

PDF hosted at the Radboud Repository of the Radboud University Nijmegen

The following full text is a publisher's version.

For additional information about this publication click this link.

<http://hdl.handle.net/2066/25055>

Please be advised that this information was generated on 2019-02-23 and may be subject to change.

The increase in PLA₂ activity with bacterial infection of the peritoneal cavity is not unexpected; studies have documented an increase in PLA₂ in chronic inflammatory states, acute bacterial infections, and systemic sepsis. Patients with bacteremia, sepsis syndrome, and malaria have high plasma PLA₂ activity which correlates with the hemodynamic changes and pulmonary dysfunction (9,10). Furthermore, the local and systemic manifestations of inflammation can be induced by the administration of exogenous purified PLA₂.

The clinical importance of these observations remains unknown. There is significant evidence that the presence of phosphatidylcholine plays a role in facilitating peritoneal ultrafiltration (11,12). Degradation of phosphatidylcholine would thus be associated with impaired ultrafiltration. Phospholipase A₂ catalyzes the hydrolysis of phosphatidylcholine to lyso-phosphatidylcholine. We speculate that high intraperitoneal PLA₂ activity in renal failure, especially during peritonitis, hydrolyzes phosphatidylcholine and contributes to the decreased peritoneal ultrafiltration. This action may be at least partially responsible for the ultrafiltration failure during peritonitis. Furthermore, lyso-phosphatidylcholine is a vasoactive substance and may be contributory to intraperitoneal vasodilatation, part of the local inflammatory reaction.

Sarbjit V. Jassal¹

Alexander R. Morton¹

Peter Vadas²

Waldemar Pruzanski²

Eva Stefanski²

Andreas Pierratos¹

Division of Nephrology¹

Department of Medicine

The Wellesley Hospital

Inflammation Research Group²

University of Toronto

Toronto, Ontario, Canada

REFERENCES

1. Kramer RM, Hession C, Johansen B, *et al.* Structure and properties of a human non-pancreatic phospholipase A₂. *J Biol Chem* 1989; 264:5768–75.
2. Pruzanski W, Vadas P. Soluble phospholipase A₂ in human pathology: clinical-laboratory interface. *Adv Exp Med Biol* 1990; 275:83–101.
3. Peuravuori HJ, Funatomi H, Nevalainen TJ. Group I and group II phospholipases A₂ in serum in uraemia. *Eur J Clin Chem Clin Biochem* 1993; 31:491–4.
4. Morton AR, Vadas P, Stefanski E, Pruzanski W, Pierratos A. Increased levels of phospholipase A₂ in renal failure patients. The American Society of Nephrology Meeting 1989.
5. Baur M, Schmid TO, Landauer B. Role of phospholipase A in multiorgan failure with special reference to ARDS and acute renal failure (ARF). *Klin Wochenschr* 1989; 67:196–202.
6. Smith GM, Ward RL, McGuigan L, Rajkovic IA, Scott KF. Measurement of human phospholipase A₂ in arthritis plasma using a newly developed sandwich ELISA. *Br J Rheumatol* 1992; 31:175–8.
7. Funakoshi A, Furukawa M, Yamada Y, *et al.* Clinical studies of serum phospholipase A₂ immunoreactivity. *Nippon Shokakibyō Gakkai Zasshi* 1989; 86:1136–40.
8. Costello J, Franson RC, Landwehr K, Landwehr DM. Activity of phospholipase A₂ in plasma increases in uraemia. *Clin Chem* 1990; 36:198–200.
9. Pruzanski W, Keystone EC, Sternby B, Bombardier C, Snow KM, Vadas P. Serum phospholipase A₂ correlates with disease activity in rheumatoid arthritis. *J Rheumatol* 1988; 15:1351–5.
10. Vadas P, Pruzanski W, Stefanski E. Extracellular phospholipase A₂: causative agent in circulatory collapse of septic shock? *Agents Actions* 1988; 24:320–5.
11. Breborowicz A, Sombolos K, Rodela H, Ogilvie R, Bargman J, Oreopoulos D. Mechanism of phosphatidylcholine action during peritoneal dialysis. *Perit Dial Bull* 1987; 7:6–9.
12. Di Paulo N, Buoncristiani U, Gaggiotti E, Capotondo L, De Mia M. Improvement of impaired ultrafiltration after addition of phosphatidylcholine in patients on CAPD. *Perit Dial Int* 1989; 9:211–13.

