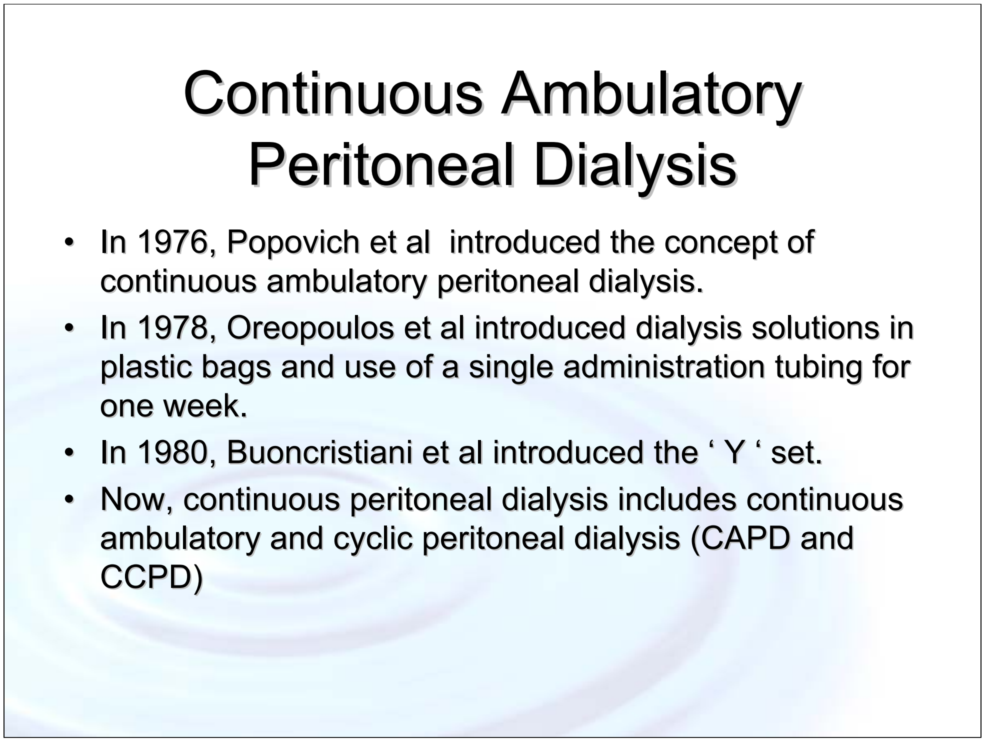
Peritoneal Dialysis Prescription and Modalities

Maria V. DeVita, M.D.
Associate Director Nephrology Lenox Hill Hospital Clinical
Associate Professor of Medicine NYU School of Medicine
Meghana Gaiki, M.D.
Fellow, Division of Nephrology, Lenox Hill Hospital
Emmanuelle Gilles, M.D.
Fellow, Division of Nephrology, Lenox Hill Hospital

Goals and Objectives

- Introduction to the different modalities of Peritoneal Dialysis (PD).
- Clinical implication of Peritoneal Equilibration Test (PET).
- Chronic Peritoneal Dialysis Prescription.
- Automated versus Ambulatory Peritoneal Dialysis in terms of –
  - Mortality
  - Technique survival
  - Impact on Residual Renal Function(RRF)
  - Volume and blood pressure control

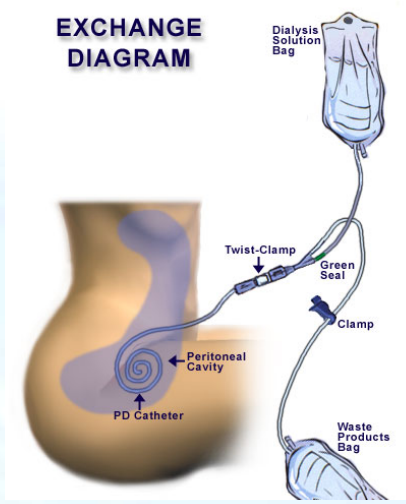


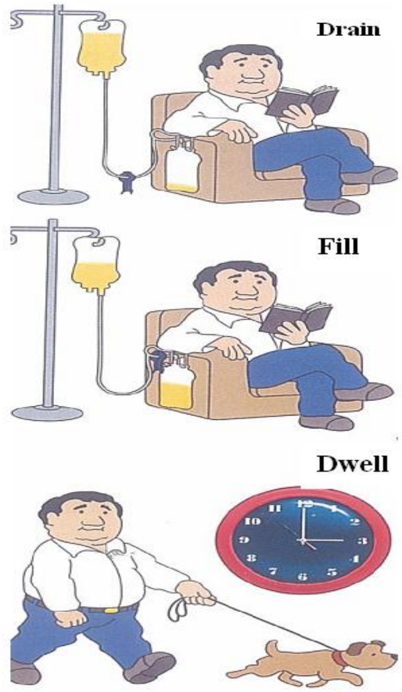
Two litres of standard hypertonic dialysate fluid are infused peritoneally and allowed to equilibrate for five hours while the patient conducts his normal activities.

The high peritoneal infection rate due to frequent openings in the dialysate delivery circuit and technical burden were the major drawbacks.

This new approach decreased the number of daily connections and disconnections- and limited the peritonitis episodes.

CAPD


EXCHANGE DIAGRAM
Dialysis Solution Bag
Twist-Clamp
Green Seal
Clamp
Peritoneal Cavity
PD Catheter
Waste Products Bag


Drain
Fill
Dwell

Automated Peritoneal Dialysis

Brenner and Rector's The Kidney, 8th edition, 2008

- APD uses a cycler/machine to perform the exchanges.
- For chronic renal failure, APD is traditionally divided into-
  - Continuous cycling peritoneal dialysis/CCPD
  - Nocturnal intermittent peritoneal dialysis/ NIPD.
  - Tidal peritoneal dialysis/ TPD
  - Hybrid Systems.

