SECTION 26

Peritoneal Dialysis in the Intensive Care Unit

CHAPTER 178

Peritoneal Dialysis System

Claudio Ronco

OBJECTIVES

This chapter will:

1. Describe the anatomic characteristics of the peritoneal dialysis system.
2. Discuss peritoneal microcirculation.
3. Explain the mesothelial membrane.
4. Discuss the dialysate compartment and the influence of different dialysate flow/dwell times on efficacy of treatment.

Several factors affect the delivery of therapy in peritoneal dialysis. They are the amount of fluid used, the frequency of exchanges, the dwell time, and the type of solution employed. However, the final efficacy of the therapy depends on the anatomic and functional components of the dialytic system, such as the peritoneal circulation (blood compartment), the mesothelium (peritoneal membrane), and the dialysate compartment. Once these components are described clearly, different parameters of each technique become the foundations for an adequate therapy prescription and a crucial factor in treatment delivery.

PERITONEAL DIALYSIS SYSTEM

Since the beginning of dialytic therapy, diffusion and convection have been combined in an attempt to replace renal function.[1] The knowledge about diffusion came from industrial chemistry, and dialyzers were designed to be ideal countercurrent exchangers.[2] Only later was convection used in clinical practice, showing potential advantages.[3,4] Although ultrafiltration was employed first to treat overhydrated patients,[5] convective was used subsequently to enhance solute removal.[6–9] In peritoneal dialysis, such mechanisms of solute removal are employed with the same objectives as hemodialysis.

The peritoneal dialysis system has three major components: the peritoneal microcirculation, the peritoneal membrane, and the dialysate compartment, which includes the composition of the solution and the modalities of delivery. All of these components may have an important effect on the final performance of the technique (Fig. 178.1).[10]

DIALYSATE COMPARTMENT

The dialysate compartment is represented by the peritoneal cavity and the amount of fluid infused in one exchange. Basically, the compartment can be divided into a bulk region and a boundary layer of fluid, close to the peritoneal membrane. Furthermore, several variables should be taken into account, such as the time of infusion and drainage, the dwell time, the flow of dialysate, its temperature and composition, and the possible use of tidal techniques.

In Figure 178.2, urea clearance is plotted against dialysate flow rate. The curve identifies three specific regions. The first region consists of the dialysate flow rates typical for continuous ambulatory peritoneal dialysis (CAPD) (3–5 exchanges/day). In this region, the correlation is very steep, and clearance displays significant changes even in the presence of minimal changes in the dialysate flow. However, minimal variations in dialysate flow rate may require changing from four to five exchanges per day. This region is therefore dialysate flow-dependent or flow-limited, because the volume of dialysate per day is the factor that chiefly limits the clearance value. In this region, it would be theoretically simple to increase the dialysate flow by a few milliliters per day to achieve much higher clearances and, consequently, significant increases in Kt/V. However, although theoretically possible, this process would not be feasible in practice because it would mean carrying out 6 to 10 exchanges per day. The only possible way to increase the dialysate flow without raising the number of exchanges is to increase the volume of solution per exchange. To achieve the same fractional clearance in patients weighing 60 and 90 kg, the clinician must schedule four exchanges per day, with 2-L and 3-L bags, respectively. The impact

of possible intraperitoneal pressure rise must be checked carefully to avoid middle- to long-term complications such as hernias, respiratory problems, and decreased ultrafiltration. In conclusion, a typical CAPD technique is basically dialysate flow-limited.

The second part of the curve is the typical region of automated or intermittent peritoneal dialysis. The dialysate flows may vary significantly owing to a variation of the dwell time from 30 min to 0 and in the number of exchanges per day. Based on a 30-minute dwell time with 20 minutes for influx and outflow, 12 two-for-one exchanges can be performed overnight for an overall duration of 10 hours. The clearance will be 19 mL/min or 11.4 L/day. When the dwell time is reduced to 0 and the dialysate flow is therefore increased, the clearance rises to 22 to 30 mL/min with a total clearance per day of 18 L/day. This would result in a rise in the weekly Kt/V in a 60-kg patient from 2.21 to 3.50. However, this treatment, which could be defined as high-flux automated peritoneal dialysis (HFAPD), would require 60 L of dialysis solution, and the cost would become excessive. A good compromise could be the use of a tidal volume of solution, which may increase the dialysate volume artificially and enable better utilization of the surface area available for the exchanges.

