A measure of comorbidity in dialysis patients must not only predict outcomes but also be reproducible and easy to obtain. Our primary purpose in the present study was to determine the inter-rater reliability of the Charlson comorbidity index (CCI) in peritoneal dialysis (PD) patients. Our secondary purpose was to evaluate the usefulness of annual rescoring of the CCI as a predictor of patient survival.

We included in the study 100 consecutive patients (mean age: 52 ± 16 years; 85% white; 39% with diabetes) who started PD between 1995 and 2000 at a single center. Two nurses independently scored the CCI at the start of PD. One nurse rescored each patient on the yearly anniversary of the start of PD. Patient survival was recorded for each year. Kappa score and time-dependent analysis were applied.

The kappa score between the two CCI scores at the start of dialysis was 0.93. (The average scores by the two nurses were 5.2 and 5.3.) Annual rescoring of the CCI demonstrated no increase in its predictive value regarding patient survival. However, given the minimal change in the CCI for the patient population in the present study, that question needs further study. Over time, the average CCI fell—an unsurprising result, because patients with higher CCI scores at the start of dialysis are the most likely to die.

We conclude that the CCI is a reliable and easily applied tool for assessing comorbidity. Dialysis units should consider obtaining this measure at the start of dialysis in all patients. Repetitive annual scoring was not helpful in improving prediction of survival.

Key words
Comorbidity, mortality, Charlson comorbidity index

Introduction
The mortality rate in dialysis patients in the United States is high (1). Comorbidity is an important determinant of outcome in patients on renal replacement therapy. Differences in comorbidity have complicated comparisons of outcome in international studies and comparisons of hemodialysis (HD) and peritoneal dialysis (PD) (1,2). Assessment of comorbidity can be determined by a simple dichotomous assignment of diseases or by use of a validated scoring system. To have wide use for case-mix adjustment, an instrument needs to accurately measure comorbidity, to predict outcomes, and to be easily obtained.

Our primary purpose in the present study was to determine the inter-rater reliability of the Charlson comorbidity index (CCI) in PD patients. Our secondary purpose was to evaluate, as a predictor of patient survival and hospitalization, the usefulness of rescoring the CCI on the yearly anniversary of the start of PD. Some authors have suggested that annual rescoring would increase the predictability of survival in a given year. Given the limited time that nurses and physicians have to care for patients, it is important to know if such additional evaluation would be useful.

Patients and methods
All patients were asked to participate in a registry of peritoneal dialysis approved by the Institutional Review Board of the University of Pittsburgh and Dialysis Clinic Inc. The registry collects information on all hospitalizations, demographics, and outcome. All patients gave informed consent for inclusion. Inclusion criteria accepted both incident patients on PD and those being reinitiated on dialysis after a failed transplant. The study was performed at a single center, Dialysis Clinic Inc. of Oakland. All consecutive patients started on PD from January 1, 1995, to December 31, 1999, were included. Follow-up continued until April 1, 2003.

At the start of PD, 2 nurses independently scored the CCI based on comorbidity. In addition, 1 nurse rescored each patient on the yearly anniversary of PD start. Patients on PD for less than 1 year were excluded from the rescoring. Rescoring was based on a careful
review of records from both the dialysis clinic and a computerized hospital medical records system.

Follow-up continued until April 1, 2003, or until the patient was transplanted, died on PD, was transferred to HD, experienced the return of residual renal function, or was transferred to another PD unit. Patient survival and hospitalization on PD were collected prospectively.

Data are expressed as mean ± standard deviation. Inter-rater reliability was tested by cross tabulation with kappa score. Proportional hazards regression, using the annual CCI (baseline to year 3) as a time-dependent covariate, was performed to analyze patient survival. Change in the CCI over time was analyzed using the Kruskal–Wallis one-way analysis of variance, corrected for ties.

