membrane is proportional to the transmembrane pressure, membrane area, and membrane hydraulic permeability. The transmembrane pressure is the sum of hydrostatic and osmotic pressure differences between the blood in the peritoneal capillary and dialysis solution in the peritoneal cavity. Net transcapillary ultrafiltration defines net fluid movement from the peritoneal microcirculation into the peritoneal cavity primarily in response to osmotic pressure. Net ultrafiltration would equal the resulting increment in intraperitoneal fluid volume if it were not for peritoneal reabsorption, mostly through the peritoneal lymphatics. Peritoneal reabsorption is continuous and reduces the intraperitoneal volume throughout the dwell. **A**, The net transcapillary ultrafiltration rate decreases exponentially during the dwell time, owing to dissipation of the glucose osmotic gradient secondary to peritoneal glucose absorption and dilution of the solution glucose by the ultrafiltration. Later in the exchange net, ultrafiltration ceases when the transcapillary ultrafiltration is reduced to a rate equal to the peritoneal reabsorption. **B**, When the transcapillary ultrafiltration rate decreases below that of the peritoneal reabsorption rate, the net ultrafiltration rate becomes negative. Consequently, the intraperitoneal volume begins to diminish. Thus, peak ultrafiltration and intraperitoneal volumes are observed before osmotic equilibrium during an exchange.

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Dialysis as Treatment of End-Stage Renal Disease

**STANDARDIZED 4-HOUR PERITONEAL EQUILIBRATION TEST**

1. Perform an overnight 8- to 12-h preexchange.
2. Drain the overnight exchange (drain time not to exceed 25 min) with patient in the upright position.
3. Infuse 2 L of dialysis solution over 10 min with patient in the supine position. Roll the patient from side to side after every 400-mL infusion.
4. After the completion of infusion (0 time) and at 120 min, drain 200 mL of dialysate. Take a 10-mL sample, and reinfuse the remaining 190 mL into the peritoneal cavity.
5. Position the patient upright, and allow patient ambulation if able.
6. Obtain a serum sample at 120 min.
7. At the end of study (240 min), drain the dialysate with the patient in the upright position (drain time not to exceed 20 min).
8. Measure the drained volume, and take a 10-mL sample from the drained volume after a good mixing.
9. Analyze the blood and dialysate samples for creatinine and glucose concentrations.
10. Correct the serum and dialysate creatinine concentrations for high glucose level (correction factor 0.000531415).
11. Calculate the dialysate to plasma ratios for creatinine, and so on, and calculate the DT/D0 glucose.

**FIGURE 4-8**

C, Osmotic equilibrium most likely precedes glucose equilibrium because of both solute sieving and the higher peritoneal reflection coefficient of glucose compared with other dialysate solutes, allowing net transcapillary ultrafiltration to continue at a low rate even after osmotic equilibrium. D, Ultrafiltration can be maximized by measures that delay osmotic equilibrium, which can be accomplished by using hypertonic glucose solutions, larger volumes, or both, during an exchange. More frequent exchanges shorten dwell times and increase the dialysate flow rate and thus avert attaining osmotic equilibrium. Additionally, potential exists for enhancing ultrafiltration by measures that reduce the peritoneal reabsorption rate. (From Mactier and coworkers [13]; with permission.)

**FIGURE 4-9**

Equation to correct the creatinine levels in dialysate and serum. The creatinine levels in dialysate and serum need to be corrected for high glucose levels, which contribute to formation of noncreatinine chromogens during the creatinine assay. The correction factor may vary from one laboratory to another. In our laboratory at the University of Missouri–Columbia, the correction factor is 0.000531415. Accordingly, the corrected creatinine is calculated as in the equation. The correction in the serum is minimal due to low blood sugar levels; however, it is significant in dialysate, especially during the early phase of dwell (0- and 2-hour dialysate samples).

