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Glucose and Mannitol Have Different Effects on Peritoneal Morphology in Chronically Dialyzed Rats

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In previous studies, we showed that glucose reduces the morphologic changes in rat peritoneum caused by chronic intraperitoneal administration of 0.9% NaCl solution. In the present study, we set out to determine if the observed results were attributable to hyperosmolarity or to the metabolic effect of the glucose.

Intraperitoneal catheters were implanted in 19 rats. The animals were then intraperitoneally exposed twice daily for 30 days to 20 mL 0.9% saline supplemented with either 250 mmol/L glucose (GLU, n = 9) or 250 mmol/L mannitol (MAN, n = 10). Control rats did not undergo catheter implantation or the dialysis procedure (CON, n = 6). At the end of the study, a 1-hour peritoneal equilibration test (PET) using Dianeal 3.86% (Baxter Healthcare SA, Castlebar, Ireland) was performed in every dialyzed rat to analyze peritoneal transport. Afterward, the rats were humanely killed by bleeding, and a semi-quantitative scale was used to evaluate adhesions in the peritoneal cavity. Imprints of the visceral mesothelium and samples of the visceral peritoneum (liver) were then taken and analyzed by light microscopy.

The PET results for glucose, urea, creatinine, and total protein were comparable in both experimental groups. We found that intraperitoneal adhesions were more severe in the MAN group (6 rats with adhesions graded >3) than in the GLU group (only 1 such rat). No difference in peritoneal thickness was observed between the experimental groups (MAN: 54.9 ± 17.8 μm; GLU: 51.2 ± 14.5 μm); however, in both experimental groups, the thickness was greater than in the CON group (3.9 ± 0.6 μm). The density of the peritoneal blood vessels tended to be greater in the MAN group than in the GLU group (0.158 ± 0.072 vessels/1000 μm² vs. 0.085 ± 0.067 vessels/1000 μm², p = 0.0541). No visible blood vessels were evident in the CON group. The density of mesothelial cells was higher in the MAN group than in the GLU group (2456 ± 333 cells/mm² vs. 2090 ± 322 cells/mm², p < 0.05), and, in both experimental groups, the cell density was higher than in the CON group (817 ± 100 cells/mm², p < 0.01). The nucleus:cytoplasm area ratio in mesothelial cells was comparable in the MAN and GLU groups (0.206 ± 0.039 and 0.176 ± 0.045), but that ratio was higher in both experimental groups than in the CON group (0.086 ± 0.010, p < 0.01).

We conclude that glucose-induced changes in the peritoneum of rats exposed to chronic peritoneal dialysis depend on both osmotic and metabolic effects.

Key words
Glucose, osmolality, peritoneum, morphology

Introduction
Chronic exposure of the peritoneum to peritoneal dialysis fluids (PDFs) results in alterations in permeability that progress with time and that may be the cause of patient withdrawal from peritoneal dialysis therapy (1,2). Those functional disturbances are accompanied by morphologic changes in peritoneal membrane, including mesothelial cell damage and disorganization of the peritoneal interstitium (3,4). Long-term exposure to PDFs may also result in impairment of natural host defenses and may cause increased susceptibility to peritonitis (5,6). All of those events indicate the bioincompatibility of PDFs.

Glucose is known to be an important factor in the bioincompatibility of commercially available PDFs. At least two possible mechanisms are involved in the negative impact of glucose on peritoneal function and structure: a direct metabolic effect of the high glucose concentration, and hyperosmolality of the solu-
tion as a consequence of the high glucose concentra-
tion. Moreover, the glucose degradation products
(GDPs) present in heat-sterilized PDFs may intensify
the disadvantageous effects of peritoneal dialysis (7,8).

On the other hand, repeated infusions of any fluid
into the peritoneal cavity may cause an inflammatory
reaction owing to mechanical irritation of peritoneum
(9,10). In previous studies, we found that isotonic,
glucose-free solutions such as physiologic saline and
phosphate-buffered saline cause inflammatory reac-
tions in the peritoneal cavity of rats (11,12) and, as a
consequence, alterations in the morphology of the
peritoneum (13). Interestingly, when glucose was
added to the above-mentioned solutions, we observed
a reduction in the severity of inflammation and of
morphologic changes. Our aim in the present study
was to determine whether the morphologic effects of
glucose depend on its metabolic action or on the
hyperosmolality of the glucose dialysis solution.

