The CARI Guidelines – Caring for Australasians with Renal Impairment

Catheter removal, adjunct therapies and timing of reinsertion of peritoneal dialysis catheter after peritonitis

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GUIDELINES

The use of antibiotics with catheter replacement is superior to antibiotics with urokinase to treat peritoneal dialysis-associated peritonitis. (Level II evidence)

SUGGESTIONS FOR CLINICAL CARE
(Suggestions are based on Level III and IV evidence)

- The available evidence does not indicate the appropriate timing for reinsertion of a peritoneal dialysis (PD) catheter that has been removed because of peritonitis.
- Anecdotal recommendations range from simultaneous removal and reinsertion to waiting for a minimum of three weeks after removal before reinsertion.

IMPLEMENTATION AND AUDIT

No recommendation.

BACKGROUND

Anecdotal and retrospective reports suggest that removal of a PD catheter may be indicated in such situations as obstruction to flow, dislodgement, leakage, adjacent herniation, antibiotic-refractory infections (including peritonitis, tunnel infection and exit-site infection), spontaneous cuff extrusion, accidental shortening, bowel perforation, and discontinuation of PD (i.e. after recovery of renal function, after renal transplantation, or after transfer to haemodialysis).

Peritonitis that fails to resolve with antibiotic treatment alone often responds to removal of the PD catheter. These patients remain in renal failure and in need of dialysis. Peritoneal dialysis is one option and recommencement of it necessitates the reinsertion of a peritoneal catheter. Performance of that procedure may not be justified if some or all of such patients have a predictably unsatisfactory outcome. Those patients who are good candidates for having catheters reinserted in order to resume PD need to be identified, as does the optimal timing of when this procedure should be undertaken.

Use of urokinase seemed logical as adjunctive treatment for PD peritonitis with the aim of dissolving infected biofilm and removing obstructive fibrin clots from PD catheters. This guideline also assesses evidence regarding the role of urokinase.

The objectives of this guideline are to identify (in association with peritonitis) when a catheter should be removed, any adjunct therapies that may be beneficial to use and when is the
appropriate time to reinsert the catheter in those patients in whom the outcome is likely to be satisfactory.

SEARCH STRATEGY

**Databases searched:** MeSH terms and text words for peritoneal dialysis were combined with MeSH terms and text words for time factors, device removal, and catheterisation. The search was carried out in Medline (1950 – November Week 3, 2009). The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline.

**Date of searches:** 8 December 2009; update search 15 October 2010.

**WHAT IS THE EVIDENCE?**

No properly conducted prospective randomised controlled trials appear to have been performed that address the issue of when to remove a PD catheter. Many anecdotal and retrospective reports of single or small numbers of patients exist, as well as a few reports of larger retrospective studies.

**Common reasons for removal of catheter**

Sahu et al retrospectively studied 106 patients who had received a second catheter after removal of the first one [1]. They found that the reasons for removal of the first catheter were peritonitis (n=50), malfunction (n=20), leakage (n=11), exit-site or tunnel infection (n= 21), and failed kidney transplantation with resumption of PD (n=4). The Italian national paediatric experience, also assessed retrospectively, was similar [2].

Yata et al compared retrospectively the experience in a single centre of double-cuff swan-neck catheters with single-cuff straight catheters when used for PD in children [3]. They found that the straight catheters more frequently needed replacement due to leakage and infection but that the swan-neck catheters more frequently needed replacement because of dislocation.

Lu et al reported a prospective study of the outcomes of 148 laparoscopic PD catheter placements in 123 patients [4]. The principal reasons for catheter removal were technical problems (31%), receipt of a renal transplant (23%), recurrent peritonitis or exit-site infection (18%), and blockage (14%).

A Cochrane systematic review suggested that no difference exists between continuous ambulatory PD and automated PD as a predisposing factor in the removal of catheters [5].

**Removal of catheter for exit-site management**

Lui et al retrospectively reviewed the outcome of 37 patients who underwent simultaneous removal and reinsertion of their PD catheters for the treatment of *Pseudomonas aeruginosa* exit-site infections refractory to antibiotic treatment. They concluded that this approach is feasible as they found it to be successful in all patients in the short term and in over 90% of patients in the long term [6].