The Necessity of Adjusting Dialysate Volume to Body Surface Area in Pediatric Peritoneal Equilibration Tests

Peritoneal dialysis is an established therapy for end-stage renal failure in both adult and pediatric patients. Transport kinetics in adult patients is standardized by using the peritoneal equilibration test (PET) as prescribed by Twardowski (1). Standard dwell volumes of 2 L are generally used regardless of the patient's size. In pediatric clinical practice a volume of 30 – 50 mL/kg body weight (BW) is used in most centers. Since the surface area of the peritoneal membrane is related to the body surface area (BSA) it would be more logical to prescribe dialysate volumes on the basis of BSA. In the present study, PETs were performed using an intraperitoneal volume of 1200 mL/m². The fluid kinetics were compared to the results of the previous PETs in which the volume was 40 mL/kg BW (2).

PATIENTS AND METHODS

Study group A consisted of 13 children (7 boys, 6 girls) with a median age of 8.3 years (range 3 – 15.9 years). The median duration of CAPD was 9.4 months (range 1 – 91 months). The intraperitoneal volume in

Group A was 1211 ± 47 mL/m². The control group (Group B) consisted of 13 children (10 boys, 3 girls) with a median age of 7 years (range 3.1 - 15.4 years) and a median duration of CAPD of 27.5 months (range 1 - 101 months). The intraperitoneal volume in this group was 40.3 ± 0.3 mL/kg BW. Four patients were studied in both groups. The two groups were similar with respect to height (118 ± 25 cm vs 123 ± 24 cm), weight (24 ± 12 kg vs 25 ± 11 kg), and BSA (0.88 ± 0.29 m² vs 0.92 ± 0.28 m²).

In both groups, the PETs were performed as described earlier (2). A 4-hour dwell of Dianeal 3.86% (Baxter Inc., Deerfield, IL, U.S.A.) was studied using Dextran 70 (Macrodex NPBI, Emmercompascuum, The Netherlands) as a volume marker. Transcapillary ultrafiltration (TCUF) and marker clearance (MC) were calculated (2). The protocol was approved by the committee of medical ethics of the University Hospital of Nijmegen and informed consent was obtained.

All data are expressed as mean \pm SD. Statistical comparisons between the groups were performed using the unpaired t-test. Correlations were calculated by the method of least squares (Pearson). Any p values less than 0.05 were considered significant.

RESULTS

The mean (\pm SD) intraperitoneal volume in mL/kg BW in Group A was 46.4 ± 6.0 versus 40.3 ± 0.3 in Group B ($p = 0.005$). The intraperitoneal volume in mL/m² in Group A was 1211 ± 47 versus 1055 ± 141 in Group B ($p = 0.008$).

Figure 1 shows the changes in TCUF and MC during the 4-hour dwell in both groups. The differences noted at each dwell time are not significant.

Cumulative TCUF during the 4-hour dwell was 935 ± 202 mL/1.73 m² in Group A and 823 ± 226 mL/1.73 m² in Group B ($p = 0.27$). Cumulative MC during the 4-hour dwell was 438 ± 275 mL/1.73 m² in Group A versus 307 ± 176 mL/1.73 m² in Group B ($p = 0.67$).

