



WESTERN
CANADA

PD
DAYS

April 6, 2017

Mauro Verrelli, MD

kidneyhealth.ca
manitoba renal program



UNIVERSITY
OF MANITOBA
Faculty of Health Sciences

ISPD Peritonitis Recommendations: 2016 Update on Prevention and Treatment

Li PK, Szeto CC, Piraino, B et al.

Peritoneal Dialysis International, Vol. 36, pp. 481–508

Outline

- Review mostly well-known content, possibly from a different lens
- Interactive approach – some case studies
- Highlight practical principles
- Discuss areas of controversy
- ABXs not reviewed

“The recommendations are not meant to be implemented in every situation indiscriminately. Each PD unit should examine its own pattern of infection, causative organisms, and sensitivities, and adapt the protocols according to local conditions as necessary. “

“These recommendations are evidence-based where such evidence exists. Publications in or before December 2015 were reviewed.”

- The guidelines use the GRADE system for classification of the level of evidence and grade of recommendations.
- The strength (grade) of the recommendation is indicated as:
 - Level 1 (We **recommend**)
 - Level 2 (We **suggest**)
 - Not graded
- The quality of the supporting evidence is shown as:
 - A (high quality)
 - B (moderate quality)
 - C (low quality)
 - D (very low quality)

Prevention of Peritonitis: Catheter Placement

- Systemic prophylactic antibiotics be administered immediately prior to catheter insertion (1A).
- Three RCTs have shown that perioperative antibiotic reduces the incidence of early peritonitis.

Prevention of Peritonitis: Connection Methods

- Use disconnect systems with a “flush before fill” design be used for CAPD (1A).
- “Several prospective studies have shown that the use of Y connection systems with the “flush before fill” design results in a lower peritonitis rate than the traditional spike systems.”

Prevention of Peritonitis: Exit-site Care

- We recommend daily topical application of antibiotic (mupirocin or gentamicin) cream or ointment to the catheter exit site (1B).
- We recommend prompt treatment of exit-site or catheter tunnel infection to reduce subsequent peritonitis risk (1C).

Prevention of Peritonitis: Catheter Design

- There is no specific recommendation on catheter design for prevention of peritonitis.
- “There are no convincing data regarding the effect of PD catheter design and configuration on peritonitis risk.”

Prevention of Peritonitis: Insertion Technique

- There is no significant difference in peritonitis rate between peritoneoscopic/laparoscopic versus surgical (laparotomy) catheter insertion based on a systematic review.
- There are no convincing data that the buried catheter technique lowers peritonitis rates.

Prevention of Peritonitis: Dialysis Solution

- No specific recommendation on the choice of dialysis solution for prevention of peritonitis.

- A 75 year-old woman with ESRD secondary to ischemic nephropathy has been on PD for 1 year. She is admitted to hospital for lower GI bleeding. She undergoes colonoscopy and is found to have diverticulosis. Her bleeding stops and Hgb stabilizes but 48 hours later she develops peritonitis. CT scan of the abdomen is normal. Her PD effluent grows E. Coli.
- **Could her peritonitis have been prevented?**

Prevention of Peritonitis: Bowel and Gynecological Source Infections

- We suggest antibiotic prophylaxis prior to colonoscopy (2C) and invasive gynecologic procedures (2D). 2016
- Invasive gastrointestinal procedures may infrequently cause peritonitis in PD patients. Intravenous antibiotic prophylaxis reduces early peritonitis in these patients. 2011

- Transient bacteremia is common after dental procedures and may lead to peritonitis.
- Prophylactic antibiotics (e.g. single oral dose of amoxicillin) before extensive dental procedures may be reasonable.

Prevention of Peritonitis: Other Modifiable risk Factors

- Prophylactic antibiotics are usually recommended after wet contamination
- There is no widely accepted standard antibiotic regimen.

Prevention of Peritonitis: Training Programs

- Follow the latest ISPD recommendations for teaching PD patients and their caregivers.
- Figueiredo AE, Bernardini J *et al.* ISPD guideline / recommendations: a syllabus for teaching peritoneal dialysis to patients and caregivers. *Perit Dial Int* 2016. doi.10.3747/pdi.2015.00277
- PD training should be conducted by nursing staff with the appropriate qualifications and experience (1C).