**Results**

At the start of PD, 100 patients were each scored by 2 nurses. Patients were rescored by 1 nurse on the yearly anniversary of the start of PD. Scoring the CCI required 5 – 10 minutes per patient. At the start of PD, the 100 study patients had a mean age of 52 ± 16 years. Of the 100 patients, 50% were men; 85% were white; and 39% were insulin-dependent. The mean CCI scores by the 2 nurses were 5.2 ± 2.4 and 5.3 ± 2.5. The inter-rater reliability of the CCI by the 2 scorers, as evaluated by the kappa reliability test, was 0.93 with a standard error of 0.10.

Although 100 patients were scored initially, only 53 patients were available for rescore at 1 year, and only 28 at 2 years. At 1 year, 16/100 patients had been transplanted; 15/100 had been transferred to HD, with 2 failing successful PD training; and 16/100 had died. Similarly, at 2 years, 8/53 patients (15%) had been transplanted; 8/53 (15%) had been transferred to HD; and 5/53 (9%) had died.

The CCI was rescored annually by 1 nurse with these results (Figure 1; values differ, \( p = 0.047 \)):

- At 1 year, the CCI was 5.4 ± 2.8 (\( n = 53 \)).
- At 2 years, the CCI was 4.5 ± 2.3 (\( n = 28 \)).
- At 3 years, the CCI was 4.3 ± 2.1 (\( n = 20 \)).
- At 4 years, the CCI was 3.9 ± 1.9 (\( n = 12 \)).

Only 7 of the 53 patients rescored at 1 year showed a changed CCI, and 3 of those were changed because of an increase in age. From year 1 to year 2, only 1 patient showed a changed CCI, again because of an increase in age. No CCI score changed between year 3 and year 4 (Figure 1).

We compared the log likelihood of the models for baseline CCI and CCI as a time-dependent covariate. We observed no difference in the model fit between the model that used baseline CCI and the model that used time-dependent CCI for prediction of death (log likelihood: 187.7 vs. 181.1, \( p > 0.05 \)). For each 1-point increase in the CCI, the relative risk of predicting death was 1.37 (baseline model) as compared with 1.33 (time-dependent model).

**Discussion**

A comorbidity scoring system must be easy to use and predictive of the outcomes of interest, particularly death and hospitalization. We found a high association between raters when 2 independent nurses used the CCI for comorbidity scoring (kappa score: 0.93). (A kappa score > 0.75 indicates a high association between 2 raters.) Those results indicate that having just 1 nurse obtain a CCI should not affect the reliability of the measure.

Based on 604 patients admitted to a medical service, the CCI was originally developed to predict hospital survival (3). To predict outpatient survival with a chronic medical illness, the measure was then validated in 685 women with breast cancer.

The CCI assigns weights based on relative risk of death to a number of medical conditions. The score also contains points for age.

In a previous study at the University of Pittsburgh, the CCI was used to predict outcomes in dialysis patients (4). We examined the usefulness of the CCI as a predictor in incident PD patients, and examined
whether it was a better predictor than simply the number of comorbid conditions or other known predictors such as age, diabetes status, serum albumin, and cardiovascular disease. That retrospective study used a mix of prevalent and incident PD and HD patients and found that the CCI was a strong predictor of survival.

We also previously compared the CCI to the Davies (Stokes) score (5). The Davies score was designed for PD patients and is commonly used in Europe to adjust for comorbidity (6). Like the CCI, the Davies score is easily and quickly obtained from a review of medical records. The Davies score assigns points for a number of conditions that have been shown to be important comorbid conditions. The scale is not weighted, and age is not considered in the score. We found that both the CCI and the Davies score were predictive of mortality and hospitalization (6). Based on our findings, we could not recommend one score over another. The CCI alone was a slightly stronger predictor of mortality; the Davies score was a somewhat better predictor of hospitalization. The choice between the two scores therefore depends on the planned analysis.

