Antibiotics in Peritoneal Dialysis



Ali Roberts, PharmD
PGY1 Resident – Memorial Hospital
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Video Clip

Peritoneal Dialysis Video

Advantages of PD

1. **Preserves residual renal function better**
2. **May allow better blood pressure and volume control with cardiovascular benefits**
3. **May give better quality of life**
4. **Has less anemia and lower EPO doses**
5. **Lower risk of Hepatitis C**
6. **Cost advantages**
7. **Clinical outcomes comparable to HD, no difference in 2 year and 5 year mortality vs. HD (study NECOSAD)**
8. **Saves vascular access**
9. **Preferred for children**

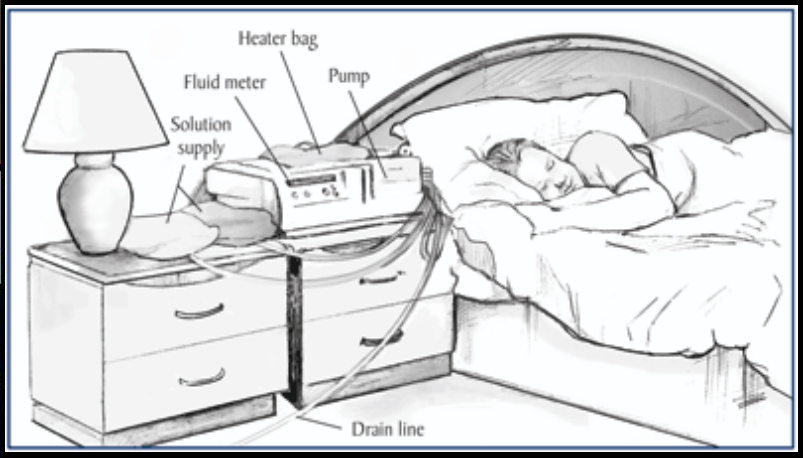
Types of PD

- Continuous or Intermittent
- Continuous ambulatory peritoneal dialysis (CAPD)
  - multiple exchanges during the day (usually three) followed by an overnight dwell
- Automated peritoneal dialysis (APD) uses a cycler to perform multiple overnight exchanges
  - Modifications to this technique include continuous cycler peritoneal dialysis (CCPD), nightly intermittent peritoneal dialysis (NIPD), and tidal peritoneal dialysis (TPD)

Types of APD

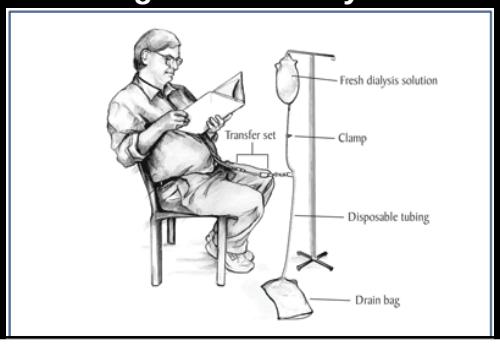
- Continuous cycler peritoneal dialysis (CCPD) has a long daytime dwell and several cycles overnight.
- Nightly intermittent peritoneal dialysis (NIPD) or intermittent peritoneal dialysis (IPD), have treatment periods ("wet" abdomen) alternating with times during which the peritoneal cavity has been drained of dialysate ("dry" abdomen).
- Tidal peritoneal dialysis (TPD), consists of exchanges in which the peritoneal cavity always contains at least some dialysate (usually at least one-half full)

Cycler (used in APD)

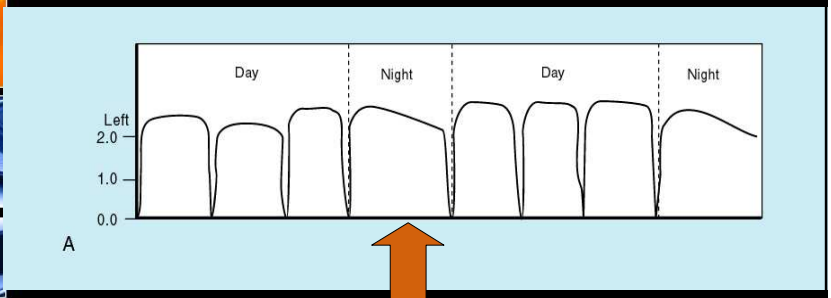


Manual Exchange (CAPD)