The third part of the curve is the region where the plateau is reached, and further increases in dialysate flow rates do not result in parallel increases in clearance. This region has been explored experimentally, especially using continuous flow peritoneal dialysis (CFPD) performed with double-lumen peritoneal catheters[11] and theoretical mathematical models based on mass transfer-area coefficient (MTC) calculation.[12] The value of the mass transfer coefficient is a function of the product of the overall permeability of the peritoneum and the available surface area of the membrane. This parameter is based on the calculation made for each single subject of the maximal clearance theoretically achievable at infinite blood and dialysate flow rates (i.e., at a constantly maximal gradient for diffusion).

The regions of the curve just discussed describe the relationship between dialysate flow and solute transport. Other factors, such as dialysate temperature, intraperitoneal volume, and dialysate osmolality, are further factors affecting solute transport, either by increasing the diffusion process or by adding some convective transport because of increased ultrafiltration rates.

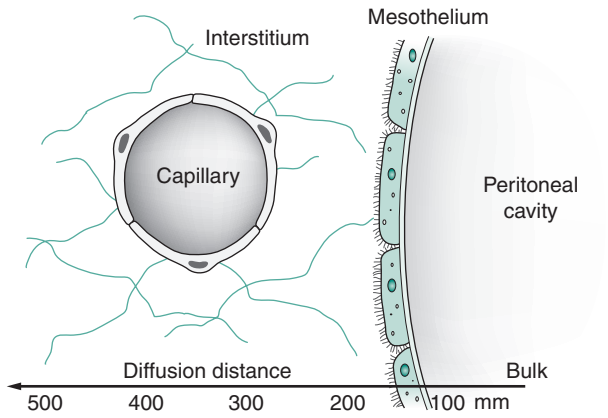

FIGURE 178.1 The peritoneal dialysis system: capillary, interstitium, mesothelium, and peritoneal cavity with the dialysate compartment.

Peritoneal Dialysis Membrane

The peritoneal dialysis membrane is a living structure that can be considered more a functional barrier than a precisely defined anatomic structure. On the basis of the flow/clearance curve described previously, the following question may arise: Why is the value of the mass transfer coefficient (MTC) so low in peritoneal dialysis compared with other dialysis treatments, and is the membrane involved in such limitations?

The three-pore model of peritoneal transport has been proposed by Rippe et al.[13] to explain the peculiar behavior of the peritoneal membrane in relation to macromolecules, micromolecules, and water transport. According to this model, human peritoneum appears to behave as a membrane with a series of differently sized pores as follows: large pores (25 nm; macromolecule transport), small pores (5 nm; micromolecule transport), and ultra-small pores (water transport). The anatomic structure of these ultra-small pores corresponds to the "water channels" created by a specific protein "aquaporin" acting as a carrier for water molecules. This model locates the main resistance to transport at the level of the capillary wall, regarding all other anatomic structures as a negligible site of resistance. Later the interstitium was added as an additional site of resistance.

A controversial opinion is offered by the so-called "distributed model" offered by Dedrick et al.[14] In this model,

