CHAPTER 180

Solute and Water Transport Across the Peritoneal Barrier

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OBJECTIVES

This chapter will:
1. Describe the structure of the peritoneal barrier.
2. Review the physiology of solute and water transport under normal conditions.
3. Discuss the effects of the special conditions in the intensive care unit on transperitoneal solute and water transport.

Acute kidney injury (AKI) commonly develops in patients in either surgical or medical intensive care units because of these patients' underlying problems. The presence of AKI in the intensive care unit (ICU) in the setting of multiple-organ dysfunction increases the risk of mortality to 50% to 100%, depending on the number of organs in failure.[1] There are several ways to manage this type of renal failure. One is intermittent hemodialysis, which is performed with a standard hemodialysis machine. Another technique is continuous renal replacement therapy, performed with smaller dialysis machines that constantly process the blood. Typically, hemodialysis requires one-to-one nursing to monitor the blood pump and ensure the security of all blood lines.

Although used infrequently in the United States, peritoneal dialysis (PD) is a distinct alternative to provide renal support in the ICU. The major advantage of PD is that there is no need for anticoagulation, which is contraindicated in patients with bleeding diathesis or hemorrhagic conditions. The process can be carried out manually or with a programmable cycler, which does not require one-to-one nursing. If the catheter becomes obstructed or the machine malfunctions, the ICU nurse can merely turn off the machine until dialysis personnel are called to correct the situation. PD tends to be gentler on the cardiovascular system and is useful in hemodynamically unstable patients, such as those with heart failure.[2] A more thorough discussion of the indications for, contraindications to, and complications of PD in AKI can be found in Chapter 184.

PD can be used to deliver drugs or remove toxins owing to the peritoneum's permeability to both small solutes and higher-molecular-weight proteins. Dobutamine, insulin, antibiotics, and other chemotherapeutic agents may be given intraperitoneally;[3,4] indeed there is a significant pharmacokinetic advantage to local delivery of a drug when the target is located in the abdominal cavity.[5] In addition, the peritoneal cavity can be a source of blood transfusion or biologic agents (via the lymphatic drainage) and glucose or other nutrients that are easily absorbed into the circulation of the surrounding tissue.[6] Besides the clinical considerations, the physician must weigh carefully whether the technique will accomplish the desired outcome. Because PD uses parts of the patient's body to carry out the dialysis, assessments of the fundamental physiology and the impact of pathologic conditions on the dialysis process are important to the successful outcome. Patients with abdominal trauma or intraperitoneal bleeding diathesis obviously cannot undergo this mode of dialysis. Occasionally, cardiothoracic surgery or recent abdominal surgery may be a contraindication because of multiple drains in the chest and peritoneal cavity, which may increase the risk of infection and also result in leaks from the cavity. Diaphragmatic peritoneal pleural connections may be present and may result in pleural effusions when dialysis fluid is placed in the cavity.[7] PD increases intraabdominal pressure,[8] potentially impeding the descent of the diaphragm and compromising ventilation or respiration.

This chapter describes the basic structure and function of the peritoneum and the special considerations needed for utilization of the peritoneal cavity as a dialyzer in the ICU.

STRUCTURE OF THE PERITONEAL BARRIER AND TRANSPORT PRINCIPLES

Distributed Nature of the Barrier

Fig. 180.1 displays the elements of the peritoneal barrier, which is much more complex than the concept of a single "peritoneal membrane." As illustrated, the barrier has the following three components: (1) the anatomic peritoneum, (2) the cell-interstitial matrix, and (3) blood capillary endothelium lining the vasculature, which is distributed within the tissue. The anatomic peritoneum consists of a single layer of mesothelial cells overlying several layers of connective tissue. The visceral peritoneum has been dissected and measured to be 90 mm thick in the normal state.[9] Although many nephrologists consider the anatomic peritoneum the barrier to transport, experiments in both humans and rodents have demonstrated that the peritoneum is not a barrier to solute and water transport.[10] Complete destruction of the peritoneum in rodents has had no effect on the transfer of small solutes or the osmotic filtration of fluid from the peritoneal cavity into a transport chamber.[10] There have been parallel findings in patients who undergo extensive peritonectomy for treatment of peritoneal carcinomatosis; in one report, clearance of mitomycin C from the peritoneal cavity was not significantly affected by an extensive peritoneal resection.[11] On the other hand, if the overall peritoneal thickness increases with uremic inflammation and fibrosis from chronic contact over months with dialysis fluid, the transfer of water but not solute would be affected.[12] However, unless there were ongoing inflammation in the abdominal cavity, the mesothelium and the underlying tissue should be relatively normal in AKI without other changes.