The mean CCI score in a cohort of PD patients falls after the first year. That result is expected, because sicker patients die. We found that rescoring the CCI annually in our PD population provided no increase in its predictive value for patient survival or risk of hospitalization. That finding may be attributable to the small yearly change in CCI score.

Some authors have suggested that annual rescoring might have some utility (7). Our data do not support the need for repeated analysis of comorbidity on an annual basis.

Conclusions
We recommend that each dialysis program measure comorbidity at the start of dialysis in all patients. Such measurement will permit valid comparisons regarding outcomes from one unit to another and between modalities, controlling for case mix. The CCI is a tool with excellent inter-rater reliability. It is also easy to score. Repetitive scoring over time appears to be unnecessary.

References

Corresponding author:
Judith Bernardini, 3504 Fifth Avenue, Suite 200, Pittsburgh, Pennsylvania 15213 U.S.A.
E-mail: bernardini@pitt.edu
The number of patients over 65 years of age with chronic renal failure has increased. Peritoneal dialysis (PD) is an effective mode of treatment for such patients. In the present study, we report our experience with automated PD in patients over 65.

We recorded the demographic and clinical characteristics of the patients and the exit-site infection rate, the peritonitis rate, and the mortality rate, comparing those parameters with the same parameters in patients under 65.

We followed 36 patients (30% of the total study population) who were over 65 years of age (mean: 74.5 ± 7.3 years). Of the 36 patients, 34 (94.4%) had another chronic disease—arterial hypertension and heart disease being the more common. Eleven of the patients (31%) had diabetes. Duration of PD therapy in the group was 31.5 ± 20.7 months.

Ten of the patients (27.8%) had at least 1 catheter-related complication, including exit-site infection (n = 3), tunnel infection (n = 1), or a noninfectious complication (n = 6). The rate of catheter-related infection was 0.22 episodes/patient–year. Two catheter were lost: 1 in a case of hematoma, and 1 in a case of catheter obstruction. The rate of peritonitis was 0.16 episodes/patient–year, and the most common infectious agent was methicillin-susceptible Staphylococcus aureus. Actuarial survival of our elderly patients was 51.8% at 4 years of follow-up as compared with 81.7% in the younger patients (p = 0.01). All cases of death were related to comorbid conditions, not to PD therapy. Two patients were transferred to hemodialysis.

We conclude that PD has proven to be a safe and comfortable therapy for renal replacement in patients over 65 years of age. Results are similar to results in younger patients.

From: 1Department of Nephrology, P. Catholic University, Santiago, Chile.

Key words
Elderly patients, chronic renal failure

Introduction
Elderly patients are a growing group in our clinical practice, and some of them have chronic renal failure (CRF). Some authors have reported that about 45% of patients with end-stage renal disease are over 65 years of age (1,2). The best modality for renal replacement in elderly patients is unknown. Some studies have demonstrated that peritoneal dialysis (PD) is associated with longer survival than hemodialysis (HD) is; however, other studies have shown no difference in mortality rates (3–7).

Peritoneal dialysis is associated with hemodynamic stability and better control of arterial pressure without the need for vascular access. Moreover, PD is also associated with lower hospitalization rates and a better quality of life. The physiologic condition of elderly patients and their greater prevalence of comorbidity make PD seem to be the best modality for renal replacement in CRF patients over 65 years of age. In the present study, we report our experience with automated PD in such patients.

Patients and methods
We prospectively studied patients admitted to the PD program of the Catholic University Clinical Hospital between January 1996 and June 2003.

Of 120 patients treated with PD, 36 (30%) were over 65 years of age. We recorded their baseline clinical characteristics, their demographic characteristics, and their associated illnesses. During monthly clinical follow-up visits, we recorded the incidence of catheter-related complications such as exit-site infection and peritonitis. Follow-up was conducted by a nephrologist and a trained PD nurse. Tenckhoff double-cuff catheters, implanted by the open surgical method, were used in all patients.
Exit-site infection was defined by the presence of erythema and purulent secretion at the catheter exit site. Peritonitis was defined as the presence of cloudy peritoneal fluid associated with a leukocyte count > 100 cells per field.

