Chapter 17
Ultrafiltration Failure

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Definition

Fluid overload is an important problem in peritoneal dialysis (PD) patients, especially when residual urine production is absent. It may be caused by a high fluid intake, inappropriate PD prescription, noncompliance, or by a low drained volume. The latter can be due to mechanical problems, such as catheter dislocation or subcutaneous leakages, or to peritoneal membrane failure. When the diagnosis of ultrafiltration failure is based on a clinical definition, all the above causes of overhydration are included, which might lead to overdiagnosis. Underdiagnosis is also possible, for instance, when a patient with impaired peritoneal ultrafiltration remains in a good hydration status because of strict adherence to a severe salt and fluid restriction. Hence, when faced with a disruption of volume homeostasis, the clinician needs to determine where the fault lies: is it failure of the peritoneum to respond to an adequate osmotic stimulus, or the failure of the prescription to provide such an osmotic stimulus, or the failure of the patient to comply with dietary restrictions and guidelines. In addition, it can be argued that failure at the peritoneal level is also complex, as the response to the osmotic stimulus may be adequate, but overshadowed by other operative processes (such as lymphatic/tissue reabsorption) whereby the net observed ultrafiltration response is inadequate.

The implications of the above discourse are clinically relevant as they affect the interventions required to alleviate the consequences of fluid overload. They can be restated thusly: failure of volume homeostasis is not necessarily the result of inadequate peritoneal fluid removal. It can result from excessive salt/water intake. Failure of excess fluid removal does not obligatorily imply a pathologic alteration of the peritoneal membrane. It may be due to an erroneous prescription that does not offer optimal conditions for peritoneal ultrafiltration, or the operation of contrary mechanisms that thwart the effects of proper peritoneal membrane response.

The definition of peritoneal ultrafiltration failure has been debated. A common clinical definition refers to the inability to attain volume homeostasis despite the use of more than two hypertonic bags per day (4.25%/3.86% dextrose/glucose). However, others used a definition based on a standardized exchange and considered UFF to be present, for instance, when there was negative net ultrafiltration with a 1.36% glucose dwell [1]. In 2000, the International Society of Peritoneal Dialysis (ISPD) committee on ultrafiltration failure recommended a formal evaluation with a standardized test with 3.86%/4.25% glucose, and considered a net ultrafiltration of less than 400 mL after a 4-h dwell as indicative of UFF [2].

Although peritoneal ultrafiltration failure (UFF) can occur in any stage of peritoneal dialysis, it usually develops after a sustained period on PD [3, 4] and is therefore especially important in long-term PD. The proper incidence of ultrafiltration failure is difficult to determine because of the variability in case definition [5–12]. Prevalence as high as 31% for patients treated with PD for more than 6 years have been reported [13] and in a Japanese long-term study, drop-out because of UFF was as high as 51% after 6 years [14]. Both studies were based on clinical signs of UFF and not on a standardized test. Recently in a population of PD patients treated for more than 4 years, prevalence for ultrafiltration failure of 36% has been observed, based on a standardized peritoneal function test as advised by the ISPD committee [15].

This does not necessarily imply a failure in clinical management, as the therapeutic options have improved with wider use of cycler therapy and the availability of alternate osmotic agents such as icodextrin. Patients who have fluid management problems on standard continuous ambulatory peritoneal dialysis (CAPD) may do well with use of alternate osmotic agents such as icodextrin [16–22], or by transfer to automatic peritoneal dialysis (APD) [23].

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Table 17.1 Causes of volume homeostasis failure

Input dependent causes
Excessive salt/water intake
Output dependent causes
Uncompensated loss of residual renal function
Mechanical failure of dialysis procedure
Obstruction and other catheter malfunctions
Leaks
Inadequate provision of ultrafiltration conditions
Long dwells
Inappropriate tonicity
Mismatch of prescription and PET status
Exaggerated contrary mechanisms
Lymphatic/tissue reabsorption
Failure of peritoneal response
High transport status
Aquaporin deficiency
Loss of functional peritoneum

Classification

Table 17.1 offers a classification of causes of failure of volume homeostasis divided by the operative mechanisms. This is an etiologic classification that is useful as a framework for discussion of the various conditions. It divides the possible causes into groups based on a pathophysiologic approach and will be used in the discussion of the various entities. The linear approach to causation classification, however, does not always capture the complexity of clinical situations. It is not uncommon for causative mechanisms to coexist in the same patient. The most intuitively obvious example of mixed causality is the mismatch between fluid intake and dialysis prescription when the former is excessive and the latter is inadequate. More complex examples would be situations of ultrafiltration capacity failure due to high transport coupled with enhanced lymphatic/tissue reabsorption. Such occurrences of mixed causality are not rare in nephrology. They can be likened to mixed acid-base disorders and, like the latter, require a sharp diagnostic acumen coupled with a systematic approach to unravel their intricacies.

Diagnosis

The diagnostic approach needs to account for the frequency hierarchy of causes to be most efficient and practical. The more frequently occurring etiologies need to be addressed in a stepwise diagnostic scheme. Such a diagnostic approach is illustrated in Fig. 17.1.

In the work-up of fluid overload, it is important to consider reversible factors that can alter fluid balance first (Fig. 17.2). The clinical history may readily disclose the probable causation that can then be pursued with definitive diagnostic testing. A history of noncompliance with either dietary advice or PD prescription may direct the evaluation to more interventional pathways and preclude the need for expensive and tedious diagnostic work-up. Understandably, the detection and resolution of patient noncompliance are not easy tasks. Parallel evidence for no-compliance in

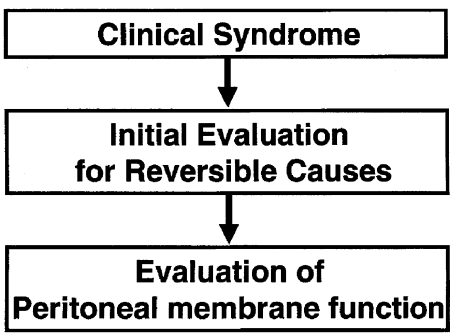

Fig. 17.1 Diagnostic approach for the clinical syndrome of volume overload

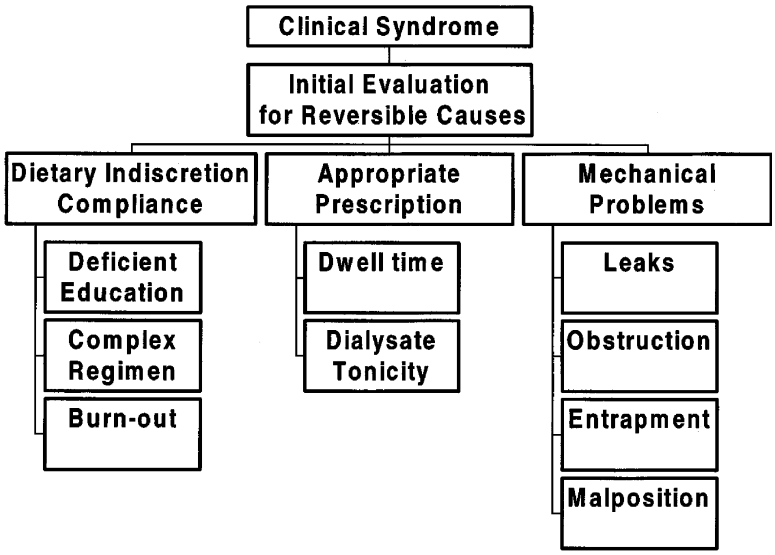

Fig. 17.2 Work-up of fluid overload. Initially the reversible causes should be considered. Patient compliance to diet and prescription must be evaluated, also an assessment of the prescription itself is useful. In addition several mechanical problem must be ruled out

other aspects of the therapy, or generalized evidence for nonadequacy of the therapy may be helpful. Concomitant small solute inadequacy and inadequate fluid removal are much less frequent due to true peritoneal membrane pathology. The clinical profile of the syndrome is also helpful when it is associated with a persistent reduction in drain volume. Reductions in drain volume due to mechanical problems have a more acute presentation. A positional dialysate flow suggests a malpositioned catheter, whereas sluggish outflow (and/or inflow) may result from a partially obstructed or entrapped catheter. Findings of edema localized to the abdomen or inguinal area on clinical examination can be important clues to the presence of a peritoneal leak.

At the time of the initial office evaluation, a quick "fill and drain" with 2 L of dialysate is beneficial in order to directly observe the nature and rate of in-flow and out-flow. The presence of fibrin clots may explain abnormalities with flow, which reduce the efficiency of drainage and volume removal and can often be resolved with intraperitoneal heparin. If incomplete drainage or positional drainage is observed, a flat-plate radiograph of the abdomen will assess the possibility of a malpositioned catheter. When an entrapped catheter or peritoneal leak is suspected, peritoneography or peritoneal computerized tomography are valuable in their diagnosis [24–27]. Diagnostic and therapeutic approaches to these conditions should be sought in the appropriate chapters in this volume.

The exclusion of rapidly resolvable causes of impaired fluid removal has diagnostic and therapeutic advantages. The causes discussed above can be frequently resolved with standard therapeutic approaches and the clinical syndrome hence resolved. Streamlining of the diagnostic approach is also aided by the exclusion of the mechanical causes. The next diagnostic step is to evaluate the ultrafiltration and transport functions of the peritoneal membrane.

Traditionally, peritoneal membrane function has been assessed by the peritoneal equilibration test (PET). The PET has been standardized both procedurally and interpretably to classify membrane function [28, 29]. It is directed, however, primarily at small solute clearance and although ultrafiltration capacity is closely linked to the latter, the traditional PET [29] does not address the issue of quantifying pathologic variations in ultrafiltration. For the purposes of diagnosing presence and causation of impaired fluid removal, the required test is one that will 1) measure ultrafiltration under optimal conditions (to avoid false-positive results); 2) evaluate small solute transport to aid in defining causation; and 3) have validated criteria that correlate with clinical behavior (to avoid both false-negative and false-positive results). The current PET does provide a thorough evaluation of small solute transport, but because of the modest osmotic challenge of a 2.5%/2.27% dextrose concentration utilized in the test, the osmotic drive for ultrafiltration is not optimal.