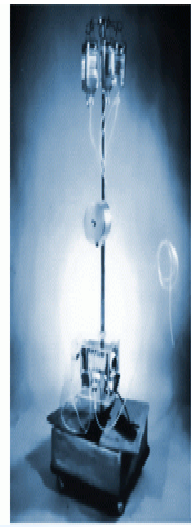
(exchanges done by the machine at night time and the pt carries the PD solution in the cavity all day)- CCPD

(exchanges done by the machine at night time and the pt remains dry all day.)- NIPD

APD has greatly increased in popularity in the past decade and is now used more than CAPD in the United States. Its appeal is that it frees up the daytime from PD procedures for patients and their caregivers. It also has the capacity to deliver more clearance and remove more fluid.

The First Cyclers





1962- Developed by Boen

The first automated peritoneal delivery system

S.T. Boen, C.M. Mion, F.T. Curtis and G. Shilipetar developed an automated device to do peritoneal dialysis at home. It utilized a 40-liter bottle that was filled and sterilized at the University of Washington. The bottles were delivered to the patient's home and returned to the hospital after use.

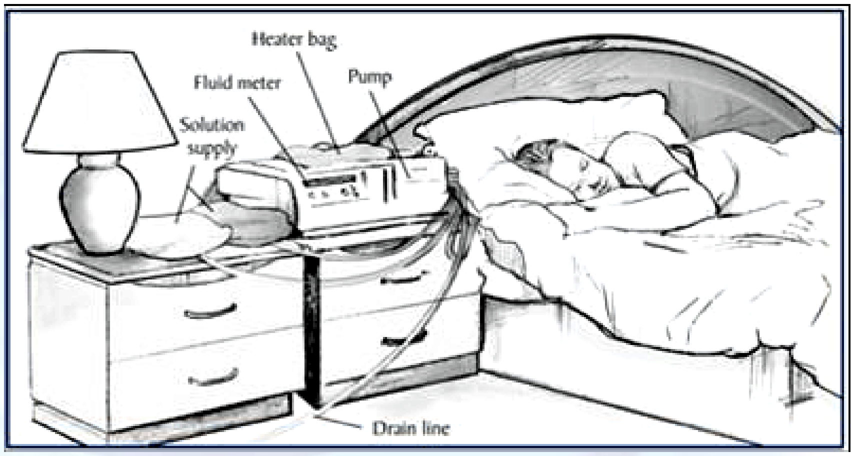
A cam cycler timer was used to meter the peritoneal fluid into and out of the peritoneal cavity. A heater plate heated the solution to body temperature and the effluent from the peritoneum was measured.

Fred Boen, MD, used the "repeated puncture" method for access. This required that a physician go to the patient's home and surgically place a 14F trocar in the patient's abdomen. The patient's helper would be trained to remove the trocar after the peritoneal dialysis treatment.

Boen ST, Mion CM, Curtis FK, Shilipetar G. Periodic peritoneal dialysis using the repeated puncture technique and an automatic cycling machine. *Trans Am Soc Artif Intern Organs*. 196; 10: 408-14.

In 1966 lasker introduced a simple gravity fed cycler. This device used sterile dialysate in 2 l glass bottles, plastic tubing for delivery and a plastic bag for collection of dialysate.This was the forerunner of all modern cyclers. This system could deliver variable amout of warm dialysate.

The New Cyclers



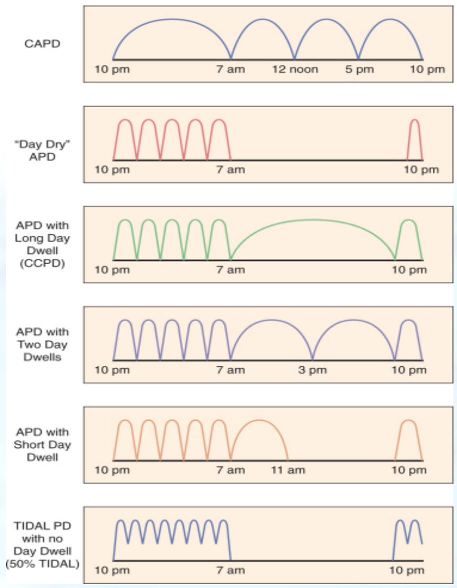
Automated PD's recent popularity also reflects the improved technology and design of modern cyclers, which are more compact, light, portable, reliable, and easier to operate than previous models.

Most cyclers now use hydraulic pumps rather than gravity to deliver and drain the PD solution. They have the facility to do tidal PD which involves deliberately allowing an incomplete drain of a proportion of the infused fluid (e.g., 50% or 80%) before refilling with the next cycle. This can be used to minimize down time with a poorly draining catheter or to avoid drain pain. Cyclers also allow the daytime solution to be delivered before disconnection and can be used for additional daytime exchanges in an approach that decreases cost and may increase convenience, compared with doing those exchanges with CAPD tubing.

The New Cyclers

Modalities of PD

Brenner and Rector's The Kidney, 8th edition, 2008



- Continuous cycled peritoneal dialysis-
  3 to 7 cycles of 1.5 to 2.5 L delivered over 9 hours at nighttime.
  Dwell times range from 45 minutes to 3 hours.
  Dwell left in at the end of the cycling period and drained out again before the next cycling period about 15 hours later.
- Nocturnal intermittent peritoneal dialysis or day dry APD
  - No day dwell because of good residual renal function or mechanical contraindications.
- High-dose APD or PD plus or APD with 2 day dwells
  - more than one day dwell, requires another exchange sometime during the day.
- APD with short day dwell-
  - leaves some of the day time dry to facilitate ultrafiltration or for comfort or mechanical reasons.
- Tidal PD-
  - Incomplete drain of a proportion of the infused fluid before refilling with the next cycle.
  - Used to minimize down time with a poorly draining catheter or to avoid drain pain.