Statistical analysis
Data are shown as mean ± standard deviation. For catheter survival, we used actuarial survival curves and the chi-square test. Values of \( p \) less than 0.05 were considered significant.

Results
In our PD program, 36 patients (23 men, 13 women) were over 65 years of age (Table I). Their mean age was 74.5 ± 7.3 years (range: 65 – 92 years), and 13% were from the suburbs. The entire group were treated with automated PD, but 22 of the patients had an assistant to connect them to the cycler. The PD learning period was 32 ± 20 days in elderly patients as compared with 28 ± 16 days in patients under 65 years of age \( [p = \text{nonsignificant (NS)}] \). Of the 36 elderly patients, 94% had comorbid illnesses, with arterial hypertension and heart disease being most common. Eleven patients (31%) had diabetes.

The most common indication for PD was patient decision (because of the comfort of the modality). In 2 patients, PD was indicated to control volume overload in congestive heart failure. The patients were observed for a total of 2806 patient–months.

Complications
Among the 36 elderly patients, 10 (27.8%) experienced a catheter-related problem. Noninfectious complications occurred in 6 patients (17%), and 7 episodes of infection occurred in 4 patients. That incidence of infectious complications was slightly lower than the incidence observed in patients under 65 years of age (11% vs. 20% respectively); however, the difference was not statistically significant (Table II). In all cases of infection, the organism isolated was *Staphylococcus aureus*. Multiresistant *S. aureus* was seen in only 1 case. No secondary complications attributable to infection at the exit site were observed. Nasal cultures positive for *S. aureus* were seen in 8 patients (22%), and all of those patients received topical treatment. In 4 patients, an exit-site infection was related to nasal carrier status.

The rate of exit-site infection was 0.22 episodes/patient–year in patients more than 65 years of age and 0.16 episodes/patient–year in younger patients \( [p = \text{NS}] \). The rate of peritonitis was, respectively, 0.16 episodes/patient–year and 0.14 episodes/patient–year \( [p = \text{NS}] \). The patients did not display secondary complications attributable to peritonitis, and peritonitis episodes were not associated with death or switch to HD.

Catheter survival rate
The duration of access was 17 ± 16 months (Figure 1). The catheter was lost in 2 patients: 1 because of obstruction, and 1 because of hematoma of the abdominal wall.

Three patients were switched to HD. One switch was transitory, for surgical treatment of hypernephroma. Two definitive switches occurred because of catheter dysfunction \( [n = 1] \) and pleural leak unresponsive to pleural seal \( [n = 1] \).

Patient survival rate
After 4 years of follow-up, the survival rate of elderly patients on PD was 51.8% as compared with 81% in

| TABLE I | Baseline characteristics of the patients |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                | <65 Years \( (n = 84) \) | >65 Years \( (n = 36) \) | \( p \) Value |
| Age (years)    | 55±17            | 74±7            | <0.001         |
| Men [\( n \) (%)] | 39 (46)          | 23 (64)         | NS             |
| Diabetes mellitus [\( n \) (%)] | 11 (13)         | 11 (31)         | 0.04           |
| Arterial hypertension [\( n \) (%)] | 49 (58)         | 34 (94)         | <0.001         |
| Dyslipidemia [\( n \) (%)] | 11 (13)         | 3 (8)           | NS             |
| Coronary heart disease [\( n \) (%)] | 7 (8)           | 16 (44)         | <0.001         |
| Heart failure [\( n \) (%)] | 5 (6)           | 14 (39)         | <0.001         |
| NS = nonsignificant. |

| TABLE II | Catheter-related complications |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                | <65 Years \( (n = 84) \) | >65 Years \( (n = 36) \) | \( p \) Value |
| Infections [\( n \) (%)] | 17 (20) | 4 (11) | NS             |
| Exit-site | 13 | 3 | |
| Tunnel | 4 | 1 | |
| Other complications [\( n \) (%)] | 14 (17) | 6 (17) | NS             |
| Herniation | 3 | 2 | |
| Leakage | 4 | 3 | |
| Bloody dialysate | 3 | 1 | |
| Obstruction | 2 | 0 | |
| Migration | 2 | 0 | |
| NS = nonsignificant. |
younger patients ($p < 0.05$, Figure 2). In all cases, the cause of death was related to an associated illness, and not to the dialytic modality.