- A 55 year-old man with ESRD secondary to chronic glomerulonephritis has been on PD for 2 years. He develops peritonitis and the PD effluent grows staphylococcus epidermidis. He is successfully treated with a 2-week course of IP vancomycin with PD fluid readily clearing after 48 hours.
- 2-weeks after terminating his antibiotics his PD effluent becomes cloudy again.
- **What is the differential diagnosis of cloudy effluent?**

Differential Diagnosis of Cloudy Effluent

- Culture-positive and culture-negative infectious peritonitis
- Specimen taken from “dry” abdomen
- Hemoperitoneum
- Eosinophilia of the effluent
- Calcium channel blockers
- Malignancy (rare)
- Chemical peritonitis
- Chylous effluent (rare)

- A 55 year-old man with ESRD secondary to chronic glomerulonephritis has been on PD for 2 years. He develops peritonitis and the PD effluent grows staphylococcus epidermidis. He is successfully treated with a 2-week course of IP vancomycin, with PD fluid readily clearing after 48 hours.
- 1-week after terminating antibiotics his PD effluent becomes cloudy again.
- What is the differential diagnosis of cloudy effluent?
- **Is this refractory, relapsing, repeat, or recurrent peritonitis?**

Peritonitis Terminology

- **Refractory:** Failure of the effluent to clear after 5 days
- **Relapsing:** Within 4 weeks of terminating therapy - same organism or culture-negative
- **Repeat:** More than 4 weeks of terminating therapy - same organism
- **Recurrent:** Within 4 weeks of terminating therapy - different organism
- **Catheter-related:** in conjunction exit-site or tunnel infection - same organism or culture-negative

N.B. Relapsing episodes should not be counted as another episode during the calculation of peritonitis rates; recurrent and repeat episodes should be counted.

- A 55 year-old man with ESRD secondary to chronic glomerulonephritis has been on PD for 2 years. He develops peritonitis and the PD effluent grows staphylococcus epidermidis. He is successfully treated with a 2-week course of IP vancomycin with PD fluid readily clearing after 48 hours.
- 1 week after terminating antibiotics his PD effluent becomes cloudy again.
- Is this refractory, relapsing, repeat, or recurrent peritonitis?
- **He has recurrent peritonitis with the PD effluent now growing yeast.**

- He has recurrent peritonitis with the PD effluent now growing yeast
- **How should this patient now be managed?**

The guidelines say...

- We recommend immediate catheter removal when fungi are identified in PD effluent **(1C)**.
- We suggest that treatment with an appropriate anti-fungal agent be continued for at least 2 weeks after catheter removal **(2C)**.

- He has recurrent peritonitis with the PD effluent now growing yeast
- How should this patient now be managed?
- **Could this episode of peritonitis have been avoided?**

The guidelines say...

- We recommend anti-fungal prophylaxis when PD patients receive antibiotic courses to prevent fungal peritonitis **(1B)**.
- “ Two randomized controlled trials and a systematic review showed a significant benefit.”
- In 2011: “ Fungal prophylaxis during antibiotic therapy may prevent some cases of Candida peritonitis in programs that have high rates of fungal peritonitis.”

RCT 2010

- Not blinded, June 1, 2004 – Oct 30,2007, Colombia
- n=420 patients CAPD/APD, no difference between groups
- Control group n=210: no anti-fungal Rx
- Rx group n=210 : fluconazole 200mg PO q48h X 3 wks/duration of ABXs
- Outcomes:
 - Primary fungal peritonitis
 - ABX-associated (secondary) fungal peritonitis: >30 to <150 days after terminating ABXs

RCT 2010

- Results:
 - 434 peritonitis episodes in 226 patients
 - 402 bacterial
 - 32 fungal
 - 14 primary episodes
 - 18 ABX- associated episodes
 - Rx group: 3 episodes (0.92%)
 - Control group: 15 episodes (6.45%) (p= 0.0051)

RCT 2010 - Considerations

- Fluconazole well tolerated – no SEs/AEs
- Very high baseline peritonitis rate prior to RCT: 0.63 episodes per patient-year (1 episode per 19 patient-months)
- No exit site prophylaxis
- warm climate, no seasonal variation
- ABX – associated: why > 30 days? ...true primary if <30 days?
- What about patients Rx with ABXs for other indications?...true primary?