The two other major components of the peritoneum therefore make up the barrier. The cell-interstitial matrix restricts movement of solutes and water between the blood

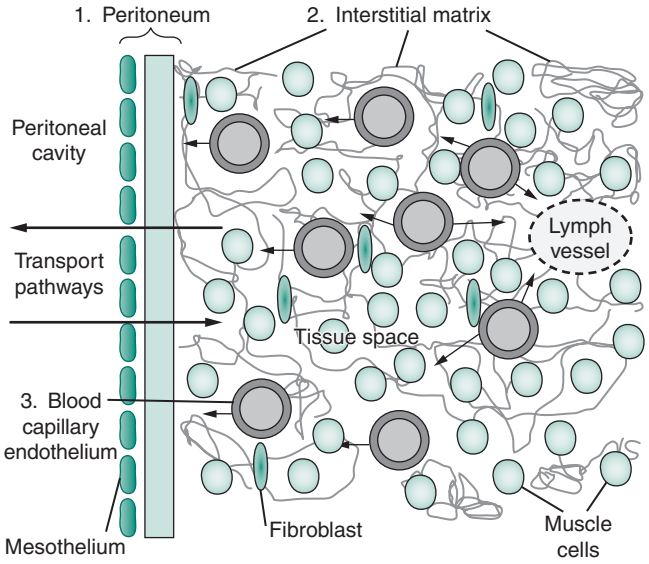

FIGURE 180.1 Potential barriers separating the dialysis solution in the peritoneal cavity from the plasma flowing within the microvasculature distributed within the subperitoneal tissue.

capillary walls and the peritoneal cavity,[12] slowing transport and making it less efficient than if the blood vessels were in direct contact with the dialysis solution. Because the muscle of the abdominal wall and the gut constitute the vast majority of the peritoneal surface in contact with the dialysis solution,[13] the vessels of these tissues dominate transport. The endothelium of most smooth muscles, capillaries, and venules is known to be size selective.[14] As illustrated in Fig. 180.1, these vessels, through which the blood flows, are distributed within these tissues, which are surrounded by cells and the interstitial matrix.[15]

Effects of the Interstitial Matrix on Transport

The interstitial matrix, once considered to be inert, "sticky" mucopolysaccharides and termed "ground substance," is now known to be an orderly structure of the tissue.[16] Collagen fibers, which provide the skeleton of the interstitial network, are linked to interstitial cells and possibly pericytes through adhesion molecules such as β_1-integrins.[17] These collagen fibers can stretch and contract as the cells to which they are attached are stimulated in different ways.[18] Wrapped around the collagen fibers and, in some cases, attached to them are large (1-40 megadaltons) molecules of hyaluronan, with proteoglycan molecules bound to the hyaluronan molecules. The hyaluronan molecules within the collagen matrix are highly negatively charged, imbibe large amounts of water, and restrict the passage of negatively charged proteins.[19] Proteins are typically restricted to about 50% of the interstitial space,[20] which translates into a protein space of 6% to 10% of the entire tissue space available to proteins for transport if the typical interstitial space is only 12% to 20%.[21]

The rates of transport through the tissue depend on the interstitial matrix. Transport includes diffusion, which can be described by the effective diffusivity as follows:

$$D_{eff} = \frac{D_{isf}\theta_{isf}}{\tau}. \quad [1]$$

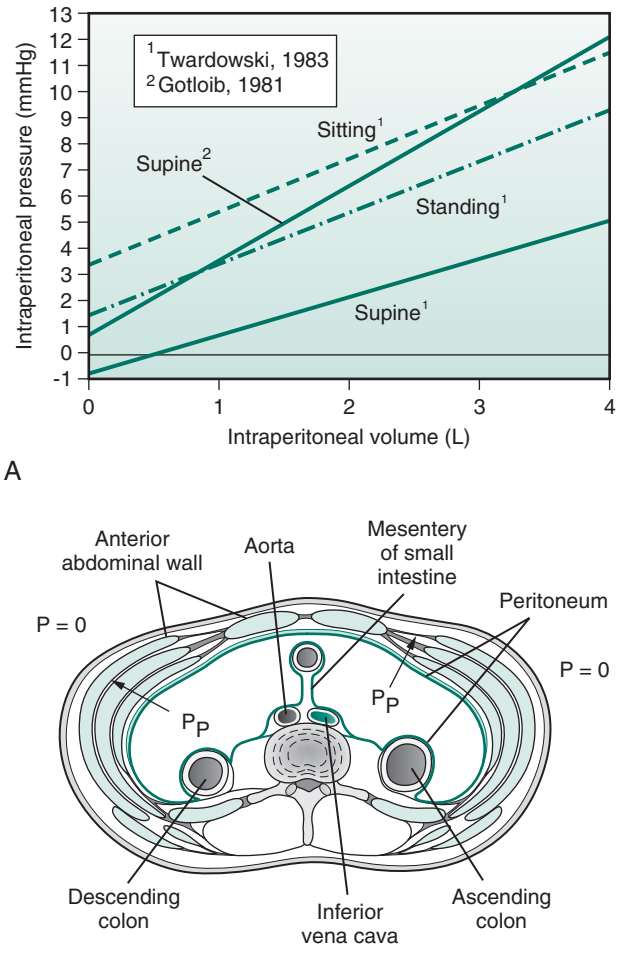

FIGURE 180.2 A, Intraperitoneal hydrostatic pressure versus volume instilled. *Data from Gotloib L, Mines M, Garmizo L, Varka I. Hemodynamic effects of increasing intra-abdominal pressure in peritoneal dialysis. *Peritoneal Dial Bull.* 1981;1:41–43. †Data from Twardowski ZJ, Prowant BF, Nolph KD. High volume, low frequency continuous ambulatory peritoneal dialysis. *Kidney Int.* 1983;23:64–70. B, Abdominal cross section demonstrating pressure gradient from the cavity into local tissue and, in particular, the abdominal wall. *P,* Pressure at skin surface; P_{PC}, peritoneal hydrostatic pressure.

where D_{eff} is effective tissue diffusivity; D_{isf} is diffusion coefficient in the interstitium; θ_{isf} is the interstitial fraction (fraction of the total tissue space available to the solute); and τ is tortuosity (factor to account for the convoluted path of the solute around cells and through the interstitial matrix).[22] For water transport and substances that are transported chiefly through convection or solvent drag, the hydraulic conductivity of the tissue space (K_{tiss}) has been shown to depend on the interstitial fraction and the concentrations of collagen, proteoglycan, and hyaluronan.[21]

Dialysis solutions infused into the peritoneal cavity typically cause intraperitoneal hydrostatic pressures (IPP) above 3 or 4 mm Hg, which alter the surrounding tissue space.[23] Intraperitoneal pressures depend on the size and position of the patient, and on the infusion volume used (Fig. 180.2A).[8,24] IPPs of 4 mm Hg would seem to be a very small increase, but the tissue responds by absorbing significant amounts of fluid.[25] This absorption occurs particularly in the abdominal wall, where there is a positive-pressure gradient

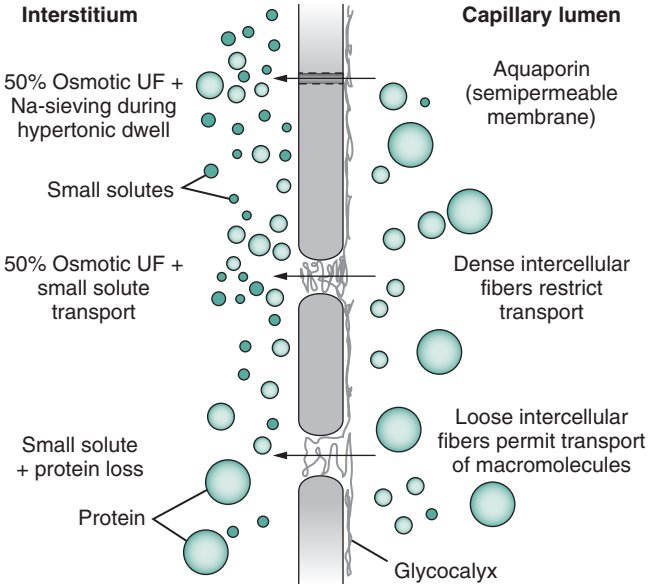

FIGURE 180.3 Pore-fiber-matrix concept of the blood capillary endothelial barrier. *UF,* Ultrafiltration.

from the serosa to the subcutaneous space (Fig. 180.2B).[26] Studies in rats have demonstrated that the extracellular space doubles with a rise in IPP from zero to 3 mm Hg,[27] and the hydraulic conductivity increases four to five times.[28] In experiments in the rat, sampling of the interstitial fluid after 4 hours of dialysis showed a 50% decrease in colloid osmotic pressure.[29] Expansion of the interstitial space and decreases in collagen and hyaluronan concentrations raise the rates of diffusion and convection within the tissue. Clinical complications can occur from this intraabdominal pressure that may result in abdominal wall hernias or inhibit diaphragmatic movement of ventilated ICU patients.

Nature of the Endothelial Barrier

The endothelial barrier is depicted in Fig. 180.3 as a transcellular pore, called an *aquaporin*, and different intercellular gaps lined with matrix material, called the *glycocalyx*[30–68]; this concept represents a necessary modification of the three-pore model of peritoneal transport[31] to account for alterations in pathologic states. The aquaporin permits only water through its channel and is responsible for much of the osmotically induced filtration from the plasma.[32] Intercellular gaps lined by the glycocalyx are the second portion of the barrier, which permit the transfer of solutes and water, depending on the density of the glycocalyx.