Interpretation of the PET test

- High transport implies a structural or functional alteration of the peritoneum-
  - A larger effective peritoneal surface area
  - A higher intrinsic membrane permeability (for the rapid equilibration of small solutes including creatinine and urea).
- **High transporters** are prone to lose the osmotic gradient required for sustained ultrafiltration because of rapid absorption of glucose from the dialysate.
  - Subsequent decrease in ultrafiltration capacity
  - Tendency to have greater systemic exposure to glucose than low transporters do.

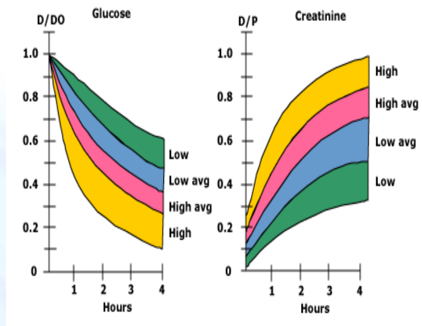


Figure-

Time-dependent changes during peritoneal dialysis in dialysate (D) concentration of glucose (left panel) or creatinine (right panel) as a proportion of original dialysate glucose concentration (DO) or plasma creatinine concentration (P), respectively. The absorption of glucose from the dialysate gradually lowers the D/DO ratio, while the diffusion of creatinine into the dialysate raises the D/P ratio. Slow transporters may be inadequately dialyzed due to diminished solute removal. Rapid transporters can achieve a D/P creatinine ratio above 0.8 and a D/DO glucose below 0.3 at four hours; they may be predisposed to malnutrition from increased amino acid losses in the dialysate and to decreased fluid removal due to absorption of glucose.

Data from Twardowski, TJ, Blood Purif 1988; 7:95.

Patients who are **rapid transporters** tend to equilibrate small solute concentrations between dialysate and blood early in a dwell time.

These patients also readily absorb glucose from the dialysate. Once the osmotic gradient is dissipated, ultrafiltration

Clinical implications of transporter type

- High transporters tend to have problems achieving ultrafiltration goals but are efficient with clearance.
- Low transporters tend to achieve ultrafiltration goals but have difficulty with clearance targets.
- Traditionally, high transporters were thought to do best on regimens that involve frequent short duration dwells (APD) maximizing ultrafiltration, and low transporters needed longer dwell times (CAPD) to maximize clearances.

Typical PD Regimens Required to Achieve Adequate Solute Clearances

Patient Body Surface Area (m^2)	Peritoneal Solute Transport Characteristics-D/P Creatinine at 4 Hours			
	Low (<0.5)	Low Average (0.5 to <0.65)	High Average (0.65-0.82)	High (>0.83)
<1.7	CAPD/APD 10-12.5 liters	CAPD/APD+ 10-12.5 liters	APD+* 10-12.5 liters	APD* 10-12.5 liters
1.7-2.0	CAPD+/APD 12.5-15 liters	APD+ 12.5-15 liters	APD+* 12.5-15 liters	APD+* 12.5-15 liters
>2.0	CAPD+,HD	APD+ 15-20 liters	APD+* 15-20 liters	APD+* 15-20 liters

Adapted From Comprehensive Clinical Nephrology- John Feehally, Jurgen Floege, Richard J. Johnson, 3rd edition, 2007.
+ an additional exchange , * use of icodextrin solution .

These are the typical PD regimens used to achieve adequate solute clearance according to patient size and membrane characteristics in anuric patients.

- •The total volume of dialysate fluid required increases with body size (2.5 to 3 L/ exchange).
- •APD using shorter overnight dwells is favored over CAPD, as solute transport increases.
- •Both CAPD and APD may have to be augmented by use of an additional exchange (for increased solute clearances or UF respectively).
- •The use of icodextrin solution for the long exchange will enhance both solute clearance and ultrafiltration.

Peritoneal Dialysis Prescription

Handbook of Dialysis, fourth edition, 2006, John T. Daugirdas, Peter G. Blake, Todd S. Ing

- Clearance Targets-

A consensus target Kt/V for all modalities of PD is 1.7 per week. KDOQI guidelines suggest that peritoneal and renal Kt/V can be added to achieve the target.

Greater residual renal function has repeatedly been shown to be associated with superior survival.

- Incremental versus maximal prescription-
  - In the incremental approach PD is used to make up the differences between residual renal clearance and targeted clearances.
  - In the maximal approach a sufficient prescription of PD is given to meet their targets with PD alone.
- Empirical versus Modeled approach-
  - With the empirical approach a reasonable prescription is chosen and prescription is adjusted to achieve clearance targets.
  - The computer program uses anthropometric data, results of PET test and RRF to predict clearances achieved with various prescriptions.

It has been difficult to show a similar effect for peritoneal clearance within the range of typical clinical use.

Incremental approach is less costly . It may decrease total glucose exposure and risk of peritonitis

It does require frequent monitoring of RRF to make sure that combined clearances do not fall below targets.

Factors determining clearance in peritoneal dialysis patients

Handbook of Dialysis, fourth edition, 2006, John T. Daugirdas, Peter G. Blake, Todd S. Ing

- Nonprescription factors-
  - Residual renal function
  - Body size
  - Peritoneal transport characteristics
- Prescription factors-
  - CAPD- frequency of exchanges, dwell volumes, tonicity of dialysis solution.
  - APD- Number of day dwells, volume of day dwells, tonicity of day dwells, time on cycler, cycle frequency, cycler dwell volumes and tonicity of cycler solution.

