Primary and Secondary Peritonitis in Peritoneal Dialysis

19th The 19th International Congress of Nephrology, Dialysis and Transplantation (ICNDT)

12-15 December 2023 Homa Hotel, Tehran Abbas Etminan Nephrologist





What's new with the 2022 update of the ISPD peritonitis guidelines?

Revised, clarified definitions for refractory peritonitis, relapsing peritonitis, peritonitis-associated catheter removal, peritonitis-associated haemodialysis transfer, peritonitis-associated death and peritonitis-associated hospitalization

Definitions for new peritonitis categories and outcomes: pre-PD peritonitis, enteric peritonitis, catheter-related peritonitis and medical cure

Revised, updated recommendations for calculating and reporting peritonitis rates before and after PD commencement New targets recommended for overall peritonitis rate, proportion of patients free of peritonitis and culture-negative peritonitis

Revised recommendations regarding management of contamination of PD systems

Revised recommendations regarding antibiotic prophylaxis for invasive procedures

Revised recommendations regarding PD training and reassessment





What's new with the 2022 update of the ISPD peritonitis guidelines?

New recommendations regarding PD patients with pets

New recommendations regarding management of modifiable peritonitis risk factors (hypokalaemia, histamine-2 receptor antagonists)

Update on novel diagnostic techniques for peritonitis

Updated recommendations regarding empirical antibiotic selection and dosage of antibiotics

New recommendation regarding adjunctive oral N-acetylcysteine therapy for mitigating aminoglycoside ototoxicity

Revised recommendations regarding treatment of peritonitis in patients receiving APD

Revised recommendation regarding consideration of expectant management in patients longer than 5 days if PD effluent white cell count is decreasing towards normal, instead of mandatory PD catheter removal if effluent does not clear up by day 5

Updated recommendations for treatment of peritonitis due to coagulase-negative staphylococci, Corynebacteria, enterococcus, Pseudomonas, Acinetobacter, Stenotrophomonas and non-tuberculous mycobacteria



ISPD Peritonitis Guideline Recommendations: 2022 Update on Prevention and Treatment



PERITONEAL DIALYSIS INTERNATIONAL



These recommendations are evidence-based where evidence is available, and if multiple reports are available, findings from the more recent publications have been incorporated by the committee. Philip Kam-Tao Li, Kai Ming Chow, Yeoungjee Cho, et al. *ISPD Peritonitis Guideline Recommendations: 2022 Update on Prevention and Treatment. Perit Dial Int. DOI:10.1177/08968608221080586* Visual Graphic by Edgar Lerma, MD



Definition and measurement of peritonitis



Clinical features consistent with peritonitis, that is, abdominal pain and/or cloudy dialysis effluent
 Dialysis effluent white cell count > 100/µL (after a dwell time of at least 2 h), with > 50% polymorphonuclear leukocytes (PMN)
 Positive dialysis effluent culture



Differential diagnosis of cloudy effluent

Table 4. Differential diagnosis of cloudy effluent.

Cellular causes

PMN leucocytes Culture-positive infectious peritonitis Infectious peritonitis with sterile cultures Chemical peritonitis **Eosinophils** Dialysate eosinophilia Chemical peritonitis Monocyte/macrophages Specimen taken from 'dry' abdomen (after prolonged peritoneal rest) Red blood cells Hemoperitoneum Malignant cells Lymphoma Peritoneal metastasis Non-cellular causes Fibrin Triglycerides (milky white appearance of effluent) Calcium channel blockers Lymphatic obstruction Acute pancreatitis

Peritoneal Dialysis Fluid Appearance



Cloudy: Coagulopathy Intraperitoneal disease (appendicitis, cholecystitis, bowel ischemia) Retrograde menstruation Retroperitoneal disease (pancreatitis, renal cell carcinoma) Ovulation Drugs (vancomycin, amphotericin B) Strenuous exercise Allergic reaction (increased eosinophils) Ovarian cyst rupture Adhesions





Chylous:

Normal

High triglycerides Lymphatic obstruction Trauma Abdominal lymphomas Pancreatitis Drugs (calcium channel blockers)