The discovery of aquaporins by Agre and colleagues[33] has brought new understanding to the transfer of water across blood capillaries into the tissue and subsequently into the peritoneal cavity. Because the aquaporin does not permit any solute to transfer, it represents the perfect semipermeable membrane across which any solute concentration difference exerts osmotic pressures that result in filtration. The functional significance of the aquaporins has been demonstrated in numerous experiments. Carlsson et al.[34] showed that in vivo inhibition of aquaporins with mercuric chloride resulted in a significant decrease in volume of osmotically filtered fluid from the tissue. Sixty-six percent inhibition of water flow through the aquaporins was verified subsequently by Yang et al.[32] in aquaporin 1—knockout mice. When mice were dialyzed with a hypertonic solution, the filtration in the knockout mice was 40% of that in normal mice. Another study in rodents has demonstrated both the structural appearance and the functionality of the endothelial aquaporins.[35]

Solute transport depends on the density of the glycocalyx in the intercellular gap.[36] A denser glycocalyx restricts the passage of larger solutes (functionally equivalent to the "small pore" of the three-pore model), with a less dense glycocalyx allowing protein leakage (the equivalent of the "large pore" of the three-pore model). In the normal situation, the vast majority of the intercellular spaces are densely packed with glycocalyx and restrict the passage of macromolecules, making up 95% of the total capillary permeable area;[37] these spaces are responsible for 40% to 50% of the osmotic filtration. Vlahu et al.[69] examined the endothelial glycocalyx in patients with chronic renal failure; using Sidestream Darkfield imaging, they demonstrated significant damage to the glycocalyx barrier. Subsequent studies in rodents did not demonstrate major changes to the peritoneal glycocalyx with exposure to dialysis solutions. These authors concluded that this area needs further research. The remainder of the capillary is made up of intercellular junctions, which permit proteins to leak out.

The rate of transfer from the plasma to the interstitial space of the surrounding tissue can be represented in a simplified fashion as follows:[38]

$$J_{endo} = pa\,(C_{plasma} - C_{isf}) \quad [2]$$

where J_{endo} is solute transfer rate across the endothelium (mass/time/tissue mass); p is overall endothelial permeability, including the effect of all intercellular passages; a is capillary surface area/mass of tissue; C_{plasma} is solute concentration in plasma; and C_{isf} is solute concentration in interstitial fluid. More complicated mathematical approaches can be employed to include the three elements of the endothelial barrier.[22,39]

PHYSIOLOGY OF TRANSPORT: NORMAL CONDITIONS

The overall rate of mass transfer can be described by the following equation:[38]

$$\frac{dM_{cavity}}{dt} = MTC \times A_{contact}(C_{plasma} - C_{cavity}) \quad [3]$$

where M_{cavity} is solute mass in the peritoneal cavity (equal to the product of the solute concentration in cavity—C_{cavity}—and the volume in the cavity); t = time; MTC is the overall mass transfer coefficient across the peritoneal barrier; $A_{contact}$ is the area of the peritoneum in contact with the dialysis solution; and C_{plasma} is solute concentration in the plasma. In experiments in rodents, four major surfaces within the peritoneal cavity have been shown to have very similar MTCs,[40] thus justifying the use of one value for the overall MTC. MTC has been shown to be very similar in different rodent species as well and likely is similar in other mammals.[41] $A_{contact}$ is typically not measured in humans, and its product with the MTC is termed the *mass transfer-area coefficient* (MTAC).[42] The overall clearance or MTAC is plotted in Fig. 180.4.

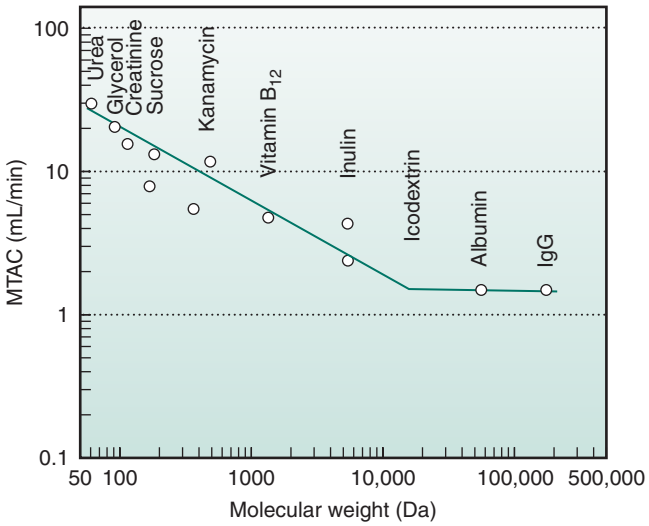

FIGURE 180.4 Mass transfer-area coefficient (MTAC) versus molecular weight. (Modified from Flessner MF. Intraperitoneal drug therapy: Physical and biological principles. In Beelen RH [ed]. Multidisciplinary Management of Peritoneal Carcinomatosis. New York, Springer, 2006.)

