

## Risk Factors and Cause of Removal of Peritoneal Dialysis Catheter in Patients on Continuous Ambulatory Peritoneal Dialysis

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*In the present study, we examined the risk factors and causes for removal of the peritoneal dialysis (PD) catheter in patients on continuous ambulatory PD (CAPD). Data were collected from the records of patients who received CAPD therapy from 1995 to 2007 in the Department of Nephrology, Saitama Medical University. During that time, 473 patients were introduced onto CAPD therapy and the PD catheter was removed from 63 patients. Catheters were removed in 30 patients (47%) because of peritoneal infection, in 11 (17%) because of dialysis failure, in 8 (13%) because of neoplasm of the gastrointestinal tract, in 6 (10%) because of perforation of the gastrointestinal tract, in 2 (3%) because of laceration of PD catheter, and in 3 each (5%) because of transplantation and home hemodialysis therapy. Duration of CAPD was  $5.6 \pm 1.2$  years. In patients who experienced peritoneal infection, causative organisms were Staphylococcus (mainly methicillin-resistant *S. aureus*), Candida, Pseudomonas, and non tuberculous Mycobacterium. Failure to continue PD therapy related to dialysis deficiency. All patients were examined for encapsulating peritoneal sclerosis (EPS) by computed tomography (CT) enhanced using contrast material. In 9 cases in which the CT findings indicated EPS, treatment with oral prednisolone (20 mg daily) was started; the dose was then gradually reduced over 1 year. After removal of the PD catheter, no patient developed EPS. All removed catheters were examined using electron microscopy. The catheters from patients who experienced PD peritonitis revealed biofilm formation; however, no biofilm formation was found in PD catheters removed from patients without infection.*

*Despite appropriate antibiotic therapy, peritoneal infection remains the major cause of PD catheter removal. Biofilm formation might be an obstacle to PD continuation.*

### Key words

PD peritonitis, *Staphylococcus*, *Pseudomonas*, candidiasis

### Introduction

Removal of the catheter is one of the major factors in the technical failure of peritoneal dialysis (PD), even when dialysis is well performed. Previously, our group reported that the main cause of PD catheter removal was PD peritonitis (1). The incidence rate of PD peritonitis has declined substantially with the introduction of the flush-before-fill double-bag technique, and the emergence of improved connection systems (2). However, the rate of recurrent and relapsing peritonitis has gradually been increasing despite standard antibiotic therapy (3). Infectious episodes are linked not only to poor patient technique or a concomitant exit-site infection, but also to the emergence of infections caused by *Pseudomonas aeruginosa* and *Staphylococcus aureus* infection. Biologic material containing microorganisms and their associated exopolysaccharides, termed "biofilm," has been observed on the surface of virtually all types of implanted medical devices and prostheses including Tenckhoff catheters employed for PD (4).

It has been hypothesized that adherent biofilm on PD catheters may act as a nidus of infection, which, because of inherent antibiotic resistance, may be the underlying cause of treatment failure and subsequent relapsing infection (5). Biofilm bacteria can be visualized with electron microscopy (EM); and so, in the present study, we analyzed the cause of catheter

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removal in 63 patients, and we used EM to examine the catheters removed from 30 patients for various reasons.

### Patients and methods

From April 1995 to September 2003, all continuous ambulatory PD (CAPD) patients in our dialysis center whose PD catheters were removed for any reason were eligible for the study. Informed consent was obtained from each patient.

The decisions to remove PD catheters were made for a variety of reasons:

- change from PD to hemodialysis (HD);
- abdominal surgery, including resection of a neoplasm;
- recurrent or relapsing peritonitis;
- peritonitis resulting from infection with *Pseudomonas*, tuberculosis, or *Candida*; and
- transplantation.

A PD-related peritonitis was diagnosed when abdominal pain and cloudy PD fluid occurred with or without fever, and when the peritoneal white blood cell count was more than 100 cells per milliliter with more than 50% neutrophils. "Relapse" was defined as a peritonitis episode occurring within 4 weeks of therapy completion for a prior peritonitis episode with the same organism, or an episode occurring after one sterile episode. "Recurrence" was defined as a peritonitis episode occurring within 4 weeks of completion of therapy for a prior peritonitis episode with a different organism.