**Biochemical markers**

In our elderly patients, serum albumin, a marker of nutrition status, was 3.4 mg/dL at the start of PD. We did not observe a fall in albumin level during the patients’ time on PD. Initial hematocrit in the patients was 28%; that value reached 31% during follow-up ($p = 0.03$).

**Discussion**

The group of patients over 65 years of age is growing, and it is not rare to see elderly patients with end-stage renal disease. Because of special conditions in that group, and the scarcity of information regarding the results of renal replacement in elderly patients, the best therapy for such patients is unknown.

At our institution, patients over the age of 65 years constitute 30% of all PD patients. Most of them are in the automated PD program because that modality is easier and more comfortable than HD, and it can be carried out at home.

The most important finding of our study is the lower rate of catheter-related infectious complications seen in our elderly patients. The rate of exit-site infection was 0.22 episodes/patient–year, similar to that seen in our younger patients (0.12 episodes/patient–year, $p = NS$) and to that reported by other authors (8). The relationship between age and infectious complications is not clear. Holley and colleagues (8,9) found no differences in that relationship.

The incidence of peritonitis varies widely in different centers, from 0.42 episodes/patient–year to 2.8 episodes/patient–year (8 10 11). Peritonitis is the main cause of hospitalization in PD patients (12). The incidence of infection has been reported to be similar in all age groups (12,13), but some studies have shown that elderly patients could be at more risk (11). In our series, the peritonitis rate was slightly higher in elderly patients; however, the difference (0.16 episodes/patient–year vs. 0.14 episodes/patient–year) was not statistically significant. The organisms isolated in both groups have been reported to be similar (11), *S. aureus* being the organism most frequently seen. One reason for that finding may be the fact that elderly patients on PD are usually supervised and attended by highly trained personnel.

The risk of death increases with age and with the presence of other diseases (11,14,15). In our program, 94% of patients over 65 years of age as compared with 51% of younger patients had comorbid diseases ($p < 0.05$). Diabetes, arterial hypertension, and heart disease were the most common comorbidities—a situation similar to that reported in the literature (16). The survival rate in our elderly patients was 51.8% after 48 months of follow-up as compared with 81.7% in our younger patients ($p < 0.05$). Mortality was mainly related to comorbid conditions, and not to PD itself.

Nutrition status is an essential factor in the prognosis of patients with CRF, mainly because of the catabolic effects of uremia (17). Malnutrition has been reported to be more common among elderly patients and patients on PD because of important losses of pro-
teins and amino acids in the peritoneal fluid (18). Albumin levels were lower in our elderly patients than in our younger patients at the beginning of PD (3.4 mg/dL vs. 3.7 mg/dL, p < 0.001), but those levels did not fall thereafter.

On the other hand, the anemia associated with CRF is less severe in patients being treated with PD because less blood loss and hemolysis occurs than in HD and because PD better removes the inhibitors of erythropoiesis (19). Those effects are important in patients who suffer from cardiac diseases. We observed that hematocrit values improved in our patients during PD therapy.

Conclusions
Patients over 65 years of age are an important group among patients being treated with PD. Although the patients may have other diseases that can influence their survival rate, PD therapy has proven to be safe, comfortable, and effective for elderly patients.

