Evaluation of peritoneal membrane characteristics: a clinical advice for prescription management by the ERBP working group

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Introduction

Peritoneal dialysis (PD) uses the peritoneal membrane as a semi-permeable membrane for solute transfer and ultrafiltration. The properties of this membrane are important determinants for selecting the optimal treatment regimen but vary among individuals as well as within the same individual over time (for review, see Coester et al. [1]).

As such, evaluation of the peritoneal membrane characteristics is of importance to guide PD prescription management (Figure 1). So far, the European Best Practice Guidelines (EBPG) have not covered the evaluation of the peritoneal membrane, but other guideline bodies have done so [2–4].

The present document summarizes the point of view of the European Renal Best Practice (ERBP) advisory board on this topic. In accordance with the mission statement of ERBP [5], this position statement is not a guideline, which would necessitate a complete in-depth analysis of the literature, but reflects recommendations and/or clinical advice on how to evaluate peritoneal membrane characteristics in clinical practice and how the results should be incorporated in PD prescription. The recommendations/clinical advice are based on expert opinions, supported by evidence when available.

The need for tests of peritoneal membrane characteristics

ERBP position statement:

1.1 An evaluation of peritoneal membrane characteristics should be used to guide prescription of PD therapy and follow the evolution of peritoneal membrane function over time.

1.2 An evaluation of peritoneal membrane characteristics should routinely be repeated at least once per year or when new clinical problems (overhydration, malnutrition, metabolic disturbances) are noticed.

1.3 PD prescriptions should be optimized according to Table 1 in function of the results of the peritoneal membrane characteristics.

The aims of evaluating peritoneal membrane function are:

- To optimize treatment prescription with regard to small-solute clearance, volume regulation and reduction of uraemic toxicity.
- To assess membrane characteristics not related to small solutes: osmotic conductance of glucose, aquaporins, hydraulic conductance, large-solute flow, lymphatic reabsorption.
- To evaluate the evolution of peritoneal function over time.

Assessment of peritoneal membrane characteristics, specifically solute transport rate and ultrafiltration capacity, is fundamental to PD prescription, as this will guide prescription.

There is considerable between-patients variability in both solute transport and ultrafiltration capacity. These differences necessitate that a therapy should be tailored to the specific needs of the patient in terms of the ideal length of dwell, the number of dwells and the type of dialysis solution used (Table 1). An inappropriate prescription can lead to substantial underachievement in terms of solute clearance and ultrafiltration or unnecessary exposure to hypertonic solutions. There is, for example, evidence that part of the higher mortality associated with a fast transport status can be abolished by using appropriate prescriptions [6,7] and
Fig. 1. Flowchart of clinical peritoneal membrane characteristics evaluation.
that using automated peritoneal dialysis (APD) in slow transporters results in hypertension [8]. It is suggested that 4–6 weeks after start of PD is the appropriate timing for a first evaluation.

Membrane characteristics change with time on therapy. Some PD patients will develop changes to the peritoneal membrane consisting of neo-angiogenesis, vasculopathy and submesothelial and interstitial fibrosis [9]. In the majority of these patients, these alterations will lead to decreased ultrafiltration capacity and an increase in the transport rate for small solutes [10,11]. Therefore, membrane transport characteristics should be evaluated at least once a year to make sure the prescription still matches the needs of the patient.

Deterioration of clinical (volume overload, ultrafiltration failure and malnutrition) and biochemical parameters (haemoglobin, serum albumin, urea and creatinine) can be caused by an inappropriate PD regimen, as a consequence of a change in peritoneal membrane characteristics. When these problems arise, re-evaluation of the peritoneal membrane characteristics should be performed to adapt the treatment regimen accordingly.

