Introduction
Peritonitis and exit site and tunnel infections are the most frequent and serious complications of continuous ambulatory peritoneal dialysis (CAPD) (Boeschoten et al., 2006). Gram-positive micro-organisms, particularly Staphylococcus aureus and Staphylococcus epidermidis, are the most frequent causative pathogens. Recently, however, the incidence of Gram-positive staphylococcal peritonitis has decreased and the relative incidence of Gram-negative infections has increased (Keane et al., 2000). Gram-negative bacilli causing peritonitis in CAPD patients move from the gastrointestinal tract to the hyperosmolar dialysate in the peritoneum or contaminate the connection devices directly, and are generally difficult to eradicate (Szeto et al., 2006; Woo et al., 2004).

Citrobacter species are members of the aerobic Enterobacteriaceae family, Gram-negative bacilli commonly found in water, soil, food and the intestinal tracts of animals and humans (N. Gupta et al., 2003). Here we present the case of one of our CAPD patients who developed CAPD-associated peritonitis and tunnel infection caused by Citrobacter freundii.

Case report
A 33-year-old female with end-stage renal disease, who had been receiving CAPD for 8 years, presented to our hospital with a 12 h history of abdominal pain, nausea, vomiting and cloudy peritoneal fluid. Past medical history included only one culture-negative peritonitis episode 3 years previously. She had not received any broad-spectrum antibiotics since that episode. On physical examination, her temperature was 37.7 °C, blood pressure 100/70 mmHg and heart rate 92 beats min⁻¹. Her abdomen was diffusely tender. The area inferior to the umbilicus around the catheter tunnel site was swollen, red, warm and tender, but no visible signs of infection were present around the catheter exit site. The blood results were: 11.2 g haemoglobin dl⁻¹, haematocrit 32.3 %, 11400 white blood cells mm⁻³; erythrocyte sedimentation rate 95 mm h⁻¹ and 38.3 mg C-reactive protein dl⁻¹ (normally <0.8 mg dl⁻¹). The cell count of the peritoneal fluid was 20900 cells μl⁻¹ with a neutrophil predominance (91 %). No bacteria were seen on Gram stain examination. The patient was hospitalized, and after peritoneal fluid was sent for bacterial culture, intraperitoneal (i.p.) cefazolin (loading dose 1 g, then 500 mg i.p. in every exchange, four times per day) and gentamicin (40 mg i.p. once daily) were started empirically. Two samples were collected and inoculated into BACTEC plus aerobic/F culture bottles (Becton Dickinson) and incubated in a BACTEC 9240 blood culture system. On the fourth day of incubation, both blood culture bottles became positive, and subculture yielded Gram-negative, oxidase-negative bacteria. The micro-organism was identified as C. freundii using the VITEK 2 system (bioMérieux). In order to determine the species, the bacteria was biochemically tested using the API 20E system (bioMérieux). For the antibioticogram, a VITEK 2 AST-GN13 card (ampicillin, ampicillin/sulbactam, aztreonam, cefazolin, cefepime, cefotetan, cefazidime, ceftriaxone, ciprofloxacin, gentamicin, imipenem, levofloxacin, nitrofurantoin, piperacillin/tazobactam, tobramycin and trimethoprim/sulfamethoxazole antibiotics) and an extended-spectrum β-lactamase (ESBL) confirmatory test were used. The strain was found to be ESBL positive, and sensitive to imipenem, meropenem, gentamicin, ceftoperazone/sulbactam and trimethoprim/sulfamethoxazole. ESBL production was also confirmed using two ESBL
Etest strips (AB Biodisk). The swab culture of the catheter exit site was negative.

Based on these results, cefazolin was discontinued and intravenous (i.v.) meropenem (500 mg once a day) was started. Abdominal ultrasonography revealed a $6 \times 2 \times 3$ cm fluid collection with internal echogenicities at the inferior aspect of the umbilicus around the catheter track. The white blood cell count in the peritoneal fluid declined to 8800, 1500 and 240 cells $\mu l^{-1}$ 3, 7 and 10 days later, respectively. On the 14th day of her hospital stay, we recommended to the patient that her peritoneal catheter be removed, but the patient refused. Three weeks later, her peritoneal fluid was clear. Her symptoms of nausea and vomiting had improved over the course of 1 week while i.v. meropenem was being administered, but localized abdominal tenderness, especially at the inferior aspect of the umbilicus, continued for 3 more weeks. Furthermore, the patient developed a $2 \times 1$ cm area of red, tender induration at the inferior aspect of the umbilicus during the third week of hospitalization. Repeat ultrasonography at that time showed no regression of the size of the fluid collection.