Materials and methods
The study was performed on 25 male Wistar rats
weighing between 250 g and 350 g. Peritoneal cath-
eters were implanted into 19 rats according to a pre-
viously described method (14). The control group
(CON) consisted of 6 rats that did not undergo cath-
eter implantation and dialysis.

For the first two days, all rats with implanted cath-
eters were injected intraperitoneally with Dianeal
1.36% (Baxter Healthcare SA, Castlebar, Ireland)
supplemented with antibiotics [gentamicin 5 mg/L
(Polfa, Tarchomin, Poland) and cefazolin 50 mg/L
(Eli Lilly, Florence, Italy)]. The fluid was allowed to
absorb. On the third day, the rats with catheters were
randomly divided into two groups and were infused
twice daily for a further 30 days with 20 mL of one of
the following solutions (also supplemented with
antibiotics):

Group GLU (n = 9) 0.9% NaCl (Baxter Healthcare,
Warsaw, Poland) supplemented with 250 mmol/L
glucose (Pilva, Krakow, Poland)

Group MAN (n = 10) 0.9% NaCl (Baxter Health-
care, Warsaw) supplemented with 250 mmol/L
mannitol (Baxter Healthcare, Warsaw).

At the end of the study, a 1-hour peritoneal equili-
bration test (PET) was performed. The rats were then
humanely killed by bleeding, under ether anesthesia.
The peritoneal cavity was opened to estimate the pre-

cence and severity of intraperitoneal adhesions. Im-
prints of mesothelial cells from the visceral peritoneum
of the liver surface were taken to characterize cell
morphology. Liver samples were also collected for
morphology analysis of the visceral peritoneum.

Peritoneal equilibration test
Each animal was injected with 30 mL Dianeal 3.86%
(Baxter Healthcare, Castlebar). Immediately after in-
fusion and after 30 minutes of dwell time, 2 mL
samples of dialysate were obtained. After 1 hour of
dwell time, the remaining dialysate was completely
drained and its volume was measured. At the same
time, blood samples were taken for serum analysis.
Peritoneal transport was determined using the dialy-
sate-to-plasma (D/P) ratios of urea nitrogen, creati-
nine, and total protein, and the final-to-instillation
(D/D0) ratio of glucose concentration.

In the samples, the urea nitrogen and creatinine
concentrations were determined by an enzymatic
method (kit numbers A-371 and A-291: Analco, War-
saw, Poland). Total protein concentration was mea-
sured by the Lowry colorimetric method (15). Glucose
in dialysate samples was determined by the glucose
oxidase–peroxidase method (Sigma, St. Louis, MO,
U.S.A.).

Evaluation of peritoneal adhesions
Intensity of the peritoneal adhesions was evaluated
according to 4-point scale:

1 point Thin adhesion (1 – 2 mm) between catheter
and peritesticular fat pad
2 points Medium adhesion (3 – 5 mm) between cath-
eter and peritesticular fat pad
3 points Thick adhesion (>5 mm) between catheter
and peritesticular fat pad
4 points Adhesions between intraperitoneal organs

In cases where the peritoneal cavity of a rat showed
more than one adhesion, we totaled the point score
for the various adhesions.

Mesothelial cell imprints
Imprints of the mesothelial monolayer from the vis-
ceral peritoneum were taken after the peritoneal cav-
ity was opened. Glass slides coated with 1% agar
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(Sigma, St. Louis, MO, U.S.A.) were applied to the liver surface for 30 seconds, allowing mesothelial cells to be peeled off that surface. Next, the cells were fixed using 96% ethanol. Slides were stained with hematoxylin (Quimica Clinica Aplicada, Amposta, Spain). The density of the mesothelial cells and the nucleus:cytoplasm surface ratio (an index of mesothelial hyperplasia) were determined by light microscopy (observed at 200∞ magnification) supported with digital image analysis equipment (Lucia 4.6, Prague, Czech Republic).

Visceral peritoneum morphology
Liver samples were taken and fixed with 10% formaldehyde solution in phosphate-buffered saline (PBS). Paraffin-embedded tissue sections were stained using the van Gieson method for visualization of collagen. The thickness of the peritoneal membrane and the density of the blood vessels (expressed as the number of blood vessel sections per 1000 µm² in that membrane) were measured using the equipment mentioned earlier.

Statistical analysis
Results are expressed as mean ± standard deviation. The statistical analyses were performed using the Mann–Whitney test. A p value of less than 0.05 was considered significant.