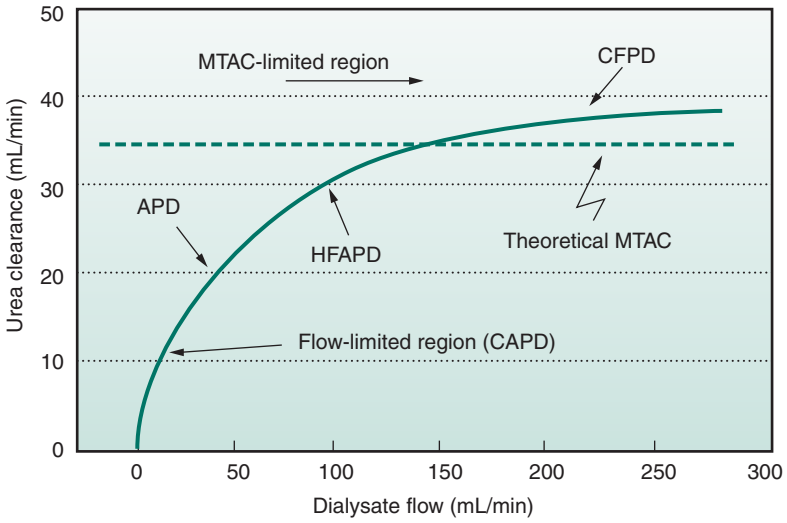

FIGURE 178.2 Dialysate flow rate/urea clearance domain map in peritoneal dialysis. A progressive increase in clearance is displayed with a parallel increase in dialysate flow. The phenomenon reaches a plateau at which no further clearance increases can be observed. *APD,* Automated peritoneal dialysis; *CAPD,* continuous ambulatory peritoneal dialysis; *CFPD,* continuous-flow peritoneal dialysis; *HFAPD,* high-flow automated peritoneal dialysis; *MTAC,* mass transfer-area coefficient.

the main resistance to transport apparently is located in the interstitial tissue. This anatomic entity consists of a double-density material containing water and glycosaminoglycans in different proportions. The interstitial matrix seems to act as the main site of resistance to solute and water transport from the bloodstream to the peritoneal cavity. The solute diffusivity in free water is greater than that in the tissue by more than one order of magnitude. Accordingly, not only the structure of the interstitium but also the thickness of the glycosaminoglycan layer may play an important role in restricting the diffusive transport of solutes. There is a certain discrepancy between the two models, and overall transport process probably is governed by a more complex and integrated series of events, each with a remarkable but not absolute importance. The pressures applied to the system that contribute to the generation of the transmembrane pressure are shown in detail in Figure 178.3. It is evident that the osmotic pressure generated by the glucose contained in the dialysate is by far the most important. Nevertheless, as shown in Figure 178.4, because the peritoneal membrane is not a perfect barrier for the employed osmotic agent (glucose), the transmembrane pressure gradient is continuously varying in relation to the velocity of reabsorption of glucose from dialysate into the blood compartment. Furthermore, capillaries, which are located at different distance from the mesothelial barrier, may be exposed to different concentrations of readsorbed glucose with different levels of cell damage (Fig. 178.5).

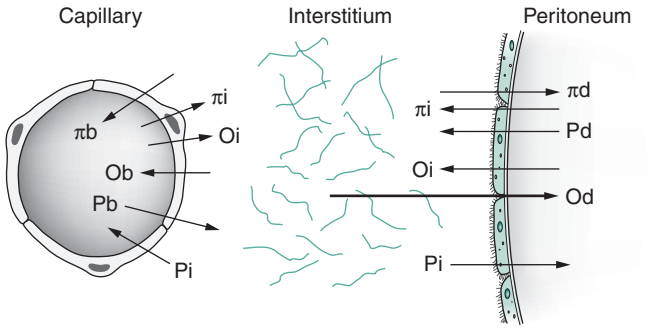

FIGURE 178.3 Depiction of the different pressures contributing to the generation of the transmembrane pressure: *b,* blood; *d,* dialysate; *i,* interstitium; *O,* osmotic; *P,* hydrostatic; π, oncotic.

Peritoneal Microcirculation

Despite several lines of evidence suggesting that peritoneal blood flow should be high enough to avoid any limitation in solute clearances and ultrafiltration, the real impact of effective blood flow on the efficiency of the peritoneal dialysis system is still controversial.[15] Experimental work has in fact suggested that peritoneal ultrafiltration and solute clearances may be blood flow-limited at least in some condition.[16]

Mesenteric blood flow averages 10% of cardiac output, but the peritoneal capillary blood flow seems to vary between 50 and 100 mL/min. The "effective" amount of flow involved in peritoneal exchanges is unknown, however, and could be much lower. Gas clearance studies have suggested that peritoneal blood flow may be as high as 68 to 82 mL/min,[17] whereas other studies have suggested a much lower value for "effective" blood flow.[18] Gas clearance studies were based on the assumption that peritoneal gas clearance is equivalent to effective blood flow, and this assumption may not necessarily represent the actual condition. Ronco et al.[19] have obtained an indirect measure of "effective" blood flow of between 25 and 45 mL/min.