Therefore, a modification of the standard PET test was introduced by the group of Krediet [30], which offers a reasonable alternative and is recommended as the main test for determining the appropriateness of peritoneal ultrafiltration response (Fig. 17.3). The modification consists of replacing the 2.5%/2.27% dextrose solution of the standard PET with a 4.25%/3.86% dextrose solution, thereby satisfying the criterion of maximal osmotic drive defined above as required for proper evaluation of ultrafiltration capacity. A value of less than 400 mL of net ultrafiltration in a 4-h dwell correlates well with clinical behavior and avoids any false-positive results. An additional advantage of this approach is that it allows for determination of sodium sieving by profiling the changes in dialysate sodium concentration induced by osmotically

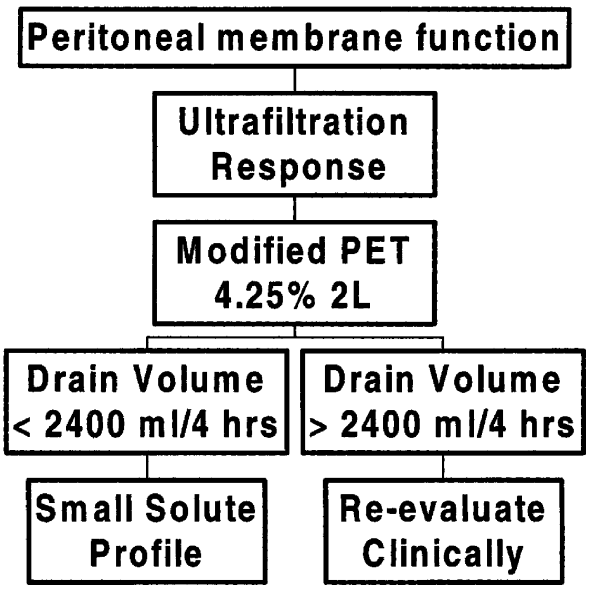

Fig. 17.3 Peritoneal membrane function testing with a 3.86%/4.25% dextrose solution indicates peritoneal membrane failure when the net drained volume is less than 400 mL after a 4-h dwell time

driven water flow. As water influx into the peritoneal cavity is mediated in part by aquaporins, the enhanced osmotic drive will draw water into the peritoneal cavity thereby diluting the sodium concentration. The greater the influx of water is via aquaporins, the greater the decline in dialysate sodium. Impaired aquaporin-mediated water transport will lead to obliteration of the decline in dialysate sodium. Hence, measurement of sodium sieving will allow better diagnostic discrimination of the causes of impaired ultrafiltration [31, 32]. The characterization of small solute transport with this approach correlates well with the results of the standard PET test with 2.5%/2.27% [33, 34].

After initial exclusion of mechanical, compliance, dietary, and other relevant clinical causes of impaired fluid removal, the patient needs to undergo an evaluation of ultrafiltration response. A PET using a 4.24%/3.86% dextrose solution is performed and dialysate and plasma sampling obtained as per usual. The modified test allows for both fluid removal and small solute profiles to be evaluated.

The primary intent of the test is to quantify the net ultrafiltration in response to a 4.25%/3.86% dextrose dialysis solution challenge. If net ultrafiltration is greater than 400 mL/4 h, the subsequent diagnostic sequence needs to focus on the following possible etiologies: 1) dietary indiscretion or dialysis noncompliance; 2) inappropriate prescription; and 3) recent loss of residual renal function for which no adjustments were made in prescription. If net ultrafiltration is less than 400 mL/4 h, the subsequent diagnostic sequence is dependent on an examination of the results of small solute profile measurement (Fig. 17.4). When using the values for net ultrafiltration volume indicated above, the physician

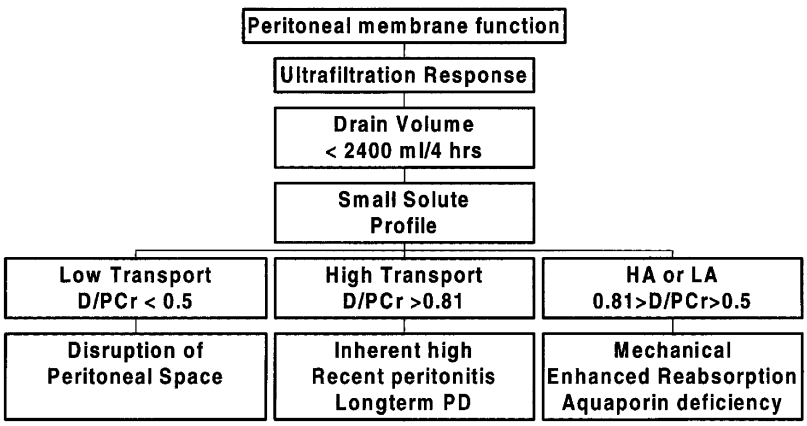

Fig. 17.4 Diagnostic sequence of ultrafiltration failure when the net drained volume is < 400 mL in a 4-h peritoneal function test using 3.86%/4.25% dextrose. Possible causes are given, according to the small solute transport status

should keep in mind the possibility of overfill of dialysis bags and account for this volume in their evaluation of the observed response. Pre- and postinfusion weighing of the dialysate solution bag and standardization of the flush before fill volume are important approaches to ensure accuracy.

Causes of Volume Homeostasis Failure

Input Dependent Causes

Excessive salt and water intake in end stage renal disease (ESRD) is so frequent that it invites neglect either because of familiarity or resigned frustration. Below the apparent simplicity of the clinical imperative to limit intake lies a complex web of factors that make the task very difficult. Patient-related factors such as established habits, difficulties in altering behavior, resentment and contrariness, and simple and pure gluttony are familiar to the practicing physician and so are the barriers to their modification. Resigned frustration with the latter, however, should not be allowed to become a pattern of clinical approach. The attention to intake issues has to focus additionally on three other aspects. First, is avoidance of being lulled by the impression that, because PD is a continuous daily therapy, the dangers of fluid overload are attenuated [35]. The potential advantages of PD are only real if they are used properly. The ability to control fluid removal on a daily basis is a significant advantage, but only as much as it is used appropriately. The tolerance of PD patients for greater food and fluid intake than hemodialysis patient should not be abused by neglect of proper dietary guidelines. Second, attempts at limiting salt and water intake should be balanced against provision of adequate nutrition. Salt and water are obligatory components of food and the zeal to control the former should not lead to restriction imposed on the latter that may hinder proper nutrition. Third, some physicians have used excessive fluid intake coupled with large ultrafiltration volume achieved with high glucose dialysate as a method of enhancing solute clearance. The contribution of ultrafiltration to clearance in PD is quite significant and the success of the above approach in the hands of expert users is testimony to this fact. Caution, however, is necessary when such an approach is used in both the selection and education of the patient in whom this approach is contemplated. Failure of the ultrafiltration to occur because of noncompliance with prescribed regimen, and excessive license in increasing intake by the unwary patient are risks to consider. In addition, the high glucose load that the patient will be exposed to with this regimen will not only have its effects on the metabolic status of the patient, but can also have negative effects on the peritoneal membrane.

Output Dependent Causes

Uncompensated Loss of Residual Renal Function

The contribution of residual renal function to fluid balance is major at the time of usual initiation of dialysis. Patients started on dialysis at a glomerular filtration rate of 5–10 mL/min/1.73 m^2 usually have over a liter of urine output per day. They are able to maintain such an output for over a year unless an intercurrent illness (peritonitis) or event (contrast dye study) causes a sudden loss of renal function. It is usually in such settings that a discrepancy between fluid balance needs and suitability of ongoing prescription arises most acutely. As renal function will inevitably undergo further declines in all patients, failure to adjust the dialytic prescription to the fluid balance requirements will lead to incipient fluid overload. The rate of loss of renal function varies among patients, and the impact of declining glomerular filtration rate (GFR) on urine output is also variable. GFR may decline without a perceptible change in urine output until advanced failure sets in. It is therefore useful to evaluate urine output on a quarterly basis and adjust prescription as needed.

Inadequate Provision of Optimal Ultrafiltration Conditions

From a clinical standpoint, inadequate provision of optimal ultrafiltration conditions can be reduced to two situations: a mismatch between prescription and PET status is best exemplified by use of long dwells in high transporters, and mismatch between dwell time and tonicity exemplified by use of low tonicity solutions in both high transport states and long dwells.

Long Dwells

Glucose is an unsuitable osmotic agent for long dwells because of its rapid absorption. By 4 h in patients with high transport, less than 25% of the original glucose concentration persists in the dialysate. Glucose concentration

continues to fall, albeit less dramatically, with further prolongation of the dwell. The two critical periods for ultrafiltration failure in a diurnal cycle of treatment are then the overnight dwell in CAPD and the daytime dwell in APD [23]. The former can be shortened by the use of an automated night-time exchange device and the latter by earlier drainage, either manually or by reattachment to the cycler for that function exclusively. Alternatively, and likely preferable from a quality-of-life standpoint, the use of alternate osmotic agents such as icodextrin would provide enhanced ultrafiltration at less disruption of lifestyle. When problems with fluid removal arise, examination of the long dwell first is worthwhile as this is the most vulnerable component of the therapy. Determining which patients have negative net ultrafiltration during the long dwell is a useful screening maneuver to adopt in PD clinics. With the use of 2.5% dextrose for a single long dwell in APD, three out of four patients may have negative net ultrafiltration. In high and high-average transporters, two out of every five patients may have a negative net long dwell UF with 4.25%. Icodextrin virtually eliminates negative net UF during the long dwell.

Inappropriate Tonicity

While improvements in fluid removal can be achieved by modifications in dwell time, and as discussed in another section, prescriptions with lower glucose content can be modeled and used, provision of appropriate tonicity for the chosen dwell duration and the peritoneal transport type is nevertheless necessary [23]. It is not uncommon to find patients labeled as having ultrafiltration failure when the cause of fluid excess is the reluctance of the physician to prescribe even 2.5%/2.27% dialysate. Indeed, the areas of the world where "ultrafiltration failure" is most frequently cited as a cause of technique failure are those that have the lowest utilization of solutions with tonicity higher than 1.5% glucose [14]. In the United States where "ultrafiltration failure" is seldom listed as a cause of technique failure, more than 50% of the dialysate used is in 2.5%/2.27% formulation. With the advent of icodextrin as an alternate osmotic agent, enhanced ultrafiltration without an increase in glucose exposure may be obtained.

