GUIDELINES

a. Patients receiving automated peritoneal dialysis (APD) treatment report significantly more time for work, family and social activities (Level II evidence; single good quality RCT, clinically relevant outcome, strong precise effect). APD should be prescribed in preference to continuous ambulatory peritoneal dialysis (CAPD) for patients in whom minimising the time spent performing peritoneal dialysis (PD) is an important consideration (e.g. workers, school pupils, students, carers of elderly or debilitated patients).

b. APD treatment is associated with lower rates of peritonitis, overall hospital admissions and hospital admissions for dialysis-related problems (Level II evidence; single small RCT of questionable quality, clinically relevant outcome, strong but inconsistent effect).

c. APD does not enhance peritoneal ultrafiltration in PD patients with high and high-average transport status (Level II evidence; single, underpowered good quality RCT, clinically relevant outcome, weak effect).

d. There is no convincing evidence that APD offers any other advantages or disadvantages over CAPD with respect to quality of life (other than addition in social time), small solute clearance, residual renal function (RRF) decline or mechanical complications (Level II evidence; two small underpowered, variable quality RCTs, clinically relevant outcomes, weak effects).

Suggestions for clinical care
(Suggestions are based on Level III and IV sources)

- Patients with low peritoneal membrane transport characteristics are less well suited to APD, particularly in the setting of poor RRF. In such patients, poorer small solute clearances may be achieved relative to CAPD (Level IV evidence; several prospective studies of variable quality, surrogate outcome measure, inconsistent effects).

- APD is associated with poorer sodium removal than CAPD (Level III evidence; several prospective studies of reasonable quality, surrogate outcome measure, consistent strong effect). Sodium removal can be enhanced in APD patients by the use of icodextrin, supplementary diurnal
exchanges and longer nocturnal dwell times (Level IV evidence; several prospective studies of variable quality, surrogate outcome measure, consistent effects).

The bulk of observational studies suggest that RRF decline is no different between CAPD and APD (Level III evidence; numerous prospective and retrospective cohort studies of variable quality, mostly consistent effect).

**Background**

Much research has been undertaken over the past 20 years to improve the quality of treatment provided by PD. One of the most promising advances has been the introduction of APD. In this section, APD refers to the use of a cycler for various regimens, including nightly intermittent peritoneal dialysis (NIPD), continuous cycling peritoneal dialysis (CCPD) and tidal peritoneal dialysis (TPD; nightly, NTPD, or continuous, CTPD). Intermittent peritoneal dialysis (IPD) two or three times/week is not recommended because satisfactory clearances are seldom achieved with this modality.

APD has been adopted increasingly by PD units worldwide, such that global use has increased from 9.7% of the world’s PD population in 1992 to 24% in 1997 (Diaz-Buxo 2000). The use of cyclers in North America has increased from 10% in 1990 to 25% in 1995, 33% in 1998, and 54% in 2000 (Hanigan et al 2001). In Australia, APD usage has increased from 4% in 1995 to 11% in 1998, 22% in 2000 and 34% in 2002. Of patients treated with APD in North America, 60% also receive at least one daytime exchange (Rocco et al 1997). APD is more expensive than CAPD, but is usually cheaper than transfer to in-centre haemodialysis.

Uncontrolled studies have purported a number of significant advantages of APD over CAPD, including reduced peritonitis rates, better ultrafiltration, improved quality of life, augmented small solute clearances and decreased complications (i.e. hernias, leaks, back pain, body image difficulties). However, these studies are potentially confounded by selection bias, as well as ascertainment, recall and informative censoring biases. Moreover, several observational studies have suggested that APD is also associated with increased cost and possibly an acceleration of RRF decline. APD has been recommended by the International Society of Peritoneal Dialysis ad hoc Committee on Ultrafiltration Management for the treatment of high transporters with impaired net ultrafiltration (Mujais et al 2000).

The objective of this guideline is to review the evidence for choosing APD versus CAPD.

**Search strategy**

**Databases searched:** Medline (1966 to September Week 3 2003). MeSH terms and text words for automated peritoneal dialysis (APD) were combined with MeSH terms and text words for continuous ambulatory peritoneal dialysis (CAPD). The results were then combined with the Cochrane highly sensitive search strategy for randomised controlled trials. The Cochrane Renal Group Specialised Register of
randomised controlled trials was also searched for relevant trials not indexed in Medline.