Results
We found no significant differences between the experimental groups in peritoneal transport of measured substances. Also, no differences were observed in the prevalence of intraperitoneal adhesions between the GLU and MAN groups (78% and 60% of the rats in those groups had intraperitoneal adhesions). However, the severity of the adhesions was less in the GLU group than in the MAN group. In the GLU group, only 1 rat had adhesions evaluated above 3 points. In the MAN group, 6 rats had adhesions evaluated above 3 points. We found no adhesions in the CON group.

Animals from the GLU group also had a lower density of mesothelial cells than rats in the MAN group [2090 ± 322 cells/mm² vs. 2456 ± 333 cells/mm², p < 0.05; Figure 1(C)]. Both experimental groups had a higher density of mesothelial cells than the CON group (817 ± 100 cells/mm², p < 0.01). No significant difference was observed in the nucleus:cytoplasm area ratio between the GLU group and the MAN group (0.176 ± 0.045 vs. 0.206 ± 0.039); but, in both experimental groups, that ratio was higher than in the CON group [0.086 ± 0.010, p < 0.01; Figure 1(D)].

Peritoneal thickness was comparable in the GLU and MAN groups (51.2 ± 14.5 µm vs. 54.9 ± 17.8 µm) and, in both experimental groups, exceeded the thickness in the CON group [3.9 ± 0.6 µm, p < 0.01; Figure 1(A)]. We noted a tendency for the density of the blood vessels in the visceral peritoneum to be lower in the GLU group than in the MAN group [0.085 ± 0.067 vessels/1000 µm² vs. 0.158 ± 0.072 vessels/1000 µm², p = 0.0541; Figure 1(B)]. No visible vessels were observed in the peritoneal membrane of rats from the CON group.

Discussion
In previous experiments, we found that glucose suppresses inflammatory reactions (measured as cell count, protein, nitric oxide, monocyte chemoattractant protein-1 concentration) and morphologic alterations in the peritoneal cavity (mesothelial hyperplasia, fibrosis, and angiogenesis) induced by chronic intraperitoneal infusions of iso-osmotic saline (12,13). In the present experiment, we tried to determine whether the unexpected impact of glucose on peritoneal morphology is related solely to its osmotic action or to its metabolic activity.

Certain effects of chronic exposure to glucose and mannitol seemed to be comparable in both experimental groups (peritoneal transport of urea, creatinine, protein, and glucose; peritoneal thickness; prevalence of adhesions). But some of the observed changes were more intensive in animals that were exposed to mannitol (as compared with animals that were administered glucose in the same concentration). Those changes include mesothelial cell density (expressed as a higher intensity of mesothelial hyperplasia in the MAN group) and peritoneal vessel density (expressed as increased angiogenesis in the MAN group). Moreover, among rats in which intraperitoneal adhesions were present, the adhesions were more severe if mannitol was used as the osmotic solute in the dialysis fluid.

Those findings lead us to conclude that glucose-induced changes in the morphology of the peritoneal cavity (mesothelial hyperplasia, angiogenesis, formation of peritoneal adhesions) are less intense than those caused solely by osmotic action (mannitol). This situation suggests that unidentified meta-
Intrinsic metabolic effects of glucose may modify certain morphologic changes in the peritoneum under conditions of chronic dialysis. Reduced proliferation of mesothelial cells in a high glucose environment (as compared with the same concentration of mannitol) was previously demonstrated by in vitro experiments (16,17). Gotloib et al. (18) also observed a lower density of mesothelial cells in mice intraperitoneally injected with high-glucose PDF as compared with mice injected with another osmotic solution (polyglucose). Those researchers explained their finding as acceleration of the lifecycle of mesothelial cells following depletion of the growth capabilities of the monolayer exposed to a high glucose solution (19). Thus, the lower density of mesothelial cells in rats injected with high glucose as compared with rats injected with mannitol may reflect an ineffective repair mechanism after injury induced by dialysis.

On the other hand, the lower intensity of morphologic change in the peritoneal cavity may be a sign of a diminished inflammatory reaction, which may result from depletion of peritoneal macrophages caused by toxic glucose activity against those cells (5). To verify that hypothesis, the antibacterial activity of peritoneal macrophages needs to be examined.