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Catheter-associated trauma

Definition and measurement of peritonitis

Cause-specific peritonitis

A. Organisms identified on culture (e.g., Staphylococcus aureus peritonitis)

- B. Culture-negative peritonitis
- C. Catheter-related peritonitis

D. Enteric peritonitis (intestinal and intra-abdominal ongans source: Inflammation, perforation or ischemia)



International Society For Peritoneal Dialysis

PERITONITIS

DIAGNOSTIC CRITERIA

Effluent WBC > 100/mcL with > 50% PMN

In the absence of Point 3 Culture Negative Peritonitis

Monitoring Target

2 out of 3

1) Abdominal Pain or Cloudy Effluent

3) Positive Effluent Culture

<0.40 episodes/year at risk.

per unit time per year.

>80% of Patients Peritonitis Free



Cause Specific



- Enteric Peritonitis



Time Specific Peritonitis

- Pre-PD - PD-Related - PD Catheter Insertion Related







Definition and measurement of peritonitis 3



Definition and measurement of peritonitis

Outcome	Definition		
Medical cure	Complete resolution of peritonitis together with NONE of the following complications: relapse/ recurrent peritonitis, catheter removal, transfer to haemodialysis for \geq 30 days or death		
Refractory	Peritonitis episode with persistently cloudy bags or persistent dialysis effluent leukocyte count >100 \times 10 ⁹ /L after 5 days of appropriate antibiotic therapy		
Recurrent	Peritonitis episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism		
Relapsing	Peritonitis episode that occurs within 4 weeks of completion of therapy ^a of a prior episode with the same organism or one sterile (culture negative) episode (i.e. specific organism followed by the same organism, culture negative followed by a specific organism or specific organism followed by culture negative).		
Repeat	Peritonitis episode that occurs more than 4 weeks after completion of therapy ^a of a prior episode with the same organism		
Peritonitis-associated catheter removal	Removal of PD catheter as part of the treatment of an active peritonitis episode		
Peritonitis-associated haemodialysis transfer	Transfer from PD to haemodialysis for any period of time as part of the treatment for a peritonitis episode		
Peritonitis-associated death Peritonitis-associated hospitalisation	Death occurring within 30 days of peritonitis onset or death during hospitalisation due to peritonitis Hospitalisation precipitated by the occurrence of peritonitis for the purpose of peritonitis treatment delivery		

Table 1. Outcome specific definition following peritonitis.

PD: peritoneal dialysis.

^aCompletion of therapy is defined as the last day of antibiotic administration.

PD PERITONITIS OUTCOMES

Medical cure

Complete resolution of peritonitis

Refractory peritonitis

Peritonitis persistent after 5 days of appropriate antibiotic therapy

Recurrent peritonitis

Peritonitis - within 4 weeks of completion of therapy of a prior episode, different organism

Relapsing peritonitis

Peritonitis within 4 weeks of therapy of a prior episode with the same organism or one culture negative episode followed by culture negative (or specific organism)

Repeating peritonitis

Peritonitis > 4 weeks of therapy of a prior episode with the same organism

Peritonitis-associated catheter

- as part of the treatment of peritonitis episode

Peritonitis-associated hemodialysis transfer

- as part of the treatment for a peritonitis

Peritonitis-associated hospitalization

Hospitalisation for the purpose of peritonitis treatment delivery

Peritonitis-associated death

Death within 30 days of peritonitis onset or death during hospitalisation due to peritonitis

Measurement and Reporting

 Table 2. Measurement and reporting of peritonitis.

	Unit of measure	Minimum frequency	Target
Peritonitis rates (overall and organism- specific)	Episodes per patient year	Yearly	<0.4 episodes per patient- year
Culture-negative peritonitis	% of all peritonitis episodes	Yearly	<15% of all peritonitis episodes
Time to first peritonitis episode	Mean unit time to first episode peritonitis	Quarterly (local report)	_
Proportion of patients free of peritonitis	% per unit time	Quarterly (local report)	>80% per year
Pre-PD peritonitis	% of all peritonitis episodes	Quarterly (local report)	_
PD catheter insertion-related peritonitis	% of all PD catheter insertions	Quarterly (local report)	<5%
Medical cure	% of all peritonitis episodes	Quarterly (local report)	_
Recurrent peritonitis	% of all peritonitis episodes	Quarterly (local report)	_
Relapsing peritonitis	% of all peritonitis episodes	Quarterly (local report)	_
Peritonitis-associated catheter removal	% of all peritonitis episodes	Quarterly (local report)	_
Peritonitis-associated haemodialysis transfer	% of all peritonitis episodes	Quarterly (local report)	_
Peritonitis-associated death	% of all peritonitis episodes	Quarterly (local report)	_

PD: peritoneal dialysis.

