The peritoneal equilibration test (PET) has been widely used as a standardized means for estimating solute transport. However, the procedure is rather complex, and patients must spend more than half a day in the hospital. The fast PET is an alternative method, but the results are not reliable in patients whose peritoneal catheters drain poorly.

We postulated that patients could perform the PET at home if educated well about the procedure. To that purpose, we prepared three types of visual aids that introduce the PET procedure: a VCR tape, a DVD disc, and a brochure with photographs.

Equilibration tests were performed using the twin-bag system. For marking fluid level indicator lines (200 mL and 10 mL), patients are given a guide sheet on which the fresh dialysate bag is placed. After an 8- to 12-hour overnight dwell, the dwelled dialysate is drained completely into the empty bag. Immediately after the patient infuses 2 L of fresh 2.5% glucose dialysis solution, 200 mL of that solution is drained into the bag on which the two fluids levels were previously marked. After mixing, about 190 mL of the dialysate is re-infused, and the remaining 10 mL (the amount indicated by a guide mark at the corner) is left within the bag. After a 4-hour dwell, the dialysate is completely drained into another twin-bag.

A standard PET was also performed on a different day, and the data were compared with those from the home PET. Significant correlations were seen in D/D₀ and in drain volume between the home PET and the standard PET (n = 10; D/D₀: 0.385 ± 0.054 vs. 0.371 ± 0.052 respectively; r = 0.872, p = 0.0004; drain volume: 2340 ± 123 mL vs. 2372 ± 90 mL respectively, r = 0.788, p = 0.0048).

We conclude that the home PET is a clinically useful alternative to the standard PET, saving time and labor while maintaining accuracy.

Key words
Peritoneal equilibration test, PET, home PET

From: Shizuoka City Hospital, Shizuoka, Japan.
(Table I). At our outpatient clinic, the patients were given visual aids (a VCR tape, a DVD disc, and a brochure with photographs, all of which showed the home PET procedure) and a form for recording exchange time and drain volume (Figure 1).

To ascertain the efficacy of visual aids, verbal instructions at the outpatient clinic were minimal. In the cases of two older patients who were not able to perform the tests themselves, a family member performed the procedure for the patient instead (Table I).

The home PET procedure is based on the standard PET, but blood and dialysate sampling at hour 2 are omitted for patient convenience. The PET category is calculated from drain volume and from the dialysate-to-instilled ratio (D/D₀) of glucose at hour 4.

**Table I** Patient characteristics

<table>
<thead>
<tr>
<th>Patient</th>
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<th>Cause of ESRD</th>
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<td>92</td>
<td>M</td>
<td>45</td>
<td>Diabetic nephropathy</td>
</tr>
</tbody>
</table>

* Home peritoneal equilibration test was performed by a family member.

PD = peritoneal dialysis; ESRD = end-stage renal disease.

For marking fluid-level indicator lines (200 mL and 10 mL), patients receive a guide sheet on which the fresh dialysate bag (2 L 2.5% dextrose bag) is placed. A felt-tip pen is then used to clearly draw the two indicator lines before testing begins.

After an 8- to 12-hour overnight dwell, the dwelled dialysate is completely drained into the empty bag.

Immediately after the patient infuses 2 L of dialysis solution, 200 mL is drained back into the bag on which the two fluid-level lines were previously marked.

After the bag is inverted three times to mix, the patient re-infuses about 190 mL of the dialysate. The remaining 10 mL, the amount indicated by a guide mark at corner, is left within the bag.

After a 4-hour dwell, the dialysate is completely drained into another twin-bag, and the three dialysate samples are brought to our outpatient clinic for further evaluation.
FIGURE 2 The home peritoneal equilibration test (home PET) procedure. (A) A guide sheet indicates two fluid levels (200 mL and 10 mL). (B) Drawing a 10 mL line by placing the fresh dialysate bag on the guide sheet. (C) Drawing a 200 mL line. (D) Immediately after the patient infuses fresh dialysate, 200 mL of the solution is drained into the bag on which the two fluid levels were previously marked. (E) The drained bag is mixed by inverting three times. (F) About 190 mL of dialysate is re-infused, and the remaining 10 mL (the amount indicated by the guide mark at the corner) is left in the bag (time 0 sample). (G) After a 4-hour dwell, the dialysate is completely drained into another twin-bag. The three dialysate samples (the overnight sample, the time 0 sample, and the 4-hour dwell sample) are brought into the outpatient clinic for further evaluation.
Dialysate samples were evaluated for $D/D_0$ ratio of glucose at hour 4, PET category, and residual volume. Residual volume ($V_r$) was calculated by: $V_r = 2000C_2 / (C_1 - C_2)$, where $C_1$ is the concentration of creatinine in the overnight drain bag and $C_2$ is the creatinine concentration in the drain bag at hour 0.