**Conclusion**

Glucose-induced changes in the peritoneum of rats exposed to chronic peritoneal dialysis depend on both the osmotic and the metabolic effects of glucose. Those changes are less intense than the changes caused by a PDF of the same osmolality containing mannitol. This unexpected finding may arise from a glucose-depen-

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**FIGURE 1** Morphologic changes in peritoneal cavity of rats exposed to 0.9% NaCl supplemented with glucose 250 mmol/L (GLU) or mannitol 250 mmol/L (MAN) and in non-dialyzed rats (CON). *p < 0.05 as compared with CON; **p < 0.01 as compared with CON; +p < 0.05 as compared with MAN; #p = 0.0541 as compared with MAN.
dent suppressive influence on the regenerative and antibacterial potentials of the peritoneum.

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Peritoneal dialysis affects both the quantity and quality of connective tissue in the visceral peritoneum. In the present study, we report the alterations observed in the morphology of the superficial liver lobuli of dialyzed rats.

The studies were performed in male Wistar rats weighing 250 – 350 g. Rats were exposed intraperitoneally to 0.9% NaCl, phosphate-buffered saline (PBS), or commercial dialysis solutions containing 3.86% glucose (Dianeal 3.86%; Baxter Healthcare SA, Castlebar, Ireland; CAPD3 and CAPD3–Balance: Fresenius Medical Care, Bad Homburg, Germany) twice daily for 4 – 6 weeks. At the end of the study, samples of the liver were taken and stained for light microscopy (hematoxylin and eosin, van Gieson). The results obtained in dialyzed rats were compared with those from the control, non dialyzed animals.

In control animals, the surface of the hepatic parenchyma was smooth. In all dialyzed rats, irrespective of the solution used, folding of the surface of the liver parenchyma was found owing to penetration of connective tissue elements between the hepatocytes. In effect, folds of hepatocytes within the liver capsule became detached and isolated from the remaining cells of the lobules. The distinctive feature of that pathologic change was that its severity increased with the thickness of the peritoneum. The change was seen in rats exposed to any of the experimental solutions, and therefore appeared to be attributable to a nonspecific reaction caused by exposure of the peritoneum to dialysis fluid and not to specific components of the fluid.

The observed alterations in morphology seem to suggest disturbed function within the affected lobules. Further studies are necessary to confirm this hypothesis.

Key words
Connective tissue, morphology, liver

Introduction
Morphologic screening of the peritoneum of dialyzed patients has permitted characterization of the typical findings in parietal peritoneum attributable to the dialysis procedure (1–3). Similarly, in animals chronically exposed to dialysis fluids, peritoneal thickening and increased vascularity of the parietal peritoneum are relatively well characterized (4–6). However, data about the impact of dialysis on the visceral peritoneum are sparse.

Hypervascularity, an increased amount of extracellular matrix, and a larger number of milky spots were found in the omenta of animals exposed to standard high glucose dialysis solution (6). Previously, our interest focused on the visceral peritoneum of the liver in chronically dialyzed rats (7–9). We showed that the expansion of submesothelial tissue was attributable to an increased quantity of collagen fibers and their disorganization and disintegration; to an increased quantity of connective-tissue cells and their activation; and to increased vascularity (10). Changes in the visceral peritoneum of the liver were anatomically asymmetric, appearing mainly on the anterior and inferior surfaces of the liver, which have prolonged contact with the dialysis fluid (10).

We speculated that alterations in all components of the connective tissue of the visceral peritoneum of the liver owing to dialysis might interfere with the function of the liver. We could find no literature on the possibility of liver fibrosis caused by dialysis. Our aim in the present study was therefore to report abnormalities observed in the morphology of the anterior and inferior surfaces of the liver in dialyzed rats.

Materials and methods
Samples of visceral peritoneum of the liver from rats exposed to various dialysis solutions were retrospec-
tively screened for liver alterations in connection with peritoneal fibrosis.

Dialysis procedure
The experiment was performed on male Wistar rats weighing 250 – 350 g. All animals were maintained in standard conditions during the study period (temperature: 18 ± 1°C; 12/12 light/dark cycles), were fed a standard rat diet, and had free access to water.

After catheter implantation, the experimental animals were intraperitoneally exposed twice daily for 4 – 6 weeks to 0.9% NaCl, to phosphate-buffered saline (PBS), or to commercial dialysis solutions containing 3.86% glucose (Dianeal 3.86%: Baxter Healthcare SA, Castlebar, Ireland; CAPD3 and CAPD3–Balance: Fresenius Medical Care, Bad Homburg, Germany). All fluids were supplemented with antibiotics [gentamicin 5 mg/L (Polfa, Tarchomin, Poland) and cefazolin 50 mg/L (Eli Lilly, Florence, Italy)].