A review article in 2006 expressed the view that refractory exit-site infections can be managed with simultaneous catheter replacement [7].

**Catheter removal for peritonitis management**

Choi et al retrospectively compared the outcomes in PD patients who experienced 64 episodes of acute peritonitis who required catheter removal to eradicate the infection, with the outcomes in 426
episodes of peritonitis where the patient was treated with antibiotics alone. They found that increased age and duration of peritonitis were associated with the need for catheter removal and prolonged hospitalisation [7].

Troidle et al retrospectively reviewed the clinical charts of PD patients who experienced 1146 episodes of peritonitis, in 16% of which the peritoneal catheter was removed. Reasons for removal included unit protocol, failure of peritonitis to respond to antibiotics, recurrent peritonitis, exit-site infections, and tunnel infections. Twenty-three per cent of the patients whose catheters were removed died within 2 weeks of the onset of peritonitis, while only 22% of the patients whose catheters were removed were still alive and receiving PD treatment one year after the removal [8].

Hiremath and Biyani retrospectively reviewed the outcome of 16 episodes of Serratia spp.- associated peritonitis in 12 patients; in 4 of the episodes the catheter was removed. Technique survival in these patients was 68.8% [9].

An analysis of 565 episodes of peritonitis, of which 100 led to treatment failure (70 with removal of the catheter and 30 with death), demonstrated the superiority of dialysate white cell count on day 3 of peritonitis as a valuable predictor of outcome [10].

Piraino also concluded that fungal peritonitis is best treated with prompt catheter removal [7]. This view with regard to fungi reflected conclusions expressed in 2003 by Nannini et al [12] (based on experience with two cases) and Das et al [13]. The latter investigators retrospectively examined the outcome in 18 patients who developed fungal peritonitis; all 15 of those who survived had their catheters removed. Indhumathi et al [14] subsequently reached a similar conclusion when they retrospectively reviewed the outcomes in 30 episodes of fungal peritonitis in PD patients, as did Hooman et al [15] in a retrospective review of 16 paediatric episodes. The retrospectively assessed experience in all Australian PD patients reported by Miles et al [16] and the retrospective Dutch paediatric experience also reached similar conclusions [17].

Yerram et al prospectively analysed the survival of 131 pre-ternal Missouri swan-neck catheters implanted in 129 patients [18]. They found 60% catheter survival at 4 years, with all except two catheter losses being attributed to peritonitis (the others were due to malposition and a late-stage external leak).

Nodaira et al retrospectively examined the reasons for catheter removal in 63 patients who underwent this procedure out of a total of 473 patients in a continuous ambulatory peritoneal dialysis (CAPD) programme [19]. Forty-seven per cent were removed because of peritoneal infection, 17% because of dialysis failure, 13% because of gastrointestinal tract neoplasm, 5% because of transplantation, 5% because of transfer to home haemodialysis, and 3% because of laceration of the catheter.

A search of the Cochrane Central Register of Controlled Trials conducted by Wiggins et al [20] revealed little information about indications for removal of PD catheters or timing of removal of catheters in patients with peritonitis. It did, however, find evidence that for relapsing or persistent peritonitis, simultaneous catheter removal and replacement was superior to urokinase treatment in reducing treatment failure rates.

A retrospective review of Australian Registry data demonstrated that patients who have streptococcal peritonitis are less likely (10% versus 23%) to require catheter removal than are those with peritonitis due to other organisms [21]. In contrast, a similar study of patients with peritonitis due to Pseudomonas spp. peritonitis revealed that they were more likely (44% versus 20%) to require catheter removal [22].

A further retrospective study conducted by Yang et al reviewed 579 episodes of peritonitis treated in a tertiary-care referral hospital. They found that PD catheter loss as a consequence of peritonitis is related primarily to hypoalbuminaemia, longer duration of PD effluent leukocyte count remaining
above 100/μL, the aetiological source of the infection, and the organism causing the infection [23]. Peritonitis associated with concomitant tunnel or exit-site infections and abdominal catastrophes was more likely to proceed to PD catheter loss. The microbiological determinants of PD catheter loss included polymicrobial infections caused by Enterobacteriaceae as well as monomicrobial pseudomonal, anaerobic, and fungal infections.