### Table 1. Peritoneal membrane transport types and their consequences for clinical management

<table>
<thead>
<tr>
<th>Transport type</th>
<th>Properties</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast transporter</td>
<td>Fast, hyperbolic, equilibration of creatinine, typically with a $D/P_{\text{crea}} &gt; 0.80$ after 4 h</td>
<td>Short dwells, preferably shorter than 180 min</td>
</tr>
<tr>
<td></td>
<td>Fast dissipation of glucose from the peritoneal cavity, with negative ultrafiltration in dwells with 1.36% glucose longer than 180 min</td>
<td>Icodextrin to be considered for longest dwell, unless sufficient residual diuresis</td>
</tr>
<tr>
<td></td>
<td>Limited sodium sieving, with 3.86% PET and small ($&lt; 5 \text{ mmol/l}$) delta $D_{\text{sodium}}$ (difference between the $D_{\text{sodium}}$ at start and after 1 h)</td>
<td>Check inflammatory status (peritoneal protein loss). When negative, check transport status using larger fill volumes</td>
</tr>
<tr>
<td>Average transporter</td>
<td>Moderately fast equilibration of creatinine, with a steeper slope in the beginning than at the end of the dwell</td>
<td>Too short (&lt;120 min) and too long dwells (&gt;300 min) should be avoided, except for one exchange/day (‘the long dwell’)</td>
</tr>
<tr>
<td></td>
<td>Moderately fast disappearance of osmotic agent. Negative ultrafiltration only in too long dwells (&gt;240 min)</td>
<td>Long dwells, preferably longer than 240 min</td>
</tr>
<tr>
<td>Slow transporter</td>
<td>Slow, semi-linear equilibration of creatinine, typically with a $D/P_{\text{crea}} &lt; 0.55–0.60$ after 4 h</td>
<td>Use larger volumes rather than more dwells</td>
</tr>
<tr>
<td></td>
<td>Sustained ultrafiltration even in dwells longer than 240 min</td>
<td>Icodextrin probably not necessary for longest dwell</td>
</tr>
<tr>
<td></td>
<td>Important sodium sieving, with 3.86%-PET and substantial delta $D_{\text{sodium}}$ ($&lt;5 \text{ mmol/l}$) after 1 h (the peak of delta $D_{\text{sodium}}$ could occur later in the dwell)</td>
<td>Be aware of sodium sieving when using dwells shorter than 180 min</td>
</tr>
</tbody>
</table>

between peritoneal membrane characteristics, patient characteristics, treatment parameters and outcome.

- Some basic parameters of peritoneal membrane characteristics can be directly derived from observing ultrafiltration volumes obtained with the regular PD schedule of the patient, as indicated in Table 1.
- The original PET (see Appendix 1 for instructions on how to perform a classic PET) is the most widely used test for evaluation of peritoneal membrane characteristics [12,13].
- The original PET used a fixed fill volume of 2 l of a 2.27% glucose solution over a 4-h dwell. There is no evidence that using 1.36% or 3.86% glucose instead of 2.27% glucose influences the results of dialysate over plasma ratio of creatinine ($D/P_{\text{crea}}$) or ratio of glucose concentration at a given moment over that at the start of the dwell ($D/D_0$) [14–16].
- The impact of a preceding overnight dwell with icodextrin has only been evaluated in one study, showing a small increment in $D/P$ value. This was, however, a small study, so no definite recommendation can be made in this regard [17].
- Although the original PET allows accurate estimation of small-solute transport, as expressed by $D/P_{\text{crea}}$ and $D/D_0$, and ultrafiltration capacity, it does not provide sufficient information to discriminate between causes of ultrafiltration failure. To answer the latter question, using a 3.86% glucose solution during the PET is recommended [18] to determine the evolution of $D/P_{\text{sodium}}$ during the dwell. This allows evaluation of the function of the aquaporins by the assessment of ‘sodium sieving’ [15,19]. This test has been named ‘modified PET’ (Appendix 2). Of note, the timing and amplitude of sodium sieving depend on the peritoneal transport characteristics of small solutes through the small pores [19]. The sodium dip results from a competition between free water transport over

### Choice and application of tests of peritoneal membrane characteristics

**ERBP position statement:**

2.1 **There is insufficient evidence to prefer one test of peritoneal membrane characteristics over another for clinical prescription.** However, some tests may render specific information not provided by the classical peritoneal equilibration test (PET) test (Table 2a). The type of test to be used is thus dependent on the type of information one wants to obtain and the questions one wishes to be answered (Table 2b).