Exaggerated Contrary Mechanisms

The peritoneal absorptive flow consists of two different pathways: 1) *direct lymphatic absorption* and 2) *fluid absorption into tissues*. The peritoneal fluid and protein absorption rates in animal experiments have been shown to be directly proportional to the intraperitoneal *hydrostatic* pressure. Hydrostatic pressure-driven convection is the most likely mechanism driving the fluid and protein transport into adjacent tissues.

Increased lymphatic/tissue absorption (or overall peritoneal fluid absorption) can lead to a low drain volume despite an adequate response to an osmotic challenge [31, 36, 37]. Lymphatic/tissue absorption of peritoneal fluid negatively influences the overall removal of water (decreases net ultrafiltration) and solute (partially negating the effect of diffusive and convective solute transport). Since the lymphatic/tissue absorption of peritoneal fluid does not alter the concentration of solutes in the dialysate, the D/P creatinine ratio remains unchanged even though net ultrafiltration can be significantly decreased. Measurement of fluid absorption from the peritoneal cavity can only be done with indirect methods. The disappearance rate (clearance) of intraperitoneally administered macromolecular tracers, such as radio-iodated serum albumin (RISA) [38, 39] or dextran 70 [40, 41], can be used. The disappearance rates of these tracers are constant in time [42] and independent of molecular size. This indirect measure can be applied as functional characterization of the effective lymphatic absorption rate. It implies that all pathways of peritoneal lymphatic drainage, both subdiaphragmatic and interstitial, are included in the definition. Lymphatic/tissue absorption rates average 0.95–1.0 mL/min in the upright position and thus contributes significantly to intraperitoneal volume balance. An overall increase in intraperitoneal pressure causes a decline in net ultrafiltration primarily by the increase in lymphatic/tissue absorption rate [43]. The relative contribution of increased lymphatic/tissue reabsorption to fluid removal problems is not definitively established. Proper assessment of frequency of the condition, however, will require further work. Impaired net ultrafiltration associated with the disappearance of intraperitoneally administered macromolecules was found in two out of the nine patients with ultrafiltration failure described by Heimbürger et al. [8]. Krediet and his group [31, 44] found a dextran disappearance rate exceeding 2 mL/min in about one-third of the patients with inadequate ultrafiltration (net UF $<$ 400 mL/4 h on 4.25%/3.86% glucose), often in combination with the presence of a large peritoneal surface area. There seems to be no evidence that the prevalence of this cause of impaired peritoneal fluid removal would increase with the duration of peritoneal dialysis, since lymphatic absorption rates appear to be stable over time [45].

Definitive proof of the condition requires identification of high macromolecule clearance from the peritoneal cavity to plasma as a surrogate marker for fluid removal by the lymphatic pathway [40, 46]. The point bears emphasis: clearance of macromolecules is used as an indicator of fluid clearance, but the two are not necessarily identical. In the absence of such a test, the diagnosis is made by exclusion of mechanical catheter problems, and aquaporin deficiency in patients with

low-average or high-average solute transport on the modified PET. The rate of lymphatic absorption is estimated by measuring the disappearance of macromolecules, such as albumin or dextran 70 from the peritoneal cavity (molecules too large for transcapillary transfer by either diffusion or convection). As described by Pannekeet et al. [43], this can be done by adding 1 g of dextran 70/L to a 2-L, 4-h 4.25%/3.86% dextrose dwell. The dialysate would be sampled at 0, 10, 20, 30, 60, 120, 180, and 240 min and the lymphatic or tissue absorption rate of dialysate would be calculated from the dextran clearance from the peritoneal cavity. Measurement of lymphatic flow is uncommon in clinical practice due to the complexity of the procedure.

Failure of Peritoneal Response

High Transport Status

The most frequent cause of peritoneal ultrafiltration failure is the presence of a large vascular surface area, characterized by a high D/P of creatinine or low D/D_0 glucose. It leads to high absorption rates of low-molecular-weight osmotic agents and therefore to a rapid dissipation of the osmotic gradient. A large peritoneal surface area can be anatomic or functional. In the first, neoangiogenesis in the peritoneum [47] leads to more vessels, so a larger surface for the transport of solutes is available. Functional enlargement of the vascular surface area can be present when more existing peritoneal microvessels are perfused (for instance, during PD-related peritonitis). Patients with a net ultrafiltration (< 400 mL/4 h with a 4.25%/3.86% modified PET) and D/P creatinine > 0.81, represent the largest group of patients with inadequate filtration due to peritoneal membrane characteristics. Patients can have an inherent high small solute transport profile at initiation of dialysis; they can have a transient fast transport status during peritonitis and there are patients who develop a high transport profile in the course of long-term peritoneal dialysis. These patients tend to have good small molecular weight solute transport, but have poor ultrafiltration during standard CAPD using glucose containing dialysate. If their dwell times are mismatched for their membrane transport characteristics, they often appear to have inadequate ultrafiltration as they lose residual renal function and no longer have urine flow to supplement net daily peritoneal fluid removal.

Inherent high transport

Fifteen percent of patients starting peritoneal dialysis display this transport profile. This proportion appears to be constant in various population groups and stable over medium periods of observation [48]. Patients in this group have very efficient membranes for small solute clearance, but may have difficulty in ultrafiltration particularly in long dwell cycles. These patients are at risk of high protein losses in the peritoneum. A high level of technique failure has been described on CAPD therapy, likely related to fluid management. Retrospective analysis also suggests higher mortality in this group [49–53]. Automated PD and icodextrin for long dwell are recommended therapeutic approaches in this group (see below).

Recent peritonitis

Impaired ultrafiltration with PD is a transient phenomenon during acute peritonitis [54]. The high solute transport rates during acute peritonitis lead to a rapid disappearance of the osmotic gradient. The infection-induced hyperpermeability is probably caused by increased secretion of vasoactive substances such as prostaglandins and cytokines [55] and an up-regulation of NO-synthase activity [56, 57]. These mediators are likely to increase the number of perfused peritoneal capillaries, leading to a functional increment of the vascular peritoneal surface area. This leads to an increase in transcapillary ultrafiltration rate during peritonitis, compared to the stable situation. In addition, vasodilatation leads to a reduced size-selectivity, resulting in a decreased restriction coefficient to macromolecules [58]. It is a common clinical observation for peritoneal dialysis patients to experience fluid retention during episodes of peritonitis [54, 59]. These patients often need a temporary change in their standard dialysis prescription (shorter dwell times or increased tonicity of fluids) to achieve net ultrafiltration. When compared to baseline, PET data during peritonitis reveal an increase in the D/P ratio for creatinine and a decrease in the D/D_0 ratio for glucose, usually accompanied by an increase in protein losses and a significant decrease in net ultrafiltration. Several studies have indicated that ultrafiltration during an episode of peritonitis can be satisfactorily achieved with the use of icodextrin [60, 61].

High transport during long-term PD

In long-term patients, the presence of a large vascular surface area, as judged from fast transport rates of small solutes, is by far the most frequent cause of ultrafiltration failure [62]. This fits well with the finding of an increased number of vessels in the peritoneal membrane of long-term PD patients [47, 63]. This peritoneal neoangiogenesis resembles the abnormalities

frequently observed in diabetic retinopathy. In PD the peritoneal tissues are exposed to extremely high glucose concentrations. This may explain the diabetiform alterations in the microvasculature, like reduplication of the capillary basement membrane and the marked increase in the number of microvessels [47], as well as the accumulation of advanced glycation end-products in the vascular walls [64]. Peritoneal equilibration testing shows an increase in D/P ratio for creatinine, a decrease in the D/D_0 ratio for glucose, and a smaller than usual decrease in dialysate sodium during the dwell. In contrast to the situation seen with peritonitis, where transport changes are usually transient, and protein losses are increased, the small solute transport changes in this group tend to be permanent and protein mass transport does not change.

These changes in peritoneal membrane function were originally described with acetate-containing dialysis solutions [5, 65], but have also been seen in patients who have only used lactate-containing dialysis. A history of recurrent peritonitis and extensive use of hypertonic exchanges has been observed in some, but not all, studies. The incidence seems to increase with time on peritoneal dialysis implicating repeated exposure of the peritoneum to dialysis solution as a cause.

The natural history of peritoneal membrane transport over time has been debated [3, 48, 66–70]. This is mainly due to noncomparability of the methods used. A small number of studies have used standardized 4-h dwell evaluations with examination of both ultrafiltration and solute transport, while a larger number utilized clearance monitoring. The latter may mask opposing directional changes in solute and fluid transport. The potential increase in solute clearance due to an increase in D/P creatinine may be masked by the potential decline due to lower ultrafiltration. The emerging picture, however, is that during long-term observations (greater than 2 years) some degree of increase in D/P creatinine does occur in patients on PD.

Aquaporin Dysfunction

This condition has first been described clinically in patients with severe peritoneal ultrafiltration failure, without signs of increased solute transport [32]. It is a rare condition to be present as the only cause of UFF, it is more frequently seen in combination with augmented small solute parameters. Impaired aquaporin function offers a very interesting model to understand peritoneal transport and its alteration by pathologic states. The peritoneal capillary membrane is not freely permeable to solutes but is a highly selective barrier, with the ability to impede diffusion and convection of relatively small molecules while restricting large macromolecules, but to a lesser degree than standard hemodialysis membranes. This suggests that the peritoneal capillaries contain populations of varying "pores," which alter solute transport. This has led, through computer simulations [71–76] and animal work [77–80], to the "three pore theory" of water and solute transport across the peritoneal membrane (mainly transcapillary movement of solute and fluid). This theory proposed three populations of pores. First a large number of transcellular pores (4–5 A radius). Second a large number of small pores (40–50 A) and third a small number of large pores (200–300 A). This theory predicted that 40–50% of the total ultrafiltrate is obtained through the transcellular path and therefore will be solute free, when driven by an osmotic pressure differential. Animal work and indirect human research has strongly pointed to the aquaporins being the water channel transcellular pores (ultra small pore). This assumption has been tested in rats and rabbits. Aquaporin-1 was inhibited by intraperitoneal administration of mercury-chloride and as a result almost complete blockage of the sieving of sodium was present [80, 81]. In humans, aquaporins have been demonstrated by in situ techniques to be present in the peritoneal capillary endothelium and mesothelium [82, 83]. The small pores are also involved in water transport through colloid osmosis and hydrostatic pressures which are in balance; these are also the pores through which most of the small solute transport occurs. Aquaporin dysfunction is that situation where there is damage to or diminished number of water channel ultrasmall pores, which can lead to deficient crystalloid induced ultrafiltration [32, 84].