For assessment of PET category, we used the standardized PET data of Twardowski et al (1).

A standard PET was also performed on a different day, and the data were compared with those obtained from the home PET.

**Results**

In all 10 cases, the home PET was performed without trouble. No omissions in filling the indicated parameters of the home PET records were observed.

Excellent correlations were seen (Figure 3) between the home PET and the standard PET in the values of $D/D_0$ glucose ($r = 0.872, p = 0.0004$) and in the drain volumes ($r = 0.788, p = 0.0048$). No statistical differences were observed in the mean values of $D/D_0$ glucose ($0.385 \pm 0.054$ vs. $0.371 \pm 0.052, p = 0.329$) and drain volume ($2340 \pm 123 \text{ mL}$ vs. $2372 \pm 90 \text{ mL}, p = 0.221$) between the two tests (Figure 4).

The PET categories based on $D/D_0$ glucose coincided in all cases except one (Table II). The PET categories based on drain volume also coincided in all cases except one (Table II).

Large differences were seen in the calculated values of residual volume between the two tests, and no correlation was observed in that parameter ($291 \pm 87 \text{ mL}$ vs. $328 \pm 110 \text{ mL}, p = 0.088, r = 0.307 \text{ (NS)}$; Figures 3 and 4).

**Discussion and conclusions**

We developed a modified PET (home PET) that is performed at home by the patient or a family member.

Routine PET determinations in individual patients may be useful in defining the optimum PD prescription and in tracking changes in peritoneal function over time (3). Periodic PET testing might be omitted, however, because of the inconvenience to patients in visiting a hospital, or because of a labor shortage in the medical facility. We saw a clinical necessity for a simpler PET that could be carried out at regular intervals.

Our home PET has proved to be a clinically useful alternative to the standard PET, and it saves time and labor surrounding PET procedures. In our case studies, the patients performed the home PET with accuracy, and the data were quite compatible with those obtained using the standard PET.

Our results also demonstrated that, by giving patients detailed instructions and visual aids, sampling errors by the patients and the efforts needed by the medical staff to teach the PET procedure could be greatly reduced.

Because our home PET employs sampling of dialysate at hour 0, the results can be directly compared with past cumulative data using the standard PET, an additional advantage of the home PET over the fast PET.

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**FIGURE 3** Correlations between home peritoneal equilibration test (PET) and standard PET (horizontal axis: home PET; vertical axis: standard PET). Significant correlations were seen in $D/D_0$ glucose and in drain volume. $D/D_0 = $ the ratio of dialysate glucose at 4 hours to dialysate glucose at time 0; NS = nonsignificant.
To pursue patient convenience by reducing hospital visits, we employed D/D₀ glucose and drain volume at hour 4 as parameters for determining PET categories. Though we sometimes encountered incompatibility in PET categories between D/D₀ glucose and dialysate-to-plasma (D/P) creatinine (in such cases, the latter data are given priority), it was assumed that repeating the tests would clarify the membrane characteristics with more accuracy. That is to say, tracking the changes in D/D₀ glucose over time might yield very valuable clinical information concerning the individual peritoneal membrane.

We could observe no correlation in the calculated values of residual volume between the two tests. That lack of correlation probably reflects differences in drain position between home and hospital. Because our home PET requires intelligence and good eyesight, applying our methods to all PD patients would be difficult unless a family member cooperated. However, our home PET might be convenient for patients without those problems. Our method is of particular benefit to patients whose home PET data closely resemble data obtained by standard PET. Therefore, a reasonable method might be to compare the results of two tests.