2.2 **As evidence is scarce, ERBP strongly recommends and supports epidemiological follow-up of the relation**...
the aquaporins and the diffusion of sodium over the small pores [20]. In the first part of the dwell, the osmotic gradient over the aquaporins is strongest and gradually decreases as glucose is absorbed. The free water transport is thus most pronounced in the beginning of the dwell. In the second part of the dwell, diffusive transport of sodium from the plasma to the dialysate will increase as a consequence of the increase in concentration difference (see Appendix 3). Therefore, using the 1-h value of $D/P_{\text{sodium}}$ to estimate the free water transport is advocated [21,22], a procedure named the mini PET. When the mini PET is performed once with a 1.36% and once with a 3.86% glucose solution, it is possible to calculate the osmotic conductance to glucose. This test has been called the 'double mini PET' [23] (Appendix 2).

Table 2a. Overview of peritoneal function tests relevant for routine clinical practice

<table>
<thead>
<tr>
<th>Test</th>
<th>Application/advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original PET (2.27%) [12,13,38–40]</td>
<td>Small-solute transport, expressed as $D/P$ value Categories fast/average/slow should guide prescription management (see Table 1) Widely used</td>
<td>Limited information</td>
</tr>
<tr>
<td>Modified PET (3.86% glucose) [41]</td>
<td>Small-solute transport, expressed as $D/P$ value Categories fast/average/slow should guide prescription management (see Table 2)</td>
<td>No information on sodium sieving, FWT or OC</td>
</tr>
<tr>
<td>APEX (accelerated peritoneal examination test) [42]</td>
<td>Apex time, being the moment when the curves of $D/D_0$ glucose and $D/P_{\text{Creat}}$ cross Very suitable to define ‘optimal dwell time’ for individual patients</td>
<td>No information on sodium sieving, FWT or OC</td>
</tr>
<tr>
<td>PDC® (Peritoneal Dialysis Capacity) test [34,35,43–45]</td>
<td>More reliable data because more measuring points Small-solute transport, expressed as area over diffusion distance ($A_0/dX$). Easily convertible to $D/P$ values Large pore flow Estimate of net peritoneal fluid loss (peritoneal reabsorption) Computer-aided prescription management</td>
<td>Multiple laboratory test needed</td>
</tr>
<tr>
<td>Mini PET [15,21]</td>
<td>FWT It lasts only 1 h</td>
<td>Small-solute transport difficult to interpret No information on peritoneal reabsorption or OC</td>
</tr>
<tr>
<td>Double mini PET [23]</td>
<td>FWT OC It lasts only 2 h</td>
<td>Small-solute transport difficult to interpret No information on peritoneal reabsorption</td>
</tr>
<tr>
<td>Modified PET with temporary drainage</td>
<td>Small-solute transport, expressed as $D/P$ value Categories fast/average/slow should guide prescription management (see Table 1)</td>
<td>No information on sodium sieving, FWT</td>
</tr>
</tbody>
</table>

FWT, free water transport; OC, osmotic conductance.

Table 2b. Recommendations regarding peritoneal function test to assess different aspects

<table>
<thead>
<tr>
<th>Parameter to be investigated</th>
<th>Preferred or relevant test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small-solute transport</td>
<td>PET, PDC®, mini PET</td>
</tr>
<tr>
<td>Ultrafiltration capacity</td>
<td>Double mini PET to evaluate osmotic conductance; keep samples to evaluate sodium sieving if previous inconclusive. Consider PDC® or SPA to evaluate fluid reabsorption when needed.</td>
</tr>
<tr>
<td>Overhydration</td>
<td>Test ultrafiltration capacity Check dietary compliance Check outflow pattern/breakpoint analysis Check other mechanical complications Check residual renal function</td>
</tr>
<tr>
<td>Free water transport</td>
<td>Double mini PET</td>
</tr>
<tr>
<td>Osmotic conductance to glucose</td>
<td>Modified PET with temporary drainage</td>
</tr>
<tr>
<td>Large pore flux (large solute transport)</td>
<td>$D/P_{\text{albumin}}$ Double mini PET (can also be done without sodium measurements for this purpose)</td>
</tr>
<tr>
<td>Small-solute clearance (Kt/V, clearance)</td>
<td>PDC®-test 24-h collection of urine and dialysate</td>
</tr>
</tbody>
</table>