RCT 1996

- Not blinded, May 1, 1991 – April 30, 1993, Honk Kong
- CAPD n=397, no difference between groups
- Nystatin 500,000 units QID during **any** antibiotic Rx
- Control group n=198, no anti-fungal Rx 16.8 mos mean F/U
- Rx group n=199, 18 mos mean F/U
- Outcomes:
 - Candida peritonitis- free survival
 - ABX-related Candida peritonitis (defined as occurring \leq 3 months after terminating ABXs)

RCT 1996

- Results:
- Control group:
 - 188 episodes of peritonitis
 - 12 episodes fungal (0.043/pt-yr)
 - 6 episodes ABX-associated (1.43/100 peritonitis)
- Rx group:
 - 216 episodes of peritonitis
 - 4 episodes fungal (0.013/pt-yr)
 - 3 episodes ABX-associated (0.66/100 peritonitis)

(p>0.05)

RCT 1996 - Considerations

- Nystatin well tolerated, no SEs
- Positive effect of nystatin not statistically significant
- All -1 episodes of fungal peritonitis occurred April to October, ? seasonal influence

Fungal Peritonitis Prophylaxis – Cross Canada Survey Feb 2017

Site	Fungal Prophylaxis	Drug	Comments
1	High risk only*	Fluconazole.	2 cases in 7 years
2	Optional	Nystatin	1 case/yr 2014-16 - 80 pt program
3	No		1-3 cases /yr - 60 pt program
4	High risk only	Fluconazole	2 cases/yr 2012-16
5	High risk only	Fluconazole	1 case in 2015, 2 in 2016
6	Yes	Nystatin	
7	Variable	Nystatin	Low rates
8	No		1-2/ yr
9	No		1 case in 5 years
10	High risk only	Nystatin	Reviewed in 2017 – low rates

*Recurrent PD peritonitis/prolonged antibiotic exposure, immunosuppressed

St. Boniface Hospital Rates of Fungal Peritonitis

Year	# Fungal episodes	% of culture (+) episodes	% of all episodes	Episodes per patient-year
2005	5	9.3	6.3	0.03
2006	3	7	4.5	0.02
2007	5	8.1	5.5	0.034
2008	5	7.9	6.1	0.033
2009	1	1.8	1.2	0.006
2010	2	3.4	2.1	0.012 ¹
2011	0	0	0	0
2012	1	1.9	1.6	0.006
2013	1	1.8	1.4	0.006 ²
2014	2	4.8	3.7	0.012
2015	6	10.5	-	
2016	5			0.0276

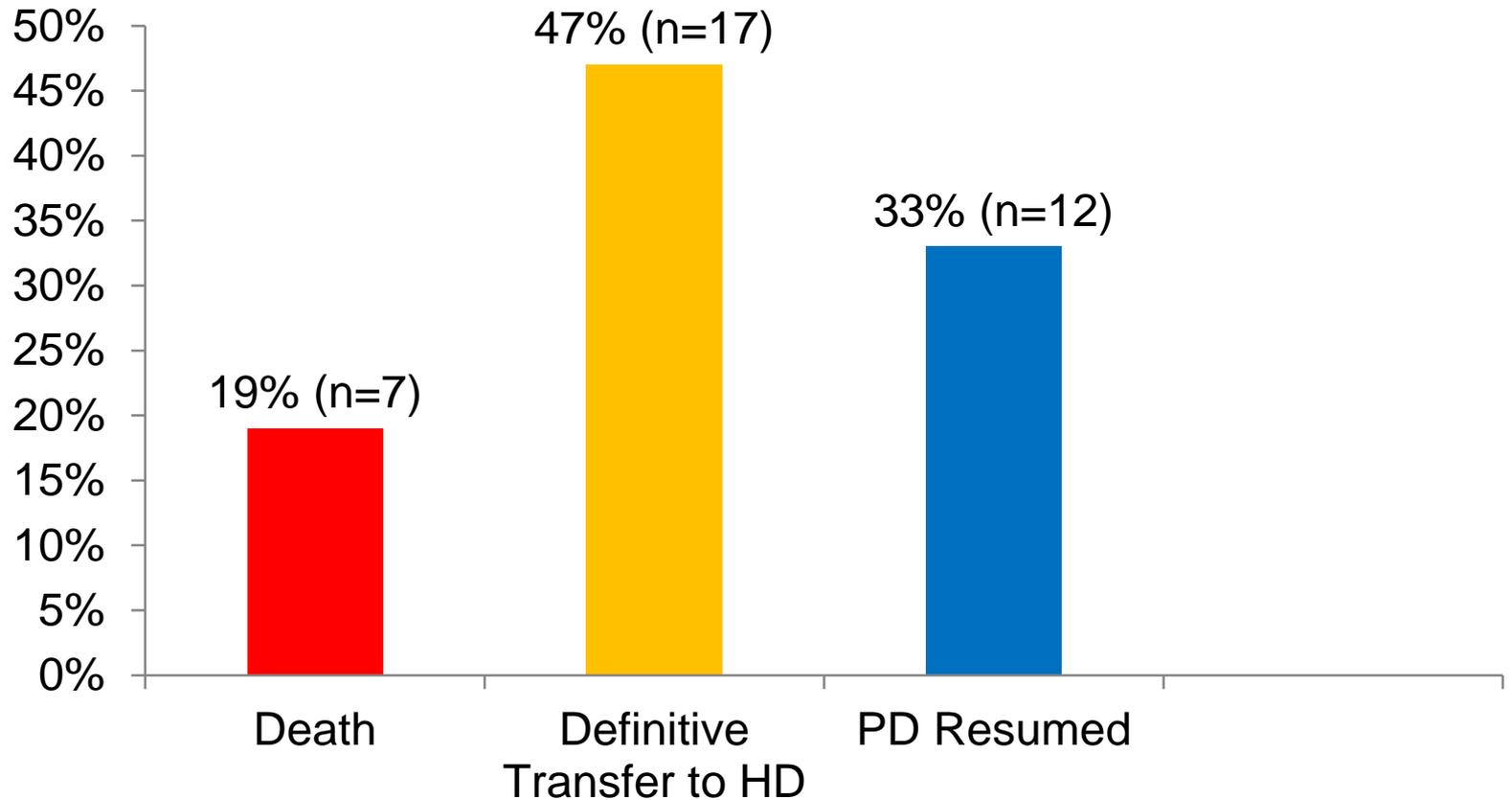
¹September 2010 switched from oral rifampin and nasal mupirocin to gentamicin cream for exit site care