References

Corresponding author:
Maria A. Fernández, MD, Department of Nephrology, P. Catholic University, Lira 85, 4ºPiso, Santiago, Chile.
E-mail: marialiciafe@hotmail.com
Hydrothorax, an uncommon complication of peritoneal dialysis (PD), results from the migration of dialysis fluid under pressure from the peritoneal cavity into the pleural space. The exact site of the transdiaphragmatic fluid leak remains obscure, but the right-sided predominance of the hydrothorax points to the presence of abnormalities in the right hemidiaphragm. Such abnormalities have occasionally been described.

In a recent case of acute massive right hydrothorax at the start of PD, the autopsy revealed extensive changes of amyloidosis that were comparable in both hemidiaphragms, prompting us to revisit the accepted explanation for right hydrothorax.

We propose that an embryonic remnant—namely, the persisting pneumatoenteric recess and the infracardiac bursa—provides a passage connecting the peritoneal cavity to the right pleural space. The potential presence of this mechanism is consistent with the recognized clinical features of right hydrothorax complicating PD.

This proposed route for dialysis fluid to form a right hydrothorax during PD can be investigated by currently available high-definition imaging techniques. This novel mechanism may also be involved in the pathogenesis of right hydrothorax complicating other medical conditions with tense ascites (liver cirrhosis, Meigs syndrome).

Key words
Right hydrothorax, persisting pneumatoenteric recess, infracardiac bursa

Introduction
Hydrothorax, a relatively infrequent complication of peritoneal dialysis (PD), can potentially be serious when it presents as acute massive hydrothorax with respiratory distress (1,2). The true incidence of this complication may be underestimated because the milder cases—such as asymptomatic pleural effusion found on routine chest radiographs—can easily be missed.

Discussion
Hydrothorax, a form of dialysis leakage from the peritoneal cavity
During dialysis, hydrothorax results from the migration of dialysis fluid from the peritoneal cavity to the pleural space. Hydrothorax is one of several forms of dialysis fluid leakage from the peritoneal cavity and accumulation in adjacent tissues (3). The clinical presentation of the leak is determined by the site of accumulation of the dialysis fluid: that is, hydrothorax, pericatheter leak, genital edema, or vaginal leak.

Peritoneal fluid leakage is attributed to the increased intra-abdominal pressure and volume that follows from intraperitoneal instillation of dialysis solution. The result is undue stress on the supporting structures of the abdomen, with leakage of dialysis fluid out of the peritoneal cavity as a consequence (4). Several risk factors for hydrothorax during PD have been identified. These include female sex, adult polycystic kidney disease, prior abdominal surgery, and peritonitis (1–4). All of the risk factors have in common a reduced abdominal space, which may readily lead to high intraperitoneal pressure following the instillation of PD solution.
An intriguing feature of hydrothorax complicating PD is that it occurs mostly on the right side—as frequently as 88% in a large series (5). Similarly, right-sided predominance of hydrothorax has been reported in other medical conditions with tense ascites such as liver cirrhosis (6,7) and Meigs syndrome (8). Of possible relevance is the first description of hydrothorax during PD (9), in which the authors remarked that right pneumothorax had been observed following therapeutic pneumoperitoneum (10).

Site of the peritoneopleural communication

Although the clinical manifestations of hydrothorax complicating PD are well characterized and the method of diagnosis by isotope techniques and the modalities of management have been extensively reported (1–4,11), the exact site of the peritoneopleural communication remains obscure.

Because of the right-sided predominance of the hydrothorax, much attention has been devoted to the right hemidiaphragm and abnormalities that might potentially be responsible for leakage of PD fluid into the right pleural space (1–4). The main explanation proposed involves the presence of anatomic defects in the right hemidiaphragm. That explanation has found support in occasional reports of direct examination of the diaphragm at surgery or autopsy. The nature of the observed defects vary from discontinuities in the tendinous or muscular portions of the diaphragm (or both) to the presence of blebs that can rupture, allowing dialysis fluid to seep out of the peritoneal cavity through the diaphragm. The size of the defects is also variable. Some defects were visible only at the microscope; others were clearly visible on direct inspection.