PET, peritoneal equilibration test; PDC® test, personal dialysis capacity test.
• Whereas the (double) mini PET is short and gives important information on aquaporin function, it fails to provide estimates of net fluid reabsorption from the peritoneal cavity. As this can be a cause of ultrafiltration failure, a mini PET should preferentially be coupled to an original or modified PET. Although the double mini PET is somewhat more complex and labourious, it provides interesting and essential information, especially related to osmotic conductance for glucose, which is the capacity of glucose to induce transperitoneal ultrafiltration through generation of osmotic pressure. This is especially important as it allows detection of intrinsic changes in the peritoneal membrane, such as sclerosis or fibrosis [24], which might be more prevalent as a cause of ultrafiltration than aquaporin deficiency. In addition, the calculation of the osmotic conductance does not require measurement of sodium concentrations in dialysate, a lab test that might be difficult to obtain in clinical routine labs. For all these reasons, measuring osmotic conductance for glucose performing a double mini PET without sodium modelling has great appeal as a second line test after PET evaluation in complicated cases of ultrafiltration (UF) failure.

2.3 In scientific publications, one should avoid reporting the results of PET only as transport categories. Expression of data as exact figures of $D/P$ (dialysate over plasma) ratios is recommended. For clinical use and prescription management, the current terminology should be replaced by the more relevant descriptions ‘fast’, ‘average’ and ‘slow’, as these terms more intuitively relate to the optimal dwell length.

• Although the reporting of transport categories is widespread, their relevance as comparators between populations and studies is to be debated, as large differences exist in distributions of transport characteristics between populations [25,26].
• The terms ‘high’ and ‘low’ transporter should be avoided. They create confusion, as they suggest that ‘high’ or ‘low’ transporters have a high or low solute removal, respectively, which is often not the case because of loss of the osmotic solute gradient resulting in negative ultrafiltration and thus decreased drained volumes in ‘high’ transporters [25] (see Appendix 4). As a consequence, solute removal is lower in ‘high’ transporters than in ‘low’ transporters. It would therefore be more realistic and representative to use the terms ‘fast’ and ‘slow’ since, in fact, a rate of transport is being measured.
• In clinical practice, the division into four categories to guide prescription is unnecessarily complex, as ‘average slow’ and ‘average fast’ patients can be treated with comparable treatment regimens.
• In view of the above, prescription recommendations for clinical practice should be based on the classification ‘fast’, ‘average’ and ‘slow’ transporter status. This categorization can be obtained even based on simple clinical observation. As such, the classification is more based on ‘general’ appreciation than on absolute $D/P$ values. Fast transporters typically have a fast equilibration of creatinine and a fast dissipation of the glucose gradient, with thus a negative ultrafiltration in dwells longer than 180 min with 1.36% glucose. Slow transporters have a slow equilibration of creatinine and a slow dissipation of glucose but a sustained ultrafiltration even after a dwell longer than 300 min with a 1.36% glucose solution.

2.4 $D/P_{\text{urea}}$ shows far less variability between patients than $D/P$ of larger molecules. As such, when formal evaluation of the peritoneal membrane characteristics is required, the use of $D/P_{\text{creat}}$ should be preferred to obtain better characterization of the small-solute transport characteristics of the membrane.