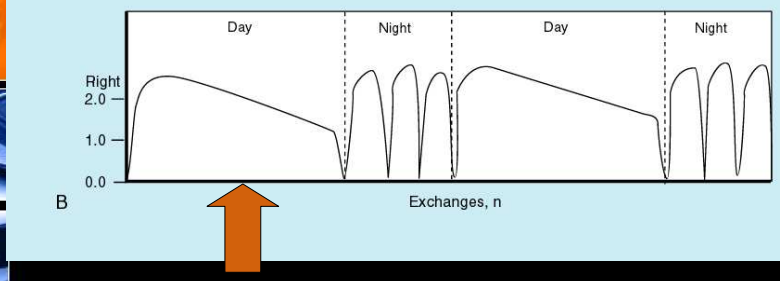
- **Between exchanges, catheter and transfer set hidden inside clothing.**
- **At the beginning of an exchange, connect transfer set to a Y-tube.**
- **The branches of the Y-tube connect to the drain bag and the bag of fresh dialysis solution.**



Continuous ambulatory peritoneal dialysis (CAPD) – uses manual exchange

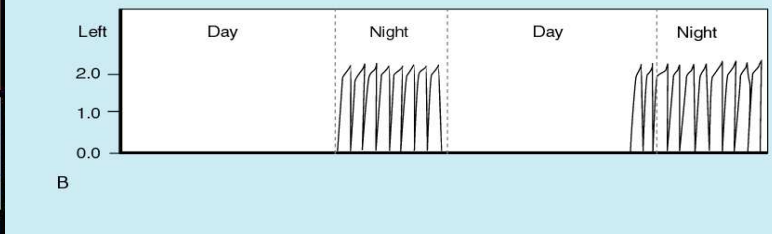


Continuous cycler peritoneal dialysis (CCPD) - uses cycler



Dwell

Nightly intermittent peritoneal dialysis (NIPD) – uses cycler



Indication/Contraindication in PD

80% of patients have no contra-indication to any of the dialysis methods and may choose according to their lifestyle between HD a PD.

Absolute contra-indications of PD:

1. **Peritoneal fibrosis and adhesions following intraabdominal operations**
2. **Inflammatory gut diseases**

Peritonitis

- **Remains the biggest cause of PD technique failure**
- **Patients must switch to HD**
- **Most cases are caused by pathogenic bacteria**
- **Fungi, mostly Candida species, may also be source**
- **Causes hospitalization, catheter loss and even death**
- **Rates have fallen over past 2 decades , mainly due to improved connectology**

Microbiology of Peritonitis: Gram +

- Coag-negative staph most common cause of peritonitis in CAPD
  - Caused by touch contamination or infection via the pericatheter route
  - Mild peritonitis that responds rapidly to therapy (unless biofilm develops)
- Staph aureus can cause a more severe and resistant form of peritonitis
  - Concurrent catheter infection is a common source
  - May present with a toxic shock-like syndrome
  - Severe cases can cause progressive injury to the peritoneal membrane
- Frequency of VRE as a nosocomial pathogen has risen dramatically

Microbiology of Peritonitis: Gram -

- Produced by a variety of organisms that may be derived from the bowel, skin, urinary tract, contaminated water, and animal contact.
- Pseudomonas is the most common cause of peritonitis and exit site infections
- E. coli is an unusual cause of peritonitis in CAPD

Empiric Antibiotic Selection

- Must cover Gram + and Gram – organisms
- Gram-positive organisms may be covered by vancomycin or a cephalosporin
- Gram-negative organisms by a third-generation cephalosporin or aminoglycoside
  - May use ceftazidime, cefepime, or carbapenem
  - Quinolones should only be used for empiric coverage of gram negative organisms if local sensitivities support such use

Drug Delivery

- May mix in antibiotics with dialysate solution
- Icodextrin-containing dialysis solutions are compatible with vancomycin, cefazolin, ampicillin, ceftazidime, gentamicin, or amphotericin
- Vancomycin, aminoglycosides, and cephalosporins can be mixed in the same dialysis solution bag without loss of bioactivity
- Aminoglycosides should NOT be added to the same exchange with penicillins

Stability

- **Vancomycin**: stable for 28 days in dialysis solution stored at room temp.
- **Gentamicin**: stable for 14 days, but the duration of stability is reduced by admixture of heparin
- **Cefazolin**: stable for at least 8 days at room temp. or for 14 days if refrigerated
- **Ceftazidime**: conc. 125 mg/L are stable for 4 days at room temp. or 7 days refrigerated, and 200 mg/L is stable for 10 days if refrigerated.
- **Cefepime**: stable in dialysis solution for 14 days if the solution is refrigerated.