**Date of searches:**  1 October 2003.

**What is the evidence?**

**Randomised prospective studies**

There have been 2 small, randomised controlled trials (RCTs) of APD versus CAPD (Bro et al 1999, de Fijter et al 1994).

De Fijter et al (1994) reported the results of a prospective, open-label, single centre, randomised study of CCPD (n = 41) versus CAPD (n = 41). The principal findings of this study were that CCPD was associated with a marked reduction in peritonitis rates (0.51 versus 0.94 episodes per patient-year, \(p = 0.03\)), overall hospital admissions (0.6 versus 1.0 admissions per patient-year, \(p = 0.02\)) and hospital admissions for dialysis-related problems (0.2 versus 0.6 admissions per patient-year, \(p = 0.006\)). There were no differences in patient or technique survivals or small solute clearances over the median follow-up periods of 19.5 months for CCPD and 17.5 months for CAPD (although the studies were insufficiently powered for these outcomes). The limitations of the study were:

a. A suboptimal randomisation process (the dialysis modality was assigned by "a physician who was not involved in dialysis patient care and who was objective about the treatment methods being studied"). Neither allocation concealment nor the method of randomisation was described. It is also uncertain whether an intention to treat analysis was used (even though 9 patients switched between treatment arms).

b. A high drop-out rate, such that only 16 CCPD patients (61% drop-out) and 11 CAPD patients (73% dropout) remained at the end of the study. To overcome this problem, the investigators used a statistical method to replace observed mean ± SD with predicted mean ± SD for each of the follow-up time points. Nevertheless, informative censoring was a strong possibility.

c. The observed peritonitis rate in the CAPD group (0.94 episodes per patient-year) was considerably higher than what is generally reported in the literature for this modality (0.5 episodes per patient-year or lower).

Bro and coworkers (1999) conducted a prospective, open-label, randomised, multicentre controlled trial of APD (n = 17) versus CAPD (n = 17) in 34 prevalent PD patients who were high or high average transporters and had a \(\text{Kt/V} \geq 1.7/\text{week}\) and a total creatinine clearance \(\geq 50 \text{ L/week}/1.73 \text{ m}^2\) body surface area. Quality of life, the primary outcome measure, was assessed at baseline and at 6 months by the self-administered short form (SF)-36 generic health survey questionnaire supplemented with disease- and treatment-specific questions on 23 items relating to organ system function. No significant differences were found between APD and CAPD patients with respect to the changes in SF-36 scores from the start to the end
of the study. The only significant difference found was on the treatment-specific questionnaire, whereby APD patients reported significantly more time for work, family and social activities. With respect to secondary outcome measures, no significant differences were found between the 2 groups for net ultrafiltration (APD 1092±442 vs CAPD 1190 ± 343 mL/day), small solute clearances (Kt/V 2.3 ± 0.2 vs 2.3 ± 0.1, creatinine clearance 74±8 vs 76±6 L/week/1.73m²), residual renal clearance (3.0±0.7 vs 3.5 ± 0.7 mL/min), peritonitis rates (0.16 vs 0.31 episodes per patient-year) or mechanical complications. A cost analysis revealed that APD was 1.22 times (22.3%) more expensive than CAPD treatment. The limitations of this study were:

- Ascertained bias (only 29% of the total PD patient population in the 3 Danish PD units fulfilled the inclusion criteria and consented to participating in the trial).
- Type 2 statistical error (the authors calculated that a minimum of 55 patients would have been needed in each group to show a significant difference [p<0.05] with 50% power).
- An intention to treat analysis was not performed.
- The drop-out rate (56%) over 6 months was high. The mean age of patients who dropped out was higher in the APD group compared with the CAPD group, but the difference did not reach statistical significance. Similarly, patients remaining on APD were more likely to have received more years of education than those who remained on CAPD. Informative censoring was therefore likely to have been operative. Outcomes were not statistically adjusted for these differences in patient characteristics.

Non-randomised studies

Non-randomised studies have reported conflicting results as regards the various purported benefits and disadvantages of APD versus CAPD. All of these studies are seriously limited by the possibility that observed differences between APD and CAPD may have related primarily to patient selection rather than dialysis modality per se.