2.5 When applying tests of peritoneal membrane characteristics, some methodological caveats should be considered.

• High glucose concentrations might interfere with the determination of creatinine. Methods to avoid this interference or correction factors should be used accordingly. Enzymatic determination of creatinine is recommended (both in plasma as in dialysate) when available.
• Determination of sodium concentration in dialysate can be biased by the methodology used because of the presence of glucose and the absence of proteins and lipids in the dialysate. The preferred method is flame photometry. Indirect ion-selective electrodes can be used when they have been calibrated against flame photometry using peritoneal dialysate fluid as reference [27].
• The fill volume used can potentially influence the obtained results. Using too-low fill volumes can falsely induce the impression of a fast transport status. Fill volumes should be adapted to body surface area, not to weight [28–31]. For the testing of the peritoneal membrane transport characteristics, using the usual fill volume of the individual patient is recommended, as this reflects what is going on in this patient in clinical practice. It should be considered, however, that changing fill volume can change the observed transport status.
• When calculating ‘ultrafiltration’ capacity, the potential overfill of bags should be taken into account [32]. Indeed, most companies overfill their bags during the production process. Classically, this amounts up to 200 ml/exchange, but actual weighing of the bags before and after the dwell is recommended. This procedure also corrects for differences induced by the flush before fill procedure, as the flushed volume is accounted both at the in- and outside. When the bags are only weighed after drainage and not before filling, ultrafiltration will be overestimated, as the flush before fill rinsing volume will be added to the drained weight, whereas this is not ultrafiltered volume.

2.6 Peritoneal membrane ultrafiltration failure is defined as a drained volume after a 4-h dwell of
<2100 ml with a 2.27% glucose solution, respectively (International Society of Peritoneal Dialysis ISPD guideline [18]). The (theoretical) condition ‘ultrafiltration failure’ should be distinguished from the (clinical) condition ‘overhydration’. Clinical overhydration is the net result of the volume balance of the patient and, as such, is influenced not only by peritoneal ultrafiltration capacity but also by other factors, such as residual urine production and dietary salt and fluid intake.

- When analysing causes of overhydration, non-membrane-associated factors should also be evaluated: dietary compliance, evolution of residual renal function and diuresis and mechanical causes.
- Mechanical causes (bad drainage or leakage) should be the first mechanisms to be suspected when a long dwell with icodextrin results in negative ultrafiltration.
- Net fluid loss from the peritoneum can occur through several mechanisms, including capillary fluid reabsorption via the Starling mechanism, true lymphatic reabsorption and local entry of fluid into the tissues. The sum of these can be measured using volume markers such as dextran 70 [33] as in the standardized peritoneal assessment (SPA) test or with the Personal Dialysis Capacity test (PDC®) [34]. The separate components cannot, however, be dissected by clinically applicable tools. However, increased peritoneal fluid reabsorption can be suspected when mechanical problems (drainage, leakage) have been excluded and icodextrin results in suboptimal ultrafiltration. Data on the importance of high rate of peritoneal fluid loss as a cause of ultrafiltration failure in large series are very scarce. In a Dutch study, more than 10% of cases of ultrafiltration failure had a high peritoneal fluid loss [11].

For optimal PD prescription management, parameters indirectly related to peritoneal membrane characteristics should also be considered. Most important is the catheter oufflow pattern that should be monitored on a regular basis. The catheter drainage profile is an important parameter to guide prescription management, especially in APD patients. It should be taken into account that drainage time is in fact non-dialysis time. As most patients have a typical drainage profile, with a steeper initial part of the flow rate curve and a more shallow part at the end, and as especially at the end of drainage no diffusion is taking place, the dialysate outflow pattern should be monitored. For this, a drained dialysate volume/time curve can be constructed (Appendix 5). Too-long periods of non-diffusion should be avoided. This can be achieved by keeping the number of dwells low and by starting refill immediately after the ‘breakpoint’ rather than awaiting complete drainage (this can in most cyclers be done using the ‘tidal’ mode).

Residual renal function, both in terms of clearance as in terms of diuresis, should be monitored on a regular basis by 24-h urine collection and calculation of the mean of urea and creatinine clearance.

- Residual renal function is not only an important predictor of outcome; it is also an important factor to take into account when making a peritoneal dialysis regimen prescription.
- Patients with a rapid declining residual renal function often also have a faster deterioration of the peritoneal membrane.
- It is strongly discouraged to intentionally leave patients overhydrated to preserve residual renal function. Overhydration also results in a faster decline of residual renal function and is by itself an important factor leading to cardiovascular mortality. Dehydration should be avoided, since it can also cause faster deterioration of residual renal function.