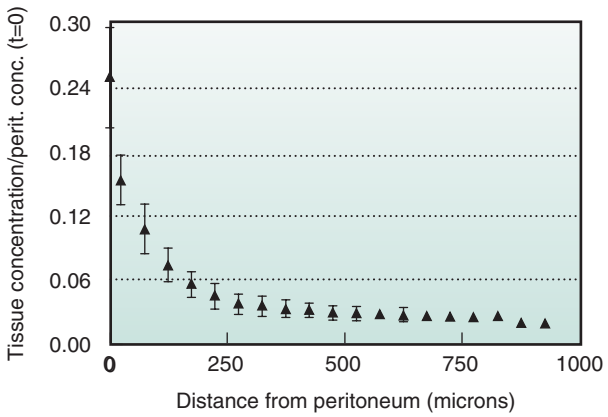

FIGURE 180.5 Concentration (C) profile of mannitol (equivalent to that of dextrose) in the abdominal wall of the rat. (Modified from Flessner MF, Deverkadra R, Smitherman J, et al. In vivo determination of diffusive transport parameters in a superfused tissue. *Am J Physiol Renal Physiol.* 2006;291:F1096–F1103.)

Importance of the Surface Contact Area

As can be observed in Eq. 3, the contact area ($A_{contact}$) is a major determinant of the rate of solute transfer. As can be seen in Fig. 180.1, if the solution does not make contact with the tissue, transfer from the blood capillaries to the peritoneal cavity cannot occur. That the rate of transfer is directly proportional to this surface contact area is apparent from Eq. 3. This relationship has also been shown both in animals[43] and in patients undergoing PD.[44,45]

Kesheviah et al.[46] carried out one of the first studies in humans, in which they determined the MTAC (MTC × $A_{contact}$) in 10 patients who were dialyzed with different solution volumes varying from 0.5 to 3.5 L. Upon increasing the fill volume from 0.5 to about 3 L, these investigators observed a linear rise in the MTAC, which was attributed to an increase in surface area. Chagnac and associates[45] dialyzed patients with a radiographic contrast agent injected intraperitoneally and employed computed tomography with special stereographic techniques to calculate the area; they found that with 2 L in a typical patient, the area covered was about 0.55 m^2 or about one third of the total anatomic area.[47] When the fill volume was raised to 3 L, the investigators also observed an increase in the measured contact area of 18% and obtained a 25% increase in MTAC.[44] When the peritoneal volume is maximized to about 3.0 L of standard solution, $A_{contact}$ approaches a maximum, ensuring maximal rates of transfer. Unfortunately, larger volumes also increase the IPP (see Fig. 180.2A)[8] and may compromise respiration or net ultrafiltration.[23]

Solute Transfer Across the Peritoneal Barrier

The functional proof for the concept of the peritoneal barrier as a distributed microvasculature within a tissue space is derived from the solute profile data shown in Fig. 180.5. Concentration profiles for mannitol (equivalent to glucose) are plotted in Fig. 180.5, demonstrating solute transporting from the cavity into the tissue over hundreds of microns. Because the normal human peritoneum is less than 100 μm thick, the extension of the concentration profile over 500 to 1000 μm implies that a considerable portion of the underlying tissue is involved with the transport. The MTC can be linked to the underlying tissue through two equations.[3,38,42] If the blood flow within the tissue is more than adequate to sustain mass transfer, then the following equation applies:

$$MTC = \sqrt{D_{eff}(pa)} \quad [4]$$

However, if blood flow is limited so that the rate of diffusion in the tissue is limited by the solute supply or removal by the blood flow through the tissue, then the following equation applies:

$$MTC = \sqrt{D_{eff} \times q} \ \textit{for} \text{ blood-flow limited transport} \quad [5]$$

where q is plasma flow rate per unit mass of tissue.

In theory, very low blood flows may actually limit the transfer of small solutes such as urea (molecular weight 60 Da). Experiments in rats however demonstrated that lowering the perfusion in local tissues in individual organs to 20% or 30% of the original level did not change mass transfer rates of urea across the peritoneum of the cecum, stomach, or abdominal wall; however, solute transfer across the liver was significantly altered with the decrease in blood flow.[48] In analogous experiments, a decrease in blood flow across these organs did result in reductions in the transfer of water through osmotic filtration, but the results were not statistically significant except in the liver.[49] One can therefore conclude that under normal circumstances, the transfer of solutes and water should not be restricted by the blood flow but are probably limited by the rate of diffusion through the tissue and the perfused capillary area (a) and permeability (p). From this theory, offered by Dedrick et al.[38] in 1982, for the diffusion-limited solute with a molecular weight of less than 6000 daltons, the steady-state concentration profile can be defined as follows:

$$\frac{C_{isf} - C_{plasma}}{C_{cavity} - C_{plasma}} = \exp^{-\sqrt{\frac{(pa)}{D_{eff}}}x} \quad [6]$$