The function of the ultrasmall pores or water channels can be estimated by the "sieving" of sodium during a hypertonic dwell [38, 85, 86]. The sodium concentration in dialysate decreases in case of free water transport. This is indeed observed in the initial phase of a 3.86%/4.25% glucose dwell, but not in a 1.5%/1.36% glucose exchange (see Fig. 17.5). The initial high osmotic pressure gradient in the 4.25%/3.86% glucose dwell will lead to osmotically driven fluid transport trough the ultrasmall pores, which leads to a dilution of the dialysate sodium concentration. The lowest dialysate sodium concentration is usually reached after 60 min. The lower osmolality of a 1.5%/1.36% glucose solution does not have the osmotic force to induce a fluid flow through these pores, so no sieving of sodium is observed. In case of a large difference between dialysate and plasma sodium concentration, diffusion of sodium from the circulation to the dialysate will take place. This will increase the dialysate sodium concentration and therefore a falsely decreased sodium sieving will be measured, incorrectly indicating loss of free water transport. To avoid this, a correction for sodium diffusion can be applied [87, 88].

Another way to assess aquaporin-mediated transport is to calculate the difference in net ultrafiltration obtained after a 4-h dwell with 1.5%/1.36% glucose and with 4.25%/3.86% glucose dialysate; 1.5%/1.36% glucose induces only a small crystalloid osmotic pressure gradient, and therefore limited transport through water channels. On the other hand, 4.25%/3.86% glucose induces a very high crystalloid osmotic pressure gradient and the net ultrafiltration

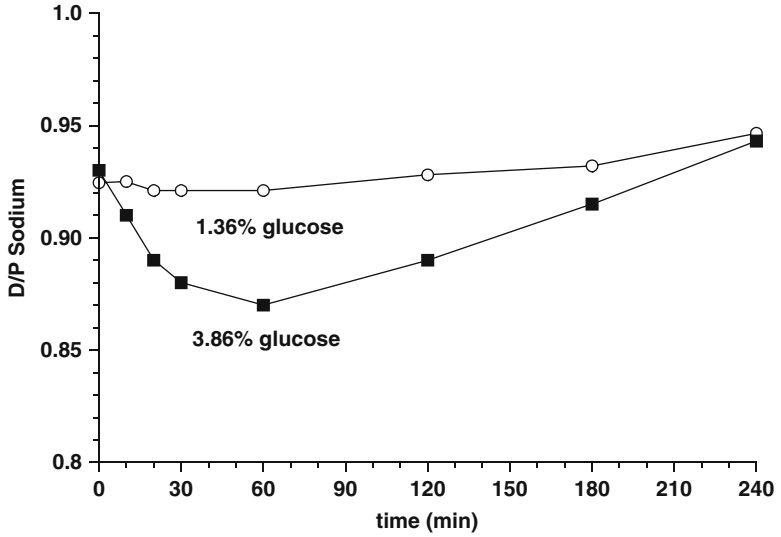

Fig. 17.5 Dip in dialysate over plasma ratio for sodium using a 3.86%/4.25% dextrose solution (closed squares) and a 1.36%/1.5% dextrose solution (open circles). The high osmolality of the first solution will induce osmotically driven "free water" transport, leading to dilution of the dialysate sodium concentration. This is not seen for the 1.36%/1.5% dextrose solution

obtained with it is therefore much more dependent on the number and function of water channels. Consequently, Δ ultrafiltration 4.25%/3.86%–1.5%/1.36% will decrease in situations with impaired aquaporin-mediated water transport. D/P Na^+ or ΔNa^+ are probably the simplest ways for rough assessment of aquaporin function.

Direct methods to calculate aquaporin mediated water transport have recently been developed. LaMilia and co-workers have described an easy direct measurement of free water transport [89], which has been refined [90–92] and tested with computer simulations by others [93]. In essence, this method uses a standardized 4.25%/3.86% glucose dwell and measures net UF after a shorter dwell period corresponding to the expected maximal sodium sieving time (60 or 90 min). By measuring directly net UF and sodium concentrations during this shortened dwell, the amount of actual free water transport can be calculated and hence one has a direct measure of aquaporin mediated fluid transport.

Loss of Functional Peritoneum

The combination of low drain volume in the face of adequate osmotic challenge and low small solute transport is very rare and reflects a major disruption of the peritoneal membrane and/or intraperitoneal fluid distribution. It is usually due to adhesions and the functional consequences may be related to fluid trapping in small spaces. Peritoneography may be helpful in making the diagnosis by identifying sequestered spaces. Poor UF in association with low transport is reported to occur in the advanced stages of peritoneal sclerosis [94–97]. It is important, however, to realize that a high transport rate has also been described prior to a diagnosis of peritoneal sclerosis [3, 65–67]. Unfortunately, no large prospective study of fluid problems in PD patients has been performed so it is not possible to state how often UFF together with low transport occurs. Because this condition results in both inadequate volume and inadequate solute removal, transfer to hemodialysis is required for adequate management in anuric patients [10]. In patients with residual renal function, management by peritoneal dialysis and oral loop diuretics may be successful. Whether restitution of peritoneal free space by adhesiolysis is warranted needs to be determined on an individual case basis.

A caveat on the diagnostic criteria is in order: patients with underlying low transport rate and leaks or mechanical problems or high lymphatic/tissue reabsorption may also present with the composite picture of low drain volume and low small solute transport. It is therefore important to exclude these latter causes before accepting low transport as the reason for the difficulty with peritoneal fluid removal.

Mechanical Failure of Dialysis Procedure

Catheter Malfunctions

Catheter-related problems contributing to poor drain volumes include obstruction, entrapment, or malposition [11, 12]. Catheter obstruction, either partial or complete, often results from fibrin plugs or build-up within the catheter

lumen but can be due to omentum obstructing the catheter ports or even a kinked catheter. These lead to sluggish or intermittent inflow/outflow of dialysate and thus alter the efficiency of fluid removal. Fibrin strands seen in the dialysate should raise suspicion of the problem. Treatment consists of aggressive "flushing" of the catheter with a dialysate-filled syringe and if this is unsuccessful, the use of fibrinolytic agents when fibrin-related occlusion is suspected.

The intra-abdominal portion of the catheter may become "entrapped" in a compartment formed by adhesions. This can lead to a reduction in intraperitoneal capacity resulting in pain on inflow once the compartment volume has been surpassed. With the use of peritoneography the compartment can be demonstrated. Treatment may be attained with surgical lysis of the adhesions if they are not too extensive.

Catheter malposition may occur because of improper placement, but this often results from the migration of catheters originally in good position [98]. A malpositioned catheter has positional outflow and does not drain the peritoneal cavity effectively, leading to an increase in residual volume. A normal residual volume (R) is approximately 200–250 mL [43] and can be measured from information obtained during the PET using the following equation:

$$\mathrm{R} = V_{\mathrm{in}}(S_3 - S_2)/(S_1 - S_3)$$

Where V_{in} = instillation volume, S_1 = solute concentration (urea or creatinine) in the pretest drain, S_2 = solute concentration of the instilled fluid (0 for urea or creatinine) and S_3 = solute concentration immediately following instillation [43]. An increase in residual volume dilutes the glucose concentration in the freshly instilled dialysate. This decreases the osmotic gradient and thus reduces the rate of transcapillary ultrafiltration without any significant effect on solute transport. Net ultrafiltration is decreased while the D/P creatinine ratio remains essentially unchanged. An increase in the calculated residual volume should raise the suspicion of a malpositioned catheter. However, the presence of this problem is often clinically apparent and the diagnosis is easily made with the aid of simple radiographic techniques (flat-plate of the abdomen) as peritoneal dialysis catheters have radio-opaque material imbedded within.

Leaks

Dialysate leaks from the abdominal cavity result in a decrease in drain volume and net fluid removal. In the case of external leaks, the impact is greater on drain volume. In leaks into the abdominal wall or pleural space, net fluid removal is diminished either because of accumulation in and reabsorption from the interstitial spaces or sequestration in the pleural space. Leaks into the interstitial space are commonly accompanied by abdominal wall edema with or without genital edema. Leaks can occur at anytime but are often seen shortly after the start of PD and usually occur at the catheter insertion site but can also be associated with an abdominal wall hernia or a history of multiple abdominal surgeries [24, 25, 99, 100]. Localized abdominal wall edema or subcutaneous fluid collections are often evident. Diagnosis is confirmed by utilizing radiographic techniques that include intraperitoneal infusion of a dialysis solution in which radiographic contrast has been added with computed tomography, or through the intraperitoneal infusion of radioisotope with peritoneal scintigraphy [24–27, 99–103], or by use of magnetic resonance imaging with or without contrast.

Peritoneal membrane function is not compromised and therefore peritoneal transport as evaluated by the PET is not changed compared to baseline. Leaks associated with hernias usually require surgical repair. Leaks occurring in the absence of a hernia usually represent a tear in the parietal peritoneum. In this situation there is frequently a history of multiple abdominal surgeries, pregnancies, recent corticosteroid usage, or abdominal straining (coughing, Valsalva maneuver). Small leaks may respond to peritoneal rest with hemodialysis support or the use of nighttime small volume peritoneal dialysis with cycler and a dry day without the need for surgical repair. Recurrence may require surgical repair.

Therapy

General Guidelines

A summary of guidelines for the prevention of fluid overload is presented in Table 17.2.