Peritoneal protein/albumin loss should be measured as an important outcome predictor.

- Peritoneal protein/albumin loss is presumably a marker of endothelial dysfunction and, as such, a reflection of general atheromatosis or of subclinical inflammation. It is an important predictor of survival in PD patients [35,36]. It should be taken into account that transferring this type of inflamed patients to haemodialysis (HD) probably does not alter their outcome [37].
- Peritoneal protein loss can be determined to discriminate fast transport status as caused by large surface area (low protein loss) from fast transport status due to inflammation (high protein loss). However, it has to be understood that this discrimination does not alter recommendations for prescription.

Of note, prescription recommendations do not indicate whether manual PD (continuous ambulatory peritoneal dialysis, CAPD) or APD should be used, as this is a lifestyle issue. Provided the recommendations on the lengths of the dwells are followed, all patients can choose either APD or CAPD in function of their preference and lifestyle.

When negative ultrafiltration is registered and mechanical causes and lymphatic reabsorption have been excluded, shortening the dwell time rather than increasing glucose concentration is advocated. As fast dissipation of osmotic agent out of the peritoneal cavity and equilibration between plasma and peritoneum go together, this intervention will result simultaneously in a more optimal ultrafiltration and solute removal, while avoiding unnecessary glucose exposure.

In patients on APD with outflow problems, as diagnosed with an outflow drained volume/time curve, tidal PD allowing each time a residual intraperitoneal volume equal to that remaining at the breakpoint should be considered.

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Conflict of interest statement. None declared.
Appendix 1: The original peritoneal equilibration test (PET) [46]

The classic PET uses 2000 ml of a 2.27% glucose solution as instillation fluid. The test is performed in the morning. Patients come to the unit with their overnight dwell fluid still in the abdomen. The fluid is drained, and after complete drainage, the 2000 ml is instilled. Immediately after completion of the fill, the patient is asked to roll over several times to mix the fluid intra-abdominally, and a small dialysate sample is drained for time point zero. After 2 h, a new dialysate sample is taken and also a blood sample. After 4 h, a new dialysate sample is taken. On all samples, urea, creatinine and glucose are determined.

The results are graphically represented in a PET graphic, presenting the ratio of the dialysate glucose concentration at a certain time over the initial dialysate glucose concentration in the Y-axis, the dialysate over plasma ratio of creatinine (D/Pcrea) in the Y-axis and time in the X-axis.

Appendix 2: Performing alternative PET regimens

1. The modified PET [15]

   (i) Complete drainage (lasting 20 min at least) of the dialysate of the overnight dwell.
   (ii) A 3.86% glucose solution should be used for the test. Weigh the bags and the lines before the beginning of the test. The weighing should be repeated at the end of the test in order to assess the infused volume.
   (iii) Connection of the bag to the patient and infusion of ‘fresh’ solution. At the end of infusion, roll patient over several times back and forth. Drain approximately 10–15 ml back in the (now empty) dialysate container (NOT in the drained dialysate!). This dialysate sample is Time 0.
   (iv) A new dialysate sample is taken in a comparable way after 60 min for dialysate sodium, creatinine and glucose and after 120 and 240 min for dialysate creatinine, glucose and total protein.
   (v) After 240 min, a complete drainage is performed, and the bags are weighed.
   (vi) A blood sample is taken after 120 min for plasma glucose, plasma urea, plasma creatinine, plasma sodium and plasma total protein.
2. The double mini PET (for details, see [23])

(i) Complete drainage (lasting 20 min at least) of the dialysate of the overnight dwell in a bag and measurement of the volume of the overnight dwell.

(ii) A 1.36% glucose solution should be used for the first and a 3.86% glucose solution for the second part of the test.

(iii) Weighing of the bags and of the lines before the beginning of the test. The weighing should be repeated at the end of the test in order to assess the infused volume.