Typical CAPD Prescription

Handbook of Dialysis, fourth edition, 2006, John T. Daugirdas, Peter G. Blake, Todd S. Ing

1) **Dwell Volumes and Frequency of daily exchanges**

- 4 (number of exchanges) x 2L (dwell volumes) is the typical prescription.
- 4 x 2.5L in larger patients with small RRF or anuric patients who weigh >75 kg.
- 3 x 2L in smaller patients or in patients with good RRF.
- Problems of increasing dwell volumes- back pain, abdominal distension and even shortness of breath.
- Increasing frequency of dwells is less effective than increased volumes for improvement of creatinine clearance as equilibration curve for creatinine is rising 4 hours after the dwell. It is also more expensive and may interfere with patient’s lifestyle.

2) **Increasing tonicity of dialysis solution** increases both ultrafiltration and clearance but may lead to hyperglycemia, hyperlipidemia, obesity and long term peritoneal membrane damage.

A switch from 4x2l to 4x 2.5 l increases the Kt/V by 18 to 20%

In anuric patients, to achieve clearance targets it is usually necessary to use 2.5 L dwells in patients who weigh more than 75 kg.

Problems of increasing dwell volumes- back pain, abdominal distension and even shortness of breath. This can be minimized by introducing increased volumes at the time of initiation of PD before the patient gets used to smaller volumes.

Typical APD Prescription

Handbook of Dialysis, fourth edition, 2006, John T. Daugirdas, Peter G. Blake, Todd S. Ing

- **Number of day dwells-** Can start with NIPD if patient has good residual volume. Adding a day dwell increases Kt/V by 25%. In high transporters a long day dwell can result in net fluid absorption. This can be countered by shortening the day dwell.
- **Tonicity of day dwells**- Net fluid absorption occurring in day dwells can be countered by using icodextrin dialysis solutions.
- **Time on cycler** – 8 to 10 hrs. The longer the time the patient spends on the cycler the better the clearance.
- **Cycle frequency-** 3 to 5 cycles per 9 hour cycling session. Each cycle lasting 1.5 to 3 hrs. More frequent cycles increases clearance, but a greater proportion of the time is spent draining and filling. Some dialysis time is lost.
- **Cycler dwell volumes** - 2 to 2.5 L. As patients are supine in APD they can tolerate larger dwell volumes more easily. A typical starting volume is 10 to 15 l depending on the patient size.
- **Tonicity of cycler solution**- As with CAPD increasing tonicity increases ultrafiltration , but the same concerns about glucose related complications arise.

Factors taken into account before choosing PD modality

In the past

- Long term outcomes
  - Technique failure
  - Mortality
  - Volume and BP Control
- Residual Renal Function.
- Risk of peritonitis.
- Transporter Status.
- Patient preference.

Current thinking

- **Patient preference.**
- Transporter status?

Increasing use of APD

Mehrotra et al, Kidney Int 2009; 76,97-107

- In the 1980s and early 1990s APD was largely used to optimize volume status in high average and high transporters.
- With the advent of smaller, portable machines; APD use has increased due to physician and patient choice, irrespective of the transport type.
- Percentage of patients on PD using APD in different countries-
  - 59%: US (2007)
  - 60%: Belgium, Denmark and Finland 60%
  - 42%: Australia and New Zealand.

CAPD versus APD

Mehrotra et al, Kidney Int 2009; 76,97-107

- Since 1996, the 1 year mortality outcomes have improved for PD but remained the same for maintenance HD.
- Reasons
  - Decrease in infectious complications.
  - Publication of clinical practice guidelines that may improve prescription management.
  - Increased use of APD- Lower rates of peritonitis with APD.
- APD also associated with-
  - Lower daily sodium removal. (worse volume and BP control)
  - Rapid loss of residual renal function.
  - Higher protein losses with multiple night time exchanges.
  - More expensive

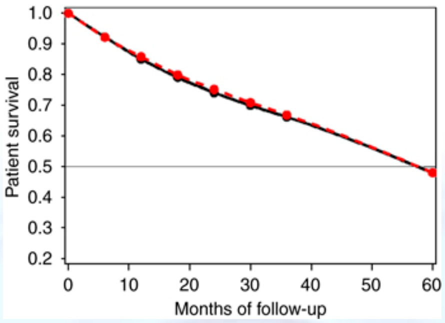
CAPD versus APD

Mehrotra et al, Kidney Int 2009:76,97-107

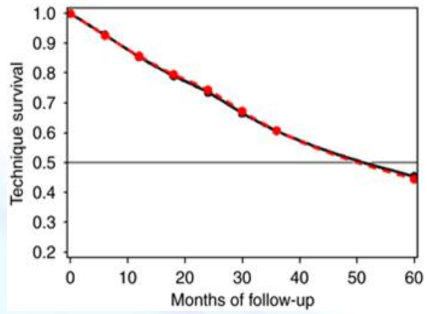
- These differences highlight the need to compare outcomes of CAPD and APD.
- Data from USRDS on 66,381 incident patients on chronic PD from 1996 to 2004 was used.
- The risk of death and technique failure between the two modalities was compared.
- Also wanted to study the impact of APD on the improved outcomes in PD.
- The adjusted median life expectancy improved by approximately 8 years from 1996–1998 to 1999-2001, irrespective of the modality of PD.