### Biochemical data evaluation

At the time of PD catheter removal, serum creatinine, blood urea nitrogen, total protein, serum albumin, serum electrolytes, and hematogram were measured.

### EM scanning

We used a Hitachi Electron Microscope S-4200 (Hitachi, Ibaraki, Japan) to carry out EM scanning for detection of biofilm.

### Statistical analysis

Results are expressed as mean  $\pm$  standard error of the mean. Statistical analyses were performed using the Student *t*-test, comparison of means, or the Mann-Whitney test for unpaired samples. Statistical significance was set at  $p < 0.05$ . All calculations were made

using the Statview 5.0 statistical software package (SAS Institute, Cary, NC, U.S.A.).

### Results

Table I shows the baseline characteristics of the patients. There were no significant differences between the groups.

### Bacteria isolated

Table II shows the profile of the bacteria isolated from the PD fluid of patients. There were 13 gram-positive and 8 gram-negative bacteria and 5 fungal isolates. Approximately 50% of isolates were gram-positive bacteria that caused relapsing or recurrent PD peritonitis.

### EM scanning

Figures 1 – 3 show representative scanning EM images of staphylococcal biofilm microcolonies, *C. albicans*, and *P. aeruginosa* on the outer surface of a peritoneal catheter.

### Discussion

In the present study, the major cause of PD catheter removal was PD peritonitis, followed by gastrointestinal neoplasm and perforation. At our center, the empirical treatment protocol for PD peritonitis (before the causative organism is identified), adheres to the guidelines issued by the International Society for Peritoneal Dialysis (6). The primary cure rate was around 60% – 70%, and the secondary cure rate was 80% – 90%. The decisions to remove the catheter were made when the causative organism was *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, or *P. aeruginosa*. These organisms are reported to form biofilm in the PD catheter (7). Currently, it is unclear whether biofilm is associated with PD peritonitis, especially the drug-resistant or relapsing and recurrent forms. Three studies examining a total of 37 PD catheters have reported varying amounts of different morphologic forms of biofilm on 80% – 100% of the devices studied (4,8,9). On the other hand, Verger *et al.* (10) reported that biofilm was detected on only 2 of 12 PD catheters.

In the present study, all catheters removed because of PD peritonitis showed biofilm on EM scanning; however, the catheters removed for other causes, such as gastrointestinal neoplasm or perforation did not demonstrate biofilm. These differences might be associated with the system and techniques in use

TABLE I Characteristics of peritoneal dialysis (PD) patients with or without infection

	Total	Reason for catheter removal	
		Noninfectious	Infectious
Patients (n)	63	36	27
Age (years)	56±4	57±5	55±8
Male sex [n (%)]	38 (60)	25 (70)	13 (48)
Diabetes mellitus [n (%)]	40 (63)	20 (56)	20 (74)
Duration of PD (years)	5.6±1.2	5.4±1.6	5.8±1.5

TABLE II Profile of bacteria isolated in peritoneal dialysate from patients with peritonitis

Bacterial isolate	Patients (n)
<i>Pseudomonas aeruginosa</i>	8
Methicillin-sensitive <i>Staphylococcus aureus</i>	5
Methicillin-resistant <i>Staphylococcus aureus</i>	8
Non tuberculous <i>Mycobacterium</i>	1
<i>Candida glabrata</i>	2
<i>Candida tropicalis</i>	2
<i>Candida parapsilosis</i>	1
TOTAL	27

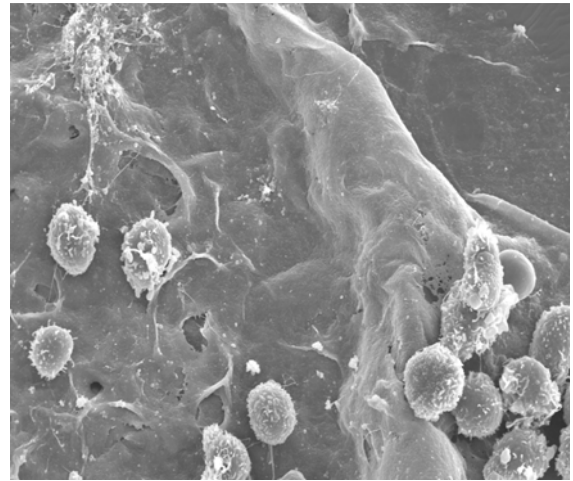


FIGURE 2 Representative scanning electron micrograph of *Candida albicans* biofilm microcolonies on the outer surface of a peritoneal catheter.