In conclusion, controversy exists about whether the blood supply to the peritoneum and subperitoneal tissues limits

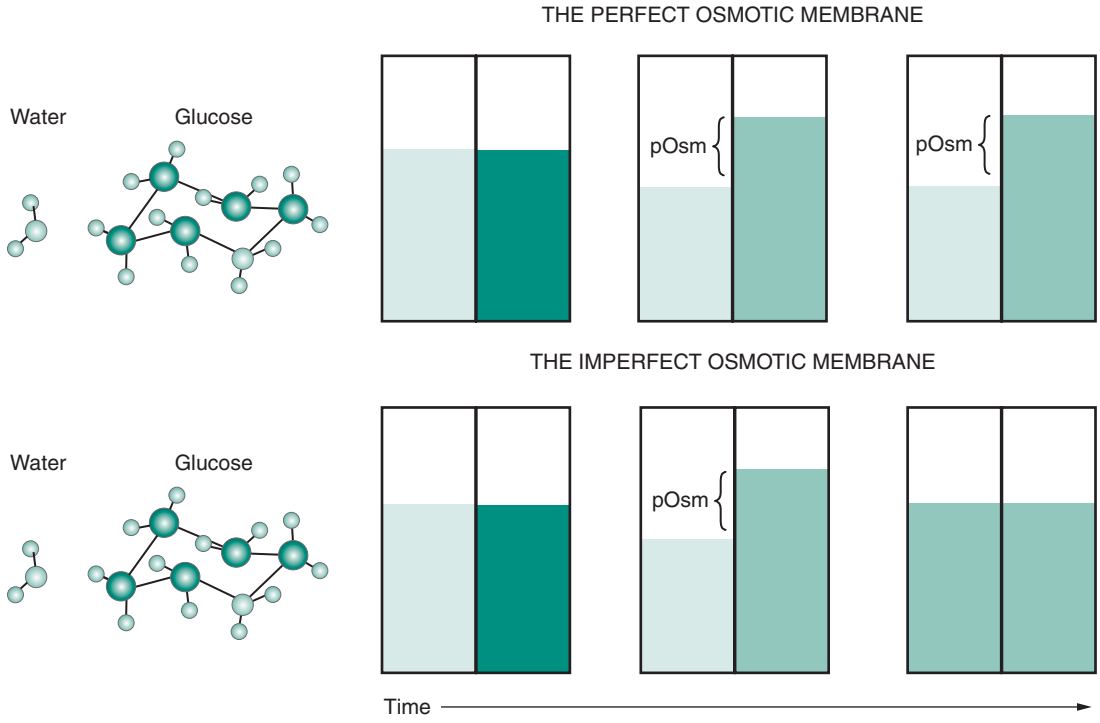

FIGURE 178.4 Graphic representation of perfect and imperfect osmotic membranes. After a time, the imperfect membrane allows a backdiffusion of the osmotic agent, and equilibrium is reached. The initial osmotic effect is achieved only because of the different diffusion velocities between glucose molecules and water molecules.

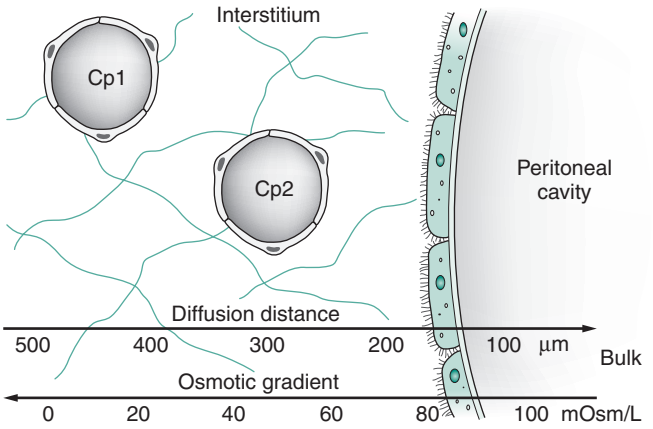

FIGURE 178.5 Graphic representation of a three-dimensional distribution of peritoneal microcirculation. Capillaries may have various distances from the mesothelial barrier, and this is the difference between the two.