The outcomes of continuous ambulatory and automated peritoneal dialysis are similar

Mehrotra et al, Kidney Int 2009; 76,97-107



There were **no significant differences** in adjusted **mortality rates** in patients treated with **CAPD or APD** for virtually all the time periods examined



There were **no significant differences** in either time dependent or overall relative risk **for technique failure between CAPD and APD patients**

Conclusions

- There have been substantial reductions in the adjusted risk for death and technique failure among incident PD patients since 1996.
- The outcomes of CAPD and APD patients are remarkably similar and the improvement in PD outcomes cannot be attributed to a greater use of APD.
- Centers with a higher PD utilization had a significantly lower risk of technique failure and marginally lower risk of death.

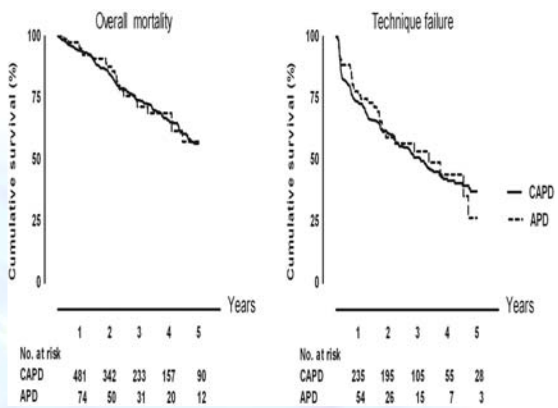
There are several strengths of this study.

First, the study included all incident patients in the United States over the 9-year period. This makes it the largest study to date that has looked into this question (*n*=66,381). Second, comparisons of CAPD and APD outcomes are often hampered on how to deal with patients who transfer between these two modalities- they resolved this by robust statistics.

NECOSAD Study Group

Michels WM et al
Clin J Am Soc Nephrol 2009; 4: 943-949

- ❖Netherlands Cooperative Study on the Adequacy of Dialysis.
- ❖ Prospective, Multicenter cohort of ESRD patients (562 on CAPD and 87 on APD)
- ❖Patient preference main reason to be on APD.
- ❖No short-term or long term effect of PD modality on overall mortality or technique failure
- ❖Findings similar to the ANZDATA registry.
- ❖Two large observational studies showed survival benefit with APD.
- ❖The choice to start APD versus CAPD should be based on factors such as quality of life, partner's preference or available resources.



Left: Kaplan-Meier curve of overall mortality on automated peritoneal dialysis compared with continuous ambulatory peritoneal dialysis. Right: Kaplan-Meier curve of pure technique failure on automated peritoneal dialysis compared with continuous ambulatory peritoneal dialysis. The numbers under the graphs show the number of patients at risk.

Short term- 1 yr after the start on dialysis.

In contrast to this study, the main analysis in the large cohort of the ANZDATA registry compared patients with at least one episode on APD with patients treated with CAPD only . Therefore in the ANZDATA study an effect of previous CAPD therapy cannot be excluded. For this reason the NECOSAD STUDY defined their groups at start of dialysis, ruling out any influence of previous dialysis modalities. Furthermore, since APD patients tend to switch to HD, while CAPD patients tend to switch to APD, in their technique failure analysis a switch to any other form of dialysis (including the other PD modality) was considered an event. In the ANZDATA registry switches to another PD modality were not considered as technique failure. Despite the differences in design between the two studies, results are similar.

Two large observational studies-The Mexican study had the longest follow-up (3 yr), but it was a retrospective single-center study in patients only treated with solutions and machines of one company . The registry study from the United States had a short follow-up of one year . In both studies adjustment for possible confounders was hampered by the quality of limited data at baseline.

Sodium Removal in Patients Undergoing CAPD and APD

Rodriguez-Carmona A et al, *Perit Dial Int* 2002; 22:705–713

- Study in three steps. Cross-sectional observational (Study A), and longitudinal interventional (Studies B and C).
  - Study A was a cross-sectional survey of Na removal in 63 patients on CAPD and 78 patients on APD.
  - Study B- studied Na removal in 32 patients before and after changing from CAPD to APD therapy.
  - Study C analyzed the impact on Na removal of introducing icodextrin for the long dwell in 16 patients undergoing CAPD or APD.
- Standard APD schedules are frequently associated with poor Na removal rates.
- For any degree of ultrafiltration, Na removal is better in CAPD than in APD.
- Icodextrin, supplementary diurnal exchanges, and longer nocturnal dwell times improve Na removal in APD.
- Patients on APD may have more frequent hypertension because of lower sodium removal.
  - Sodium sieving in the short duration dwells of APD.
  - Less ultrafiltration in the long duration day dwells.

Ana Rodríguez–Carmona and Miguel Pérez Fontán

Division of Nephrology, Hospital Juan Canalejo, A Coruña, Spain

Blood Pressure, Volume and Sodium Control in an Automated Peritoneal Dialysis Population.

Boudville NC et al, Perit Dial Int 2007; 27:537–543

- An observational cross-sectional study with 56 APD patients using icodextrin assessed sodium removal with APD and its association with BP and volume control.

- Mean total sodium removal was 102.9 ± 64.6 mmol/day. 68% had a sodium removal of >120 mmol/day.

- Total sodium removal correlated with total body water (TBW), extracellular water (ECW) and intracellular water (ICW).
- No significant correlation was found between sodium removal and the ECW/ICW ratio in those with sodium removal ≤120 mmol/day compared to those with sodium removal>120 mmol/day.

- Mean SBP 111.9 ± 18.2 mmHg and mean DBP 63.3 ±11.9 mmHg. Only 4 (7%) patients had SBP >140 mmHg and only 1 (2%) had DBP >90 mmHg.
- Blood pressure control was similar in the group of patients with sodium removal ≤120 mmol/day compared to those with >120 mmol/day.

Neil C. Boudville,[1] Peter Cordy,[2] Kristie Millman,[2] Laura Fairbairn,[2] Ajay Sharma,[2] Robert Lindsay,[2] and Peter G. Blake[2]
University of Western Australia,[1] Perth, WA, Australia; University of Western Ontario,[2] London, Ontario, Canada.