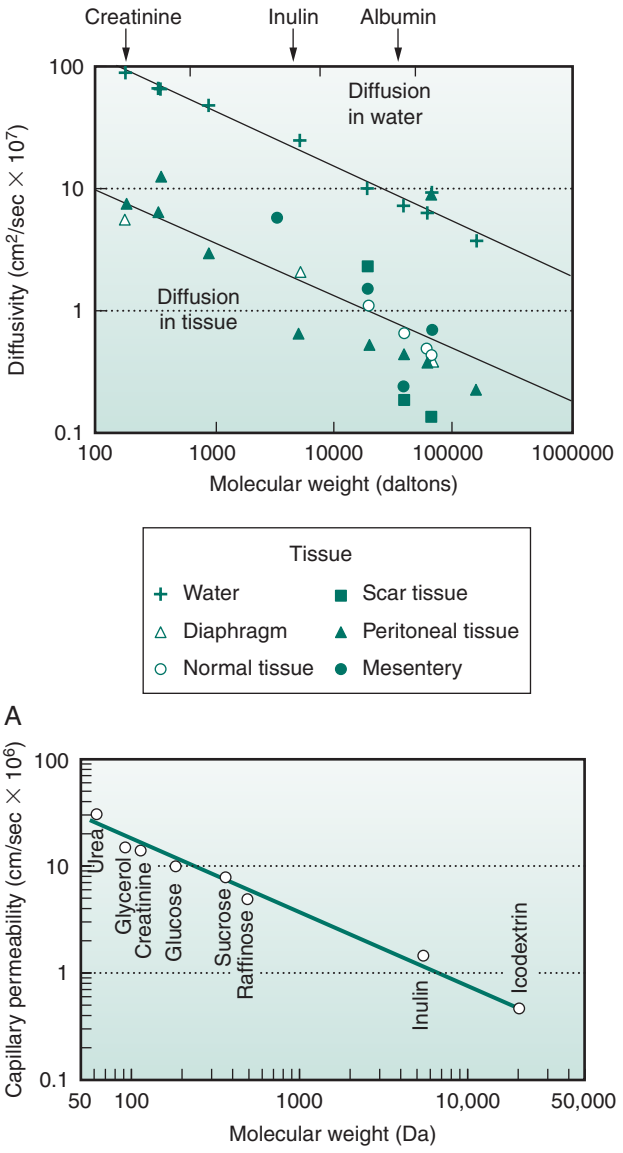

FIGURE 180.6 A, Solute diffusivities in water and various tissues versus solute molecular radius. The plot demonstrates the order of magnitude differences between the diffusion coefficients in water and those in tissues. BSA, bovine serum albumin. B, Capillary permeability versus molecular weight of solutes. **A** (Data from Dedrick RL, Flessner MF, Collins JM, Schultz JS. Is the peritoneum a membrane? ASAIO J. 1982;5:1-5; Dedrick RL. Interspecies scaling of regional drug delivery. J Pharm Sci. 1986;75:1047-1052; and Flessner MF. Peritoneal transport physiology: Insights from basic research. J Am Soc Nephrol. 1991;2:122-135.) **B** (Data from Dedrick RL, Flessner MF, Collins JM, Schultz JS. Is the peritoneum a membrane? ASAIO J. 1982;5:1-5.)

where x is the distance from the peritoneum into the tissue. The fitting of Eq. 6 to measured profiles during the dialysis in rodents has permitted the estimation of both D_{eff} and (pa).[42] The perfused capillary surface area per unit volume of tissue was measured, and the actual p was calculated from the (pa) factor. Fig. 180.6A is a plot of the derived diffusivities, and Fig. 180.6B shows values for capillary permeability (p) from data described by Dedrick et al.[38] The capillary area-density "a" of muscle capillary is about 70 cm^2 per gram of tissue,[50] and that of the abdominal wall is 600 cm^2 per mL of abdominal wall tissue.[42]

Water Flow and Calculation of Net Ultrafiltration

There are many theories as to how water is extracted from the body during PD, but none of them fully explains the phenomena of net ultrafiltration (net UF).

Net UF is defined as follows[23]:

$$\text{Net UF} = \frac{\text{Drain volume} - \text{Fill volume}}{\text{Dwell time}} \quad [7]$$

This equation does not identify what forces govern the transfer of fluid. Ultrafiltration across a blood capillary follows the classic Starling equation:

$$\text{Fluid transport rate} = K_f \text{x a} \times [P_{plasma} - P_{isf} - (\pi_{plasma} - \pi_{isf})] \quad [8]$$

where: K_f is membrane filtration coefficient; P is hydrostatic pressure; and π is effective osmotic pressure. However, the integration of this equation into the distributed model concept cannot easily be accomplished because of the uncertainty of the true osmotic forces in the interstitium and the variable, time-dependent concentration of the osmotic solute (see Fig. 180.5). At this time, most models are semiempirical in nature and often resort to fitting the model to patient data. More sophisticated mathematical models have been developed by Waniewski[70] and Stachowska-Pietka;[71] these works should be consulted for a more detailed mathematical treatment.