### TABLE II Comparison of peritoneal equilibration test (PET) categories based on two different parameters

<table>
<thead>
<tr>
<th>Patient</th>
<th>PET categories from D/D₀ glucose</th>
<th>PET categories from drain volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>Standard PET</td>
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<tr>
<td>10</td>
<td>LA</td>
<td>LA</td>
</tr>
</tbody>
</table>

*a Home peritoneal equilibration test was performed by a family member.

D/D₀ = the ratio of dialysate glucose at 4 hours to dialysate glucose at time 0; LA = low-average peritoneal transport; HA = high-average peritoneal transport.

### FIGURE 4
Comparisons of mean values of D/D₀ glucose, drain volume, and residual volume between home peritoneal equilibration test (PET) and standard PET. No significant differences were seen in those parameters between the home PET and the standard PET by paired t-test. Values are expressed as mean ± standard deviation. D/D₀ = the ratio of dialysate glucose at 4 hours to dialysate glucose at time 0.
at the start, and then to select cases for the home PET.

We conclude that home PET is a clinically useful alternative to the standard PET, saving time and labor while maintaining accuracy.

Acknowledgment
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References

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Jose A. Diaz—Buxo

Continuous flow peritoneal dialysis (CFPD) is a very promising modality of PD in terms of high rates of solute removal and ultrafiltration (UF). The published clinical data are characterized by marked variability in terms of clearances and UF. Analysis of those data suggest significant streaming and recirculation with the available double-lumen catheters.

A new double lumen catheter is described. It has wide separation between the limbs to minimize streaming and recirculation, and a novel geometric configuration to maximize internal cross-sectional luminal area with the lowest external diameter.

Preliminary in vitro studies have shown flow rates consistent with those required for CFPD, satisfactory mixing of the fluid, and minimal streaming and recirculation. Clinical validation with long-term studies are needed to assess the viability of CFPD as a chronic renal replacement therapy.

Key words
Continuous flow peritoneal dialysis (CFPD), peritoneal access, peritoneal catheters, double-lumen catheters, kinetics

Introduction
Continuous flow peritoneal dialysis (CFPD) is perhaps the most promising modality of PD ever, because of its potential for high clearances and ultrafiltration (UF) (1). However, the published clinical data have been remarkably variable in terms of solute clearance (K) and ultrafiltration rate (UFR) (2—6). The theoretical constructs (1,7) predict K, mass transfer coefficients (MTCs), and UFR consistent with the clinical results obtained when two separate catheters are used (2,5), but the constructs overestimate the results obtained by most investigators when using double-lumen catheters of various designs (6,8). The disparity in the results strongly suggests streaming of the fluid and recirculation when double-lumen catheters are used, leading to poor mixing of the fluid and inability to create consistent osmotic and solute concentration gradients.

Discussion
The CFPD concept
The terminology applied by various authors to describe CFPD is confusing. Terms include recirculation PD, continuous flow PD, flow-through PD, and hybrid PD, among others. The modality deserves a better definition.

Continuous flow PD uses the continuous flow technique, meaning that a constant flow of fluid is continuously maintained through the peritoneal cavity by means of two catheters or a double-lumen catheter. Because CFPD is usually applied as a high-flow system (with peritoneal fluid flow rates, Q_p, in the range of 100—300 mL/min), it requires large volumes of dialysate, for which various sources have been proposed (9). Those sources include preparation of new dialysate and regeneration of dialysate by means of sorbents or hemodialysis technology. Regardless of the source of the dialysate, a continuous flow of fresh or regenerated dialysis solution is provided, obviating the need for new terminology. The proper terminology should be CFPD with regeneration of dialysate using hemodialysis technology, CFPD with on-line production of dialysate, CFPD with regeneration of dialysate by sorbent adsorption, CFPD using batch dialysate, and so on.

Clinical experiences with various peritoneal access devices
Figure 1 plots clearances and MTC_{urea} for CFPD from various studies using two catheters (2,3,5). The data
are markedly dispersed; however, $K_{\text{urea}}$ is significantly higher at the same $Q_p$ than that observed by investigators using either double-lumen catheters or a single-needle device (4,6,8) (both represented by the open square). The discrepancy can easily be explained by streaming of the fluid from the inflow limb of the catheter to the outflow limb. The result is high recirculation and poor mixing of the solution.

