# Successful Use of Intraperitoneal Daptomycin in the Treatment of Vancomycin-Resistant Enterococcus Peritonitis

*Sarah C. Huen, MD,[1] Isaac Hall, MD,[1] Jeffrey Topal, MD,[2] Rex L. Mahnensmith, MD,[1] Ursula C. Brewster, MD,[1] and Ali K. Abu-Alfa, MD[1]*

Peritoneal dialysis–associated peritonitis from such resistant organisms as vancomycin-resistant enterococci increasingly is occurring and is challenging to treat. We describe 2 cases of vancomycin-resistant entercoccus peritonitis successfully treated with intraperitoneal daptomycin. Both patients were on automated peritoneal dialysis therapy with culture-positive vancomycin-resistant *Enterococcus faecium* peritonitis and were treated with 10 to 14 days of intraperitoneal daptomycin given every 4 hours through manual peritoneal dialysate exchanges. Despite the known degradation in dextrose solutions, intraperitoneal daptomycin was effective in clearing both infections. Neither patient experienced a relapse or repeated peritonitis. Additional studies of dosing and pharmacokinetics of intraperitoneal daptomycin in the treatment of patients with vancomycin-resistant enterococcus peritonitis are needed.

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Peritoneal dialysis (PD)-associated peritonitis caused by resistant organisms is increasingly common and is clinically challenging to treat. Successful treatment of patients with vancomycin-resistant enterococcus (VRE) peritonitis with intraperitoneal (IP) daptomycin has not been described. The International Society for Peritoneal Dialysis (ISPD) guidelines do not delineate recommendations for PD catheter removal in patients with such infections.[1] We describe 2 cases of VRE peritonitis associated with PD treated with IP daptomycin resulting in eradication of the infection without removal of the catheter.

## CASE REPORTS

### Case 1

A 52-year-old African American woman with end-stage renal disease had been on automated PD (APD) therapy for 2 years when she presented from an extended-care facility with hypotension and suspected peritonitis. Two months before, she had been hospitalized with sepsis and treated empirically with intravenous (IV) vancomycin and piperacillin/tazobactam. *Clostridium difficile* infection ultimately was diagnosed and treated with oral vancomycin. Residual creatinine clearance was 0.7 mL/min (0.01 mL/s) 5 months before presentation.

On presentation, the patient was afebrile, blood pressure was 85/54 mm Hg, and heart rate was 100 beats/min. Abdominal examination findings were significant for mild diffuse tenderness. There was no expressible pus, drainage, or erythema surrounding the catheter exit site. The tunnel was not tender. An abdominal film showed a malpositioned catheter with the tip in the left midabdomen. Initial dialysate cell count was 2,200 cells/$\mu$L (75% granulocytes). IV linezolid and IP daptomycin treatment was initiated because dialysate cultures sent from the extended-care facility grew vancomycin-resistant *Enterococcus faecium*. The minimal inhibitor concentration (MIC) was not reported for daptomycin. IP daptomycin initially was administered at 100 mg/L for a 6-hour dwell. On treatment day 2, linezolid therapy was discontinued and the IP daptomycin dose was changed to 20 mg/L, with heparin 250 U/L given every 4 hours through manual 2-L PD exchanges using 1.5% dextrose solutions. On day 3 of treatment, 8 mg of alteplase was instilled into the PD catheter and flushed with 10 mL of normal saline. On day 7, cell count normalized to 23 cells/$\mu$L (Fig 1). All dialysate cultures sent after the initiation of IP daptomycin therapy had negative results. She was treated for 10 days with IP daptomycin. Subsequently, the PD catheter was laparoscopically repositioned without its removal. At 1 and 3 months posttreatment, dialysate culture results were negative and cell counts were normal ($<$50 cells/$\mu$L). At the time of writing, the patient remains on APD therapy and is clinically well without signs of peritonitis 9 months after treatment of VRE peritonitis.

### Case 2

A 35-year-old African American woman with end-stage renal disease on APD therapy for 3 years presented with 5 days of abdominal pain, nausea, vomiting, and constipation. Her PD history is significant for 3 prior episodes of peritonitis: *Klebsiella pneumoniae* peritonitis 1 year prior, coagulase-

*From the Sections of [1]Nephrology and [2]Infectious Diseases, Yale School of Medicine, New Haven, CT.*

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*Address correspondence to Ali Abu-Alfa, MD, PO Box 208029, 333 Cedar St, New Haven, CT 06520-8029. E-mail: ali.abu-alfa@yale.edu*