the transport of solutes between the peritoneal cavity and the blood. Using a distributed model approach, Waniewski et al.[20] predicted the following marked changes in the mass transfer-area coefficient (MTAC, mL/min) for small solutes when the tissue blood perfusion rate (Q_b) was changed from 0.5 mL/min/g tissue to 0.1: $MTAC_{urea}$ decreases from 23 to 14, $MTAC_{creatinine}$ decreases from 17 to 11, and $MTAC_{glucose}$ decreases from 13 to 8. Unfortunately, there are no direct measurements of Q_b during peritoneal dialysis to test these calculations. In a study in rats, Kim et al.[21,22] found no blood flow limitations in the transfer of urea across the peritoneum of the abdominal wall, cecum, and stomach after suddenly decreasing the blood perfusion 60% to 72% from its baseline in the underlying tissue. In these studies, the blood perfusion relative to control value was measured with laser Doppler flowmetry, which does not provide an absolute measurement of Q_b that could be used to test Waniewski's assertion.

As an alternative view, Ronco et al.[18,19] have proposed that peritoneal blood flow may be a limiting factor in rapid peritoneal dialysis exchanges. The results obtained in a study in which a fragment of human peritoneum was perfused in a closed vascular loop displayed a linear correlation between the inlet blood flow and the rate of ultrafiltration, with a stable value of the filtration fraction. The linear correlation between small solute clearance and blood flow, even at high blood flows, seems to suggest that small solute clearance in peritoneal dialysis probably can be limited more by the low effective blood flow than by the low permeability of the peritoneal membrane. For larger solutes such as inulin, the low diffusion coefficients of the molecule may represent the most important limitation to transport. All these observations led to the formulation of the *nearest capillary hypothesis*.[23]

Because the peritoneal microvasculature is a network of capillaries with a three-dimensional distribution and different distances from the mesothelium (see Fig. 178.5), the diffusion distances of solutes as well as the glucose backdiffusion distances may be different in different populations of capillaries. In this condition, the capillaries situated closer to the mesothelium would experience greater osmotic effects than those located farther away, presenting a filtration fraction in closer capillaries to be much higher. The final effect would be represented by an average value of clearance and ultrafiltration to which proximal and distant capillaries are contributing differently. Clearance and ultrafiltration