Control animals were exposed to neither catheter implantation nor dialysis procedure.

Specimen collection and staining
At the end of the experiment, all rats were humanely killed by bleeding. The peritoneal cavity was opened, and samples of the visceral peritoneum of the liver were taken with a minimum of handling or trauma. The samples were fixed in 1% phosphate-buffered formaldehyde, and sections (4 – 5 µm in thickness) were stained with hematoxylin and eosin and van Gieson (staining for collagen, which appears reddish).

Results
In control animals, the surface of the hepatic parenchyma was smooth. It was covered by a thin layer of connective tissue and a monolayer of mesothelial cells, forming the liver capsule [Figure 1(A)].

In dialyzed rats, folding of the surface of the liver parenchyma was observed. The folding was attributable to penetration of connective tissue elements between the hepatocytes. In effect, tangled knots of liver cells were found within the connective tissue of the liver capsule [Figure 1(B)]. Those cells were usually in close proximity to the vessels [Figure 2(A,B)]; however, the possible connections between neovascularization of the peritoneum and the presenting phenomenon are not clear.

We observed groups of hepatocytes only partially surrounded by fibrous tissue [Figure 2(C)]. But, on the other hand, we also found cells encircled by a separate layer of fibrous tissue, which formed a sort of connective tissue “capsule” for the hepatocytes that were detached and isolated from the remaining cells of the lobulus [Figure 2(D)]. Isolated cells showed features of glycogen degeneration. It is not clear whether the presenting alterations can be interpreted as various stages in the expansion of connective tissue or simply as folding of the various sections.

Composition of the dialysis fluid appeared to have no impact on the presenting phenomenon. Similar alterations were found in rats exposed to each of the studied solutions. However, a distinctive feature of
the pathologic changes was that the thicker the submesothelial tissue was, the more likely were alterations to be found. The alterations were always present on the anterior and inferior surfaces of the liver where thickening was the most severe.

Discussion

Peritoneal dialysis is well known to affect both the quantity and the quality of connective tissue in the parietal peritoneum of chronically dialyzed patients and animals (1–6). Owing to severe fibrosis of the visceral peritoneum of the liver, it seems possible that exposure to dialysis fluids affects the biologic properties of the hepatocytes in the superficial liver lobuli. Interestingly, subcapsular steatonecrosis in the liver has previously been reported in dialyzed patients with diabetes as an effect of intraperitoneal treatment with insulin (11,12).

The presenting alterations do not seem to be caused by the high glucose concentration and hyperosmolality of the dialysis fluid, because they were also present in rats dialyzed with isotonic glucose-free solutions (0.9% NaCl, PBS). Additionally, the alterations are not explained by low pH, because they were also present in animals exposed to dialysis fluids with a normal pH (PBS, CAPD3-Balance). The alterations might be speculated to be caused by nonspecific irritation resulting from the exposure of the peritoneum to dialysis fluid and not to specific components of the fluid.
Conclusion
In this paper, we report for the first time the folding of the surface of the liver parenchyma followed by sequestration of superficial liver cells. Because the functions of cells within the lobules are differentiated, the observed alterations in morphology seem to suggest disturbed function within the affected lobules. Further studies are necessary to confirm this hypothesis and to discover its consequences.

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The dialysate concentration of cancer antigen 125 (CA125), a high molecular weight (220 kDa) glycoprotein, can be considered a reflection of mesothelial cell mass or turnover in stable continuous ambulatory peritoneal dialysis (CAPD) patients [reviewed in (1)]. Originally, CA125 was measured in overnight effluent because such measurements yielded the highest values (2). Later, studies were performed in peritoneal effluent obtained after a standardized 4-hour dwell because dialysate CA125 showed a linear increase during the 4 hours of the dwell regardless of the dialysate glucose concentration used (3). Standardization of dialysate CA125 measurements might therefore be achieved by using a fixed dwell time in every patient or by calculating the CA125 appearance rate (CA125AR)—that is, the amount of CA125 present in the total drained effluent divided by the duration of the dwell in minutes. The latter approach would make it possible to use overnight dwells of varying duration and still obtain accurate results that can be used for follow-up. However, the effect of dwell times exceeding 4 hours on the CA125AR was not known. Therefore, our objective in the present study was to analyze the effect of dwell time on CA125AR in stable CAPD patients.