Intra-Peritoneal Dosing

- IP dosing of antibiotics for peritonitis is preferable to IV dosing
  - Results in very high local levels of antibiotics
  - Can be done by the patient at home, after appropriate training, and avoids venipuncture.
- IP antibiotics can be given in each exchange (i.e., continuous dosing) or once daily (intermittent dosing)
  - In intermittent dosing, the antibiotic-containing dialysis solution must be allowed to dwell for 6 hrs to allow adequate absorption of the antibiotic into the systemic circulation.
- Most antibiotics have significantly enhanced absorption during peritonitis
  - IP vancomycin is about **50% absorbed without peritonitis**, but closer to **90% in the presence of peritonitis**
  - Permits reentry into the peritoneal cavity during subsequent fresh dialysis solution exchanges.

Continuous vs. Intermittent Dosing

- With CAPD, the guidelines state that it is unclear whether continuous is more effective than intermittent dosing in **first generation cephalosporins**
  - **Recommend adding the cephalosporin to each exchange**
- By comparison, there is extensive experience with the efficacy of intermittent dosing of **aminoglycosides and vancomycin** in CAPD
- **Vanco** intermittent dosing can be given in APD.
  - Dosing interval of every **four to five days** may be adequate, but the optimal interval should be determined by monitoring levels.
  - Check blood level on **day 4** to evaluate re-dosing
  - Re-dosing is required once serum levels fall to 15 mcg/mL
- Less is known concerning the efficacy of different types of dosing with automatic peritoneal dialysis (APD).

Intermittent dosing of antibiotics in automated peritoneal dialysis

Drug	IP dose
Cefazolin	20 mg/kg IP each day, in long day dwell
Cefepime	1 g IP in one exchange per day
Fluconazole	200 mg IP in one exchange per day, every 24-48 hours
Tobramycin	LD 1.5 mg/kg IP in long dwell, then 0.5 mg/kg IP each day, in long dwell
Vancomycin	LD 30 mg/kg IP in long dwell; repeat dosing 15 mg/kg IP in long dwell every 3-5 days (adjust interval to maintain serum trough levels above 15 µg/mL)

IP: intraperitoneal; LD: loading dose.

General Recommendations

- **Recommendation: “Intermittent" dosing regimen**
- Add antibiotics to their next dwell and advise the patient to have it dwell for at least six hours.
- If the patient is doing well, continue the antibiotic regimen having the patient instill antibiotics during the long daytime dwell adjusting as indicated when culture results are available.
- **Recommendation: “Continuous” dosing regimen**
- Continue the patient on their current PD prescription and add the antibiotic to the overnight dwell bag, as you would for CAPD dosing (eg, if the patient dialysis dose is four 2 L exchanges and a 2 L last bag fill, then each 5 L bag of fluid would get the same mg/L dose of antibiotic [times 5 L] as recommended for each liter of CAPD dwell; the same is true for the last bag fill if an additional bag of fluid is needed).
- **Minimum therapy for peritonitis is 2 weeks**
- 3 weeks is recommended in severe infection

Intraperitoneal antibiotic dosing recommendations for continuous administration in peritoneal dialysis patients (adult)

	Initial IP loading dose (per liter of dialysate)	Maintenance IP dose* (per liter of dialysate) For patients with residual renal function (defined as greater than 100 mL per day urine output) empirically increase dose shown by twenty-five percent
Aminoglycosides		
Continuous IP administration of aminoglycosides is not recommended. See text and accompanying table on intermittent IP antibiotic administration and dosing.		
Cephalosporins		
Cefazolin	500 mg	125 mg
Cefepime	500 mg	125 mg
Cephalothin•	500 mg	125 mg
Cephradine•	500 mg	125 mg
Ceftazidime	500 mg	125 mg
Ceftizoxime	250 mg	125 mg
Penicillins		
Amoxicillin•	250 to 500 mg	50 mg
Ampicillin	None	125 mg
Azlocillin•	500 mg	250 mg
Oxacillin	None	125 mg
Nafcillin	None	125 mg
Penicillin G	50,000 units	25,000 units
Others		
Vancomycin	1 gram	25 mg (modify dose based on serum drug concentrations)
Aztreonam	1 gram	250 mg
Ciprofloxacin	50 mg	25 mg
Daptomycin	100 mg	20 mg
Linezolid	None	ORAL: 200 to 300 mg once daily
Teicoplanin•	400 mg	20 mg
Combinations		
Ampicillin-sulbactamΔ	1 gram	100 mg
Imipenem-cilastatin◇	250 mg	50 mg
Trimethoprim-sulfamethoxazole (co-trimoxazole)	None	ORAL: one 960 mg double strength tablet (trimethoprim 160 mg and sulfamethoxazole 800 mg) two times per day