**Role of urokinase in the management of peritonitis**

In one study, 7000 IU of urokinase infused into the obstructed PD catheters of 10 CAPD patients (4 of whom had peritonitis) restored flow without causing complications [24].

A literature review of largely anecdotal reports of streptokinase and urokinase treatment of PD peritonitis concluded that streptokinase had an unacceptably high adverse reaction rate and that catheter removal was a more effective therapy than thrombolysis. The authors proposed that clinicians should reserve urokinase treatment for antibiotic-compliant patients who develop two or more episodes of recurrent or persistent peritonitis and in whom dialysis catheter removal is contraindicated [25].

Williams et al performed a randomised controlled trial in which 17 patients received intraperitoneal urokinase (5000 IU) on the second and fourth days of appropriate antibiotic treatment for CAPD peritonitis; 14 patients underwent catheter replacement [26]. A further 6 patients who had a recurrence of peritonitis after urokinase treatment underwent catheter replacement. Peritonitis subsequently recurred in significantly more patients after urokinase treatment (41%) than after catheter replacement (5%).

**Recommencement of peritoneal dialysis after catheter removal**

Various reports exist of individual cases and of small and uncontrolled series in which patients recommenced PD following treatment of peritonitis. Reports also exist of two larger studies, those of Swartz et al and of Szeto et al [27, 28].

Swartz et al [27] described 59 patients who underwent simultaneous PD catheter removal and reinsetion. In 36 patients, this was because of persisting or recurring infection and in 23 it was due to mechanical complications. The procedure succeeded in 30 peritonitis patients, with ensuing catheter survival of between 5 months and more than 5 years. The procedure was most successful in patients with staphylococcal infections already controlled with antibiotics and in those without serious systemic or intra-peritoneal complications.

A retrospective review by Szeto et al [28] looked at a subgroup of 100 patients who failed to respond to standard antibiotic treatment for PD peritonitis; peritoneal sclerosis and bowel adhesions prevented the resumption of PD. Patients had their catheters removed and continued antibiotics for a further 2 weeks, and had the catheters replaced 4 to 18 weeks later. Only one third of those who had the catheter reinserted were still receiving PD 24 months later, albeit often with impaired ultrafiltration (88%).

Cox et al [29] retrospectively reviewed 556 patients on PD, of whom 106 had their catheters removed for peritonitis and of these, 42 underwent catheter reinsertion. The outcome for technique survival in these was 69% at 3 months and 55% at 20 ± 7.3 months. The patients most likely to fail after restarting PD were those of greatest PD vintage.

**Use of adjunct therapies: urokinase**

Based on the published studies, the routine use of urokinase in the management of PD peritonitis cannot be recommended.
A prospective randomised trial of 80 PD patients (40 in each group) that compared treatment with antibiotics and intraperitoneal urokinase 5000 IU against treatment with antibiotics alone showed no statistically significant difference in outcomes between the two treatment groups. Outcomes included duration of peritonitis, severity of symptoms and signs of peritonitis, and peritonitis recurrence or relapse rate [30].

A prospective randomised trial compared intraperitoneal urokinase 60,000 IU with placebo in 88 CAPD patients with bacterial peritonitis due to organisms resistant to initial empirical intraperitoneal antibiotics. All patients also received antibiotics to which their organisms were susceptible. The duration of necessary hospitalisation did not differ significantly between the two groups [31].


A 2008 Cochrane review [20] investigated the treatment of peritonitis in PD patients. They identified one study of relapsing or persistent peritonitis in which simultaneous catheter removal and replacement was superior to urokinase at reducing treatment failure rates [33].

**SUMMARY OF THE EVIDENCE**

Evidence relating to indications for the removal of PD catheters relies largely upon anecdotal and retrospective reports. The only randomised controlled trial comparing the use of antibiotics plus urokinase against antibiotics plus catheter replacement favoured the latter approach [26].

**Removal of catheter and management of exit site**

The small amount of retrospective evidence available suggests that simultaneous removal and replacement of a catheter can lead to acceptable results.