The incidence of hypertension in this hemodialysis population was 56%.

Impact of PD modality on residual renal function

Long term outcomes in automated peritoneal dialysis: Similar or better than in continuous ambulatory peritoneal dialysis?

Mehrotra R, *Perit Dial Int 2009;* 29(S2):111-114

- Faster decline of RRF in APD patients : four single-center observational studies (103 CAPD *and* 108 APD subjects in total)
- Numerous other studies have been unable to demonstrate a more rapid loss of RRF in APD patients (1141 CAPD *and* 484 APD subjects total). Three of those studies were large multicenter trials.
- There is probably **no difference in the rate of loss of RRF between CAPD and APD patients.**

Predictors of Loss of Residual Renal Function among New Dialysis Patients

Moist LM, *J Am Soc Nephrol* 2000; 11:556-564

- The Dialysis Morbidity and Mortality Study (DMMS) is a U.S. Renal Data System (USRDS) special study, including more than 20,000 randomly selected dialysis patients. (HD and PD)
- The study included 33 baseline variables for evaluation as possible independent predictors of residual renal function.
- Loss of residual renal function was defined as an estimated urine output <200 ml/24h at the time of follow-up (8 to 18 mo from initiation of dialysis).
- Patients receiving treatment with PD had a reduced risk of RRF loss when compared to HD-treated patients
- Factors associated with increased loss of RRF on PD-
  - Increasing duration of time on PD, higher eGFR at time of initiation of PD, female gender, Non-white race , presence of DM and CHF were all associated with loss of residual renal function.
- Lower risk of loss of RRF among ESRD patients on PD being treated with ACE inhibitors and/or calcium channel blockers.
- No significant difference in loss of RRF by PD modality type

The study includes four "waves" of data collection over 3 yr.

33 baseline variables-These included age, gender, race, etiology of ESRD (diabetes, hypertension, glomerulonephritis, other), data on pre-ESRD care including late referral to a nephrologist (defined as less than 4 mo before ESRD) and dietary consult pre-ESRD, a number of baseline comorbid conditions, laboratory values at study start including serum albumin, calcium, phosphate, total cholesterol, hematocrit, body mass index (BMI), baseline mean arterial pressure (2/3 DBP + 1/3 SBP) calculated from the average of three BP readings taken postdialysis at study start, dialysis modality (PD or HD), and a number of medications in use at the time of study start including ACE inhibitors, calcium channel blockers, diuretics, erythropoietin, ß-hydroxy-ß-methylglutaryl (HMG) CoA reductase inhibitors, nonsteroidal anti-inflammatory agents, and vitamin D.

Impact of PD modality on Peritonitis rates

Long term outcomes in automated peritoneal dialysis: Similar or better than in continuous ambulatory peritoneal dialysis? *Perit Dial **Int***
29(Supplement 2): 111-114 2009

- Single center nonr**and**omized observational studies showed that APD patients had significantly lower peritonitis rates than CAPD patients did .
- In a recent meta-analysis of data from two r**and**omized controlled trials APD patients had a 46% lower peritonitis rate compared to CAPD.
- Data seems to suggest that APD patients may experience lower peritonitis rates than CAPD patients do.
- Use of connection-assist devices to spike the cycler bags is probably important to maintain this advantage in favor of APD.
- Use of CAPD twin-bag systems **and** of exit-site antibiotic prophylaxis are far more important in lowering peritonitis rates in a PD program than is a greater use of APD.

PD modality and Technique Success

Mehrotra, *Perit Dial Int* 2009; 29(S2):111-114

- "Technique success" is defined as the proportion of patients who did not need to transfer to HD.
- Two randomized controlled clinical trials – underpowered.
- Three observational studies-
  - Two of these (one each from the United States and Mexico) have shown better technique success with APD.
  - The ANZDATA registry (Australia and New Zealand) was unable to demonstrate any difference in technique success.
- In the largest study with 40,869 patients , APD had a lower incidence of transfer to maintenance hemodialysis for a variety of reasons:
  - A lower chance of transfer secondary to infection
  - Catheter problem
  - Adequacy considerations
  - Other medical reasons
  - Psychosocial causes However,
  - **The advantage of higher technique success with APD was limited to the first year of therapy**

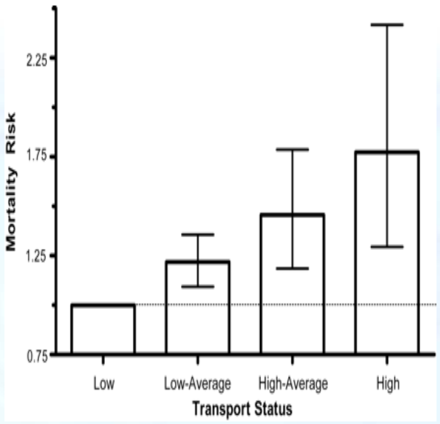
Definition of technique success excludes those who either died or underwent renal transplantation.

The evidence to date suggests that a greater use of APD may lower the number of PD patients that transfer to maintenance hemo**dialysis** early during the course of renal replacement therapy.

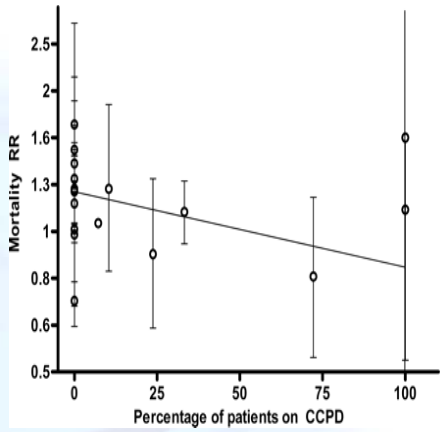
Meta-Analysis: Peritoneal Membrane Transport, Mortality, and Technique Failure in Peritoneal Dialysis

Brimble et al, *J* Am Soc Nephrol 2006 ;(17): 2591-2598.