Figure 2 shows the relationship between the age of the patient and the cumulative TCUF during the 4-hour dwell. In Group B there was a positive correlation between age and cumulative TCUF ($r = 0.68$; $p = 0.01$). In Group A there was no correlation between age and cumulative TCUF ($r = 0.32$; $p = 0.28$). No correlation between age and MC existed in either group.

DISCUSSION

In pediatric PETs different intraperitoneal volumes are applied. Some investigators have used intraperitoneal volumes scaled to body weight (3,4), body surface area (5), or both (6,7). By using a dwell volume of 33 ± 6 mL/kg Mendley and Majkowski (4) concluded that glucose equilibration occurs more rapidly in younger children. When Kohaut *et al.* performed PETs in their patients with a dwell volume related to BW and with a dwell volume related to body surface area, age dependency for glucose equilibration existed in patients where dwell volumes were prescribed scaled to BW, but disappeared in patients where the dwell volume was scaled to BSA (6). So we suggested that, for the purpose of kinetic studies, the best way to perform PETs is to prescribe intraperitoneal volumes based upon BSA, as also proposed by other authors (8-10). As expected, in our study fluid kinetics are independent of age in children older than 3 years when prescribing intraperitoneal volumes related to BSA.

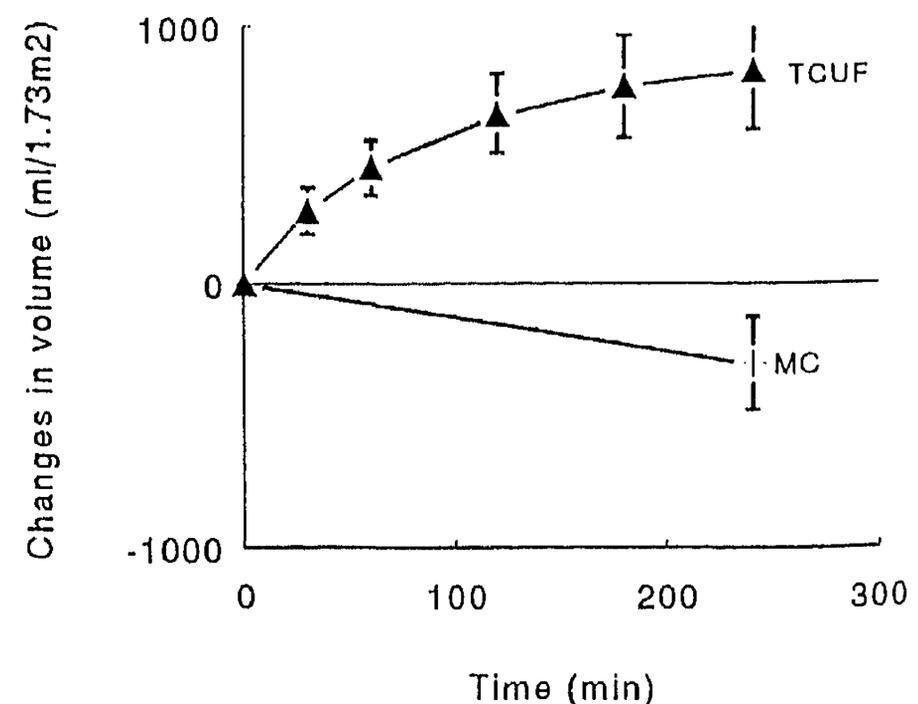
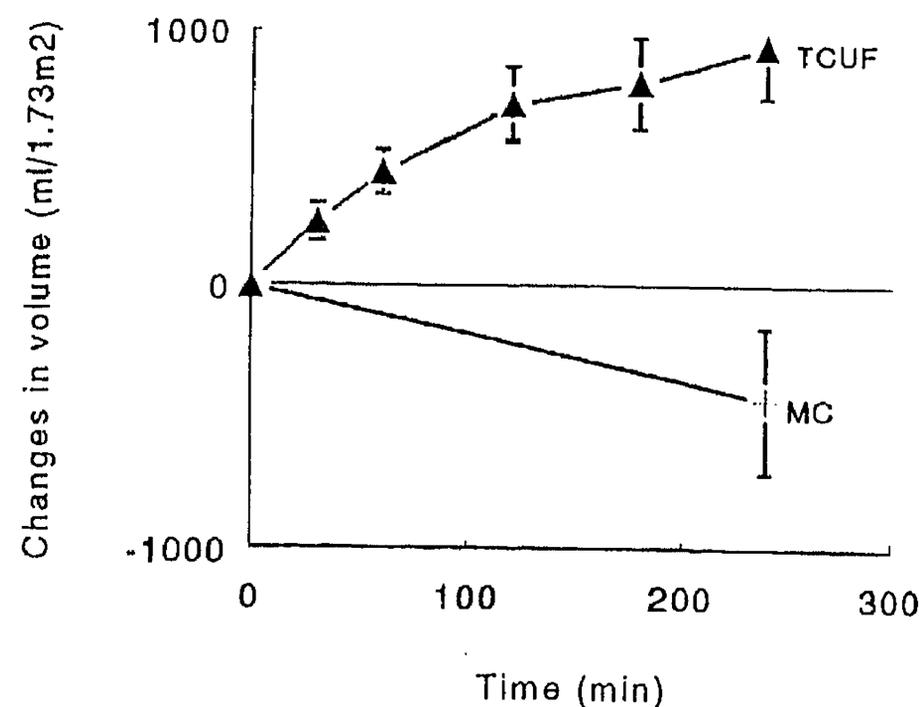