In 43 stable CAPD patients, we analyzed standard peritoneal permeability analyses (SPAs) performed with a 3.86% glucose dialysate, and night-dwell effluents from the night dwell prior to the SPA. Dialysate CA125 concentration was measured by radioimmunoassay (RIA II: Fujirebio Diagnostics, Malvern, PA, U.S.A.). Night-dwell CA125 correlated with the duration of the dwell \( (r = 0.32, p = 0.04) \) and with the CA125 concentration in the 4-hour dwell \( (r = 0.83, p < 0.001) \). The mean CA125AR in the SPA effluent was 97.8 ± 46.3 U/min; in the overnight effluent, it was 108.8 ± 73.7 U/min (nonsignificant). A good correlation was present between the CA125AR in the 4-hour dwells and in the overnight dwells \( (r = 0.82, p < 0.001) \).

We conclude that using night dwells to regularly assess dialysate CA125—for instance, at every outpatient visit—is possible in CAPD patients, provided that appearance rate is calculated.

Key words
Cancer antigen 125, CAPD, dwell time

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was 1 episode per 38 patient–months. None of the patients had peritonitis at the time of the SPA or during the preceding 4 weeks. The dwell time of each SPA was, by definition, 240 minutes. The dwell time of the night dwells ranged from 220 minutes to 910 minutes (mean: 587 minutes). Dialysate samples were obtained prior to the SPA and after completion of the SPA. The samples were centrifuged and stored at −20°C until analysis.

Dialysate CA125 concentrations were measured by radioimmunoassay using two monoclonal antibodies—namely, OC125 and M11 (RIA II: Fujirebio Diagnostics, Malvern, PA, U.S.A.). The dialysate appearance rates of CA125 were calculated by multiplying the dialysate concentration by the drained volume and dividing the result by the duration of the dwell in minutes. The CA125 ARs are expressed as units per minute.

All data are presented as mean ± standard deviation. Comparisons between the 4-hour dwells and the overnight dwells used the paired samples t-test. Correlations were analyzed by linear regression analysis. In addition, the CA125 ARs were compared using the Bland–Altman method (5).

Results
The mean CA125 concentration in SPA effluent was 12.1 ± 5.7 U/mL; in the overnight effluent, it was 31.4 ± 20.9 U/mL (p < 0.001). Figure 1 shows individual data. The average CA125 concentration showed a linear increase with the duration of the dwell, as illustrated in Figure 2. Night-dwell CA125 correlated with the duration of the dwell (r = 0.32, p = 0.04) and with the CA125 concentration in the 4-hour dwell (r = 0.83, p < 0.001).

Figure 2 shows the individual data. Although the mean values were not significantly different, the coefficient of interindividual variation (standard deviation / mean ∞ 100) was 47% for the 4-hour dwell and 68% for the overnight dwell. Good correlation was present between the CA125AR in the 4-hour dwells and in the overnight dwells (r = 0.82, p < 0.001), as shown in Figure 4. The Bland–Altman analysis (Figure 5) showed that the mean difference between the 4-hour dwells and the overnight dwells was only −11.03 U/min, but that the CA125 ARs calculated for the 4-hour dwells tended to be higher than those obtained for the overnight dwell for low values, and tended to be lower for higher values. The standard deviation of the difference between the two methods was 44.8 U/min, resulting in limits of agreement between −100 U/min and 80 U/min.

Discussion
Mesothelial cells are a biological barrier against potentially bioincompatible dialysis fluid and are also known to be involved in local host defense. In addi-
tion, they produce substances that prevent the formation of adhesions. The glycoprotein CA125 is a high molecular weight (220 kDa) protein produced by mesothelial cells. Its effluent concentration in stable PD patients is likely to reflect mesothelial cell mass or turnover (2,6). However, the method used to evaluate dialysate CA125 levels has not yet been standardized.

Dialysate CA125 increases linearly during the first 4 hours of a dialysis dwell (3,7). The present study showed that the linear increase was sustained during dwells of up to 12 hours. That finding suggests that long dwells can also be used in analyzing CA125, because, provided that the duration of the dwell is known, the CA125AR can be calculated. Indeed, we found no significant differences between 4-hour and long dwells when we calculated CA125AR. Furthermore, a strong correlation was evident between dwells of both lengths.

Conclusion
We conclude that night dwells can be used for the regular assessment of dialysate CA125 in CAPD patients—for instance, at every outpatient visit—provided that appearance rate is calculated. The method detects downward trends that suggest loss of mesothelial cell mass. Although risk concentrations of CA125 have not yet been defined, it is likely that a downward trend indicates the presence of morphologic change in the peritoneal membrane.

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