Cruz et al (5) achieved consistent MTC$_{\text{urea}}$ of approximately 40 mL/min using two separate catheters and performing 4-hour observations under rigorous conditions. Their results are consistent with the kinetic model (7).

The same investigators observed a UFR very close to that predicted by the model. Because CFPD uses a very high $Q_p$, the glucose concentration of the solution is maintained relatively constant throughout the treatment. Therefore, the expected UF should be close to the instantaneous UF (or UF at time $t = 0$). The instantaneous UF for a 1.5% glucose solution is approximately 7 mL/min, a value very close to that observed in two special studies of UF in Cruz et al series (5).

In contrast, the UFR observed by other investigators using double-lumen catheters was very low or nonexistent (6,8). Once again, streaming of dialysate along the catheter can account for the differences. Glucose is continuously absorbed from the peritoneum into the circulation. If the incoming solution is being bypassed into the outflow lumen, the osmotic gradient diminishes, and UF drops.

Peritoneal access for CFPD

Peritoneal access for CFPD can be classified into two major categories: two separate catheters and double-lumen catheters. The simplest design of the double-lumen catheter is a double D configuration, which consists of a short tube used for inflow, and a long tube for outflow (10,11). That basic design has been modified by the addition of discs along the tubes in an attempt to diffuse the inflow stream of dialysate and to improve mixing (6).

The latest modifications of the double-lumen catheter may be more significant. Ronco et al have designed a double-lumen catheter with a proximal inflow diffuser (similar to a flexible shower head that diffuses fluid in a 180-degree pattern) that is positioned close to the entry point of the catheter into the peritoneum (12). A long, curled tube, similar to a conventional coiled catheter, is used for drainage. The considerable distance between the two lumina and the diffusing effect of the multiple holes in the inflow section may reduce streaming.

In collaboration with Medigroup Inc. (Naperville, IL, U.S.A.), we have developed a double-lumen cath-

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![Figure 1](image-url)  
**Figure 1**  
Effect of peritoneal access on clearance ($K_{\text{urea}}$) and mass transfer coefficient (MTC$_{\text{urea}}$) of urea.
eter with maximum internal separation of the two tubes. The catheter can be implanted peritoneoscopically or laparoscopically. The new catheter consists of two distinct lumina (tubes) using a novel cross-sectional configuration whereby one tube, slightly oval-shaped, nests within the other crescent-shaped tube (Figure 2). That geometric arrangement allows maximum internal diameters (cross sections) and a minimal external diameter. This unique design permits passive flow rates well within the required CFPD parameters (Figure 3). In vitro studies indicate inflow and outflow rates to be within acceptable margins.

The tubes are bonded where they pass through the abdominal wall and subcutaneous tissue. Externally, they are separate for convenience and ease of use. Internally, they are also separate, each tube terminating with an appropriately sized fluted section (Figure 4). The internal tubes form a double J configuration which fits near the parietal peritoneum. The double J shape causes the cranial and caudal limbs to separate by 180° degrees. The configuration, combined with a functional separation of flutes, means that the minimal separation is at least 13 cm (approximately 5.25 in.), and the probable functional separation is approximately 20 cm (8.0 in).

**FIGURE 2** Fluted double-lumen catheter with novel configuration. (Courtesy of Medigroup, Inc., Naperville, IL, U.S.A.)

**FIGURE 3** Flow comparison of Tenckhoff and fluted double-lumen catheter. Each lumen was tested separately at different head heights. A 500-mL volume was timed, and the flow rate was calculated. Water was the medium.
Preliminary in vitro studies using only passive hydrostatic pressure have shown good flow rates and seem to indicate good mixing with minimal streaming and recirculation. While the studies are not conclusive, they do indicate that the basic design should work. Additional work with urea dilution tests and in vitro radiographic studies are needed to confirm the initial reports. Ultimately, controlled, real-life clinical studies will be required to assess the function of the catheters.

Conclusion
The next stage in the evaluation of CFPD as a viable modality of renal replacement therapy is the demonstration of consistent MTCs in the predicted range of 35°—45°mL/min and a predictable UFR. Such data will provide the foundation needed to develop prescriptions and algorithms for the proper monitoring and management of UF. Following the initial validation process, the next requirement will be to treat patients for prolonged periods of time to assess acceptance and safety of the procedure. As in the case of hemodialysis, the simplest and least expensive component of the system access is the one that causes the most problems.