Prevention of Peritonitis

Domestic pet & zoonosis

PD patients extra precautions if domestic pets (1C)

PD-Catheter placement (1B)

PD system "Wet" contamination (2D)

Before colonoscopy (2C)

Before invasive OB&GYN procedures (2D)

PROPHYLAXIS

PD exchange technique

- regularly reassessed,

 emphasis on direct inspection of the practice of PD technique (1C)

Avoidance & treatment of **hypokalemia** may reduce the risk of peritonitis (2C)

Avoiding or limiting the use of **histamine-2 receptor antagonists** may prevent enteric peritonitis (2C) Secondary fungal prophylaxis

Anti-fungal prophylaxis - co-prescribed whenever PD patients receive an antibiotic course, regardless of the indication (1B)

Retraining Program

Table 3. Indications for PD Retraining.

- Following prolonged hospitalisation
- 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 change in caregiver for PD exchange
- Following other interruption in PD (e.g. period of time on haemodialysis)

PD: peritoneal dialysis.

Initial presentation and management of peritonitis

Treatment of peritonitis: initial and subsequent

- Identification of causative organisms
- Empiric antibiotic selection
- Dosage of antibiotics
- Antibiotic delivery and stability

Figure 1. The algorithm of initial management for PD patients presenting with a clinical diagnosis of peritonitis. PD: peritoneal dialysis.

ISPD ORGANISM SPECIFIC PERITONITIS GUIDELINES 2022

Reference: Li PK et al. ISPD peritonitis guideline recommendations:2022 update on prevention and treatment. 2022 Perit Dial Int. 2022 Mar:42(2):110-153. PMID: 35264029. Legend: AG:aminoglycoside; CRAB:Carbapenem-resistant Acinetobacter baumannii; VRE:Vancomycin resistant enterococci; ESBL:Extended spectrum beta lactamase producing.

Dosage of antibiotics

IP antibiotics should be the preferred route of administration as long as the compatibility and stability of the IP antibiotics allow, unless the patient has features of systemic sepsis (1B)

IP aminoglycoside should be administered as daily intermittent dosing (2B)

Prolonged courses of IP aminoglycoside should be avoided (1C)

Adjunctive oral N-acetylcysteine therapy may help to prevent aminoglycoside ototoxicity (2B)

There is insufficient evidence to make a recommendation as to whether patients on APD should be temporarily switched to CAPD during treatment of peritonitis (Not Graded)

Table 5. IP antibiotic dosing recommendations for treatment of peritonitis.