The net UF is made up of two components as follows:

$$\text{Net UF} = \text{Osmotically driven filtration} - \text{Fluid loss} \quad [9]$$

Fluid loss is fluid transfer from the cavity, which is equal to direct lymph flow plus the hydrostatic pressure-driven convection to the surrounding tissues. From the tissue, transfer into the blood capillaries or intratissue lymphatics carries the fluid back to the plasma compartment.[3,23] The lymphatic flow is a minor part (10-20%) of the fluid loss term.

Lymphatic Drainage From the Peritoneal Cavity

The lymphatic system draining the peritoneal cavity is divided into two parts. The subdiaphragmatic lymphatic system drains 70% to 80% of the lymphatic flow from the peritoneal cavity.[51] The diaphragm acts as a pumping mechanism that pulls fluid from the lower parts of the peritoneal cavity toward the diaphragm. As the diaphragm moves upward in expiration, the lymphatic plexus expands, and a negative pressure is established in the lymphatic vessels. Lacunae, or penetrations in the basement membranes, open via stomata to take in fluids, solutes, and particles up to 25 μm in diameter. For this reason, bacteria are rapidly taken up from the cavity and transported toward the venous system in the neck. When the diaphragm contracts, the tension in the lymphatic wall is released, the stomata are closed, and pressure is exerted on the lacunae.[52] The fluid is propelled upward toward the right lymphatic duct or into the thoracic duct.

The remaining 20% to 30% of lymph flow from the peritoneal cavity is absorbed into the visceral lymphatics. These drain to the mesenteric lymphatics and to the cisterna chyli at the base of the thoracic duct. This duct subsequently drains into the left venous system.[53] Under

normal conditions in stable patients undergoing PD, the rate of lymphatic flow varies between 7 and 20 mL/hr,[23] with the total peritoneal fluid loss between 60 and 91 mL/hr.[54–56]

Clinical Effects of Intraperitoneal Pressure

Durand et al.[57] demonstrated the importance of intraperitoneal hydrostatic pressure (IPP) in determining the fluid loss from the cavity. They carried out a careful study of the effect of IPP on the net UF in 34 patients. All patients were placed in supine position to minimize changes of IPP during dialysis with 3.86% dextrose solution. After 2 hours, the net UF was measured; it was shown to vary indirectly with the intraperitoneal hydrostatic pressure and to have a net fluid absorption rate from the peritoneal cavity between 31 and 36 mL/hr per cm H_2O of IPP.[57] Rusthoven and associates[58] have verified the measurements published by Durand and associates[57] in children and have demonstrated an inverse correlation between change in IPP and the body's surface area.

Both animal data and human data have shown that fluid loss during PD—that is, flow back to the patient—can amount to 1.5 to 2 L per day. Increases in intraperitoneal dwell volume increase the IPP and may lead to a decrease in net UF. This decrease can greatly affect the child with a small body surface area and has been shown to have a negative correlation with body surface area.

Alteration of the Transport Barrier: Normal Physiology

As discussed previously, enhancement of solute transport can be accomplished by increasing the contact surface area through larger peritoneal volumes.[44,46] This approach may be impossible for some patients in the ICU because of respiratory or ventilatory difficulties. If the concentration of the surfactant diacetyl sodium sulfosuccinate in the PD solution is relatively high,[13,59] 100% of the anatomic peritoneum is in contact with the solution; however, such a high concentration is toxic and should not be used in humans. If surfactant materials are to be used, they must have been very carefully tested and proven to be nontoxic to patients.

A second way to raise the rate of transfer is to increase the perfused capillary surface area. Nitroprusside, when placed in the dialysis solution, has been shown to significantly enhance transport.[60–62] Unfortunately, intraperitoneal nitroprusside appears to be limited by a loss of effect after approximately five exchanges. In addition, there may be some decrease in blood pressure with the use of this drug. Vasoconstrictors have been demonstrated to reduce the perfused endothelial area and significantly decrease mass transfer.[42]

ACUTE PERITONEAL DIALYSIS IN THE INTENSIVE CARE UNIT: SPECIAL CONDITIONS

Hypotension and Peritoneal Blood Supply

Severe trauma or sepsis often results in hypotension, which leads to generalized vasoconstriction that might compromise the circulation supplying the tissues adjacent to the peritoneum. Blood flow limitation is observed when delivery of solute in the plasma to the exchange vessels is less than the rate of solute transfer across the capillaries into the interstitium. In a previous study in normotensive rodents, reducing the blood flow locally to 20% to 30% of baseline did not limit solute transfer but did decrease fluid transfer.[48,49] Additional studies have demonstrated that use of high doses of vasoconstrictors (1 mg/mL of norepinephrine) locally reduces the perfused vascular area, resulting in a marked decrease in the rate of mass transfer and osmotic ultrafiltration.[42] Other researchers have shown however that if an animal is put into shock by bleeding,[63] the mass transfer coefficient is reduced by 25% after the mean arterial blood pressure decreases from 133 to 61 mm Hg.[63] The perfused vascular area was not measured in this study, but the perfusion, as measured by laser Doppler flowmetry, was reduced by 50%, in turn resulting in a 25% reduction in the mass transfer of labeled ethylene-diamine-tetra-acetic acid (EDTA). From this information, one may conclude that the condition of circulatory shock with severe hypotension may have a modest effect on PD solute transfer, which may be further compromised by the presence of endogenous or exogenously administered high levels of vasoconstrictors.