Peritonitis

Some studies have suggested that peritonitis rates are lower in CAPD compared with APD (Brunkhorst et al 1994, Diaz-Buxo 1989, Fine et al 2002, Holley et al 1990, Huang et al 2001, Rodriguez-Carmona et al 1999). However, these differences could potentially reflect patient selection, particularly since not all studies have observed a lower peritonitis occurrence in APD patients (D’Adamo et al 2003, Yishak et al 2001).

If peritonitis rates are reduced with APD, the most likely explanation is the smaller number of connections associated with this treatment. An important, though as yet unanswered, question is whether the increasing use of CCPD versus NIPD will be associated with an abrogation of this advantage (due to the additional daytime exchanges).
Ultrafiltration and sodium removal
There is no high-level clinical evidence that ultrafiltration is improved overall with APD compared with CAPD, but general clinical opinion and theoretical considerations dictate that better fluid removal is achieved in high transporters (Kumano et al 1993, Mujais et al 2000, Twardowski 1990). However, the only RCT of APD versus CAPD in high and high-average transporters actually demonstrated lower (but not statistically significant) net ultrafiltration volumes in patients treated with APD (1092±442 vs CAPD 1190±343 mL/day, respectively) (Bro et al 1999).

A prospective, multicentre, sequential study of CAPD, CCPD, TPD (50% exchange volume) and TPD (25% exchange volume) in 45 patients revealed that net daily ultrafiltration was actually slightly but not significantly higher with CAPD (1066 ± 626 mL/day) than with the other three APD techniques (939 ± 713, 700 ± 718 and 790 ± 637 mL/day, respectively) (Rodriguez et al 1998). The patients studied comprised the full spectrum of peritoneal membrane transport types, so it is possible that significantly better ultrafiltration may have been found if subgroup analyses were performed. Similarly, a case control study (Hufnagel et al 1999) found that median daily ultrafiltration volumes were slightly higher in patients receiving CAPD compared with APD (0.6 versus 0.53 L/day, p = ns), despite the prescription of significantly larger volumes of hypertonic dialysate in the latter. However, although patients were matched at baseline for demographic characteristics and RRF, they were not matched for peritoneal membrane transport characteristics, which were not reported.

Rodriguez-Carmona and Perez Fontan (2002) measured sodium removal and net ultrafiltration in 32 patients before and after changing from CAPD to APD therapy. Sodium removal decreased from 192 to 92 mmol/day (p = 0.02), while ultrafiltration volumes fell from 1310 to 1097 mL/day (not significant) despite the prescription of greater dialysate volumes (8 vs 11.9 L/day), more hypertonic glucose exchanges and more frequent icodextrin use. Subsequent multivariate analysis in the APD group demonstrated that the use of icodextrin, supplementary diurnal exchanges and longer nocturnal dwell times resulted in enhanced sodium removal. Ortega et al (2001) reported that sodium removal is lower in patients receiving APD compared with those receiving CAPD, leading to a tendency to poorer blood pressure control.

Struijk and Krediet (2000) have suggested that the short dwells used in APD impair sodium removal because of enhanced sodium sieving. Nevertheless, the International Society of Peritoneal Dialysis ad hoc Committee on Ultrafiltration Management in Peritoneal Dialysis (Mujais et al 2000) recommends APD for patients with a high transport profile and a net ultrafiltration less than 400 mL/4h following a 4.25% glucose dialysate exchange, although evidence supporting this guideline is lacking. Even if ultrafiltration in high transporters is enhanced by APD, a longitudinal study of 50 APD patients observed that high transporters still experienced a survival disadvantage relative to other transport categories (Hung et al 1999). Thus, the evidence justifying the prescription of APD to treat high transporters is weak.