**Correction of creatinine levels**

Corrected creatinine (mg/dL) = Observed creatinine (mg/dL) - (glucose [mg/dL] x 0.000531415)
Equation to calculate the intraperitoneal residual volume. Residual volume is the volume of dialysate remaining in the peritoneal cavity after drainage over 20 minutes. The residual volume can be determined by knowing the dilution factor for solutes such as potassium, urea, and creatinine during the next instillation. The calculation of residual volumes is based on the assumption that the mixing of fluid in the peritoneal cavity is instantaneous and complete. This equation is used for the calculation, where $V_{\text{in}}$ is instillation volume; $S_1$ is solute concentration in pretest exchange dialysate; $S_2$ is solute concentration in instilled dialysis solution; and $S_3$ is solute concentration immediately after instillation (0 dwell time). The residual volumes by urea, creatinine, glucose, potassium, and protein are calculated and averaged for accuracy. The measurement of residual volumes is of limited clinical usefulness; however, it is of great value in a research setting in which accurate determination of intraperitoneal volume is required.

Classification of peritoneal transport function. Based on the peritoneal equilibrium test results, peritoneal transport function may be classified into average, high (H), and low (L) transport types. The average transport group is further subdivided into high-average (HA) and low-average (LA) types. For the population studied by Twardowski and coworkers [6], the transport classification is based on means; standard deviations (SDs); and minimum and maximum dialysate to plasma ratio ($D/P$) values over 4 hours for urea, creatinine, glucose, protein, potassium, sodium, and corrected creatinine (panels A–G).

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**FIGURE 4-11 (Continued)**
The volume of drainage correlates positively with dialysate glucose and negatively with D/P creatinine values at 4-hour dwell times (panel H). (From Twardowski and coworkers [6]; with permission.)

**CLINICAL APPLICATIONS OF THE PERITONEAL EQUILIBRATION TEST**

- Peritoneal membrane transport classification
- Choose peritoneal dialysis regimen.
- Monitor peritoneal membrane function.
- Diagnose acute membrane injury.
- Diagnose causes of inadequate ultrafiltration.
- Diagnose causes of inadequate solute clearance.
- Estimate dialysate to plasma ratio of a solute at time t.
- Diagnose early ultrafiltration failure.
- Predict dialysis dose.
- Assess influence of systemic disease on peritoneal membrane function.

**FIGURE 4-12**
In clinical practice it is customary to perform the baseline standardized peritoneal equilibrium test (PET) approximately 3 to 4 weeks after catheter insertion. The PET is repeated when complications occur. The standardized test for clinical use measures dialysate creatinine and glucose levels at 0, 2, and 4 hours of dwell time and serum levels of creatinine and glucose at any time during the test. The extensive unabridged test, as originally proposed by Twardowski and coworkers [6], has become a very important research tool.
**Baselined peritoneal equilibrium test**

- **High transporter** D/P creatinine: 16%
- **High average transporter** D/P creatinine: 68%
- **Low average transporter** D/P creatinine: 16%
- **Low transporter** D/P creatinine: 16%

**Baseline peritoneal equilibrium test results of patients on long-term peritoneal dialysis in the United States suggest that approximately 68% have average transport rates, 16% have high transport rates, and another 16% have low transport rates [6]. Similar distributions of transport types have been documented worldwide [14–16]. D/P—dialysate to plasma ratio.**

**FIGURE 4-13**
Population distribution of peritoneal membrane transport types. Baseline peritoneal equilibrium test results of patients on long-term peritoneal dialysis in the United States suggest that approximately 68% have average transport rates, 16% have high transport rates, and another 16% have low transport rates [6]. Similar distributions of transport types have been documented worldwide [14–16]. D/P—dialysate to plasma ratio.

**FIGURE 4-14**
Using transport type to select a peritoneal dialysis regimen. Because clearance rates continue to increase with time, patients with low transport rates are treated with long dwell exchanges, ie, continuous cyclic peritoneal dialysis (CCPD). Owing to the low rate of increase in the dialysate to plasma ratio (D/P), the clearance rate per unit of time is augmented relatively little by rapid exchange techniques such as nightly intermittent peritoneal dialysis (NIPD). On the contrary, the clearance per exchange rate over long dwell exchanges would be less in patients with high transport rates. During the short dwell time, patients with high transport rates capture maximum ultrafiltration and small solutes are completely equilibrated. Therefore, these patients are best treated with techniques using short dwell exchanges, ie, NIPD or daytime ambulatory peritoneal dialysis (DAPD). Patients with average transport rates can be effectively treated with either short or long dwell exchange techniques. CAPD—continuous ambulatory peritoneal dialysis.