²Switched from gentamicin cream to mupirocin cream due to availability

Author	Peritonitis episodes per patient-year		Fungal peritonitis episodes / patient-year		Antibiotic-related fungal peritonitis (episodes /pt-year)	
	Control	Rx	Control	Rx	Control	Rx
St. B 2016	0.37029		0.0276			
Restrepo	0.63?	0.63?				
Lo	0.686	0.725	0.0438	0.0134	0.020	0.010
Zaruba	2.718	0.725	0.2892	0.0228	0.290	0.030
Thodis	0.665	0.495	0.0300	0.0600	0.015	0.020
Williams	0.574	0.582	0.0061	0.0169	0.011	0.011
Robitaille	2.451	1.198	0.1408	0.0000	0.095	0.000
Wadhwa	0.688	0.669	0.0983	0.0282	0.084	0.014
Morey	1.533	0.731	0.1008	0.0000	0.000	0.000
Moreiras-Plaza	1.001	0.693	0.0662	0.0000	0.037	0.000
Davenport	0.608	0.436	0.0099	0.0032		

- A 55 year-old man with ESRD secondary to chronic glomerulonephritis has been on PD for 2 years. He develops peritonitis and the PD effluent grows staphylococcus epidermidis. He is successfully treated with a 2-week course of IP vancomycin with PD fluid readily clearing after 48 hours.
- 1 week after terminating antibiotics his PD effluent becomes cloudy again.
- Is this refractory, relapsing, repeat, or recurrent peritonitis?
- He has recurrent peritonitis with the PD effluent now growing yeast.
- **This patient's PD catheter was immediately removed, he was converted to HD and treated with antifungal agent for 3 more weeks.**
- **Should this patient ever return to PD?**

CHARACTERISTICS AND OUTCOMES OF FUNGAL PERITONITIS IN A MODERN NORTH AMERICAN COHORT



- A 62 year-old woman with ESRD secondary to diabetic nephropathy has been on PD for 2 years. She develops peritonitis and the PD effluent grows staphylococcus epidermidis. He is successfully treated with a 2-week course of IP vancomycin with PD fluid readily clearing after 48 hours.
- 1 week after terminating antibiotics his PD effluent becomes cloudy again.
- **Is this refractory, relapsing, repeat, or recurrent peritonitis?**