Small solute clearances
There is some evidence to suggest that, for most patients (except possibly low and low-average transporters), better small solute clearances are achievable on certain APD regimens compared with CAPD (Blake et al 1996, Schaefer et al 1994). Rodriguez et al (1998) demonstrated in their prospective sequential study that all three APD regimens (i.e. CCPD, TPD 50% and TPD 25%) resulted in significantly
better peritoneal Kt/V (up to 34%) and C\textsubscript{Cr} (up to 24%) values than CAPD, even in low transporters. These were only achieved with greater total daily dialysate volumes (approx. 16 L versus 9 L) and the inclusion of a daytime exchange. CAPD patients were limited to 2 L exchanges and there are no controlled studies that directly compare clearances achieved with APD versus CAPD using higher fill volumes (i.e. 2.5 or 3 L). On the other hand, the 1996 peritoneal dialysis core indicators study showed that in a large, randomly selected sample of prevalent patients, the differences between CAPD and APD with respect to median weekly C\textsubscript{Cr} (58.9 versus 60.8 L/1.73 m\textsuperscript{2}) and Kt/V\textsubscript{urea} (1.9 versus 2.0) were very modest (Rocco et al 1997). Some of the apparent disparity in findings may be explained by the fact that the delivered clearance depends strongly on membrane transporter type. Care should be exercised with prescription of APD in low and low-average transporters, particularly if they are anuric, because delivered clearance may actually be reduced by increasing effective dialysate flow (Durand et al 1996). Nevertheless, APD produced superior creatinine clearances compared with CAPD in low transporters in the Spanish multicentre study (Rodriguez et al 1998).

**Quality of life**
APD (in the form of NIPD) has been suggested to offer a number of unproven psychosocial benefits over CAPD, which relate directly to fewer connections, the more frequent use of reduced fill volumes, and patient independence from dialysis during the daytime, particularly for workers, school pupils or carers of elderly or debilitated patients (McComb et al 1997, Wrenger et al 1996). De Wit and co-workers (2001) examined health-related quality of life in 37 APD and 59 CAPD patients from 16 different Dutch dialysis centres and found that APD patients enjoyed better mental health and tended to be less depressed and anxious than CAPD patients. However, these differences may have been explained by the fact that APD patients were treated at only 3 of the centres, while CAPD patients were selected from 13 other centres where APD was less available. Additional benefits attributed to APD include being empty of fluid during the day (possibly reducing back pain and body image difficulties) (Wrenger et al 1996) and performing APD at night in the supine position thereby resulting in reduced intra-abdominal pressures compared with the upright position in CAPD (Twardowski et al 1983). These potential benefits are partly negated by the necessity of most patients (except for high transporters) to perform at least one daytime exchange to meet small solute clearance targets (Blake et al 1996).

**Residual renal function**
Several early observational cohort studies have suggested that APD is associated with a more rapid acceleration of RRF decline compared with CAPD (Hiroshige et al 1996, Hufnagel et al 1999). In a 6-month prospective, non-randomised comparison study, the mean change in renal C\textsubscript{Cr} measurements for NIPD (n = 8), CCPD (n = 5) and CAPD (n = 5) were -0.29, -0.34 and 0.01 mL/minute/1.73 m\textsuperscript{2}/month, respectively (p value not quoted)(Hiroshige et al 1996). The study was limited by small numbers and selection bias.

A subsequent prospective, case-controlled study demonstrated that the monthly rate of residual renal C\textsubscript{Cr} decline was significantly higher in the APD group (CCPD n = 12, NIPD n = 6) compared with the CAPD group (n = 18) at 6 months (-0.28 versus -0.1 mL/minute/1.73 m\textsuperscript{2}, P = 0.04) and 12 months (-0.26 versus -0.13 mL/minute/1.73 m\textsuperscript{2}, P = 0.0005) (Hiroshige et al 1996). RRF decreased at the same rate in the NIPD and

Cost
Most costing studies report that APD is 8%–36% more expensive than CAPD (Bro et al 1999, Rodriguez et al 1998). These additional costs include those of the machine, the greater volumes of dialysate employed, and the special tubing and connection sets used.

Summary of the evidence
Two small RCTs of APD versus CAPD have been performed to date (collectively containing 29 patients who completed the studies on APD versus 24 patients on CAPD). Firm conclusions cannot be drawn, but one trial of questionable quality has demonstrated that APD treatment is associated with a significant reduction in peritonitis rates, overall hospital admissions and hospital admissions for dialysis-related problems. No other differences between APD and CAPD were demonstrated. The second trial involved high and high-average transporters followed for 6 months, was of better quality, and observed that APD patients reported significantly more time for work, family and social activities. However, this benefit came at a significantly (22%) increased financial cost. CAPD and APD patients did not differ with respect to other quality of life measures, net ultrafiltration, small solute clearances, residual renal clearance, peritonitis rates or mechanical complications.

What do the other guidelines say?
Kidney Disease Outcomes Quality Initiative: No recommendation.