Dehydration and Hypotension

Occasionally patients in the ICU may be extremely dehydrated, because of heat exhaustion, severe diarrheal illness, or profound diuresis. Such was the case in one patient with severe heart failure who had been given massive amounts of diuretics, which resulted in renal failure, hyperosmolality, and hypotension (blood pressure approximately 90 mm Hg systolic, 50 mm Hg diastolic). After placement of a peritoneal catheter, the patient was started on a 90-minute 2 L dwell of 1.5% dextrose solution; the 2L volume returned 1000 mL. The solution was changed to 2 L of 2.5% dextrose solution, with the same result. Subsequently, the solution was changed to a 4.25% dextrose dialysis solution with a positive output. It is well known that dehydration lowers the interstitial pressure from about 0 mm Hg to a *negative* value (-5 to -10 mm Hg[64]); this event in the patient likely set up a very large positive-pressure difference between the cavity and abdominal wall tissue (see Fig. 180.2). The 2 L of fluid absorbed in the first two exchanges not only increased the mean arterial pressure but also hydrated the tissue surrounding the peritoneal cavity and raised the tissue pressure, in turn decreasing the fluid loss rate. Although solute transfer was not compromised in this case, the osmotic ultrafiltration failed until the peritoneal tissue was hydrated and the patient's blood pressure rose to a normal range.

Practical Limits of Solute Transfer

Maximal rates of mass transfer in any ICU renal replacement therapy ensure adequate therapy. As discussed previously, vasodilators such as nitroprusside enhance the rate of mass transfer for several exchanges but then lose their effectiveness and may further compromise systemic blood pressure.[61] The dwell volume can be increased to improve the contact area, but this approach increases the IPP, potentially causing either leakage around the recently placed catheter or compromise of ventilation. Under conditions prevalent in the ICU, it would appear that the nephrologist would have little control over the perfused vascular area. However, use of innovations such as continuous-flow PD[65] in postoperative chemotherapy[66] has achieved marked increases in mass transfer with the use of dual catheters and continuous circulation of a heated

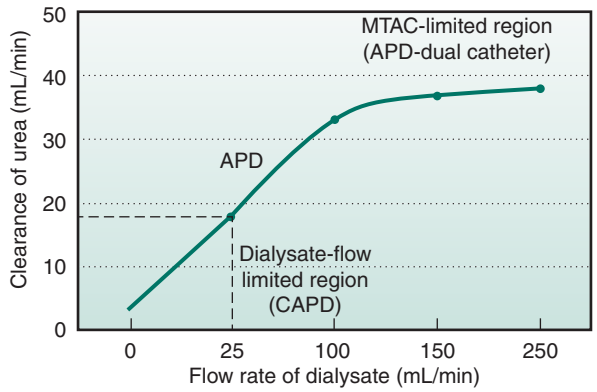

FIGURE 180.7 Urea clearance versus dialysate flow rate. (Modified from Ronco C. Limitations of peritoneal dialysis. *Kidney Int.* 1996;50[Suppl 56]:S69–S74.)

solution (40° C). The mass transfer rates for small substances, such as glucose and creatinine, increased to approximately twice that of the normal clearance and approached the region of the "MTAC-limited area" outlined in Fig. 180.7.[67] This marked elevation was likely due to a combination of increased peritoneal contact area and the recruitment of blood vessels by the heated fluid.

Key Points

1. The normal anatomic peritoneum is not a significant barrier to solute and water transport during dialysis.
2. The functional transport barrier in peritoneal dialysis is made up of size-selective capillary endothelia that are distributed within the cell-interstitial matrix of subperitoneal tissue.
3. Although the rate of water and mass transfer is directly proportional to the peritoneal area in direct contact with the dialysis solution, only one third of the adult, anatomic peritoneum is typically exposed to 2 to 3 L at any moment during dialysis.
4. Increasing the volume in the cavity generally enlarges the contact area and raises the rate of mass transfer but may also increase intraperitoneal pressure and lead to a reduction in net ultrafiltration.
5. Raising the osmotic pressure in the cavity generally raises the rate of fluid removal from the body.
6. Peritoneal dialysis can be used in the intensive care unit as a mode of renal replacement therapy, with the advantages of improved hemodynamic stability and no requirement for anticoagulation.

Key References

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