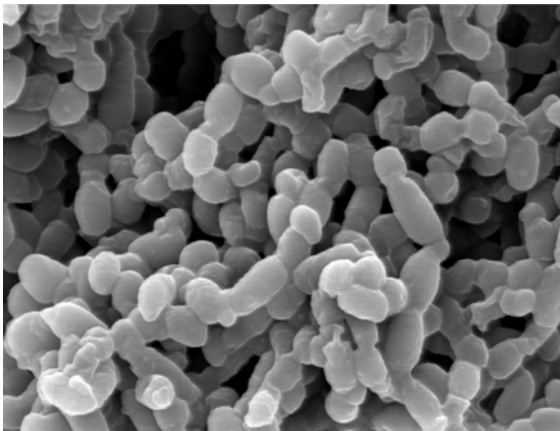


FIGURE 1 Representative scanning electron micrograph of staphylococcal biofilm microcolonies on the outer surface of a peritoneal catheter.

before the introduction of the flush-before-fill double-bag principle and improved connector systems (2). According to Dasgupta *et al.* (11) biofilm is found on all PD catheters, with or without infection (2). Peritonitis caused by the organisms *P. aeruginosa*, *Candida*, and *Staphylococcus* are well known to produce biofilm easily (5).

The mechanisms by which biofilm is formed remain unclear. Interestingly, Hoffman *et al.* (12) showed that, in *P. aeruginosa* and *Escherichia coli* infections, sub-inhibitory concentrations of aminoglycoside antibiotics induce biofilm formation, suggesting the hypothesis that *P. aeruginosa* had evolved adaptive responses to tobramycin before clinical use of antibiotics (formation of antibiotic-resistant biofilm). Although a combination treatment with aminoglycosides and cephalosporins is routinely used for PD peritonitis as initial therapy, removal of the PD catheter is recommended when *Pseudomonas* is isolated from PD fluid. Our current findings seem to support that recommendation.

Compared with the mechanisms of biofilm formation in *P. aeruginosa*, the biology of *Candida* biofilms is less well understood. However, biofilm formation by *C. albicans* has been reported to be similar to that

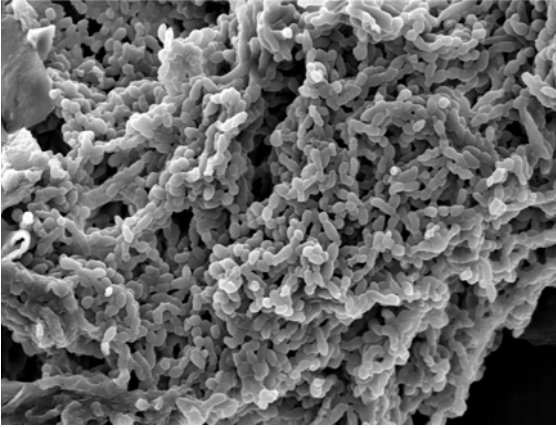


FIGURE 3 Representative scanning electron micrograph of *Pseudomonas aeruginosa* biofilm microcolonies on the outer surface of a peritoneal catheter.

of many other bacterial species, indicating a sharing of certain common basic steps. Dasgupta (4) proposed that biofilm formation occurs after initial contact of a free-floating bacteria with a foreign surface such as a catheter. After the initial attachment, planktonic bacteria adhere irreversibly to the foreign surface, generate molecular signaling, and proliferate to transform into bacterial microcolonies. This process forms the biofilms that are found in PD peritonitis.

### Conclusions

In the present study, biofilm formation was found on catheters removed because of antibiotic-resistant infection, but not on catheters removed for other causes, suggesting that biofilm formation on PD catheters does not always occur. However, when species such as *P. aeruginosa* and *Candida* are isolated, the catheter should be removed.

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