- A 62 year-old woman with ESRD secondary to diabetic nephropathy has been on PD for 2 years. She develops peritonitis and the PD effluent grows staphylococcus epidermidis. She is successfully treated with a 2-week course of IP vancomycin with PD fluid readily clearing after 48 hours.
- 1 week after terminating antibiotics her PD effluent becomes cloudy again.
- Is this refractory, relapsing, repeat, or recurrent peritonitis?
- **She has recurrent peritonitis with the PD effluent now growing staphylococcus aureus.**
- **How do we now manage this patient?**

“Retraining plays an important role in reducing mistakes”

Indications for PD Re-Training

- Assess need with home visit (compliance, technique)
- Following prolonged hospitalization
- Following peritonitis and/or catheter infection
- Following change in dexterity, vision, or mental acuity
- Following change to another supplier or a different type of connection
- Following other interruption in PD (e.g. period of time on hemodialysis)

- A 70 year-old man with ESRD secondary to polycystic kidneys has been on PD for 6 months. He develops peritonitis and the PD effluent grows staphylococcus epidermidis. He is successfully treated with a 2-week course of IP vancomycin with PD fluid readily clearing after 48 hours.
- 10 days after terminating antibiotics his PD effluent becomes cloudy again.
- **Is this refractory, relapsing, repeat, or recurrent peritonitis?**

- A 70 year-old man with ESRD secondary to polycystic kidneys has been on PD for 6 months. He develops peritonitis and the PD effluent grows staphylococcus epidermidis. He is successfully treated with a 2-week course of IP vancomycin with PD fluid readily clearing after 48 hours.
- 10 days after terminating antibiotics his PD effluent becomes cloudy again.
- Is this refractory, relapsing, repeat, or recurrent peritonitis?
- **He has relapsing peritonitis with the PD effluent again growing staphylococcus epidermidis with same sensitivity pattern.**
- **What is likely going on?**

- “Relapsing coagulase-negative Staphylococcus peritonitis suggests colonization of the PD catheter with biofilm..”

- A 70 year-old man with ESRD secondary to polycystic kidneys has been on PD for 6 months. He develops peritonitis and the PD effluent grows staphylococcus epidermidis. He is successfully treated with a 2-week course of IP vancomycin with PD fluid readily clearing after 48 hours.
- 10 days after terminating antibiotics his PD effluent becomes cloudy again.
- Is this refractory, relapsing, repeat, or recurrent peritonitis?
- He has relapsing peritonitis with the PD effluent again growing staphylococcus epidermidis with same sensitivity pattern.
- What is likely going on?
- **How do we now manage this patient?**

- Catheter removal should be considered
- If PD effluent becomes clear with antibiotic treatment simultaneous catheter removal and re-insertion can be performed

The guidelines say...Indications for Catheter Removal:

- 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

Refractory Peritonitis

- We recommend that the PD catheter be removed promptly in refractory peritonitis episodes, defined as failure of the PD effluent to clear up after 5 days of appropriate antibiotics (1C).

Relapsing, Recurrent, and Repeat Peritonitis

- We recommend that timely catheter removal be considered for relapsing, recurrent, or repeat peritonitis episodes (1C).

Catheter Removal and Re-Insertion

- We recommend that PD catheters be removed for refractory, relapsing, or fungal peritonitis unless there are clinical contraindications (1C).
- We suggest that it is appropriate to consider return to PD for many patients who have had their catheter removed for refractory, relapsing, or fungal peritonitis (2C).

Monitoring and CQI: Peritonitis Rate

- There is a substantial variation in the peritonitis rate reported by different countries, as well as a great deal of variation within countries that is not well explained
- The **overall peritonitis rate should be no more than 0.5 episode per patient-year**. The rate depends considerably on the patient population. In some centers a rate as low as 0.18 to 0.20 episode per year has been reported .

Monitoring and CQI: Peritonitis Rate

- PD programs should monitor incidence of peritonitis at least yearly (1C).
- Monitor (1C):
 - Overall peritonitis rate
 - Peritonitis rates of specific organisms
 - The percentage of patients per year who are peritonitis-free
 - Antimicrobial susceptibilities of the infecting organisms.

Monitoring and CQI

- Peritonitis rate should be standardly reported as number of episodes per patient-year (not graded).
- Organism-specific peritonitis rates should be reported as absolute rates, i.e. as number of episodes per year (not graded).

Monitoring and CQI

- We recommend each PD center have a continuous quality improvement (CQI) program in place to reduce peritonitis rates (1C).
- We suggest that multidisciplinary teams running CQI programs in PD centers meet and review their units' performance metrics regularly (2C).



Thank You!