Routine Standardized Monitoring

Routine standardized monitoring of desired weight, course of residual renal function, and achieved ultrafiltration with current dialysis prescription should be emphasized in the care protocols of all patients on peritoneal dialysis. This

Table 17.2 Guidelines for prevention of volume overload in patients on peritoneal dialysis

General guidelines
Routine standardized monitoring including awareness of PET status
Dietary counselling concerning appropriate salt and water intake
Protection of RRF
Loop diuretics if RRF present
Enhanced compliance – Education
Appropriate prescription
Hyperglycemia control
Preservation of peritoneal membrane function
CAPD
Avoidance of long dwells with low glucose concentrations
Use of icodextrin for the long dwell
Use of night-time exchange device
Tailoring prescription to transport profile determined by PET
APD
Avoidance of long dwells with low glucose concentrations
Use of icodextrin for the long dwell
Use of short day dwells even when no additional exchange is needed for clearance

approach will allow for early detection of developing problems and early intervention with corrective measures. The volume status of patients on peritoneal dialysis should be used as a core indicator of dialysis adequacy. Constant re-evaluation by physicians and nurses of the patient's target weight in the light of blood pressure and other features suggestive of fluid overload is required. Particular emphasis should be placed on the desirability of normalizing blood pressure by using fluid removal alone, without antihypertensive drugs. Routine performance of PET with a view to identifying high and high-average transporters in whom monitoring of fluid status is particularly critical is highly encouraged. Use of icodextrin for the long dwell and utilization of APD may be preferred approaches in these patients.

Dietary Counseling

Avoidance of dietary indiscretion can be enhanced by detailed counselling and regular re-enforcement of taught guidelines. The tendency to be more liberal in dietary restrictions with peritoneal dialysis patients compared to patients on hemodialysis should be tempered by the need to maintain desired weight and reduction of cardiovascular risk. The general assumption that patients on peritoneal dialysis tolerate greater dietary salt and fluid indiscretion should not be construed as an endorsement for such indiscretion [104]. Tepid indifference that allows patients to hover close to mild edema may have pernicious long-term consequences. It is recognized that dietary interventions are the hardest to implement as they involve an elaborate process of education and lifestyle modification.

Protection of Residual Renal Function

Residual renal function (RRF) plays an important role in both small solute adequacy and volume control. The protective zeal that has become a cornerstone of nephrologic management in the pre-ESRD phase needs to be sustained after initiation of dialysis. This is particularly important in the context of the new directions in dialysis initiation where patients are started on dialytic therapy at higher levels of residual renal function than previously. Attention to the nephrotoxic potential of over-the-counter medications should become a component of regular patient interviews. Further, the use of aminoglycosides in the management of peritonitis should be limited to cases where no safer effective alternative is available. Protection from the nephrotoxic potential of contrast agents is limited by the obvious inability of using hydration methods. The promise of acetylcysteine or adenosine antagonists (e.g., aminophylline) has not been explored in this population and may be considered by inference until tested. Avoidance of nephrotoxic agents should be practiced rigorously.

Diuretic Use

Routine use of high-dose loop diuretics to maintain urine output in patients with residual renal function is a viable consideration. Usually large oral doses are needed (furosemide range 250–1000 mg) with or without addition of a

thiazide-like diuretic (metolazone 5–10 mg given 30 min prior to the loop diuretic). Urine volume can be successfully increased even in advanced renal failure by the use of large doses of loop diuretics alone or in combination with thiazides. While these agents do not help preserve RRF, they do increase urine output [105, 106]. The concern over the potential ototoxicity finds its origin in the experience with large intravenous doses. Oral administration seems not to carry the same risk.

Education and Enhanced Compliance

Emphasis should be placed in the initial training period on the education of the patient in the diagnosis and significance of fluid overload (e.g., awareness of importance of hypertension, peripheral edema, shortness of breath, etc.). Additionally, patients should be provided appropriate education in what the indications are to use more hypertonic PD solutions. Routine monitoring of patient compliance with PD exchanges and education of the patient in the importance of this issue are highly desirable.

Appropriate Prescription

Choosing the correct prescription for the peritoneal transport type of the patient is crucial. Patients with high and high-average transport can achieve adequate ultrafiltration using APD (four to five night cycles and long day dwell with icodextrin) and lower total glucose exposure than with CAPD [23].

Hyperglycemia Control

In diabetic patients, hyperglycemia can adversely affect the maintenance of an osmotic gradient across the peritoneal membrane. Control of the hyperglycemia may allow improved ultrafiltration without the need to use hypertonic glucose solutions unnecessarily. As glucose control is under current practice conditions mostly monitored and modified by the patients independently, education of the patient on the relevance of this activity to the adequacy of dialysis is important.

Preservation of Peritoneal Membrane Function

The most important therapeutic option is the prevention of ultrafiltration failure. Reduction of the occurrence of peritonitis can be achieved with appropriate patient training and retraining in aseptic techniques, the universal adoption of exit site antibiotic prophylaxis (either gentamicin or mupirocin creams) and the use of the widely applied double-bag system, which prevents extra disconnections [107]. The prevention of ultrafiltration failure in the long-term patients will depend largely on the possibility to reduce the peritoneal glucose exposure and the development of more biocompatible dialysis solutions. The first can, to some extent, be accomplished by preservation of the residual renal function. Therefore, nephrotoxic agents should be avoided, even when a patient is already on PD. In case of volume overload, the use of diuretics can lead to extra fluid removal by the kidneys, instead of increasing the osmolality of the dialysate. Alternative solutions that can replace glucose for one exchange per day are the glucose-polymer Icodextrin and amino-acids. Glucose polymers are attractive, because they are not hypertonic, exert their effect by colloid osmosis, and are taken up from the peritoneal cavity to a limited extent. They are therefore extremely useful in patients with an enlarged vascular surface area [16]. However, the use of icodextrin is limited to one exchange in the long dwell. Whether the agent can be used more than once daily and during shorter exchanges is under active investigation. Amino-acid-containing dialysis solutions are limited to one bag daily (separate exchange or mixed with glucose on the cycler) because of the increase in the nitrogen load. The use of more biocompatible dextrose-containing solutions seems to be promising in the preservation of the peritoneal membrane. Unfortunately, long-term patient-studies are still lacking. However, animal studies have shown that the use of more biocompatible solutions (lower content of glucose degradation products, higher pH, bicarbonate/lactate buffer) lead to less pathological alterations of the peritoneal membrane after long-term exposure compared to the conventional solutions [108, 109]. Temporary cessation of peritoneal dialysis has been used in a few patients with high small solute transport characteristics with some success and may be a reasonable option to consider if other approaches are unsuccessful [110–112]. Alternatively, reduction of peritoneal membrane glucose exposure may lead to some improvement in transport parameters [113].

Therapeutic Guidelines for Specific Diagnostic Categories

Failure of Peritoneal Response

Patients with peritoneal ultrafiltration failure should be treated according to the cause. Possibilities are summarized in Table 17.3

Fast Transport Status

In addition to the universal guidelines discussed above, therapeutic interventions in patients with high small solute transport need to address the basic pathophysiologic mechanism of rapid dissipation of the osmotic gradient. The latter phenomenon is particularly prominent during the long overnight dwell in CAPD and the daytime dwell in APD. The most appropriate intervention is the use of large molecular weight substitutes for glucose such as icodextrin [17–22]. Dialysis solutions containing icodextrin have been shown to be superior to glucose-based solutions in achieving net ultrafiltration during long dwells in majority of patients and particularly in high transporters. In areas where icodextrin dialysis solutions are not available, shortening dwell time is the preferred approach. In CAPD patients this can be achieved with the use of an automated night-time exchange device. This approach will shorten dwell time and has the additional benefit of improving small solute clearance with little impact on patient lifestyle. Alternatively, patients can be switched to APD where the use of short dwell times in the night phase enhances ultrafiltration. In patients on APD who do not have access to icodextrin, foregoing the daytime exchange and optimizing the night-time regimen may be sufficient [23]. If small solute clearance suffers, then a short daytime exchange with mid-day drainage will supplement night-time clearance without compromising ultrafiltration. If the preceding options are insufficient, then high glucose concentrations may be required. In a few patients adjunctive, temporary, or permanent hemodialysis may be required.

Preventive measures remain limited and speculative because of a lack of thorough understanding of the factors underlying high transport [114, 115]. In patients with inherent high transport, there are no clear associations with reversible conditions that can be therapeutically addressed. The possible association with higher indices of chronic systemic inflammatory response remains unproven. The clearest category for intervention is that of the transient small solute high transport rate associated with peritonitis. Approaches to reduce and prevent infections with improved connectology, patient training, and local prophylaxis have been successful, but more remains to be achieved. In patients who develop a high transport profile in the course of chronic peritoneal dialysis the approach is more a question of considered opinion rather than evidence-based. Reinforcing universal measures before relying on the chronic intensive use of 4.25%/3.86% glucose dialysate is generally preferable. Further, wherever available, use of icodextrin for the long dwell is recommended.

Loss of Functional Peritoneum

The combination of reduced solute clearance and diminished ultrafiltration represents a state of significant shortcomings in delivery of appropriate renal replacement by peritoneal dialysis. If therapeutic targets for either azotemia and volume homeostasis cannot be met, then adjunctive hemodialysis or permanent transfer to hemodialysis may be required in anuric patients. In patients with residual renal function, use of loop diuretics may allow achievement of adequate fluid balance while continuing on peritoneal dialysis.

Table 17.3 Therapeutic strategies in a patient with peritoneal ultrafiltration failure, according to the cause

Cause of Ultrafiltration Failure	Therapeutic Option
Fast transport status	• Avoid long dwells • Use icodextrin
Loss of functional peritoneum	• Transfer to hemodialysis when RRF is absent • Adhesiolysis if indicated
Aquaporin dysfunction	• Avoid hypertonic glucose • Use icodextrin • Temporarily discontinuation of PD?
Exaggerated contrary mechanisms	• Avoid large dialysate volumes • Avoid long dwells

Aquaporin Dysfunction

Adherence to the universal measures detailed above is necessary in all conditions whatever the underlying etiology of the impaired ultrafiltration. Patients with aquaporin dysfunction continue to have significant ultrafiltration via non-aquaporin pathways. This can be enhanced by the use of icodextrin in long dwells allowing for sustained fluid removal [19, 22, 115, 116]. For the glucose-based exchanges, increasing the dextrose concentration will not be beneficial.

