Peritoneal dialysis (PD) peritonitis and subsequent relapses are undesirable complications for patients requiring home peritoneal dialysis. Coagulase-negative staphylococci (CoNS) remain a common cause of peritonitis. Strains of CoNS are emerging that are resistant to cephalosporins. It has been suggested that, if sensitivity testing shows resistance to cephalosporin but the patient is improving on intraperitoneal cephalosporin, then there is no need to change the antibiotic. The rationale for this approach is that the intraperitoneal concentration of cephalosporin is higher than concentrations used in the microbiology laboratory to determine sensitivity or resistance.

Previously, we reviewed a smaller number of cases of CoNS and noted that the relapse rate seemed greater for strains with cephalosporin “resistance” initially treated with cephalosporins. The present retrospective review looks at the incidence and treatment of CoNS peritonitis reported as resistant to cephalosporins in a large urban PD program between January 1, 2006, and August 31, 2009.

During the study period, 200 new cases of peritonitis occurred, 65 of which (32.5%) were identified as CoNS. All were treated empirically with cefazolin (or vancomycin if allergic) for gram-positive coverage and either tobramycin or ceftazidime for gram-negative coverage. Of the 65 CoNS cases, 27 (41.5%) were sensitive to cefazolin; 38 (58.5%) were reported to be cephalosporin-resistant.

Of the 38 episodes of CoNS reported as resistant, 10 were treated throughout with cephalosporin, and 28 either started with or were changed to vancomycin. Of the 28 treated with vancomycin only, 2 relapsed, which compares with 4 of 10 who were treated with cephalosporin throughout (Fisher exact test p = 0.03).

Our study suggests that, although cephalosporin-resistant cases of CoNS initially resolve with cephalosporin treatment, they are indeed associated with a greater risk of relapse. Patients with CoNS peritonitis reported resistant to cefazolin may benefit from a change to vancomycin to reduce the risk of relapse.

Key words
Peritonitis, antibiotic resistance, relapsing peritonitis, cephalosporin resistance

Introduction
Even in 2010, peritonitis remains a significant cause of morbidity, technique failure, and death in peritoneal dialysis (PD). With the advent of new connectology, the incidence of peritonitis has been declining over time (1). However, coagulase-negative staphylococci (CoNS) remain a common cause of this infectious complication. Cases of CoNS peritonitis are usually easily treated with common antibiotic therapy, but strains of this organism are emerging that are resistant to cephalosporins. In this case, vancomycin is commonly used to treat a CoNS peritonitis. Many centers believe that use of vancomycin should be limited so as to reduce the incidence of vancomycin-resistant enterococci (VRE). Indeed, after a serious outbreak of VRE in our own nephrology unit, we changed our gram-positive coverage from vancomycin to once-daily intraperitoneal cephalosporin.

A vexing clinical problem is the patient who presents with a PD-related peritonitis and receives gram-positive coverage with a cephalosporin, commonly cefazolin (2). In many instances, the patient appears to be improving clinically, with resolution of pain and PD fluid leukocytosis, at which point the antibiotic sensitivities return and the organism is reported to be “resistant” to cephalosporin. It is difficult to reconcile the antibiotic resistance report...
with the clinical improvement. However, a laboratory report of resistance is typically based on the serum concentration of cephalosporin that results from intravenous therapy. The concentration of cephalosporins in PD fluid after intraperitoneal antibiotic therapy is generally much higher than that in serum. Therefore, although the organism in the peritoneal fluid would be resistant to the lower blood-level concentrations seen with intravenous cephalosporin therapy, they may be effectively killed by the higher intraperitoneal concentrations of the antibiotic, explaining why patients can improve clinically despite this report of “resistance.” It has been suggested that patients with a “resistant” CoNS strain can continue to be treated with intraperitoneal cephalosporin for the duration of the peritonitis without switching to another antibiotic (3).

A decade ago, our unit reviewed more than 50 episodes of CoNS peritonitis (4). Almost 40% of the episodes were reported to be cephalosporin-resistant. Of the 20 resistant cases, 9 continued to be treated with cephalosporin, and although the peritonitis resolved, 5 of the 9 relapsed. That result was unfavorable when compared with the results for a cephalosporin-resistant CoNS group treated with vancomycin, in which only 3 of 11 cases relapsed. Although the patient numbers were small, our impression from that study was that, although “cephalosporin-resistant” CoNS cases may resolve with cephalosporins, the chance of relapse is greater.

We have now revisited this issue. We studied patients over a longer period of time and in greater numbers to see if the trend is consistent.

Methods
This retrospective chart review looked at the incidence and treatment of CoNS peritonitis reported by the laboratory to be resistant to cephalosporins. The review period covered 44 months, from January 1, 2006, until August 31, 2009. The usual definitions of peritonitis and peritonitis relapse were those published in the guidelines from the International Society for Peritoneal Dialysis (2).

Results
Over the study period, 200 episodes of peritonitis occurred, with 55% being the result of gram-positive organisms; 28%, gram-negative organisms; 9.5%, no growth; and 7.5%, other organisms. In 65 of the 200 episodes (32.5%), CoNS were the causative organism. Thirty-two patients had 1 episode only, 15 had 2 separate (not relapsing) episodes, and 1 patient had 3 different episodes involving this organism.

Of the 65 CoNS episodes, 41.5% were reported to be cephalosporin-sensitive and 58.5% to be cephalosporin-resistant. We observed no trend toward increasing cephalosporin resistance over the study period, although the prevalence of reported cephalosporin resistance was higher than in our original study (4). Of the 38 episodes of CoNS peritonitis reported as “resistant,” 10 were treated with cephalosporin throughout; 28 either started with or were changed to vancomycin. Of the 28 patients treated with vancomycin, only 2 experienced a relapse. In contrast, the 10 patients treated with cephalosporin experienced 4 relapses (Fisher exact test \( p = 0.03 \)).

We also examined whether relapsing patients were more likely to be on cycler-assisted PD, because it could be postulated that the cycler led to lower blood levels of cephalosporin and therefore made the patient vulnerable for relapse. We found that, although 64.5% of the total PD population used a cycler, only 17% of the relapsed group were on APD. They were, in fact, underrepresented in the relapsed group.

Finally, of the 6 patients who relapsed, half were ultimately successfully treated; the other half required removal of the PD catheter.

Summary and Conclusions
This study extends initial observations made more than a decade ago and confirms that, although cephalosporin-resistant cases of CoNS treated with cephalosporin initially resolve, they are indeed associated with a greater risk of relapse. Based on the present study, the continued use of cephalosporin in a PD patient with CoNS peritonitis that is reported as resistant to cephalosporin cannot be recommended, even when initial clinical improvement is observed.

References
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**Corresponding author:**
Joanne M. Bargman, MD, FRCPC, University Health Network, 8N-840, 200 Elizabeth Street, Toronto, ON M5G 2C4 Canada.

**E-mail:** joanne.bargman@uhn.on.ca