Figure 1 — The time course of transcapillary ultrafiltration (closed triangles) and marker clearance (+) in Group A (left) and Group B (right) in mL/1.73 m².

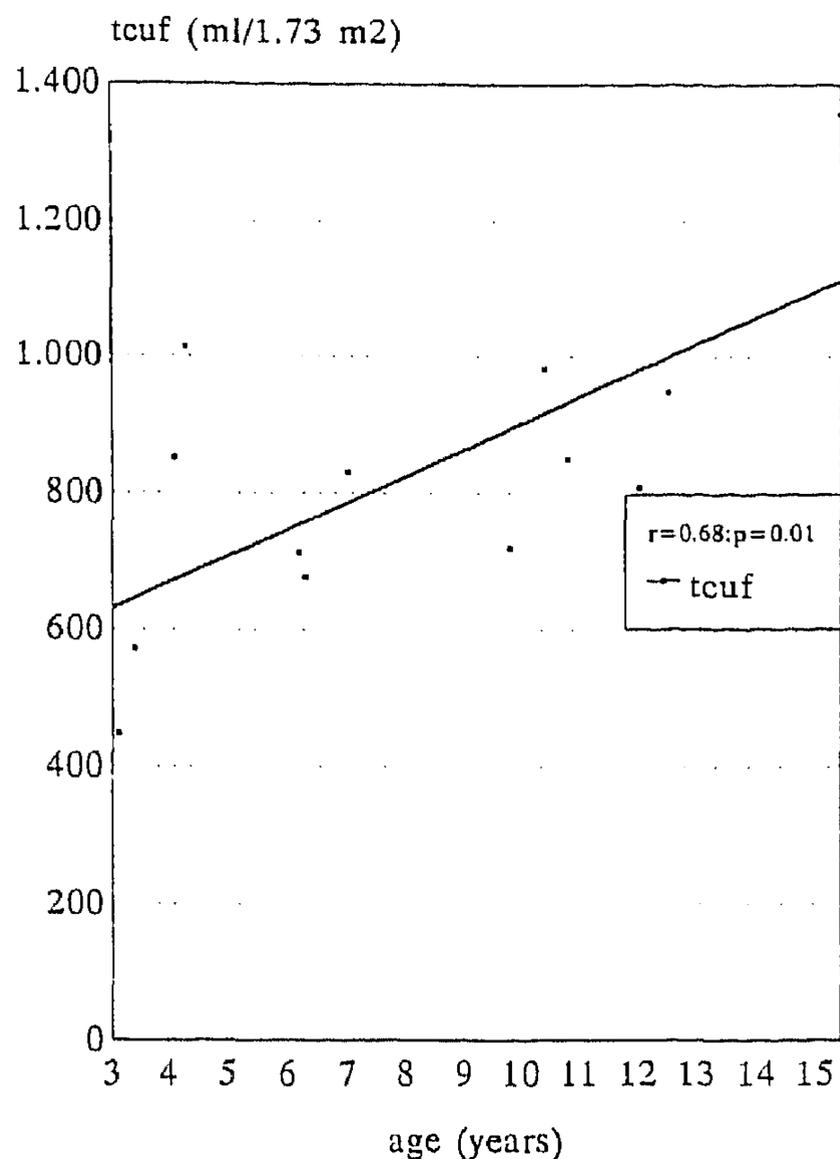