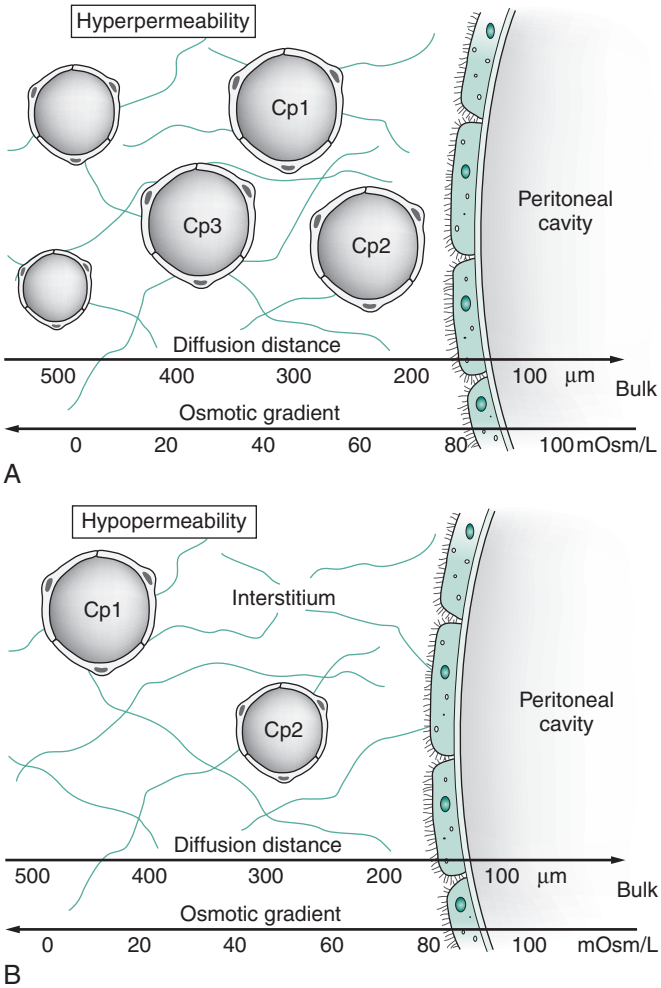

FIGURE 178.6 Graphic representations of the possible anatomic bases of hyperpermeability (A) and hypopermeability (B) according to the "nearest capillary" hypothesis (see text).

could be limited definitely by the low blood flow, at least in the capillaries closest to the peritoneal mesothelium. In distant capillaries, blood flow could be great enough to avoid significant limitations, but the effective blood flow in the capillaries closest to mesothelium may be too low. The vascular reserve, represented by the capillaries located farther from the mesothelium, would participate only partially in the peritoneal exchanges because of interference by the interstitial tissue. In such a condition, the central role of the interstitium becomes evident, as well as its hydration state. Anatomic observations demonstrate that interstitial tissue surrounding peritoneal capillaries may vary in thickness from 15 to 300 µm. The different locations of the capillary network in this tissue and the varying distances from the mesothelium therefore may help explain the different transport rates observed in different portions of the human peritoneum.[23]

The nearest capillary hypothesis also may help explain the pathologic conditions of hyperpermeability and hypopermeability of the peritoneal membrane. Hyperpermeability could occur from reduction in the interstitial spaces and a consequent crowding of the capillaries in a position close to the mesothelium (Fig. 178.6A). Hypopermeability could occur in the case of interstitial hyperhydration or in pathologic processes that affect the capillaries proximal to the mesothelium (Fig. 178.6B).

CONCLUSION

This chapter discussed the major factors influencing the efficiency of peritoneal dialysis, focusing on the anatomic and functional components of the peritoneal dialysis system. Other factors, such as patient and staff compliance, significantly influence treatment efficacy. Nevertheless, understanding the dialytic process in peritoneal dialysis starts with an understanding of the different components of the system and their specific function.

Key Points

1. Peritoneal dialysis relies on a semipermeable membrane (the peritoneum), which is a living structure and so presents significant variations in performance.
2. The peritoneal dialysis system comprises the microcirculation of the peritoneal area, the mesothelium, and the peritoneal cavity with the infused solution.
3. The microcirculation can become a crucial factor when rapid exchanges are used, and blood flow may become a limiting factor under certain circumstances.
4. The mesothelium has different levels of permeability in different subjects. Furthermore, it is not a perfect osmotic barrier.
5. The dialysate compartment is the component with a broader spectrum of possibilities in terms of variations of volume, flows, and other manipulations.

Key References

1. Alwall N. On the artificial kidney. I: Apparatus for dialysis of blood "in vivo." *Acta Med Scand*. 1947;128:317-321.
2. Kolff WJ. First clinical experience with the artificial kidney. *Ann Intern Med*. 1965;62:608-612.
3. Henderson LW, Besarab A, Michaels A, et al. Blood purification by ultrafiltration and fluid replacement (diafiltration). *Trans Am Soc Artif Intern Organs*. 1967;17:216-221.
4. Henderson LW, Colton CK, Ford C. Kinetics of hemodiafiltration. II: Clinical characterization of a new blood cleansing modality. *J Lab Clin Med*. 1975;85:372-375.
5. Maher JF, Schreiner GE, Waters TJ. Successful intermittent hemo-dialysis—longest reported maintenance of life in true oliguria (181 days). *Trans Am Soc Artif Itern Organs*. 1960;6:123-126.

A complete reference list can be found online at ExpertConsult.com.