**Removal of catheter and timing of reinsertion**

Retrospective reports fail to provide any clear guidance regarding the most appropriate timing for reinsertion.

**WHAT DO THE OTHER GUIDELINES SAY?**

**Kidney Disease Outcomes Quality Initiative:** No recommendation.
**UK Renal Association:** No recommendation.
**Canadian Society of Nephrology:** No recommendation.
**European Renal Best Practice Guidelines (2005):**
Guideline 3K: Catheter removal for exit site infection should be considered (i) when a peritonitis episode with the same microorganism is present; (ii) if antibiotic treatment is unsuccessful; and (iii) in the case of recurrent exit site infections with the same organisms. (Evidence level C) [34]

Guideline 3L: Mechanical complications, such as hernias, leakage and obstruction, should be managed according to the recommendations of the International Society for Peritoneal Dialysis. (Evidence level C)

Simultaneous catheter removal and insertion of a new catheter can be done in peritonitis with a tunnel infection and in cases of recurrent peritonitis, both caused by Gram-positive microorganisms. The dialysate leukocyte count should be <100/mm³ before replacement. It is not recommended in the presence of peritonitis with ongoing inflammation, an active infection, Gram-negative or fungal organisms, or when evidence of intra-abdominal adhesions is present. It is
advisable to use antibiotic coverage during catheter removal and reinsertion if it is being done for infectious reasons such as relapsing or recurrent peritonitis.

**International Society for Peritoneal Dialysis Guidelines 2010** [35]

**Refractory peritonitis**

Refractory peritonitis, defined as failure of the effluent to clear after 5 days of appropriate antibiotics, should be managed by removal of the catheter to protect the peritoneal membrane for future use (Evidence).

**Indications for Catheter Removal for Peritoneal Dialysis-Related Infections**

- Refractory peritonitis
- Relapsing peritonitis
- Refractory exit-site and tunnel infection
- Fungal peritonitis
- Catheter removal may also be considered for
  - Repeat peritonitis
  - Mycobacterial peritonitis
  - Multiple enteric organisms

Treatments of relapsing, recurrent, or repeat peritonitis represent distinct clinical entities that portend a worse outcome (particularly for recurrent peritonitis). Stronger consideration should be given to timely catheter removal (Opinion).

Coagulase-negative staphylococcal peritonitis, including *S. epidermidis*, is due primarily to touch contamination, is generally a mild form of peritonitis, and responds readily to antibiotic therapy but can sometimes lead to relapsing peritonitis due to biofilm involvement. In such circumstances, catheter replacement is advised (Evidence).

**Staphylococcus aureus** causes severe peritonitis. Although it may be due to touch contamination, it is often due to catheter infection. Staphylococcal peritonitis with concurrent exit-site or tunnel infection is unlikely to respond to antibiotic therapy without catheter removal (Evidence).

**Pseudomonas aeruginosa** peritonitis, similar to *S. aureus* peritonitis, is often related to a catheter infection and in such cases catheter removal will be required. Two antibiotics should always be used to treat *P. aeruginosa* peritonitis (Evidence).

Fungal peritonitis is a serious complication and should be strongly suspected after recent antibiotic treatment for bacterial peritonitis. Catheter removal is indicated immediately after fungi are identified by microscopy or culture (Evidence).

The Committee recommends removing the catheter for relapsing peritonitis, refractory peritonitis, fungal peritonitis, and refractory catheter infections. The focus should always be on preservation of the peritoneum rather than on saving the peritoneal catheter (Opinion).

**Catheter removal and reinsertion for peritoneal infection**

Timely replacement of the catheter for refractory exit-site infections can prevent peritonitis, a far better approach than waiting until the patient has the more serious infection. This approach has the added advantage of permitting simultaneous replacement, thus avoiding prolonged periods on hemodialysis.