Exaggerated Contrary Mechanisms

When enhanced tissue reabsorption results in reduced net ultrafiltration, interventions to maximise overall ultrafiltration are required to reach a state favorable to fluid removal. Ultrafiltration needs to exceed reabsorption to allow proper volume homeostasis. All interventions that maximize ultrafiltration (short dwell time, high tonicity of dialysate) need to be combined. As tissue absorption is a continuous process, and as ultrafiltration tends to decline with time, short cycle therapy is required to keep the balance of operation earlier than the convergence of the two processes. Adjusting cycle number and overall cycler time in APD, or cycle number in CAPD to the requirements of both ultrafiltration and solute clearance need to be done meticulously [23]. Also avoiding large dwell volumes can be beneficial, since large volumes will increase lymphatic absorption

Although there is a lot of promising investigative evidence that tissue absorption can be reduced [117–121], no pharmacological intervention can be recommended at this time for the lack of definitive clinical studies.

Future Prospects

Alternate use of current therapeutic options is a rich area deserving of consideration for the management of ultrafiltration failure in these challenging patients. Preliminary studies on the use of two icodextrin exchanges in a 24-h period suggest that this approach may be a successful option in this setting [122, 123]. In APD, the two exchanges are used sequentially during the long day interval, each dwelling for 7–8 h. In APD patients, a decrease in glucose exposure and a parallel decline in body weight have been observed [122]. In CAPD patients, one icodextrin dwell is used during the night and the other substitutes for a day dwell with extension of dwell time. Better blood pressure control and reversal of left ventricular hypertrophy have been achieved with such a regimen [123]. The use of two exchanges of icodextrin per day has resulted in modest asymptomatic changes in plasma oligosaccharides [122], but careful long-term studies are needed. Another area under exploration is the use of icodextrin as part of the solutions used on the cycler to allow for reduction in glucose exposure and possibly increased UF [124]. Such an approach would be particularly useful in very high transporters.

References

1. Ho-dac-Pannekeet MM, Atasever B, Struijk DG, Krediet RT. Analysis of ultrafiltration failure in peritoneal dialysis patients by means of standard peritoneal permeability analysis. Perit Dial Int 1997; 17: 144–150.
2. Mujais S, Nolph K, Gokal R, et al. Evaluation and management of ultrafiltration problems in peritoneal dialysis. International Society for Peritoneal Dialysis Ad Hoc Committee on Ultrafiltration Management in Peritoneal Dialysis. Perit Dial Int 2000; 20 (suppl. 4):S5–S21.
3. Selgas R, Fernandez-Reyes MJ, Bosque E, Bajo M-A, Borrego F, Jimenez C, Del Peso G, De Alvaro F. Functional longevity of the human peritoneum: how long is continuous peritoneal dialysis possible? Results of a prospective medium long-term study. Am J Kidney Dis 1994; 23: 64–73.
4. Davies SJ, Bryan J, Phillips L, Russell GI. Longitudinal changes in peritoneal kinetics: the effects of peritoneal dialysis and peritonitis. Nephrol Dial Transplant 1996; 11: 498–506.
5. Faller B, Marichal JF. Loss of ultrafiltration in continuous ambulatory peritoneal dialysis. A role for acetate. Perit Dial Bull 1984; 4: 10.
6. Bazzato G, Coli U, Landini S, et al. Restoration of ultrafiltration capacity of peritoneal membrane in patients on CAPD. Int J Artif Organs 1984; 7: 93.
7. Verger C, Larpent L, Celicout B. Clinical significance of ultrafiltration failure on CAPD. In La Graeca G, Chiaramonte S, Fabris A, Feriani M, Ronco C (eds). Peritoneal Dialysis. Milano: Wichtig Editore. 1986: 91–94.
8. Lameire N. Volume control in peritoneal dialysis patients: role of new dialysis solutions. Blood Purif 2004; 22 (1): 44–54.
9. Ronco C, Ferianai M, Chiaramonte S, et al. Pathophysiology of ultrafiltration in peritoneal dialysis. Perit Dialysis Int 1990; 10: 119.
10. Mactier RA. Investigation and management of ultrafiltration failure in CAPD. In Khanna R, Nolph KD, Prowant BF, et al. (eds). Advances in Peritoneal Dialysis, vol 7. Nashville: Perit Dial Bull, Inc., 1991: 57.
11. Korbet SM, Rodby RA. Causes, diagnosis, and treatment of peritoneal membrane failure, In Henrich WL. (ed). Principles and Practice of Dialysis, 2nd ed. Baltimore: Williams and Wilkins, 1998: 185–206.
12. Korbet SM, Work-up of ultrafiltration failure. Adv Ren Replace Ther 1998; 5: 194–204.

13. Heimburger O, Waniewski J, Werynski A, Tranaeus A, Lindholm B. Peritoneal transport in CAPD patients with permanent loss of ultrafiltration capacity. Kidney Int 1990; 38: 495–506.
14. Kawaguchi Y, Hasegawa T, Nakayama M, Kubo H, Shigematu T. Issues affecting the longevity of the continuous peritoneal dialysis therapy. Kidney Int 1997; 52 (suppl. 62): S105–S107
15. Smit W, Schouten N, Van den Berg N, Langelijk M, Struijk DG, Krediet RT. Analysis of the prevalence and causes of ultrafiltration failure during long-term peritoneal dialysis: a cross-sectional study. Perit Dial Int 2004; 24: 562–570
16. Imholz ALT, Brown CB, Koomen GCM, Arisz L, Krediet RT. The effect of glucose polymers on water removal and protein clearances during CAPD. Adv Perit Dial 1993; 9: 25–30.
17. Ho-dac-Pannekeet MM, Schouten N, Langendijk MJ, Hiralall JK, de Waart DR, Struijk DG, Krediet R. Peritoneal transport characteristics with glucose polymer based dialysate. Kindey Int 1996; 50: 979–986.
18. Peers E, Gokal R. Icodextrin: Overview of clinical experience. Perit Dial Int 1997; 17: 22–26.
19. Peers E, Gokal R. Icodextrin provides long dwell peritoneal dialysis and maintenance of intraperitoneal volume. Artif Organs 1998; 22: 8–12.
20. Posthuma N, ter Wee PM, Verbruh HA, Oe PL, Peers E, Sayers J, Donker AJM. Icodextrin instead of glucose during the daytime dwell in CCPD increases ultrafiltration and 24-h dialysis creatinine clearance. Nephrol Dial Transplant 1997; 12 (suppl. 1): 550–553.
21. Woodrow G, Stables G, Oldroyd R, Gibson J, Turney JH, and Brownjohn AM. Comparison of icodextrin and glucose solutions for the daytime dwell in automated peritoneal dialysis. Nephrol Dial Transplant 1999; 14: 1530–1535.
22. Wilkie ME, Plant MJ, Edwards L, Brown CB. Icodextrin 7.5% dialysate solution (glucose polymer) in patients with ultrafiltration failure: extension of technique survival. Perit Dial Int 1997; 17: 84–87.
23. Mujais S. Ultrafiltration management in automated peritoneal dialysis. In Ronco C, Amici G, Feriani M, Virga G (eds). Automated Peritoneal Dialysis, vol 129. Contrib Nephrol. Basel: Karger, 1999: 255–266.
24. Litherland J, Gibson M, Sambrook P, Lupton E, Beaman M, Ackrill P. Investigation and treatment of poor drains of dialysate fluid associated with anterior abdominal wall leaks in patients on chronic ambulatory peritoneal dialysis. Nephrol Dial Transplant 1992; 7: 1030–1034.
25. Litherland J, Lupton EW, Ackrill PA, Venning M, Sambrook P. Computed tomographic peritoneography: CT manifestations in the investigation of leaks and abnormal collections in patients on CAPD. Nephrol Dial Transplant 1994; 9:1449–1452.
26. Scanziani R, Dozio B, Caimi F, De Rossi N, Magfri F, Surian M. Peritoneography and peritoneal computerized tomography: a new approach to non-infectious complications of CAPD. Nephrol Dial Transplant 1992; 7:1035–1038.
27. Cochran ST, Do HM, Ronaghi A, Nissenson AR, Kadell BM. Complications of peritoneal dialysis: evaluation with CT peritoneography. Radiographics 1997; 17: 869–878.
28. Twardowski ZJ. Clinical value of standardized equilibration tests in CAPD patients. Blood Purif 1989; 7 (2–3): 95–108.
29. Twardowski ZJ, Nolph K, Khanna R, Prowant B, Ryan L, Moore H, Neilsen M. Peritoneal equilibration test. Periton Dial Bull 1987; 7: 138–147.
30. Smit W, Van Dijk P, Langendijk M, Schouten N, van den Berg N, Struijk DG, Krediet RT. Peritoneal function and assessment of reference values using a 3.86% glucose solution. Perit Dial Int 2003; 23: 440–449.
31. Smit W, Schouten N, van den Berg N, Langedijk M, Struijk DG, Krediet RT. Analysis of the prevalence and causes of ultrafiltration failure during long-term peritoneal dialysis: a cross-sectional study. Perit Dial Int 2004; 25: 562–670.
32. Monquil MC, Imholz AL, Struijk DG, Krediet RT. Does impaired transcellular water transport contribute to net ultrafiltration failure during CAPD? Perit Dial Int 1995; 15: 42–48, 24–27.
33. Pride ET, Gustafson J, Graham A, Spainhour L, Mauck V, Brown P, Burkart JM. Comparison of a 2.5% and a 4.25% dextrose peritoneal equilibration test. Perit Dial Int 2002; 22: 365–370.
34. Smit W, Langedijk MJ, Schouten N, van den Berg N, Struijk DG, Krediet RT. A comparison between 1.36 and 3.86% glucose dialysis solution for the assessment of peritoneal membrane function. Perit Dial Int 2000; 20: 734–741.
35. Coles GA. Have we underestimated the importance of fluid balance for the survival of PD patients. Perit Dial Int 1997; 17: 321–326.
36. Mactier R, Khanna R, Twardowski Z, Nolph K. Contribution of lymphatic absorption to loss of ultrafiltration and solute clearances in continuous ambulatory peritoneal dialysis. J Clin Invest 1987; 80: 1311–1316.
37. Heimbürger O, Waniewski J, Werynski A, Sun Park M, Lindholm, B. Lymphatic absorption in CAPD patients with loss of ultrafiltration capacity. Blood Purif 1995; 13: 327–339.
38. Heimburger O, Waniewski J, Werynski A, Lindholm B. A quantitative description of solute and fluid transport during peritoneal dialysis. Kidney Int 1992; 41: 1320–1332.
39. Zakaria ER, Rippe B. Intraperitoneal fluid volume changes during peritoneal dialysis in the rat: indicator dilution vs. volumetric measurements. Blood Purif 1995; 13: 255–270.
40. Krediet RT, Struijk DG, Koomen GC, Arisz L. Peritoneal fluid kinetics during CAPD measured with intraperitoneal dextran 70. ASAIO Trans 1991; 37: 662–667.
41. Koomen GC, Krediet RT, Leegwater AC, Struijk DG, Arisz L, Hoek FJ. A fast reliable method for the measurement of intraperitoneal dextran 70, used to calculate lymphatic absorption. Adv Perit Dial 1991; 7: 10–14.
42. Struijk DG, Krediet RT, Koomen GC, Boeschoten EW, vd Reijden HJ, Arisz L. Indirect measurement of lymphatic absorption with inulin in continuous ambulatory peritoneal dialysis (CAPD) patients. Perit Dial Int 1990; 10: 141–145.
43. Imholz ALT, Koomen GCM, Struijk DG, Arisz L, Krediet RT. Effect of an increased intraperitoneal pressure on fluid and solute transport during CAPD. Kidney Int 1993; 44(5): 1078–1085.
44. Pannekeet MM, Imholz AL, Struijk DG, Koomen GC, Langedijk MJ, Schouten N, de Waart R, Hiralall J, Krediet RT. The standard peritoneal permeability analysis: a tool for the assessment of peritoneal permeability characteristics in CAPD patients. Kidney Int 1995; 48: 866–875.
45. Michels WM, Smit W, Korevaar J, Struijk DG, Van Westrhenen R, Krediet RT. Does lymphatic absorption change with the duration of peritoneal dialysis? Perit Dial Int 2004; 24: 347–352.
46. Abensur H, Romao J, Prado E, Kakehashi E, Sabbaga E, Marcondes M. Use of dextran 70 to estimate peritoneal lymphatic absorption rate in CAPD. Adv Perit Dial 1992; 8: 3–6.