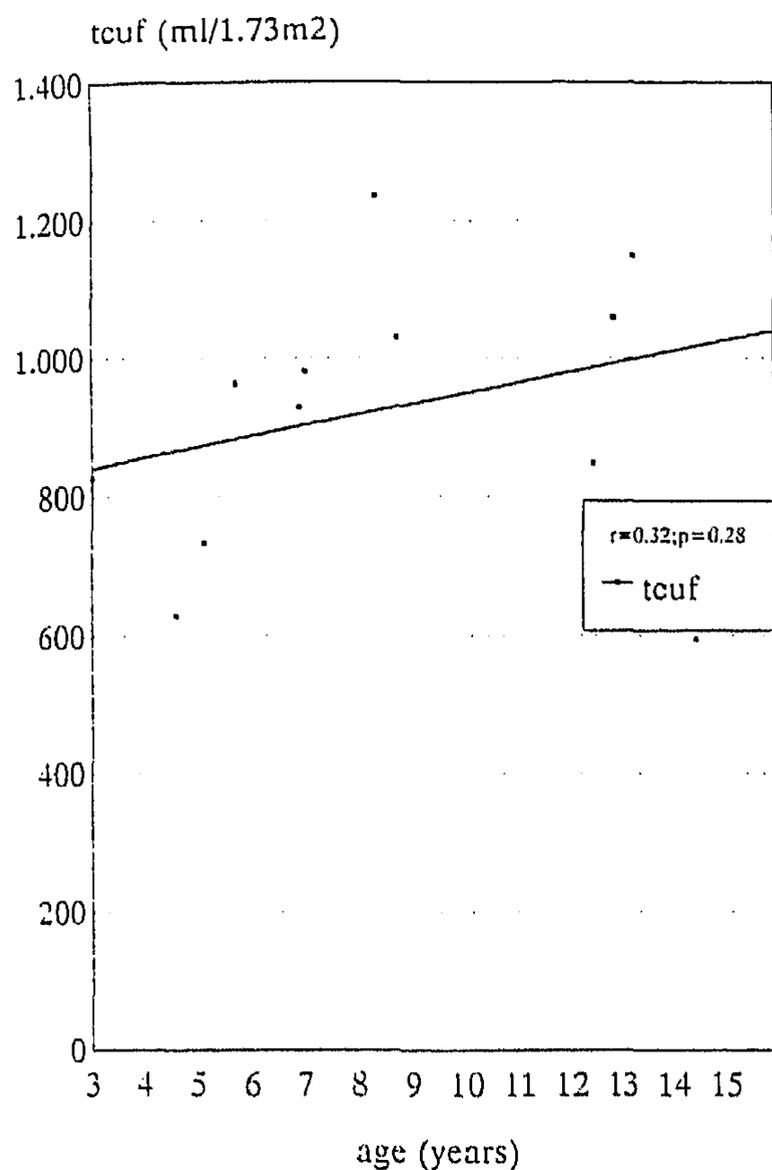


Figure 2 — The relationship between the age of the patient and transcapillary ultrafiltration in Group A and Group B.