(iv) Connection of the bag to the patient and infusion of ‘fresh’ solution (10 min), leaving approximately 10 ml of it in the bag (Time 0).

(v) Exchange lasting 60 min after the end of the infusion. Then complete drainage (20 min) of the abdominal cavity. A dialysate sample should be taken for analysis of creatinine, glucose and sodium. Blood sampling for plasma glucose, plasma urea, plasma creatinine, plasma sodium and plasma total proteins.

(vi) Na sieving is considered as \( \Delta D_{Na} \) after 60 min of the test with the 3.86% solution. NaR (mmol/l) being the difference in Na concentration (mmol/l) between the ‘fresh’ solution and the dialysate drained after 60 min.

(vii) Free water transport (FWT):

\[ \text{FWT (ml)} = \text{UFT (ml)} - \text{UFSP (ml)} \]

Ultrafiltration over the small pores (UFSP) is assessed using the Na clearance:

\[ \text{UFSP (ml)} = \frac{\text{NaR (mmol)} \times 1000}{\text{Na}_p (\text{mmol/l})} \]

NaR (mmol) is the Na removed during the second part of the test with the 3.86% solution. NaR is calculated as follows:

\[ \text{NaR (mmol)} = \left( \frac{\text{Volume of dialysate before infusion (l)} \times \text{Na concentration (mmol/l) in dialysate before infusion}}{\text{Volume of dialysate before infusion (l)} \times \text{Na concentration (mmol/l) in dialysate drained at Time 0}} \right) \]

\[ \text{Na}_p = \text{plasma sodium.} \]

(viii) Osmotic Glucose Conductance (OCG) (ml/min/mmHg)

\[ \text{OCG} = \left( \frac{(V_{3.86} - V_{1.36})}{(19.3(G_{3.86} - G_{1.36})60)} \right) \times 1.7 \]

\( V_{3.86} \) and \( V_{1.36} \) (ml) are the dialysate volumes drained at the end of the 3.86% and 1.36% glucose solution part of the test. \( G_{3.86} \) and \( G_{1.36} \) are the molar glucose concentrations (mmol/l) in dialysate before the infusion and are calculated as follows:

\[ G (\text{mmol/l}) = \frac{\text{glucose (mg/dl) at Time 0]}{18} \]

The value 1.7 is a correction factor for the fact that we measure \( J_G \) not at the beginning of the dwell, but only after 60 min, and for the dilution of the glucose in the dialysate by eventual incomplete drainage.

Osmotic conductance for glucose represents the ability of glucose to exert an osmotic pressure sufficient to cause transperitoneal ultrafiltration. It is a lumped parameter, being determined by the vascular area surface and by the reflection coefficient of glucose. It will thus be influenced by changes in vascularization (more vascularization leading to higher values), by aquaporin function (which determine the transcapillary reflection coefficient) and by properties of the interstitium, e.g. presence of fibrosis (which determines the interstitial reflection coefficient). Typically, in patients with increasing neo-vascularization and interstitial fibrosis, total osmotic conductance will go down. In the study by Lamilla et al., an osmotic conductance above 2 μl/min/mmHg was never associated with ultrafiltration failure. In the patients without ultrafiltration failure, the osmotic conductance was 3.5 ± 1.34 μl/min/mmHg.

Appendix 3: the concept of sodium sieving and aquaporin function

Sodium sieving is the phenomenon of decreasing sodium concentrations in the dialysate in the first phase of a PD dwell. This phenomenon is induced by the fact that aquaporins only allow transport of water and not of sodium. In the first part of a dwell, there is a strong osmotic gradient over the aquaporins, inducing free water transport from the capillaries to the dialysate and resulting in a decrease (dilution) of dialysate sodium concentration. In the later part of the dwell, the increase in...
concentration difference for sodium between the dialysate and the plasma will result in enhanced diffusive transport of sodium over the small pores, and sodium concentration in the dialysate will rise again (adapted from Heimburger et al. [47]).

As a consequence, this ‘sodium dip’ can be used to evaluate the functionality of the aquaporins. The stronger the osmotic gradient over the aquaporins, the more pronounced the expected sodium dip will be. Therefore, a 3.86% hypertonic glucose is the preferred solution to test sodium sieving.