Another mechanism that has been postulated is a lymph drainage disorder in the right hemidiaphragm where the lymphatic system is most abundant. The early appearance of acute massive hydrothorax suggests the presence of a large congenital communication; late occurrence of hydrothorax in the course of dialysis suggests an acquired mechanism.

No new insights into the pathogenesis of right hydrothorax associated with PD have been offered since the early observations, not only because of the rare opportunity for direct examination of the diaphragm, but also because of the inability of current diagnostic isotope techniques to identify the exact site of the dialysis fluid leak from the peritoneal cavity and its entry into the right pleural space.

A case study

We recently reported the case of a 54-year-old female who developed an acute massive right hydrothorax at the onset of PD requiring transfer to hemodialysis (12). At autopsy 2 weeks later, unsuspected systemic amyloidosis was found to affect the heart especially and all vessels in the various tissues sampled. Pathology examination of both hemidiaphragms revealed comparable abnormalities: that is, atrophy of muscle fibers, extensive fibrosis, and amyloid deposition in vessel walls. It is noteworthy that right hydrothorax complicating PD was previously described in a patient with primary amyloidosis in whom blebs were noted in the tendinous part of the right hemidiaphragm at surgery; no histology examination of the diaphragm was mentioned (13).

In our case, we found that the observed extensive damage to both hemidiaphragms was inconsistent with hydrothorax affecting the right side only. In the absence of a satisfactory explanation for the apparent discrepancy, we considered an alternative explanation. Our explanation is based on the presence of an embryonic remnant potentially connecting the peritoneal cavity and the right pleural space. The rationale for our specific consideration included both the clinical presentation—that is, acute massive right hydrothorax at the onset of PD, which suggests the presence of a large congenital defect—and the accepted explanation for the genital edema observed occasionally in male patients during PD [leakage of dialysis fluid through a patent embryonic remnant, the processus vaginalis peritonei (3)].

The persisting pneumatoenteric recess and the infracardiac bursa

The common features of the future three body cavities are

• the formation, by fusion, of extracellular spaces within the intra-embryonic mesenchyme;
• the continuity of the three spaces; and
• the lining of the cavities by the coelomic epithelium (mesothelium) that is maintained after folding of the trilaminar state into the cylindrical embryo.

The general peritoneal cavity is established early, long before the lesser peritoneal sac is defined. Early in development, the primitive gut is suspended in the
midline by a dorsal mesentery. The midline suspension of the foregut structures (especially the stomach) defines the original right and left peritoneal cavities.

Another relevant developmental fact is the continuity of the components of the dorsal mesentery (mesoesophagus, mesogastrium, and the more caudal components). Developing structures in the primitive dorsal mesentery extend independently within the space available in that primitive mesentery.

During active morphogenesis of the stomach and liver, microscopic sections clearly reveal that a new mesothelial-lined cavity (the omental bursa) forms rapidly in the dorsal mesogastrium. That formation is similar to the formation of a coelom in general, only occurring much later and within the thick spongy mesogastrium. The three-dimensional form and communications of the omental sac are best visualized from serial section reconstructions at progressive developmental phases.

From the available embryo section reconstructions, Kanagasuntheram (14) described the coalescence of clefts (extracellular spaces) within the dorsal mesogastrium. The components of those clefts rapidly fuse and can be identified in the expanding mesogastrium as the initial omental bursa with a cranial extension into the mesoesophagus (seen as the pneumatoenteric recess).

Histology sections from 8 mm human embryos clearly reveal a crescent-shaped pneumatoenteric recess within the mesoesophagus. The recess is related to the right lung bud and the esophagus during a period before closure by the diaphragm.

Conceptually (Figure 1), the three-dimensional form can be visualized as the omental bursa (within the mesogastrium) with extensions cranially (superior recess, the pneumatoenteric recess) and an inferior recess extending over the dorsal side of the stomach, which facilitates growth of the greater omentum (arrows S and I in Figure 1). The inferior recess eventually fuses within the formed greater omentum.