Fluid kinetics in both groups are not significantly different. The tendency toward a higher cumulative TCUF and MC in Group A is due to a significantly higher intraperitoneal volume in Group A compared to Group B. The difference in TCUF cannot be explained by the use of hypertonic dialysis solution since the PETs in both groups were performed with glucose 3.86 %.

Although not significantly different it is tempting to speculate on the higher MC in Group A. The slight increase in MC could be due to a higher intraperitoneal pressure in Group A (11). A positive correlation between intraperitoneal volume and intraperitoneal pressure is postulated (12,13). In a small group of patients where PETs were performed using an intraperitoneal volume of 1200 mL/m², hydrostatic intraperitoneal pressure was measured and ranged between 15.5 and 22 cm H₂O (n = 7). The intraperitoneal pressure in the control group with an intraperitoneal volume of 40 mL/kg BW was 9.5 – 17 cm H₂O (n = 9).

It is concluded that pediatric peritoneal equilibration tests should be performed with an intraperitoneal volume scaled to body surface area so that fluid kinetics in different age groups (> 3 years) are comparable. Studies in younger children, especially infants, should also be performed. In these younger

children the age relation will be especially interesting because limited observations suggest a decreased ultrafiltration capacity at that age (14).

Alberdina W. de Boer¹
Theodora C.J.G. van Schaijk¹
Hans L. Willems²
Roel E. Reddingius¹
Leo A.H. Monnens¹
Cornelis H. Schröder¹

Department of Pediatrics¹
Department of Clinical Chemistry²
University Hospital Nijmegen
Nijmegen, The Netherlands

REFERENCES

1. Twardowski ZJ, Nolph KD, Khanna R, *et al.* Peritoneal equilibration test. *Perit Dial Bull* 1986; 7:138–47.
2. Reddingius RE, Schröder CH, Willems JL, *et al.* Measurement of peritoneal fluid handling in children on continuous ambulatory peritoneal dialysis using Dextran 70. *Nephrol Dial Transplant* 1995; 10:866–70.
3. Geary DF, Harvey EA, MacMillan JH, *et al.* The peritoneal equilibration test in children. *Kidney Int* 1992; 42:102–5.

4. Mendley SR, Majkowski NL. Peritoneal equilibration test results are different in infants, children, and adults. *J Am Soc Nephrol* 1995; 6:1309–12.
5. Warady BA, Alexander S, Hossli S, *et al.* The relationship between intraperitoneal volume and solute transport in pediatric patients. *J Am Soc Nephrol* 1995; 5:1935–9.
6. Kohaut EC, Waldo FB, Benfield MR. The effect of changes in dialysate volume on glucose and urea equilibration. *Perit Dial Int* 1994; 14:236–9.
7. Schaefer F, Langenbeck, Heckert KH, *et al.* Evaluation of peritoneal solute transfer by the peritoneal equilibration test in children. In: Khanna R, Nolph KD, Prowant BF, Twardowski ZJ, Oreopoulos DG, eds. *Advances in peritoneal dialysis*. Toronto: Peritoneal Dialysis Bulletin, 1992; 8:410–15.
8. Morgenstern BZ. Equilibration testing: close, but not quite right. *Pediatr Nephrol* 1993; 7:290–1.
9. Kohaut EC. The effect of dialysate volume on ultrafiltration in young patients treated with CAPD. *Int J Pediatr Nephrol* 1986; 7:13–16.
10. Fukuda M, Kawamura K, Kawahura K, *et al.* Influence of instilled volume on the peritoneal equilibration test. *Perit Dial Int* 1994; 14:406–7.
11. Imholz ALT, Koomen GCM, Struijk DG, *et al.* Effect of an increased intraperitoneal pressure on fluid and solute transport during CAPD. *Kidney Int* 1993; 44:1078–85.
12. Durand P, Chanliau J, Gamberoni J, *et al.* APD: clinical measurement of the maximal acceptable intraperitoneal volume. In: Khanna R, ed. *Advances in peritoneal dialysis*. Toronto: Peritoneal Dialysis Publications 1994; 10:63–7.
13. Schneider Ph, Fischbach M, Lahlou A, *et al.* Relation between hydrostatic intraperitoneal pressure and dialysate dwell volume. *Perit Dial Int* 1996; 16(Suppl 2):S79.
14. Kohaut EC, Alexander SR. Ultrafiltration in the young patient on CAPD. In: Moncrief JW, Popovich RP, eds. *CAPD update*. New York: Masson Publishers, 1981:221–6.