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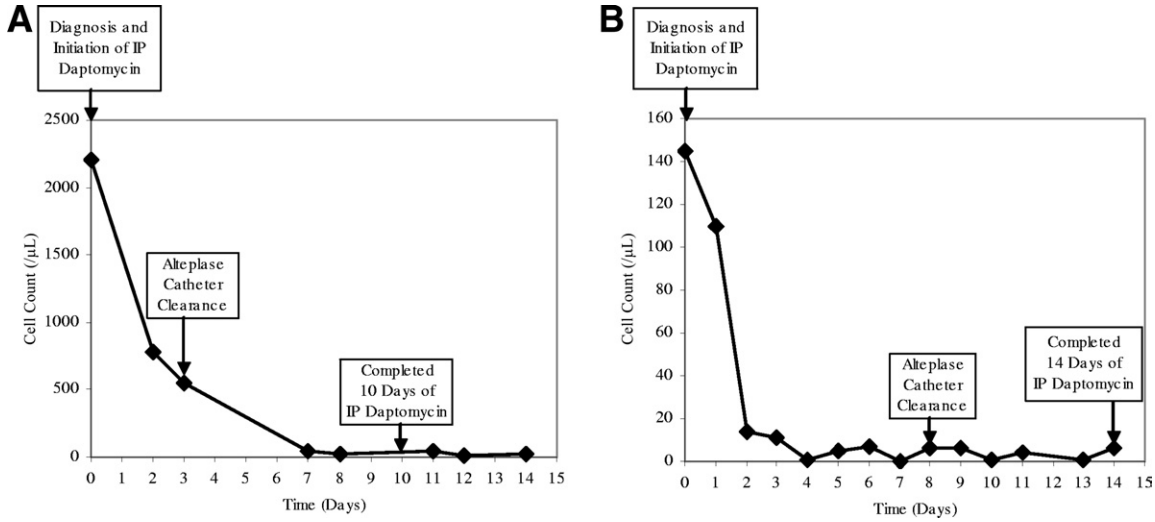


**Figure 1.** Peritoneal cell count response to intraperitoneal (IP) daptomycin therapy for (A) patient 1 and (B) patient 2.

negative *Staphylococcus* species peritonitis 3 months prior, and culture-negative peritonitis 1 month prior treated empirically with IP vancomycin, ceftazidime, and gentamicin, then oral ciprofloxacin and IP vancomycin as an outpatient. Residual clearance was 1.6 mL/min 3 months before presentation.

The patient initially presented to the PD clinic with a 2-day history of mild abdominal pain and constipation. Dialysate, which was not cloudy, was sent from the clinic for culture. Her bowel regimen was intensified and she was empirically treated for presumed peritonitis with IP vancomycin and gentamicin. Five days later, cultures from the clinic subsequently grew vancomycin-resistant *E faecium* sensitive to daptomycin (MIC, 4 $\mu$g/mL) and gentamicin (MIC, $<$500 $\mu$g/mL). She was admitted to the hospital.

On presentation, the patient was afebrile, blood pressure was 128/90 mm Hg, and heart rate was 81 beats/min. Abdominal examination findings were significant for diffuse tenderness. There was no expressible pus, drainage, or erythema around the PD exit site. Initial dialysate cell count was 145 cells/$\mu$L (88% granulocytes). IP daptomycin and gentamicin therapy were initiated at 20 mg/L and 4 mg/L, respectively. Heparin, 500 units/L, was given continuously every 4 hours using 2-L manual exchanges of 1.5% and 2.5% dextrose solutions. On the day of admission, peritoneal cultures again grew vancomycin-resistant *E faecium*. Dialysate culture results after day 2 of IP daptomycin treatment were negative. By day 3, IP gentamicin therapy was discontinued because cell count (14 cells/$\mu$L) and abdominal examination findings had normalized (Fig 1). On day 8 of treatment, 8 mg of alteplase was instilled into the PD catheter and flushed with 10 mL of normal saline. She was treated for a total of 14 days with IP daptomycin, with clearance of peritoneal cultures. The PD catheter was left in place. At the time of writing, the patient remains on APD therapy. The most recent culture results 7 months posttreatment are negative and cell count is normal (22 cells/$\mu$L).

## DISCUSSION

VRE was described first in the 1980s and has since become increasingly more prevalent, causing infections that include PD-associated peritonitis. Both patients described had multiple risk factors implicated in developing VRE infection, including recent hospitalization, VRE stool carriage, and exposure to broad-spectrum antibiotics, especially vancomycin.[2]

Treatment of patients with VRE peritonitis poses several challenges, including limited antimicrobial agents available. New agents with activity against VRE recently have been introduced, including linezolid, quinopristin/dalfopristin, and daptomycin. However, data about their efficacy, dosing regimens, and means of administration for patients with VRE peritonitis are lacking. Several case reports of PD-associated VRE peritonitis have been described.[3-8] Antimicrobial agents used in these cases included IV chloramphenicol, IV gentamicin, IV ampicillin, oral and IV linezolid, and IV and IP quinopristin/dalfopristin. One patient in the case series described by Troidle et al[4] was reported to have cleared VRE peritonitis with IP vancomycin and ceftazidime without catheter change or removal. This is surprising because enterococci are inherently resistant to cephalosporins. The investigators believe the MIC was lower than the vancomycin level achieved. All other surviving patients reported in