Table shows suggested dose of antibiotics for IP administration (except as noted otherwise) in all exchanges of peritoneal dialysate for treatment of continuous ambulatory PD associated peritonitis. For dosing of antibiotics administered intermittently with PD, see text and accompanying table.
IP: intraperitoneal; PD: peritoneal dialysis.
* Dose, in mg per liter of dialysate, administered with each exchange following loading dose.
• Parenteral preparation not available in United States.
Δ Based on ampicillin component.
◇ Based on imipenem component.
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Intraperitoneal antibiotic dosing recommendations for intermittent administration in peritoneal dialysis patients (adult)

	IP dose* For patients with residual renal function (defined as greater than 100 mL per day urine output): empirically increase dose shown by twenty-five percent
Aminoglycosides•Δ	
Amikacin	2 mg/kg in one exchange per day
Gentamicin	0.6 mg/kg in one exchange per day
Netilmicin◇	0.6 mg/kg in one exchange per day
Tobramycin	0.6 mg/kg in one exchange per day
Cephalosporins	
Cefazolin	15 mg/kg in one exchange per day
Cefepime	1 gram in one exchange per day
Cephalothin◇	15 mg/kg in one exchange per day
Cephradine◇	15 mg/kg in one exchange per day
Ceftazidime	1 to 1.5 grams in one exchange per day
Ceftizoxime	1 gram in one exchange per day
Penicillins	
Intermittent IP administration of penicillins is not recommended. See text and accompanying table on continuous IP antibiotic administration and dosing.	
Other	
Vancomycin	15 to 30 mg/kg repeat every 3 to 7 days, based on serum drug levels
Linezolid	ORAL: 200 to 300 mg once per day
Teicoplanin◇	15 mg/kg in one exchange per day
Combinations	
Ampicillin-sulbactam§	2 grams in one exchange every twelve hours
Imipenem-cilastatin¥	1 gram in one exchange every twelve hours
Quinupristin-dalfopristin	25 mg per liter of dialysate in alternate bags‡
Trimethoprim-sulfamethoxazole (co-trimoxazole)	ORAL: one 960 mg double strength tablet (trimethoprim 160 mg and sulfamethoxazole 800 mg) two times per day
Antifungal	
Fluconazole	200 mg in one exchange every 24 to 48 hours

Table shows suggested dose of antibiotics for intermittent IP administration (except as noted otherwise) in peritoneal dialysate for continuous ambulatory PD associated peritonitis. For dosing of antibiotics administered continuously (with each dialysate exchange), see text and accompanying table.
IP: intraperitoneal; PD: peritoneal dialysis.
* Dwell time for dialysate exchange containing antibiotic(s) must be at least six hours.
• Penicillins and some cephalosporins may inactivate aminoglycosides. Mixture in the same dialysate should be minimized or avoided.
Δ Repeated or prolonged courses of aminoglycosides are not recommended if an alternative is available. See text.
◇ Not available in United States.
§ Based on ampicillin component.
¥ Based on imipenem component.
‡ Given in conjunction with 500 mg intravenous twice daily.