A Prospective Study of Vancomycin-(Vancoled-) Induced Chemical Peritonitis in CAPD Patients

Vancomycin has been an important antibiotic in the treatment of gram-positive bacterial infections since its availability in 1956. It has also been accepted as one of the first-line antibiotics for the treatment of peritonitis in chronic ambulatory peritoneal dialysis (CAPD) patients. It has been reported that some CAPD patients receiving intraperitoneal vancomycin have developed chemical peritonitis (1–4) manifesting as turbid effluent 3 to 6 hours after administration of the drug (5,6). However, the underlying mechanism responsible for this reaction has not been defined. There are studies suggesting that

generic preparations of vancomycin may result in a higher incidence of chemical peritonitis when compared with the original formulation (1,4,5). The authors of those studies have postulated that this might be related to the greater amount of impurities in generic preparations (5). However, this phenomenon is not universally recognized, and the exact incidence remains unknown (7,8).

While witnessing a less than 1% incidence of chemical peritonitis when we were using Vancocin (Eli Lilly, Indianapolis, IN, U.S.A.), we noted a definite increase in such incidence in our CAPD population since we changed to the use of a different preparation, Vancoled (Lederle, Wayne, NJ, U.S.A.), in 1995. We have therefore performed a prospective study of Vancoled-induced chemical peritonitis among our CAPD patients to define the incidence and characteristics of such peritonitis and, hopefully, to understand more about the underlying mechanism.

PATIENTS AND METHODS

Between 1 October 1995 and 29 February 1996, 26 consecutive CAPD patients requiring treatment with intraperitoneal vancomycin for either exit-site infection or peritonitis were recruited prospectively into the study. CAPD was performed as per our routine using 3 to 4 daily 2-L exchanges of 1.5 – 4.25% Dianeal (Baxter, IL, U.S.A.) solution. For patients with suspected bacterial peritonitis who had received intraperitoneal antibiotic therapy, the peritoneal drainage fluid had to become clear [confirmed by microscopy with a white cell count (WBC) below 100/mm³] before they were recruited and studied for their response to the second weekly dose of intraperitoneal vancomycin. All patients recruited had had a history of exposure to vancomycin because it is our standard practice to prescribe an intravenous dose of vancomycin as a prophylaxis for Tenckhoff catheter insertion, unless contraindicated. Patients who required co-administration of other intraperitoneal agents apart from heparin, and those with a duration of CAPD less than 3 months were excluded from the study. There was no restriction on the number of occasions studied for any patient so that we could also study the consistency of the individual response to the drug.

Prior to the administration of intraperitoneal vancomycin, 30 mL of peritoneal fluid was obtained using strict aseptic procedure for baseline analysis including routine microscopy and culture. Centrifuged deposits of 20 mL of effluent were used for culture using McConkey and blood agars and thio-glycollate-enriched broth. Vancoled powder (Lederle, Wayne, NJ, U.S.A.) was dissolved in sterile water at a concentration of 100 mg/mL for injection. The solu-