Although all peritoneal fluid cultures following the administration of meropenem and gentamicin remained negative, her symptoms did not resolve and the tunnel infection persisted. On the 21st day of meropenem (500 mg i.v.) and gentamicin (40 mg i.p.) therapy, to prevent a recurrence of the peritonitis, we removed the Tenckhoff catheter and the patient was switched to haemodialysis. Cultures of the catheter and tissue around it were negative. After removing the catheter, the localized infection around the catheter track resolved. No recurrence of abdominal symptoms or signs occurred during 6 months of follow-up.

**Discussion**

*Citrobacter* species are a group of Gram-negative bacilli belonging to the family *Enterobacteriaceae* and are frequently found in the gastrointestinal flora of human beings (Forbes *et al.*, 2002). *Citrobacter* species cause a wide spectrum of infections in the urinary tract, blood, superficial wounds, skin, peritoneum and several other normally sterile sites; most frequently, their hosts are hospitalized and immunocompromised patients (N. Gupta *et al.*, 2003; Forbes *et al.*, 2002; Kim *et al.*, 2003). *C. freundii* is a member of *Citrobacter*ae and is H$_2$S-positive, and indole-, adonitol- and malonate-negative in character (Winn *et al.*, 2006).

Peritonitis due to *C. freundii* is uncommon. Lipsky *et al.* (1980) mentioned in their review that they recovered *Citrobacter* in peritoneal culture specimens from elderly and debilitated patients. Kato *et al.* (1993) reported the first case of spontaneous bacterial peritonitis due to *C. freundii* in a patient with nephrotic syndrome. Their patient had a good response to 8 days of treatment with i.v. imipenem/cilastatin and i.p. tobramycin. In a series of acute intermittent peritoneal dialysis patients from India, *C. freundii* was the only aetiologic agent in three of four CAPD-associated peritonitis cases, and in the fourth patient was found along with *E. faecalis*. The clinical course and outcomes were not reported (Sharma *et al.*, 2003).

The various species of *Citrobacter* show different antimicrobial susceptibility profiles. Aminoglycosides, fluoroquinolones, carbapenems, and third- or fourth-generation cephalosporins have the highest *in vitro* antimicrobial activity against *C. freundii* (R. Gupta *et al.*, 2003). Shih *et al.* (1996) showed that combination therapy with a $\beta$-lactam agent and an aminoglycoside produced better results than that with a single agent. Our patient was treated as directed by the antibiogram, with a combination of i.v. meropenem and i.p. gentamicin, but these antibiotics could not cure her tunnel infection while the catheter remained in place.

Identification and antimicrobial susceptibility testing were performed at our laboratory with the VITEK 2 automated system using the ID-GNB and AST-GN13 card in accordance with the guidelines of the manufacturer. By using this automated system, non-ESBL $\beta$-lactamases such as broad-spectrum enzymes like TEM-1 or SHV-1 and plasmid-encoded AmpCs were not identified in the isolate. Therefore, the therapeutic failure in the present case might be related to presence of non-ESBL $\beta$-lactamases in the organism that we could not detect by the antimicrobial susceptibility testing methods available to us.

To our knowledge, tunnel infection due to *C. freundii* has never been reported before; it is much more common with *S. aureus* or *Pseudomonas aeruginosa* (Piraino, 2003). The most recent International Society of Peritoneal Dialysis guidelines on the management of peritonitis recommend removing the catheter if a refractory tunnel infection exists, without giving any cut-off period (Piraino *et al.*, 2005). For a suspected tunnel infection in a clinically stable patient in our centre, we give empiric antibiotics then switch within a few days to those indicated by antibiogram testing. If the infection has not cleared within 5–7 days, we remove the catheter. In the present case, the patient initially refused to have the catheter removed, and because the peritonitis was improving (but not as fast as expected) the catheter was not removed until the patient gave her consent on day 21.

In summary, a patient with CAPD-associated monomicrobial *C. freundii* peritonitis and tunnel infection has been presented. The patient did not respond well to our antibiogram-based antibiotic therapy initially, and required eventual removal of her Tenckhoff catheter. It is not yet clear how frequently *C. freundii* is an aetiologic agent of peritonitis or tunnel infection in patients undergoing peritoneal dialysis. In the future, due to the better care and survival of immunocompromised patients, such as those with renal failure, pathogens like *C. freundii* will likely gain importance clinically.
References