47. Mateijsen MA, van der Wal AC, Hendriks PM, Zweers MM, Krediet RT. Vascular and interstitial changes in the peritoneum of CAPD patients with peritoneal sclerosis. Perit Dial Int 1999; 19: 517–525.
48. Selgas R, Bajo MA, Paiva A, et al. Stability of the peritoneal membrane in long-term peritoneal dialysis patients, Adv Ren Replace Ther 1998; 5(3): 168–178.
49. Brimble KS, Walker M, Margetts PJ, Kundhal KK, Rabbat CG. Meta-analysis: peritoneal membrane transport, mortality, and technique failure in peritoneal dialysis. J Am Soc Nephrol 2006; 17(9): 2591–2598.
50. Reyes MJ, Bajo MA, Hevia C, Del Peso G, Ros S, de Miguel AG, Cirugeda A, Castro MJ, Sanchez-Tomero JA, Selgas R. Inherent high peritoneal transport and ultrafiltration deficiency: their mid-term clinical relevance. Nephrol Dial Transplant 2007; 22(1): 218–223.
51. Davies SJ, Phillips L, Russel GI. Peritoneal solute transport predicts survival on CAPD independently of residual renal function. Nephrol Dial Transplant 1998; 13: 962–968.
52. Churchill DN, Thorpe KE, Nolph KD, Keshaviah PR, Page D, Oreopoulos DG. Increased peritoneal transport is associated with decreased CAPD technique and patient survival. J Am Soc Nephrol 1997; 8: 189A.
53. Wang T, Heimbürger O, Waniewski J, Bergström J, Lindholm B. Increased peritoneal permeability is associated with decreased fluid and small-solute removal and higher mortality in CAPD patients. Nephrol Dial Transplant 1998; 13: 1242–1249.
54. Krediet RT, Zuyderhoudt FM, Boeschoten EW, Arisz L. Alterations in the peritoneal transport of water and solutes during peritonitis in continuous ambulatory peritoneal dialysis patients. Eur J Clin Invest 1987; 17: 43–52.
55. Zemel D, Koomen GC, Hart AA, ten Berge IJ, Struijk DG, Krediet RT. Relationship of TNF-alpha, interleukin-6, and prostaglandins to peritoneal permeability for macromolecules during longitudinal follow-up of peritonitis in continuous ambulatory peritoneal dialysis. J Lab Clin Med 1993; 122: 686–696.
56. Combet S, Van Landschoot M, Moulin P, Piech A, Verbavatz JM, Goffin E, et al. Regulation of aquaporin-1 and nitric oxide synthase isoforms in a rat model of acute peritonitis. J Am Soc Nephrol 1999; 10: 2185–2196.
57. Douma CE, de Waart DR, Struijk DG, Krediet RT. Are phospholipase A2 and nitric oxide involved in the alterations in peritoneal transport during CAPD peritonitis? J Lab Clin Med 1998; 132: 329–340.
58. Steinhauer HB, Schollmeyer P. Prostaglandin-mediated loss of proteins during peritonitis in continuous ambulatory peritoneal dialysis. Kidney Int 1986; 29(2): 584–590.
59. Panasiuk E, Pietrzak B, Klos M, et al. Characteristics of peritoneum after peritonitis in peritonitis in CAPD patients. Adv Perit Dial 1988; 4: 42.
60. Krediet RT, Mujais S. Use of icodextrin in high transport ultrafiltration failure. Kidney Int Suppl 2002; (81): S53–S61.
61. Posthuma N, ter Weel PM, Donnker AJM, Peers EM, Oe PL, Vergrugh HA. Icodextrin use is CCPD patients during peritonitis: ultrafiltration and serum disaccharide concentrations. Nephrol Dial Transplant 1998; 13: 2341–2344.
62. Krediet RT, Lindholm B, Rippe B. Pathophysiology of peritoneal membrane failure. Perit Dial Int 2000; 20 (suppl. 4): S22–S42.
63. Williams JD, Craig KJ, Topley N, Von Ruhland C, Fallon M, Newman GR, et al. Morphologic changes in the peritoneal membrane of patients with renal disease. J Am Soc Nephrol 2002; 13: 470–479.
64. Nakayama M, Kawaguchi Y, Yamada K, Hasegawa T, Takazoe K, Katok N, et al. Immunohistochemical detection of advanced glycosylation end-products in the peritoneum and its possible pathophysiological role in CAPD. Kidney Int 1997; 51: 182–186.
65. Rottembourg J, Brouard R, Issad B, et al. Role of acetate in loss of ultrafiltration during CAPD. Contr Nephrol 1987; 57: 197.
66. Wideroë FE, Smeby LC, Mjåland S, Dahl K, Berg KJ, Aas TW. Long-term changes in transperitoneal water transport during continuous ambulatory peritoneal dialysis. Nephron 1984; 38: 238–247.
67. Davies SJ, Bryan j, Phillips L Russel GI. Longitudinal changes in peritoneal kinetics: the effects of peritoneal dialysis and peritonitis. Nephrol Dial Transplant 1996; 11: 448–456.
68. Lameire N, Vanholder R, Veys D, et al. A longitudinal five year survey of urea kinetic parameters in CAPD patients. Kidney Int 1992; 42: 426–433.
69. Struijk DG, Krediet RT, Koomen GCM, Boeschoten EW, Hoek FJ, Arisz L. A prospective study of peritoneal transport in CAPD patients. Kidney Int 1994; 45: 1739–1744.
70. Faller B, Lameire N. Evolution of clinical parameters and peritoneal function in a cohort of CAPD patients followed over 7 years. Nephrol Dial Transplant 1994; 9: 280–286.
71. Rippe B, Stelin G. Simulations of peritoneal solute transport during CAPD. Application of two pore formalism. Kidney Int 1989; 35: 1234–1244.
72. Rippe B, Stelin G, Haraldsson B. Computer simulations of peritoneal transport in CAPD. Kidney Int 1991; 40: 315–325.
73. Rippe B, Simonsen O, Stelin G. Clinical implication of a three pore model of peritoneal transport. Adv Perit Dial 1991; 7: 3–9.
74. Rippe B, Krediet R. Peritoneal physiology-transport of solutes. InGokal R,Nolph KD (eds). The Textbook of Peritoneal Dialysis. Dordrecht: Kluwer Academic Publishers. 1994: 69–113.
75. Stelin G, Rippe B. A phenomenological interpretation of the variation in dialysate volume with dwell time in CAPD. Kidney Int 1990; 38: 465–472.
76. Vonesh EF, Rippe, B. Net fluid absorption under membrane transport models of peritoneal dialysis. Blood Purif 1992; 10: 209–226.
77. Flessner MF. Peritoneal transport physiology: insights from basic research. J Am Soc Nephrol 1991; 2: 122–135.
78. Hasegawa H, Kamijo T, Takahashi H, Kagami H, Hayakawa H, Hirahara I et al. Regulation and localisation of peritoneal aquaporins expression during long-term peritoneal dialysis in rats. J Am Soc Nephrol 1998; 9: 19A.
79. Yang B, Folfesson HG, Yang J, Ma T, Matthay MA, Verkman SA. Reduced osmotic water permeability of the peritoneal barrier in AQP1 knockout mice; AQP1 provides a “water-only" pathway in peritoneal dialysis. J Am Soc Nephrol 1998; 9: 29A.
80. Carlsson O, Nielsen S, Zakaria ER, Rippe B. In vivo inhibition of transcellular water channels (aquaporin-1) during acute peritoneal dialysis in rats. Am J Physiol 1996; 271: H2254–H2262.
81. Zweers MM, Douma CE, de Waart DR, Korevaar JC, Krediet RT, Struijk DG. Amphotericin B, mercury chloride and peritoneal transport in rabbits. Clin Nephrol 2001; 56: 60–68.
82. Pannekeet MM, Mulder JB, Weening JJ, Struijk DG, Zweers MM, Krediet RT. Demonstrations of aquaporin-CHIP in peritoneal tissue of uremic and CAPD patients. Perit Dial Int 1995; 15 (suppl. 1):S54–S57.