Antibiotic	Intermittent (I exchange daily for at least 6 h)	Continuous (all exchanges)
Aminoglycosides		
Amikacin	2 mg/kg daily ¹⁷³	Not advised
Gentamicin	0.6 mg/kg daily ^{174,175}	Not advised
Netilmicin	0.6 mg/kg daily ¹⁶⁵	Not advised
Tobramycin	0.6 mg/kg daily	Not advised
Cephalosporins		
Cefazolin	15 mg/kg daily (for long dwell) ^{176,177} 20 mg/kg daily (for short dwell) ^{178,176}	LD 500 mg/L, MD 125 mg/L ^{d 168,179}
Cefepime	1000 mg daily	LD 500 mg/L, MD 125 mg/L ^{d 168}
Cefoperazone	No data	LD 500 mg/L, MD 62.5-125 mg/L ¹⁸⁰
Cefotaxime	500-1000 mg daily ¹⁸¹	no data
Ceftazidime	1000–1500 mg daily (for long dwell)	LD 500 mg/L, MD 125 mg/L ^{d 168,182}
Contailionne	20 mg/kg daily (for short dwell) ¹⁷⁸	10 000 mg 1, 1 10 1 10 mg 1
Ceftriaxone	$1000 \text{ mg} \text{ daily}^{183}$	No data
Penicillins		
Penicillin G	No data	LD 50 000 upit/L MD 25 000 upit/L 13
Amoxicillin	No data	MD 150 mg/l ¹⁸⁴
Ampicillin ^a	4 gm daily ¹⁸⁵	MD 125 mg/L ¹⁸⁶
Ampicillin/	- gin daily	ID 1000 mg/500 mg MD 133.3 mg/66.7
sulbactam		187,188
Piporacillin/	No. data	10° m/0.5 m MD 1 m/0.125 m ¹⁸⁹
tazobactam	No data	
Ticoncillin /clouulanic	Nie data	ID 3 mm/0.2 mm MD 300 mg/20 mg/1 190
ncarcinin/ciavulanic	INO data	ED 3 gm/0.2 gm, FID 300 mg/20 mg/E
Others		
A		LD 500
Aztreonam	2 gr daily	MD 50 mg/L , MD 250 mg/L
Ciprofloxacin	No data	MD 50 mg/L 195
Clindamycin	No data	MD 600 mg/bag
Daptomycin	300 mg daily	LD 100 mg/L M, MD 20 mg/L
Fostomycin	4 g daily	No data
Imipenem/cilastatin	500 mg in alternate exchange	LD 250 mg/L, MD 50 mg/L ¹⁰²
Ofloxacin	No data	LD 200 mg, MD 25 mg/L ²⁰⁴
Polymyxin B	No data	MD 300,000 unit (30 mg)/bag ¹⁰⁰
Quinupristin/	25 mg/L in alternate exchanges	No data
dalfopristin	202	20/
Meropenem	500 mg daily (for long dwell in APD) ²⁰⁷ 1000 mg daily (for short dwell in CAPD) ^{208,209}	MD 125 mg/L ²⁰⁶
Teicoplanin	15 mg/kg every 5 days ²¹⁰	LD 400 mg/bag, MD 20 mg/L ^{211,140}
Vancomycin	15–30 mg/kg every 5–7 days ^{c141,212} for CAPD	LD 20-25 mg/kg, MD 25 mg/L ²¹⁴
	15 mg/kg every 4 days ²¹³ for APD	
Antifungal		
Fluconazole	IP 150–200 mg every 24 to 48 h ^{215,216} (oral route is preferred: see Table 6)	No data
Voriconazole	IP 2.5 mg/kg daily ²¹⁷ (oral route is preferred: see Table 6)	No data

LD: loading dose in mg; MD: maintenance dose in mg; IP: intraperitoneal; APD: automated peritoneal dialysis.

^aIP ampicillin is not recommended for treatment of enterococcal peritonitis.²¹⁸

^bGiven in conjunction with 500 mg intravenous twice daily.

^cSupplemental doses may be needed for APD patients and dwell time of at least 6 h is preferred.

^dIncrease in doses by 25% may be needed for patients with significant residual kidney function.¹⁶⁸