An absent or decreased sodium dip can be due to decreased aquaporin function but can also be due to a fast diffusive transport. Although these two conditions can be dissected by calculating the free water clearance, e.g. with the double mini PET, in clinical practice it is more easy to rely on a simple rule of thumb: when there is a decreased or absent sodium dip with a 3.86% glucose solution and a high ultrafiltration with a 6-h icodextrin dwell, the underlying cause is fast diffusive transport. When ultrafiltration with a 6-h icodextrin dwell is low, the underlying cause is most likely aquaporin deficiency.

For more detailed investigation of ultrafiltration failure, measuring osmotic conductance by means of a double mini PET should be recommended. It is stressed again that, in order to determine osmotic conductance, it is not necessary to measure sodium in the dialysate. When one also wants to measure free water clearance (or sodium sieving), it is necessary to determine sodium concentrations in the plasma and in the dialysate.

Of note, the disparity between free water clearance and sodium removal (and thus the sodium sieving) increases with increasing tonicity of the dialysate solution and decreases with diffusive transport rate and the duration of the dwell. As such, sodium sieving is not problematic in fast transporters with short dwells but can be substantial in slow transporters with short dwells.

Appendix 4: the concept of fast, average and slow transport status

![Fig. 1. Intraperitoneal dialysate volume vs dwell time. ■, high transport group (n=7); ○, high-average transport group (n=20); ○, low-average transport (n=13); △, low transport group (n=6).](image)

Peritoneal outflow can be measured and presented as a drain volume/time curve (A) or as outflow rate over time (B) (adapted from Brandes et al. [48]).

Appendix 5: the concept of peritoneal outflow curves

![Fig. 2.](image)
For determining a drain/volume curve, the intraperitoneal volume is represented in the Y-axis and time on the X-axis. At Time 0, the (presumed) intraperitoneal volume is represented. At different time points (e.g. every minute), it is indicated how much volume has been drained by weighing the drainage bag, and this amount is subtracted from the initial volume and plotted. For the drain flow rate visualization, we have the drain flow rate in the Y-axis and the time in the X-axis. Flow rate is measured by weighing the drainage bag and calculating the amount of volume drained per minute.

It can easily be observed that it takes more time to drain the last 100 ml than to drain the bulk. From the moment that the slope changes (transition point), there is no more contact of a sufficient volume of dialysate with the peritoneal membrane; as a consequence, there is also no clearance, and thus there is no effective treatment. Depending upon patient characteristics, this period can last 10–20 min, provoking substantial loss of treatment time especially in APD patients. This loss of treatment time can be avoided by allowing the cycler to stop drainage after the ‘transition point’ has been obtained, after which a new fill can start. This treatment option can in some cyclers be switched on automatically; in others, it can be obtained by using the tidal mode. In the latter case, the ‘tidal volume’ should correspond to the volume obtained at the transition point.

Conflict of interest statement. None declared.

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ANCA-associated vasculitis and anti-GBM disease: the experience in China

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Anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) and anti-glomerular basement membrane (GBM) disease, the typical autoimmune diseases causing necrotizing crescentic glomerulonephritis (CrGN), have been largely reported in Caucasian patients. However, since the establishment of standard assays in China to screen for serum ANCA and anti-GBM autoantibodies over 10 years ago, Chinese patients with the two diseases were increasingly identified and studied. This editorial comment focuses on the updated information of Chinese patients with the two diseases.

ANCA-associated vasculitis and pauci-immune crescentic glomerulonephritis

The annual incidence of AAV in Europe is 10–20 per million per year [1]; the incidence in China is not available yet. In our referral diagnostic centre in Peking University First Hospital, over 200 new patients with AAV are diagnosed annually; this indicates that AAV is not rare in Chinese [2].

Chinese patients with ANCA-associated vasculitis

Clinical characteristics of Chinese patients with AAV

Regarding the disease spectrum, there is a striking preponderance of microscopic polyangiitis (MPA), constituting...