Increasing peritoneal membrane solute transport rate was associated with an increasing risk for mortality with a trend to increased technique failure.



Use of CCPD seemed to offset some of this negative effect on mortality.

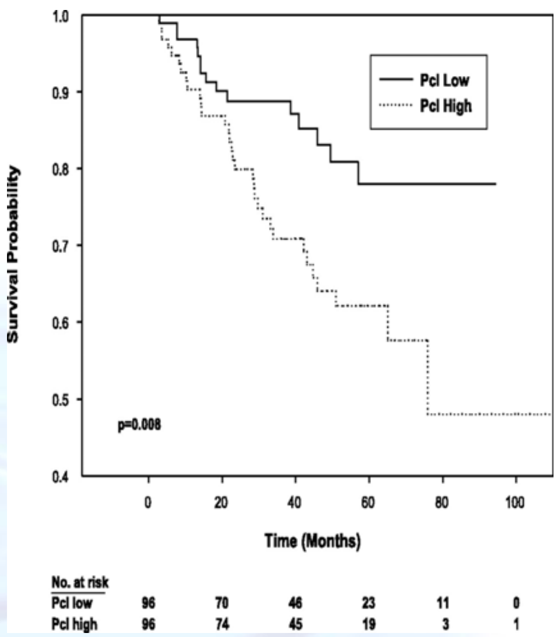


Peritoneal Protein Clearance and not Peritoneal Membrane Transport Status Predicts Survival

A prospective, single-center cohort study by Perl J et al in 192 PD patients suggested that increased peritoneal protein clearance (Pcl) at the start of PD therapy, age and comorbidity grade were predictors of death, independent of baseline small solute transport status.

Patients with baseline Pcl values were included in the study (192 /341).They had higher baseline small solute clearance and greater initial use of APD.

Even after inclusion of all 341 patients, transport status (D/Pcr) did not remain a predictor of survival on unadjusted analysis.



Perl J et al. CJASN 2009;4:1201-1206

Studies of continuous ambulatory PD (CAPD) patients have demonstrated baseline high transporter status to be an independent predictor of mortality and technique failure.

Emerging evidence suggests that high transporter status does not seem to be associated with reduced survival and technique failure.

High transporter status can be due to increased vascularity of the membrane associated with an increased anatomic membrane area or the result of inflammation and vascular injury. In both cases increased blood flow and increased effective small-pore area in contact with dialysate are responsible for the high transport status.

One way to distinguish these processes is to dissociate the small solute transport rate which is a function of the small-pore area, from peritoneal protein clearance (Pcl), which, depending on the protein size, will be a function of both small pores and large pores.

Problems Faced by High Transporters

Kam-Tao LI P et al, *Perit Dial Int* 2007; 27(S2): 148-152

- Ultra-Filtration problems
- Hypoalbuminemia
- Rapid satiety
- Marker for inflammation
  - Canusa Study
    - The relative risk of technique failure or death for high vs. low transporters was 4.
  - ANZDATA Registry subanalysis
    - High transport status is independently predictive of death-censored technique failure for patients on CAPD, but not for those on APD.
  - Meta-Analysis of 19 studies
    - High transporters were estimated to have a 77% higher risk for mortality after adjusting for age, diabetes & albumin.

Causes of hypoalbuminemia-Excessive protein losses in **peritoneal** effluent, relative hemodilution from suboptimal ultrafiltration, and rapid satiety and appetite suppression from a greater glucose load and the resultant poor protein intake .

Alternatively, **low**er albumin in **high transporters** could indicate a state of chronic inflammation . Dialysate protein losses correlated with serum concentrations of C-reactive protein (CRP) and suggested that **high** transport status is a marker for inflammation

Modeling Prescription for High Transport Status

MAXIMIZING THE SUCCESS OF PERITONEAL DIALYSIS IN HIGH TRANSPORTERS

Philip Kam-Tao Li and Kai Ming Chow , *Perit Dial Int* 2007:27(S2): 148-152

- Frequent, Shorter dwell times- APD
  - The osmotic gradient is dissipated after excessive dwell time. Short dwell times as used in APD maximize small solute clearance and net ultrafiltration.
  - Use of short-dwell therapy at night or NIPD keeps a dry abdomen during the day thus minimizing protein losses not attributable to glucose absorption.
- Use of icodextrin-containing PD solution to achieve volume control in high transporters.
- The association of survival disadvantage and high transport status is confined to patients on CAPD and does not appear to affect those on APD.

Those observations thus provide support for the idea that APD is more appropriate for patients with **high** transport status.

In a small cross-over clinical trial involving 11 **high** and **high**-average **transporters**, a change from CAPD to NIPD was accompanied by a substantial decline in serum CRP and significantly better ultrafiltration. Those beneficial effects tended to be reversed after a switch from NIPD to CCPD.

Taken at face value, that finding seems to accord reasonably well with the hypothesis that the reduction in contact time between dextrose dialysis fluid and the **peritoneal** membrane is the main advantage of APD. However, loss of the beneficial effect on systemic inflammation after a switch to CCPD from NIPD was not accompanied by a change in dialysate proinflammatory cytokine levels. An alternative explanation for the decrease in systemic inflammation may be the better volume control achieved with NIPD.