**FIGURE 4-15**
Diagnosis of early ultrafiltration failure. The dialysate to plasma ratio (D/P) curve of sodium, during the unabridged peritoneal equilibrium test (2.5% dextrose dialysis solution), typically shows an initial decrease owing to the high ultrafiltration rate. Because of sodium sieving, the ultrafiltrate is low in sodium. Consequently, the dialysate sodium is lowered, resulting in a lower D/P ratio of sodium. Later, during the dwell when ultrafiltration ceases, dialysate sodium tends to equilibrate with that of capillary blood, returning the D/P ratio of sodium to baseline. Absence of the initial decrease of the D/P of sodium is an indication of ultrafiltration failure and is typically seen in the early phase of sclerosing encapsulating peritonitis. (From Dobbie and coworkers [17]; with permission.)
Dialysis as Treatment of End-Stage Renal Disease

\[
\text{C} = \frac{(D \times V)}{P}
\]

where \( C \) = clearance in mL/min;

\( D \times V \) = dialysate solute removed per minute;

\( D \) = dialysate solute concentration;

\( V \) = volume of dialysate in mL/min; and

\( P \) = plasma solute concentration

or

\[
\text{C} = (D/P) \times V
\]

where \( C \) = clearance in mL/exchange at time \( t \);

\( D/P \) = solute equilibrium rate at time \( t \); and

\( V \) = volume of dialysate at time \( t \)

\[
K_t/V
\]

where \( K \) = urea clearance in mL/min;

\( t \) = minutes of therapy; and

\( V \) = volume of urea distribution or total body water

**FIGURE 4-16**
Creatinine and urea clearances rates. These rates are estimated by dividing the amount of solute removed per unit of time by the plasma solute concentration. Alternatively, clearance also can be estimated by multiplying the solute equilibration rate per unit of time by the volume of dialysate into which equilibration occurred over the same unit of time. By convention, the creatinine clearance rate is normalized to body surface area.

The urea clearance is normalized to total body water (volume of urea distribution in the body) and is expressed as \( K_t/V \). The \( K_t/V \) value is a number without a unit \((\text{mL/min} \times \text{min})/\text{mL})\). During intermittent dialysis, with a dialysate flow rate of 30 mL/min, the typical urea clearance is about 18 to 20 mL/min [18]. Increasing the dialysate flow rates to 3.5 to 12 L/h by rapid exchanges increases the urea clearance rate to a maximum of 30 to 40 mL/min. Beyond this maximum rate, the clearance rate begins to decrease owing to the loss of membrane-fluid contact time with infusion and drainage; inadequate mixing may also occur [19–22]. Clearance could be enhanced by increasing the membrane-solution contact [23]. Continuous dialysate flow techniques using either two catheters or double-lumen catheters also have enhanced the urea clearance rate to a maximum of 40 mL/min. At these high flow rates, poor mixing, channeling, abdominal pain, and poor drainage limit successful application. Maintaining a fluid reservoir in the peritoneal cavity (called tidal peritoneal dialysis) and then replacing only a fraction of the intraperitoneal volume rapidly, increases clearance rates by about 30% compared with the standard technique using the same doses owing to maintaining fluid-membrane contact at higher dialysis-solution flow rates [24–29]. During continuous ambulatory peritoneal dialysis (CAPD) in adults, the optimum volume that ensures complete membrane-solution contact is about 2 L [30,32]. Successful use of 2.5- and 3.0-L volumes has been reported in adult patients undergoing CAPD; however, hernia complications are increased [32,33].

**FIGURE 4-17**
The mass-transfer area coefficient (MTAC). The MTAC represents the clearance rate by diffusion in the absence of ultrafiltration and when the solute accumulation in the dialysis solution is zero [34–39]. MTAC is equal to the product of peritoneal membrane permeability \((P)\) and effective peritoneal membrane surface area \((S)\). Thus, when both capillary blood and dialysate flows are infinite, the clearance rate is directly proportional to the effective peritoneal surface area and inversely proportional to the overall membrane resistance. However, infinite blood and dialysate flows cannot be achieved, and the maximum clearance rate is unattainable. The closest measurable value, the MTAC, was introduced. The MTAC represents an instantaneous clearance without being influenced by ultrafiltration and solute accumulation in the dialysate. The MTAC is measured over a test exchange during which at least two blood and dialysate samples are obtained at different dwell times. The precision of the measurement is enhanced with more data points. The MTAC is seldom used clinically; however, it is a very useful research tool.
References