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Table 3: Recommendations for IP antibiotic dosing for anuric adult CAPD patients (increase dose by 25% for patients producing more than 100 ml of urine daily)

Generic name	Intermittent (one exchange per day)	Continuous (all exchanges, mg per liter)
Amikacin	2 mg/kg	LD 25, MD 12
Amoxicillin	ND	LD 250-500, MD 50
Amphotericin	ND	MD 1.5
Ampicillin	ND	MD 125
Ampicillin/sulbactam	2 g every 12 hours	LD 1000, MD 100
Aztreonam	ND	LD 1000, MD 250
Azlocillin	ND	LD 500, MD 250
Cefazolin	15 mg/kg	LD 500, MD 125
Ceftazidime	1-1.5 g	LD 500, MD 125
Ceftizoxime	1 g	LD 250, MD 125
Cephalothin	15 mg/kg	LD 500, MD 125
Cephradine	15 mg/kg	LD 500, MD 125
Cifepime	1 g	LD 500, MD 125
Ciprofloxacin	ND	LD 50, MD 25
Clindamycin	ND	LD 300, MD 125
Fluconazole	200 mg	NA
Gentamicin	0.6 mg/kg*	LD 8, MD 4
Imipenem/cilastatin	1 g bd	LD 500, MD 200
Nafcillin	ND	MD 125
Netilmicin	0.6 mg/kg	LD 8, MD 4
Oxacillin	ND	MD 125
Penicillin G	ND	LD 50000, MD 25000 units
Teicoplanin	15 mg/kg	LD 400, MD 40 **
Tobramycin	0.6 mg/kg	LD 8, MD 4
Vancomycin	30 mg/kg every 5-7 days ***	LD 1000, MD 25

* Check blood level every 3-4 days (target 2-4 mg/l), if level < 2 mg/l increase dose by 0.2 mg/kg, if level > 4 mg/l reduce dose by 0.2 mg/kg, if level > 7 mg/l miss a day and reduce dose by 0.2 mg/kg.

** In each bag for 7 days, then in 2 bags/day for 7 days, then in 1 bag/day for 7 days.

*** Check blood level on day 4 (target > 10 mg/l), if level ≤ 12 mg/l repeat dose every 5 days, if level 13-14 mg/l repeat dose every 6 days, if level ≥ 15 mg/l repeat dose every 7 days (usual dose for anuric patients).

LD: loading dose in mg, MD: maintenance dose, ND: no data, NA: not applicable

Antibiotic Incompatibility

Ampicillin / Gentamicin incompatibility

- These agents are incompatible in PD fluid necessitating sequential dosing. Gentamicin should be added to dialysate as indicated by serum levels.
- The interruption to ampicillin dosing may be compensated for by increasing the ampicillin maintenance dose in the dwell immediately preceding gentamicin dwell.

Quinolones

- When given concomitantly with sevelamer or calcium may chelate, resulting in reduced quinolone absorption
- Administration of the quinolone should be separated from these drugs by at least 2 hours (with the quinolone administered first).
- If resolution of infection is slow consideration should be given to IV quinolone therapy.

Consider Yeast Prophylaxis

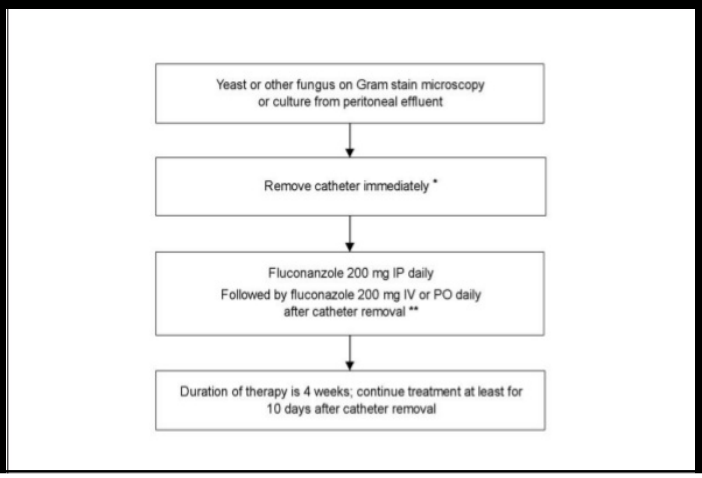
- Greatest risk for yeast infection = ABX therapy
- If yeast identified, PD must be discontinued.

Yeast Prophylaxis:

- Nystatin 100,000 u/mL give 5 mL PO QID for duration of peritonitis treatment, as prophylaxis against fungal peritonitis.
- Continue for 1 week post antibiotics

Treatment of Yeast

- Can be initiated with oral fluconazole if no preparation is available for IP usage, the patient should be maintained on HD during therapy with systemic antifungals.



Are you adequately confused???

References

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