Automated Peritoneal Dialysis: A spanish Multicenter Study

Rodriguez A, *Nephrol Dial transplant* 1998; 13:2335-2340

Table 3. Peritoneal urea clearance (l/week) in relation to the transport category

	CAPD	CCPD	TPD (tidal 50%)	TPD (tidal 25%)
All patients	55.40±8.76	74.82±12.62	69.20±14.63	66.89±13.23
Kt/V	1.51±0.32	2.03±0.39	1.88±0.35	1.80±0.40
At night time		61.38±12.2	56.45±13.53	53.19±11.33
Transport category				
High	60.58±3.51	84.51±10.43	80.04±13.02	68.78±20.26
High–average	55.12±10.7	75.78±14.27	71.58±20.20	69.39±15.02
Low–average	53.78±8.29	71.55±10.79	67.40±9.34	72.07±5.52
Low	56.28±7.32	73.01±12.59	65.36±14.26	64.85±7.01

High *vs* low–average, $P<0.001$; high *vs* low, $P<0.01$; high–average *vs* low–average, $P<0.05$.

Table 4. Peritoneal creatinine clearance (l/week/1.73 m^2) in relation to the transport category

	CAPD	CCPD	TPD (tidal 50%)	TPD (tidal 25%)
All patients	42.80±9.95	52.19±11.11	51.31±13.35	49.17±11.83
At night time		40.80±11.09	39.94±12.88	37.22±10.57
Transport category				
High	61.53±4.04	66.44±8.35	69.09±20.98	66.75±22.46
High–average	45.35±10.71	53.71±9.67	53.69±7.05	51.08±6.7
Low–average	43.77±5.9	50.37±10.32	49.54±9.66	48.13±10.53
Low	32.77±9.16	44.67±8.49	40.31±10.11	41.37±7.94

High *vs* other categories, $P<0.001$; high–average *vs* low–average, $P<0.05$; high–average *vs* low, $P<0.001$; low–average *vs* low, $P<0.001$.

Rodriguez et al

This was a prospective sequential study with 45 patients from 9 services of nephrology in different hospitals in spain between 1/1994 and 12/1996.

The following therapeutic modalities were instituted for a period of 2 months- CAPD, CCPD, TPD with 50 % exchange volume and TPD with 25 % exchange volume.

Peritoneal urea clearance and kt/V and peritoneal creatinine clearance was significantly better with APD particularly CCPD compared to CAPD.

The urea and creatinine clearances were higher for high transporters compared to low transporters in all the modalities.

The clearances of urea and cr were higher in the APD modalities vs CAPD in the low transporters.

Low transporters technically have thought to do better on CAPD in terms of clearances (longer dwells help with better clearances in low transporters.)

But this study showed better clearances on APD with low transporters. In patients in the low and low- average category the objectives of adequacy are rarely achieved.

In the authors' opinion this increment in dialysis adequacy depended on the dialysis prescription rather than the transport status . CAPD involved 9 l exchanges /day and APD involved 35- 40 ml/kg as exchange vol with 1 hr as time on ccpd, overnight treatment involved 9 to 9.5 hrs and diurnal volumes were 25 to 30 ml/kg.

In this study there is evidence that transport status does not influence the differences among clearances and CCPD was more efficient than TPD and CAPD for all transport types.

Patient Preference

QUALITY OF LIFE IN AUTOMATED AND CONTINUOUS AMBULATORY PERITONEAL DIALYSIS. Michels et al.
Perit Dial Int. 2011 Mar;31(2):138-147

- Advantages of CAPD
  - Cheaper
  - Freedom from machine
  - Easier to be trained.
- Advantages of APD
  - More time available for work, family and social activities as most of the fluid exchanges are at night.

- In a recent study, Michels et al used the prospective cohort of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD) and showed **no differences in quality of life between patients starting on CAPD versus APD.**

Summary

- Thus all evidence so far seems to suggest that the **choice of the initial PD modality should be based on patient preference**, as neither modality has any advantage over the other in terms of survival advantage, preserving renal function, technique success, risk of peritonitis or blood pressure control.
- APD is associated with lower risk of transfer to maintainence hemodialysis early during the course of renal replacement.
- There is data suggesting that APD may have a survival advantage over CAPD in high transporters, but newer data suggests that the peritoneal protein clearance and not the peritoneal membrane transport status may predict survival outcomes.
- Choice of PD modality should mainly be based on Patient preferences.

APD is associated with a lower risk of transfer to maintenance hemodialysis early during the course of renal replacement.

Additional References

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Google.com-images

Question 1

- A 44yo African-American woman has CKD-stage 5 due to hypertension and diabetes mellitus. She is on a kidney transplant list, but has no living donor. She has decided to proceed with peritoneal dialysis but is concerned for her overall health and well-being. She wants to know if it is better to proceed with CAPD or APD. You advise her that:

- A. Patients who undergo CAPD are at a higher risk for death and technique failure than APD patients
- B. Patients who undergo CAPD are at a lower risk for death and technique failure than APD patients.
- C. Both CAPD and APD patients have a high risk for technique failure and transfer to hemodialysis.
- D. There is no difference in risk of death or technique failure in CAPD patients when compared to APD patients.

Correct Answer: D

Shown in Mehrotra et al. KI 2009 (slides 20 and 21) When analysis subdivided into earlier and more recent cohorts, no differences were found between the 2 PD techniques.

Question 2

- In the above patient, factors that will increase her rate of loss of residual renal function include all but:

- A. Gender
- B. Ethnicity
- C. Use of PD instead of HD
- D. Use of APD instead of CAPD

Correct Answer: C

Factors associated with an increased loss of residual renal function include female gender, non-white, history of diabetes, history of CHF. There is no effect of PD modality on rate of loss of residual renal function (e.g. CAPD and APD are equal). Patients on PD have a slower rate of change in RRF.