British Renal Association: APD should be available as clinically indicated (high transporter status of the peritoneum, impaired filtration and psychosocial reasons forming 20–25% of the total CAPD population) and not constrained by financial considerations.

Canadian Society of Nephrology: Patients who are high transporters and who are having fluid overload problems on CAPD should be considered for transfer to APD. (Opinion)

European Best Practice Guidelines: No recommendation.

International Guidelines:

ISPD Ad Hoc Committee on Ultrafiltration Management in Peritoneal Dialysis: For patients with net UF less than 400 mL/4 hours and a high transport profile of small solute clearance, APD and icodextrin for the long dwell are the recommended therapeutic approaches.
Implementation and audit

ANZDATA should report outcome data such as patient survival, peritonitis rates and renal and peritoneal small solute clearances, by dialysis modality.

Suggestions for future research

1. A large, well-conducted, multicentre, RCT of APD versus CAPD is warranted to definitively determine the impact of APD on peritonitis rates, quality of life, RRF, fluid overload, technique survival and overall survival in PD patients.

2. A similar trial should also be performed to assess the role of APD in ameliorating fluid overload and extending technique and patient survivals in high transporters with ultrafiltration failure.
References


### Appendices

#### 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>Bro et al, 1999</td>
<td>34</td>
<td>Randomised open-label prospective controlled trial</td>
<td>3 Danish CAPD units</td>
<td>Adult patients receiving CAPD with high or high-average peritoneal transport characteristics</td>
<td>APD treatment</td>
<td>CAPD treatment</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>de Fijter et al, 1994</td>
<td>97</td>
<td>Randomised prospective controlled trial</td>
<td>University hospital</td>
<td>New patients with end stage renal failure needing PD</td>
<td>CAPD with a Y-connector</td>
<td>Cyclic peritoneal dialysis</td>
<td>24</td>
<td>OUT OF DATE</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 (participants)</th>
<th>Blinding (investigators)</th>
<th>Blinding (outcome assessors)</th>
<th>Intention-to-treat analysis</th>
<th>Loss to follow up (%)</th>
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</thead>
<tbody>
<tr>
<td>Bro et al, 1999</td>
<td>Sealed envelopes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>26.5 (9/34)</td>
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<tr>
<td>de Fijter et al, 1994</td>
<td>Third party</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Unclear</td>
<td>15.5 (82/97)</td>
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### Table 3 Results for dichotomous outcomes

<table>
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<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>Bro et al, 1999</td>
<td>Hospitalisation</td>
<td>3/13</td>
<td>5/12</td>
<td>0.55 (95%CI: 0.17, 1.83)</td>
<td>-0.19 (95%CI: -0.55, 0.18)</td>
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<td></td>
<td>Peritonitis (1 or more episodes)</td>
<td>2/13</td>
<td>1/12</td>
<td>1.85 (95%CI: 0.19, 17.84)</td>
<td>0.07 (95%CI: -0.18, -0.32)</td>
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<td>Exit-site infection</td>
<td>1/13</td>
<td>1/12</td>
<td>0.92 (95%CI: 0.06, 13.18)</td>
<td>-0.01 (95%CI: -0.22, -0.21)</td>
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<td>Tunnel infection (1 or more episodes)</td>
<td>0/13</td>
<td>1/12</td>
<td>0.31 (95%CI: 0.01, 6.94)</td>
<td>-0.08 (95%CI: -0.28, -0.12)</td>
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<td>Hernia</td>
<td>0/13</td>
<td>1/12</td>
<td>0.31 (95%CI: 0.01, 6.94)</td>
<td>-0.08 (95%CI: -0.28, -0.12)</td>
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<td>Over-hydration</td>
<td>0/13</td>
<td>2/12</td>
<td>0.19 (95%CI: 0.10, 3.52)</td>
<td>-0.17 (95%CI: -0.40, 0.07)</td>
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<td>de Fijter et al, 1994</td>
<td>Mortality</td>
<td>2/41</td>
<td>4/41</td>
<td>0.50 (95%CI: 0.10, 2.58)</td>
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<td>Peritonitis (1 or more episodes)</td>
<td>6/41</td>
<td>2/41</td>
<td>3.00 (95%CI: 0.64, 14.00)</td>
<td>0.10 (95%CI: -0.03, 0.22)</td>
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