Catheter replacement as a single procedure can also be done for relapsing peritonitis if the effluent can first be cleared. This procedure should be done under antibiotic coverage. For refractory peritonitis and fungal peritonitis, simultaneous catheter replacement is not possible. The optimal time period between catheter removal for infection and reinsertion of a new catheter is not known. Empirically, a minimum period of 2-3 weeks between catheter removal and reinsertion of a new catheter is recommended, although some would recommend later reinsertion in cases of fungal peritonitis.
SUGGESTIONS FOR FUTURE RESEARCH

1. A prospective, possibly multicentre trial could investigate the reasons for and outcome after catheter removal in a cohort of PD patients.
2. Establish a registry of patients who have had PD catheters reinserted and record their outcomes.
3. A trial could be established to compare outcomes when catheters are reinserted at different time delays after removal.

CONFLICT OF INTEREST

Charles George has no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by CARI.
REFERENCES


## Table 1. Characteristics of included studies

<table>
<thead>
<tr>
<th>Study ID (author, year)</th>
<th>N</th>
<th>Study Design</th>
<th>Setting</th>
<th>Participants</th>
<th>Intervention (experimental group)</th>
<th>Intervention (control group)</th>
<th>Follow up (months)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gadallah et al 2000</td>
<td>80</td>
<td>Randomised controlled trial</td>
<td>UK</td>
<td>PD patients who developed a first episode of peritonitis</td>
<td>Urokinase 6000 IU diluted in 2.5 mL of normal saline, 4h dwell time</td>
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<td>Tong et al 2005</td>
<td>88</td>
<td>Randomised controlled trial</td>
<td>China</td>
<td>CAPD patients with bacterial peritonitis resistant to empirical antibiotics</td>
<td>Placebo</td>
<td>Urokinase 60000 IU IP diluted in 20 mL saline</td>
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<tr>
<td>Williams et al 1989</td>
<td>37</td>
<td>Randomised controlled trial</td>
<td>UK, multicentre</td>
<td>CAPD patients with recurrent peritonitis</td>
<td>Simultaneous catheter removal and replacement</td>
<td>Urokinase 5000 IU in 2 mL saline into the Tenckhoff catheter, 2h dwell, repeated day 2 and 4</td>
<td>3-12</td>
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</table>
**Table 2. Quality of randomised trials**

<table>
<thead>
<tr>
<th>Study ID (author, year)</th>
<th>Method of allocation concealment *</th>
<th>Blinding</th>
<th>Intention-to-treat analysis †</th>
<th>Loss to follow up (%)</th>
<th>Comments ‡</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(participants)</td>
<td>(investigators)</td>
<td>(outcome assessors)</td>
<td></td>
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<tr>
<td>Gadallah et al 2000</td>
<td>Inadequate</td>
<td>No</td>
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<tr>
<td>Tong et al 2005</td>
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<td>Yes</td>
<td>Yes</td>
<td>Not stated</td>
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<tr>
<td>Williams et al 1989</td>
<td>Unclear</td>
<td>No</td>
<td>No</td>
<td>Not stated</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Choose between: central; third party (e.g. pharmacy); sequentially labelled opaque sealed envelopes; alternation; not specified. † Choose between: yes; no; unclear. ‡ Quality score – “How successfully do you think the study minimised bias?” Choose between: very well (+); okay (Ø); poorly (-).

**Table 3. Results and quality rating for dichotomous outcomes**

<table>
<thead>
<tr>
<th>Study ID (author, year)</th>
<th>Outcomes</th>
<th>Intervention group (number of patients with events/ number of patients exposed)</th>
<th>Control group (number of patients with events/ number of patients not exposed)</th>
<th>Relative risk (RR) [95% CI]</th>
<th>Risk difference (RD) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Williams et al 1989</td>
<td>Treatment failure</td>
<td>12/17</td>
<td>6/20</td>
<td>2.35 [95%CI: 1.13, 4.91]</td>
<td>0.41 (95%CI: 0.11, 0.70)</td>
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<td>Tong et al 2005</td>
<td>Treatment failure</td>
<td>17/44</td>
<td>22/44</td>
<td>0.77 [0.48, 1.24]</td>
<td>-0.11 (95%CI: -0.32, 0.09)</td>
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<td>Tong et al 2005</td>
<td>Death</td>
<td>3/44</td>
<td>3/44</td>
<td>Not estimable</td>
<td>0.00 (95%CI: -0.11, 0.11)</td>
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