83. Ho-dac-Pannekeet MM, Krediet R. Water channels in the peritoneum. Perit Dial Int 1996; 16: 255–259.
84. Goffin E, Combet S, Jamar F, Cosyns J-P, Devuyst O. Expression of aquaporin-1 (AQP1) in a long-term peritoneal dialysis patient with impaired transcellular water transport. Am J Kidney Dis 1999; 33: 383–338.
85. Nolph KD, Hano JE, Teschan PE. Peritoneal sodium transport during hypertonic peritoneal dialysis. Physiologic mechanisms and clinical implications. Ann Intern Med 1969; 70: 931–941.
86. Chen TW, Khanna R, Moore H, Twardowski ZJ, Nolph KD. Sieving and reflection coefficients for sodium salts and glucose during peritoneal dialysis in rats. J Am Soc Nephrol 1991; 2: 1092–1100.
87. Zweers MM, Imholz AL, Struijk DG, Krediet RT. Correction of sodium sieving for diffusion from the circulation. Adv Perit Dial 1999; 15:65–72.
88. Westra W, Smit W, Zweers M, Struijk D, Krediet. Correction of sodium sieving for diffusion from the circulation. Adv Perit Dial 2003; 19: 6–9.
89. La Milia V, Di Filippo S, Crepaldi M, Del Vecchio L, Dell'Oro C, Andrulli S, Locatelli F. Mini-PET: a simple and fast method to assess free water and small solute transport across the peritoneal membrane. Kidney Int 2005; 68(2): 840–846.
90. Smit W, Struijk DG, Ho-dac MM, Krediet RT. Quantification of free water transport in peritoneal dialysis. Kidney Int 2004; 66: 849–854.
91. Parikova A, Smit W, Struik DG, Krediet RT. Analysis of fluid transport pathways and their determinants in peritoneal dialysis patients with ultrafiltration failure. Kidney Int 2006; 70(11): 1988–1994.
92. Parikova A, Smit W, Struik DG, Zweers MM, Krediet RT. The contribution of free water transport and small pore transport to the total fluid removal in peritoneal dialysis. Kidney Int 2005; 68(4): 1849–1856.
93. Venturoli D, Rippe B. Validation by computer simulation of two indirect methods for quantification of free water transport in peritoneal dialysis. Perit Dial Int 2005; 25(1): 77–84.
94. Verger C, Celicout B. Peritoneal permeability and encapsulating peritonitis. Lancet 1985; 1: 986.
95. Krediet RT, Struijk DG, Boescheten EW, Koomen GCM, Stouthard JML, Hock FJ, Arisz L. The time course of peritoneal transport kinetics in continuous ambulatory peritoneal dialysis patients who develop sclerosing peritonitis. Am J Kidney Dis 1989; 13: 299–307.
96. Hendriks PMEM, Ho-dac-Pannekeet MM, van Gulik TM, Struijk DG, Phoa SSKS, Sie L, Kox C, Krediet RT. Peritoneal sclerosis in chronic peritoneal dialysis patients: analysis of clinical presentation, risk factors and peritoneal transport kinetics. Perit Dial Int 1997; 17: 136–143.
97. Campbell S, Clarke P, Hawley C, Wigan M, Kerlin P, Butler J, Wall D. Sclerosing peritonitis: identification of diagnostic, clinical and radiological features. Am J Kidney Dis 1994; 24: 819–825.
98. Schleifer C, Ziemek H, Teehan B, Benz R, Sigler M, Gilgore G. Migration of peritoneal catheters: personal experience and survey of 72 other units. Perit Dial Bull 1987; 7: 189–193.
99. Tzamaloukas A, Gibel L, Eisenberg B, Goldman R, Kanig S, Zager P, Elledge L, Wood B, Simon D. Early and late peritoneal leaks in patients on CAPD. Adv Perit Dial 1990; 6: 64–71.
100. Twardowski ZJ, Tully R, Nichols W. Computerized tomography CT in the diagnosis of subcutaneous leak sites during continuous ambulatory peritoneal dialysis (CAPD). Perit Dial Bull 1984; 4: 163–166.
101. Schultz S, Harmon T, Nachtnebel K. Computerized tomographic scanning with intraperitoneal contrast enhancement in a CAPD patient with localized edema. Perit Dial Bull 1984; 4: 253–254.
102. Wankowicz Z, Pietrzak B, Przedlacki J: Colloid peritoneoscintigraphy in complications of CAPD. Adv Perit Dial 1988; 4: 138–143.
103. Kopecky R, Frymoyer P, Witanowski L, Thomas F, Wojtaszek J, Reinitz E. Prospective peritoneal scintigraphy in patients beginning continuous ambulatory peritoneal dialysis. Am J Kidney Dis 1990; 15: 228–236.
104. Fine A, Fontaine B, Ma M. Commonly prescribed salt intake in continuous ambulatory peritoneal dialysis is too restrictive: results of a double-blind crossover study. J Am Soc Nephrol 1997; 8: 1311–1314.
105. Medcalfe JF, Harris KPG, Walls J. Frusemide increases urine volume but does not preserve residual renal function in patients on CAPD–results of a six months randomized controlled study. Perit Dial Int 1998; 18 (suppl. 2): S1.
106. van Olden RW, Guchelaar HJ, Struijk DG, Krediet RT, Arisz L. Acute effects of high-dose furosemide on residual renal function in CAPD patients. Perit Dial Int 2003; 23(4): 339–347.
107. Vargemezis V, Thodis E. Prevention and management of peritonitis and exit-site infection in patients on continuous ambulatory peritoneal dialysis. Nephrol Dial Transplant 2001; 16 (suppl. 6): 106–108.
108. Mortier S, Faict D, Lameire NH, De Vriese AS. Benefits of switching from a conventional to a low-GDP bicarbonate/lactate-buffered dialysis solution in a rat model Kidney Int 2005; 67(4): 1559–1565.
109. Wieczorowska-Tobis K, Brelinska R, Witowski J, Passlick-Deetjen J, Schaub TP, Schilling H, Breborowicz A. Evidence for less irritation to the peritoneal membrane in rats dialyzed with solutions low in glucose degradation products. Perit Dial Int 2004; 24(1): 48–57.
110. Miranda B, Selgas R, Celadilla O, et al. Peritoneal resting and heparinization as an effective treatment for ultrafiltration failure in patients on CAPD. Contrib Nephrol 1991; 89: 199.
111. De Alvaro F, Castro MJ, Dapena F, Bajo MA, Fdez-Reyes MJ, Romero JR, Jimenez C, Miranda B, Selgas R. Peritoneal resting is beneficial in peritoneal hyperpermeability and ultrafiltration failure. Adv Perit Dial 1993; 9: 56–61.
112. Burkhart J, Stallard R. Result of peritoneal membrane (PM) resting (R) on dialysate (d) CA125 levels and PET results. Perit Dial Int 1997; 17(suppl. 1):S5.
113. Ho-dac-Pannekeet MM, Struijk DG, Krediet R. Improvement of transcellular water transport by treatment with glucose free dialysate in patients with ultrafiltration failure. Nephrol Dial Transplant 1996; 11: 255.
114. Selgas R, Bajo MA, Del Peso G, Jiménez C. Preserving the peritoneal dialysis membrane in long-term peritoneal dialysis patients. Semin Dial 1995; 8: 326–332.
115. Krediet RT. Preserving the integrity of the peritoneal membrane in chronic peritoneal dialysis. Nephrology Forum. Kidney Int 1999; 55: 341–356.
116. Krediet R, Ho-dac-Pannekeet MM, Imholz AL, Struijk DG. Icodextrin's effects on peritoneal transport. Perit Dial Int 1997; 17: 35–41.

117. Mactier RA, Khanna R, Moore H, Twardowski ZJ, Nolph KD. Pharmacological reduction of lymphatic absorption from the peritoneal cavity increases net ultrafiltration and solute clearances in peritoneal dialysis. Nephron 1988; 50: 229–232.
118. Chan PCK, Tam SCF, Robinson JD, Yu L, Ip MSM, Chan CY, Cheng IKP. Effect of phosphatidylcholine on ultrafiltration in patients on continuous ambulatory peritoneal dialysis. Nephron 1991; 59: 100–103.
119. Mactier RA, Khanna R, Twardowski ZJ, Moore H, Nolph KD. Influence of phosphatidylcholine on lymphatic absorption during peritoneal dialysis in the rat. Perit Dial Int 1988; 8: 179–186.
120. Struijk DG, van der Reijden HJ, Krediet RT, Koomen GCM, Arisz L. Effect of phosphatidylcholine on peritoneal transport and lymphatic absorption in a CAPD patient with sclerosing peritonitis. Nephron 1989; 51: 577–578.
121. Baranowska-Daca E, Torneli J, Popovich RP, Moncrief JW. Use of bethanechol chloride to increase available ultrafiltration in CAPD. Adv Perit Dial 1995; 11: 69–72.
122. Fernando SK, Santacroce S, Finkelstein FO. Two daytime Icodextrin exchanges. J Am Soc Nephrol 2006; 17: 278A.
123. Sav T, Oymak O, Tokgoz B, Sipahioglu MH, Unal A, Akcakaya M, Utas C. Effect of the double dose icodextrin use on blood pressure and left ventricular mass in peritoneal dialysis patients. J Am Soc Nephrol 2006; 17: 102A.
124. Fontan MP, Rodriguez-Carmona A, García-López E, García-Falcón T, Díaz-Cambre E. Icodextrin-based nocturnal automated peritoneal dialysis (APD) allows sustained ultrafiltration (UF) while reducing peritoneal glucose load. a crossover study. J Am Soc Nephrol 2006; 17: 278A.