treatment antibiotic dosing peritonitis ations for Recommend Systemic 4 Ο

Antibacterial Amoxicillin Gianaflavaain	Oral 500 mg thrice daily ²¹⁹ Oral 500–750 mg daily ²²⁰ Oral 750 mg BD for CCPD ²²¹
Amoxicillin	Oral 500 mg thrice daily ²¹⁹ Oral 500–750 mg daily ²²⁰ Oral 750 mg BD for CCPD ²²¹
Cianaflassaain	Oral 500–750 mg daily ²²⁰ Oral 750 mg BD for CCPD ²²¹
Ciprofioxacin	Oral 750 mg BD for CCPD ²²¹
	000.000
Clarithromycin	Oral 250 mg BD ^{222,223}
Colistin	IV 300 mg loading (for critically ill patients), then 60–200 mg daily ^{b224-226}
Dalbavancin	IV 1500 mg over 30 min single dose ²²⁷
Daptomycin	IV 4–6 mg/kg every 48 h ²²⁸
Ertapenem ^a	IV 500 mg daily ²²⁹
Levofloxacin	Oral 250 mg daily ²³⁰ or 500 mg every 48 h
Linezolid	IV or oral 600 mg BD ^{231,232} for 48 h, then 300 mg BD ²³³
Moxifloxacin	Oral 400 mg daily ^{234,235}
Rifampicin	Oral or IV 450 mg daily for BW <50 kg; 600 mg daily for BW \geq 50 kg
Ticarcillin/clavulanic acid	IV 3 gm/0.2 gm every 12 h
Tigecycline	IV 100 mg loading, then 50 mg every 12 h ^{236,237}
Trimethoprim/sulfamethoxazole	Oral 160 mg/800 mg BD ^{238,239}
Anti-fungal	
Amphotericin B desoxycholate	IV 0.75–1.0 mg/kg/day over 4–6 h ²⁴⁰
Amphotericin B (liposomal)	IV 3–5 mg/kg/day ^{241,242}
Anidulafungin	IV 200 mg loading, then 100 mg daily ^{243,244}
Caspofungin	IV 70 mg loading, then 50 mg daily ²⁴³
Fluconazole	Oral 200 mg loading, then 100 mg daily ²⁴⁰
Flucytosine	Oral I gm daily ²⁴⁰
Isavuconazole	Oral or IV 200 mg every 8 h for 6 doses (48 h) loading, then 200 mg daily
Micafungin	IV 100 mg daily ^{243,245}
Posaconazole	Oral tablet 300 mg every 12 h loading for two doses, then 300 mg daily ²⁴⁶
Voriconazole	Oral 200 mg every 12 h

Table 6. Systemic antibiotic dosing recommendations for treatment of peritonitis.

BD: twice a day; IV: intravenous; BW: body weight. ^aErtapenem is not active against *Pseudomonas* or *Acinetobacter* species.

^bExpressed as colistin base activity in mg.

Adjunctive treatments

Augmented peritoneal lavage should not be performed Icodextrin be considered for volume overload which occurs during acute peritonitis

Safety and Efficacy of Icodextrin versus Glucose-only Peritoneal Dialysis (PD) Regimens

Meta-analysis (19 Randomized Controlled Trials) Including unpublished data from investigator-initiated and industry sponsored studies

Comprehensive literature search

International databases
 Clinical trial registries
 Conference proceedings
 Reference lists
 Clinical Study Reports

Limitations Variable trial quality Heterogenous F/U periods Paucity of assessments

n = 1693

Safety outcomes and residual kidney function were similar in both groups

Conclusion: Icodextrin for once-daily long-dwell PD has clinical benefit for some patients, including those not meeting ultrafiltration targets and at risk for fluid overload. Future research into patient-centered outcomes and cost-effectiveness associated with icodextrin is needed.

Goossen K, Becker M, Marshall MR, Buhn S, Breuing J, Firanek CA, Hess S, Nariai H, Sloand JA, Yao Q, Chang TI, Chen JB, Paniagua R, Takatori Y, Wada J, Pieper D. Icodextrin Versus Glucose Solutions for the Once-Daily Long Dwell in Peritoneal Dialysis: An Enriched Systematic Review and Meta-analysis of Randomized Controlled Trials. Am J Kidney Dis. 2020 Feb 4:S0272-6386(19)31115-1. DOI: 10.1053/j.ajkd.2019.10.004. Visual Abstract by Edgar Lerma, MD, FASN

ISPD Catheter-Related Infection Recommendations: (2023 Update

Visual Abstract by Edgar Lerma, MD

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and duration, catheter removal, and salvage options were provided.

Pseudomonas peritonitis

We suggest that Pseudomonas peritonitis be treated with 2 antibiotics with different mechanisms of action and to which the organism is sensitive for 3 weeks (2C)

We suggest that Pseudomonas peritonitis with concomitant exit-site and tunnel infection be treated with catheter removal (2D)

If there is no clinical response after 5 days of effective antibiotic treatment, we suggest that Pseudomonas peritonitis be treated with early catheter removal instead of using three antibiotics as an attempt to salvage (2D)

Figure 8. Management algorithm for polymicrobial peritonitis.