References

1. Alwall N. On the artificial kidney. I: Apparatus for dialysis of blood "in vivo." *Acta Med Scand*. 1947;128:317-321.
2. Kolff WJ. First clinical experience with the artificial kidney. *Ann Intern Med*. 1965;62:608-612.
3. Henderson LW, Besarab A, Michaels A, et al. Blood purification by ultrafiltration and fluid replacement (diafiltration). *Trans Am Soc Artif Intern Organs*. 1967;17:216-221.
4. Henderson LW, Colton CK, Ford C. Kinetics of hemodiafiltration. II: Clinical characterization of a new blood cleansing modality. *J Lab Clin Med*. 1975;85:372-375.
5. Maher JF, Schreiner GE, Waters TJ. Successful intermittent hemo-dialysis—longest reported maintenance of life in true oliguria (181 days). *Trans Am Soc Artif Itern Organs*. 1960;6: 123-126.
6. Bergstrom J. Ultrafiltration without dialysis for removal of fluid and solutes in uremia. *Clin Nephrol*. 1978;9:156-161.
7. Babb AL, Farrel PC, Uvelli DA, et al. Hemodialyzer evaluation by examination of solute molecular spectra. *Trans ASAIO*. 1972;18:98-105.
8. Babb AL, Strand MJ, Uvelli DA, et al. Quantitative description of dialysis treatment: A dialysis index. *Kidney Int*. 1975;7(suppl 2):23-28.
9. Henderson LW. Biophysics of ultrafiltration and hemofiltration. In: Maher JF, ed. *Replacement of Renal Function by Dialysis: A Text-Book of Dialysis*. 3rd ed. New York: Kluwer Academic; 1989:300-326.
10. Ronco C, Brendolan A, La Greca G. The peritoneal dialysis system. *Nephrol Dial Transplant*. 1998;13(suppl 6):94-99.
11. Amerling R, Ronco C, Levin NW. Continuous flow peritoneal dialysis. *Perit Dial Int*. 2000;20(suppl 2):S178-S182.
12. Ronco C. Limitations of peritoneal dialysis. *Kidney Int*. 1996;50(suppl 56):69-74.
13. Rippe B, Simonsen O, Stelin G. Clinical implications of a three pore model of peritoneal transport. *Perit Dial Int*. 1991;7:3-9.
14. Dedrick RL, Flessner MF, Collins JM, et al. Is the peritoneum a membrane? *ASAIO J*. 1982;5:1-8.
15. Ronco C, Feriani M, Chiaramonte S, et al. Peritoneal blood flow: Does it matter? *Perit Dial Int*. 1996;16(suppl 1):70-75.
16. Ronco C, Brendolan A, Crepaldi C, et al. Ultrafiltration and clearance studies in human isolated peritoneal vascular loops. *Blood Purif*. 1994;12:233-242.
17. Aune S. Transperitoneal exchanges. II: Peritoneal blood flow estimated by hydrogen gas clearance. *Scand J Gastroenterol*. 1970;5:99-102.
18. Ronco C, Borin D, Brendolan A, et al. Influence of blood flow and plasma proteins on ultrafiltration rate in peritoneal dialysis. In: Maher JF, Winchester JF, eds. *Frontiers in Peritoneal Dialysis*. New York: Fieldrich and Associates; 1986:82-86.
19. Ronco C, Feriani M, Chiaramonte S, et al. Pathophysiology of ultrafiltration in peritoneal dialysis. *Peritoneal Dial Int*. 1990;10:119-126.
20. Waniewksi J, Werynski A, Lindholm B. Effect of blood perfusion on diffusive transport in peritoneal dialysis. *Kidney Int*. 1999;56:707-713.
21. Kim M, Lofthouse J, Flessner MF. A method to test blood flow limitation of peritoneal-blood solute transport. *J Am Soc Nephrol*. 1997;8:471-474.
22. Kim M, Lofthouse J, Flessner M. Blood flow limitations of solute transport across the visceral peritoneum. *J Am Soc Nephrol*. 1997;8:1946-1950.
23. Ronco C. The nearest capillary hypothesis: A novel approach to peritoneal transport physiology. *Perit Dial Int*. 1996;16:121-125.