References

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Icodextrin is a glucose polymer osmotic agent used to achieve sustained ultrafiltration during long peritoneal dialysis dwells. Previous assays for icodextrin in plasma and dialysate samples involved laborious methods, such as gel permeation chromatography with post-column derivatization of the eluted glucose polymers. We developed and validated a simple and more rapid assay for icodextrin using amyloglucosidase to hydrolyze all glucose polymers to glucose.

Glucose was determined pre- and post-hydrolysis using a glucose hexokinase assay, and icodextrin concentration was calculated as the difference between glucose levels before and after hydrolysis. The complete hydrolysis of icodextrin to glucose was confirmed using anion exchange chromatography. Recovery studies using icodextrin powder added to plasma or dialysate showed 100%±15% recovery for plasma concentrations from 10 mg/dL to 800 mg/dL and for dialysate concentrations from 50 mg/dL to 800 mg/dL. The percent relative standard deviation (%RSD) based on multiple replicates was within 6%, except at plasma icodextrin concentrations of 10 mg/dL and below.

This simple and reliable assay has been used routinely in our laboratory to analyze thousands of plasma and dialysate samples from patients using Extraneal peritoneal dialysis solution (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.).

Materials and methods
The principle of the assay involves exhaustive hydrolysis of glucose polymers using the enzyme amyloglucosidase. Glucose is measured in the sample pre- and post-hydrolysis using a glucose hexokinase-based assay, and the calculated difference in values is used to obtain the icodextrin concentration.

Plasma and dialysate samples were collected from PD patients treated with either Extraneal or Dianeal PD solutions (both, Baxter Healthcare Corporation). Samples were shipped on dry ice and stored frozen at —20°C to —70°C until analysis. Amyloglucosidase, isolated from Aspergillus niger, was obtained from Sigma Chemical Company (St. Louis, MO, U.S.A.). A stock solution containing bonds and a small percentage of α-(1—6) glucosidic bonds. Icodextrin has a weight-average molecular weight between 13,000 Da and 19,000 Da, and a number-average molecular weight between 5,000 Da and 6,500 Da. Icodextrin functions as a colloidal osmotic agent to achieve sustained ultrafiltration during long peritoneal dialysis (PD) dwells.

Monitoring icodextrin levels in patient plasma and spent dialysate samples may be useful in clinical research to assess icodextrin absorption and excretion. Previous methods for determination of icodextrin levels in biologic samples have involved the summation of small oligosaccharides with 2—9 glucose units (that is, G2—G9) and larger glucose polymers (that is, G10 and higher), isolated using gel permeation chromatography (1). To establish a more rapid assay for the determination of icodextrin in clinical samples, we developed an assay involving exhaustive hydrolysis of glucose polymers to glucose, followed by direct glucose measurement using standard methods. That assay has been validated and used to determine icodextrin concentrations in plasma and dialysate in support of several clinical studies of Extraneal PD solution (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.).
1 mg/mL amyloglucosidase was prepared using 0.1 mol/L sodium acetate buffer at pH 4.5.

Baseline glucose concentrations were determined in plasma and dialysate samples using glucose hexokinase on a Boehringer Mannheim/Hitachi 704 analyzer (Boehringer Mannheim, Mannheim, Germany). A 0.25 mL sample of plasma or a 0.1 mL sample of dialysate was mixed with 0.25 mL or 0.9 mL of the amyloglucosidase solution, respectively (1:1 for plasma and 1:9 for dialysate). The resulting solutions were incubated at approximately 55°C for 15 minutes or more, and then total glucose concentration was measured again. The icodextrin concentration was determined as the difference in the glucose concentration before and after amyloglucosidase hydrolysis.

**Results and discussion**

**Hydrolysis of icodextrin to glucose**

Amyloglucosidase, also known as gluc-amylase, is known to be capable of hydrolyzing both the α-D-(1—4) and the α-D-(1—6) glucosidic bonds of oligosaccharides (2—6). Incubation of amyloglucosidase with icodextrin under the proper conditions is therefore expected to result in complete hydrolysis of glucose polymers to glucose. We used high-performance anion exchange (HPAE) chromatography with pulsed amperometric detection (PAD) to confirm the complete hydrolysis of icodextrin to glucose. The HPAE-PAD method was previously developed in our laboratory to quantitatively determine concentrations.