Management of culture-negative Peritonitis

Figure 10. Management algorithm for culture-negative peritonitis.

Non-tuberculous mycobacterial peritonitis

We suggest antituberculous therapy, instead of PD catheter removal, as the primary treatment of peritonitis caused by Mycobacterium tuberculosis (2C) We suggest that Ziehl–Neelsen staining for acidfast bacilli be requested when there is a clinical suggestion of non-tuberculous mycobacterial (NTM) peritonitis, including persistent culturenegative peritonitis (2D)

We suggest that NTM peritonitis be treated with both effective antibiotics and catheter removal (2D).

Tuberculose Peritonitis in Peritoneal Dialysis

Table 8. Drug dosing recommendations for treatment oftuberculous peritonitis.

Drug	Dosing
Isoniazid	Oral 5 mg/kg daily (maximum dose 300 mg daily) ³⁸²
Rifampicin	Oral 450 mg daily for BW <50 kg; 600 mg daily for BW \geq 50 kg
Pyrazinamide	Oral 30 mg/kg three times weekly
Levofloxacin	Oral 250 mg every 48 h
Ofloxacin	Oral 200 mg daily ³⁷⁵
Ethambutol	Oral 15 mg/kg every 48 h ³⁸²
Moxifloxacin	Oral 400 mg daily ^{234,235}
Pyridoxine	Oral 50–100 mg daily ^{375,382}

BW: body weight.

ISPD Peritonitis Guideline Recommendations: 2022 update on prevention and treatment #NephJC Definitions Prevention Outcomes Treatment **International Society For** Antibiotic Before **Peritoneal Dialysis** Medical Cure **IP** Antibiotics is the **Cause Specific** Catheter Placement (1A) Prefered Route (18) **Complete Resolution** Peritonitis No Relapse, Recurrence, Catheter **Topical Antibiotic** Gram Negative and Removal or Transfer to HD for >30 Days For Exit-Site Care Positive Coverage (1C) According to Organism PERITONITIS Refractory Culture Negative Anti-Fungal DIAGNOSTIC CRITERIA Cloudy Bags or Effluent Leukocyte Count Prophylactic Antibiotic - Catheter Related > 100 /mcl after 5 days of therapy Coverage (1B) After Wet Contamination 2 out of 3 Enteric Peritonitis 1) Abdominal Pain or Cloudy Effluent of PD System (2D) Recurrent Effluent WBC > 100/mcL with > 50% PMN Peritonitis within 4 weeks of therapy, Antibiotics Prior to Adjust Antibiotics to ----3) Positive Effluent Culture Different organism Culture Results (1C) Colonoscopy (2C) -----5 Relapsing **Time Specific** or Invasive Gynecological In the absence of Point 3 Peritonitis within 4 weeks of therapy, **Culture Negative Peritonitis** Procedure and Drainage Same organism or Culture Negative In Refractory Peritonitis of PD Fluid (2D) Repeat **Remove Catheter (1D)** ${igerta}$ Peritonitis > 4 weeks of therapy, or Observe If WBC is **Monitoring Target** Pets NOT Allowed in PD Pre-PD Same organism Decreasing (2C) Exchange Room (2A) 💥 Associated with **PD-Related** <0.40 episodes/year at risk. PD Catheter Insertion Related Avoid Hypokalemia Crganism Specific Recommendations >80% of Patients Peritonitis Free - Catheter Removal - HD Transfer Recommendations per unit time per year. - Death (30 days) and Hospitalisation **Reference:** Li PK et al. ISPD peritonitis guideline recommendations: Conclusion: The ISPD updated recommendations have revised definitions for peritonitis 2022 update on prevention and treatment. 2022 Perit Dial Int. 2022 and peritonitis-associated medical conditions. New peritonitis categories and outcomes are

Mar;42(2):110-153. PMID: 35264029. Visual abstract by Momen Abbasi, MD

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defined. Revised recommendations regarding prevention and treatment of peritonitis

microorganisms.

including empirical antibiotic selection and dosage and treatment of peritonitis due to specific

AND COLETY OF NEWMOOD