The omental bursa (within the mesogastrium) forms rapidly and opens into the original right side of the mesogastrium (the original right peritoneal cavity). The rotation of the stomach and developing liver with lesser omentum rapidly envelops a diminished right side of the peritoneal cavity. The continuous omental bursa and original right peritoneal cavity is now behind the stomach. This site comprises the lesser peritoneal sac, which opens into the greater peritoneal sac at the free edge of the lesser omentum (the epiploic foramen of Winslow). The expanding omental bursa and its opening into the original right peritoneal cavity constitute the lesser peritoneal cavity. This arrangement accounts for the frequent equation of the omental bursa with the lesser peritoneal sac when seen in the definitive adult state.

Keith (15) described in the fetus a mesothelial-lined sac, the infracardiac bursa, located to the right of the esophagus and just above the recently-formed diaphragm. To that detached part, Broman had given the name “infracardiac bursa.” The infracardiac bursa usually disappears at the end of fetal life, but can be found in the mediastinum of adults (15).

In Figure 1, the relative embryonic position of the pneumatoenteric recess is indicated, specifying its mesoesophageal location and proximity to the right mediastinal pleura (mesothelium). That mesothelial lining of the pneumatoenteric recess is very close to the mesothelial lining of the right parietal pleura (mediastinal pleura) attached to the mesoesophagus. The two mesothelial linings are closely approximated. A communication that could potentially develop between the two mesothelial linings would theoretically allow fluid eventually to pass from the peritoneal cavity into the right pleural space.

Hypothesis
We propose a novel mechanism to account for the development of right hydrothorax during PD. Our proposed mechanism involves leakage of dialysis fluid through an embryonic remnant, namely the persisting pneumatoenteric recess and the infracardiac bursa, potentially connecting the peritoneal cavity with the right pleural space.

The present article is, to the best of our knowledge, the first one to suggest that the persisting pneumatoenteric recess and the infracardiac bursa is a possible mechanism for the development of right hydrothorax during PD. This novel hypothesis is consistent with the main clinical characteristics of hydrothorax complicating PD: risk factors, various presentations with right-sided predominance, diagnosis using isotope techniques, and response to specific modalities of management (that is, obliteration of the right pleural cavity by various measures, transfer to hemodialysis, or modified PD prescription, especially with reduced dialysis fluid volume).
Our hypothesis requires testing. The evidence should preferentially be obtained in patients on PD presenting with acute massive right hydrothorax. In such cases, the considerable leakage of dialysis fluid into the right pleural space would presumably facilitate the demonstration of the site of the peritoneopleural communication. For that purpose, we recommend using currently available noninvasive high-definition imaging techniques such as computed tomography scanning after intraperitoneal instillation of meglumine diatrizoate. The availability of thin cuts with post-processing reconstruction in selected planes (coronal, sagittal, oblique) will permit visualization of the putative site of the peritoneopleural communication.

Based on the known anatomic location of the persisting pneumatoenteric recess and the infracardiac bursa (Figure 1), our hypothesis will be proven by demonstration of leakage of the contrast agent originating from the cranial end of the superior recess into the infracardiac bursa located to the right of the esophagus. Further leakage of the contrast agent should be demonstrated from the right lateral wall of the bursa into the right pleural space. No evidence of leakage of the contrast agent from the peritoneal cavity to the right pleural space directly through the right hemidiaphragm should be demonstrated.

If our hypothesis is correct, we speculate that it may also be applicable to other known medical
conditions characterized by tense ascites and right hydrothorax: for example, liver cirrhosis and Meigs syndrome.

References

Corresponding author:
Raymonde F. Gagnon, MD, Division of Nephrology, Livingston Hall, Room L4–516, Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec H3G 1A4 Canada.
E-mail:
raymonde.gagnon@muhc.mcgill.ca