![Chromatogram showing peaks corresponding to glucose and glucose polymers in Extraneal (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.) before and after incubation with amyloglucosidase.](image-url)

**FIGURE 1** Chromatogram showing peaks corresponding to glucose and glucose polymers in Extraneal (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.) before and after incubation with amyloglucosidase.
of G2—G7 (7) and isomaltose (8). The method is also able to qualitatively detect the presence of glucose and glucose polymers with a higher degree of polymerization (Figure 1).

We assessed the hydrolysis of icodextrin in a sample of Extraneal containing 7.5% icodextrin, the highest concentration that would be expected to be found in dialysate or plasma samples. As shown in Figure 1, a small amount of glucose and oligosaccharides G2—G7, as well as larger polymers, were present in Extraneal at baseline. Upon mixing of the dialysis solution with amyloglucosidase, concentrations of glucose and G2 increased. After 15 minutes or longer of incubation at 55°C, peaks corresponding to G2 and higher molecular weight glucose polymers had disappeared from the sample, indicating complete hydrolysis to glucose.

Method performance
The assay was validated for precision and accuracy by spiking known amounts of icodextrin powder into plasma from patients using Dianeal or into saline to mimic a spent dialysate matrix. The percent relative standard deviation (%RSD) ranged from 1.2% to 11.5%, depending on the icodextrin level and sample matrix. The accuracy of the method measured by percentage recovery was within 100% ± 15%. Plasma and dialysate samples were shown to be stable following two freeze/thaw cycles, as demonstrated by complete recovery (100% ± 12%). Additionally, the consistency of the quality control sample results that were generated along with patient sample analyses (Figure 2) demonstrates reliability and ruggedness of the assay.

Method application
The assay was used to determine icodextrin levels in patient plasma and spent dialysate samples collected from an open-label study in which patients were treated with a daily nighttime dwell of 12 hours using Extraneal for 6 weeks, followed by 4 weeks of a glucose-based dialysis solution. Figure 3(A) shows rep-

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**Figure 2** Control-sample results for icodextrin in plasma and dialysate. Two plasma control samples at different icodextrin concentrations were used. The higher concentration sample was used along with the analysis of plasma samples from peritoneal dialysis patients using a daily exchange of Extraneal (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.); the lower concentration sample was used along with the analysis of samples from a single exchange of Extraneal, where plasma icodextrin level is lower.
representative data for plasma and dialysate icodextrin levels from 3’ patients. The upper panel shows plasma results, indicating that icodextrin levels reached steady state after approximately 1’ week and remained essentially unchanged during Extraneal administration. After Extraneal was stopped, icodextrin levels returned to baseline in about 2’ weeks. The lower panel shows icodextrin concentrations in the dialysate effluent at the end of the long dwell (12-hour exchange with Extraneal). Using that value and the initial icodextrin concentration before the dwell, the absorption of icodextrin can be estimated. The icodextrin absorption for the 3’ patients was approximately 40%. Those steady-state plasma icodextrin levels and absorption results are consistent with previously reported values (9).

Figure 3(B) shows plasma and dialysate icodextrin concentrations during the course of a 12-hour dwell in 3’ patients administered a single exchange of Extraneal, after which patients returned to their normal dialysis treatment of glucose-based solution (10). Plasma concentrations of icodextrin (upper panel) peaked at around 12’ hours and declined to baseline level within 7’— 14’ days. Dialysate concentrations during the 12-hour dwell decreased in a linear fashion, consistent with absorption through lymphatic or convective transport pathways. Such data are useful in the assessment of the pharmacokinetics of icodextrin (10).

Conclusions
A rapid and simple assay using exhaustive hydrolysis of glucose polymers by amyloglucosidase has been developed and validated for measuring icodextrin concentrations in plasma and dialysate. Because the assay does not require sophisticated instrumentation, it can be used in any standard clinical chemistry laboratory with glucose testing capability.

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