

Peritonitis: Overview and Medical Perspective

Professor Edwina Brown

Imperial College Renal and Transplant Centre

Hammersmith Hospital, London, UK

ISPD guidelines

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ISPD GUIDELINES/RECOMMENDATIONS

ISPD PERITONITIS RECOMMENDATIONS: 2016 UPDATE ON PREVENTION AND TREATMENT

Philip Kam-Tao Li,¹ Cheuk Chun Szeto,¹ Beth Piraino,² Javier de Arteaga,³ Stanley Fan,⁴ Ana E. Figueiredo,⁵
Douglas N. Fish,⁶ Eric Goffin,⁷ Yong-Lim Kim,⁸ William Salzer,⁹ Dirk G. Struijk,¹⁰
Isaac Teitelbaum,¹¹ and David W. Johnson¹²

Outline of talk

- Diagnosis of peritonitis
- Antibiotic choice and administration
- Specific causes of peritonitis
- Refractory peritonitis

Diagnosis of peritonitis

REQUIRES 2 OF FOLLOWING 3 FEATURES

- Clinical features consistent with peritonitis
 - abdominal pain or cloudy dialysis effluent
- Dialysis effluent wbc $>100/\mu\text{l}$ (after dwell time of at least 2 hours) with $>50\%$ neutrophils
- Positive dialysis effluent culture

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- Blood culture bottles preferred technique for bacterial culture
 - If not possible to deliver directly to lab, should be incubated at 37°C

Initial management of peritonitis

Clinical evaluation

Examine exit site and tunnel

Collect PD fluid for differential cell count, Gram stain, culture



Start IP antibiotics as soon as possible

Allow to dwell for at least 6 hours

Empirical gram positive and gram negative antibiotics

Outline of talk

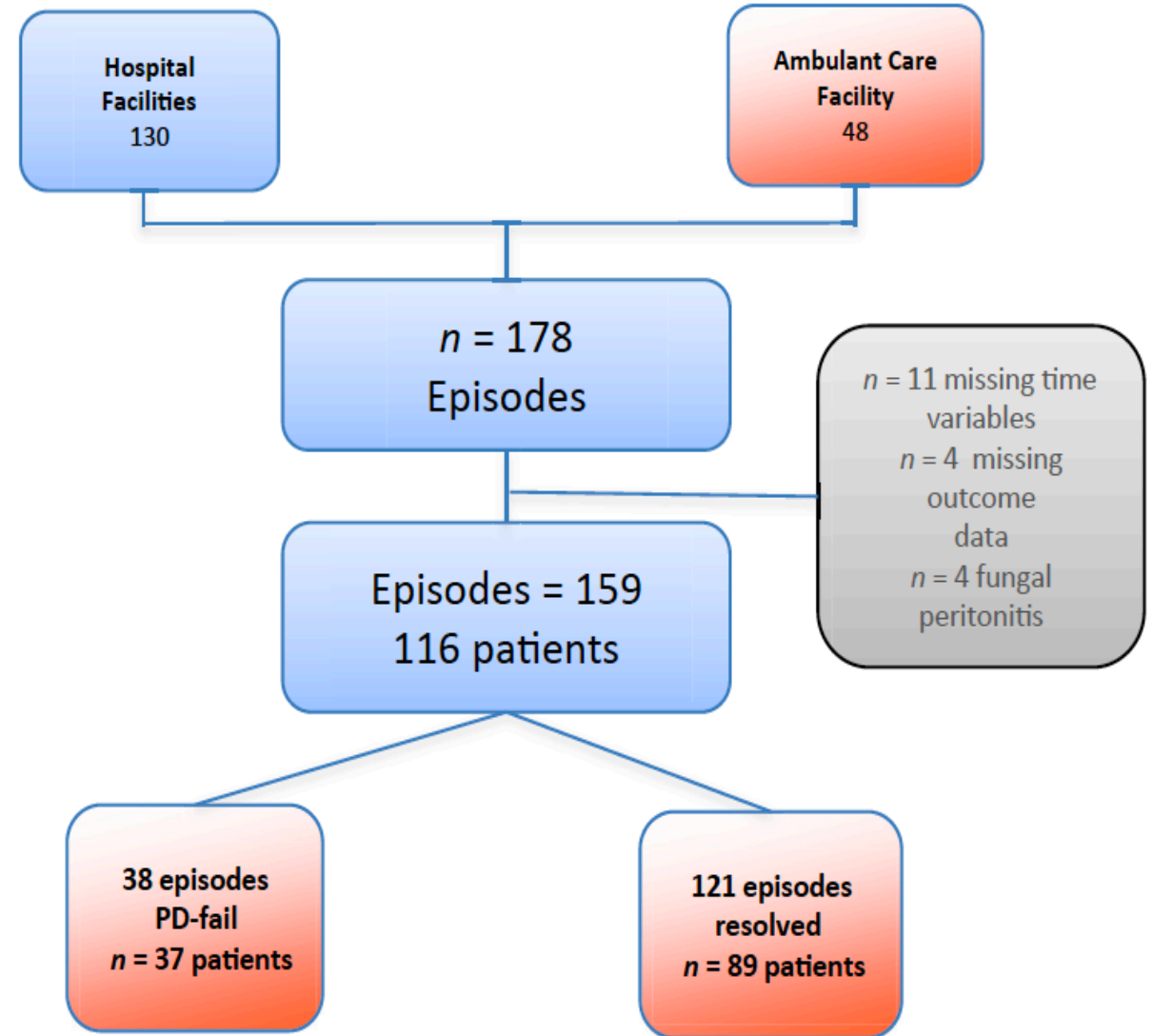
- Diagnosis of peritonitis
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Empirical antibiotic therapy

- Should be started as soon as appropriate microbiological samples taken
- No single antibiotic regime proven to be superior; choice should be centre-specific
- Must cover gram-positive and gram-negative organisms including pseudomonas
- **Intraperitoneal administration preferred route unless systemic sepsis**
- When foreseeable delay, give systemic antibiotics as temporary measure to ensure prompt treatment

The Relationship Between *Presentation* and the Time of Initial Administration of Antibiotics With *Outcomes* of *Peritonitis* in Peritoneal Dialysis Patients: The PROMPT Study

Muthucumarana K et al, KI Report 2016



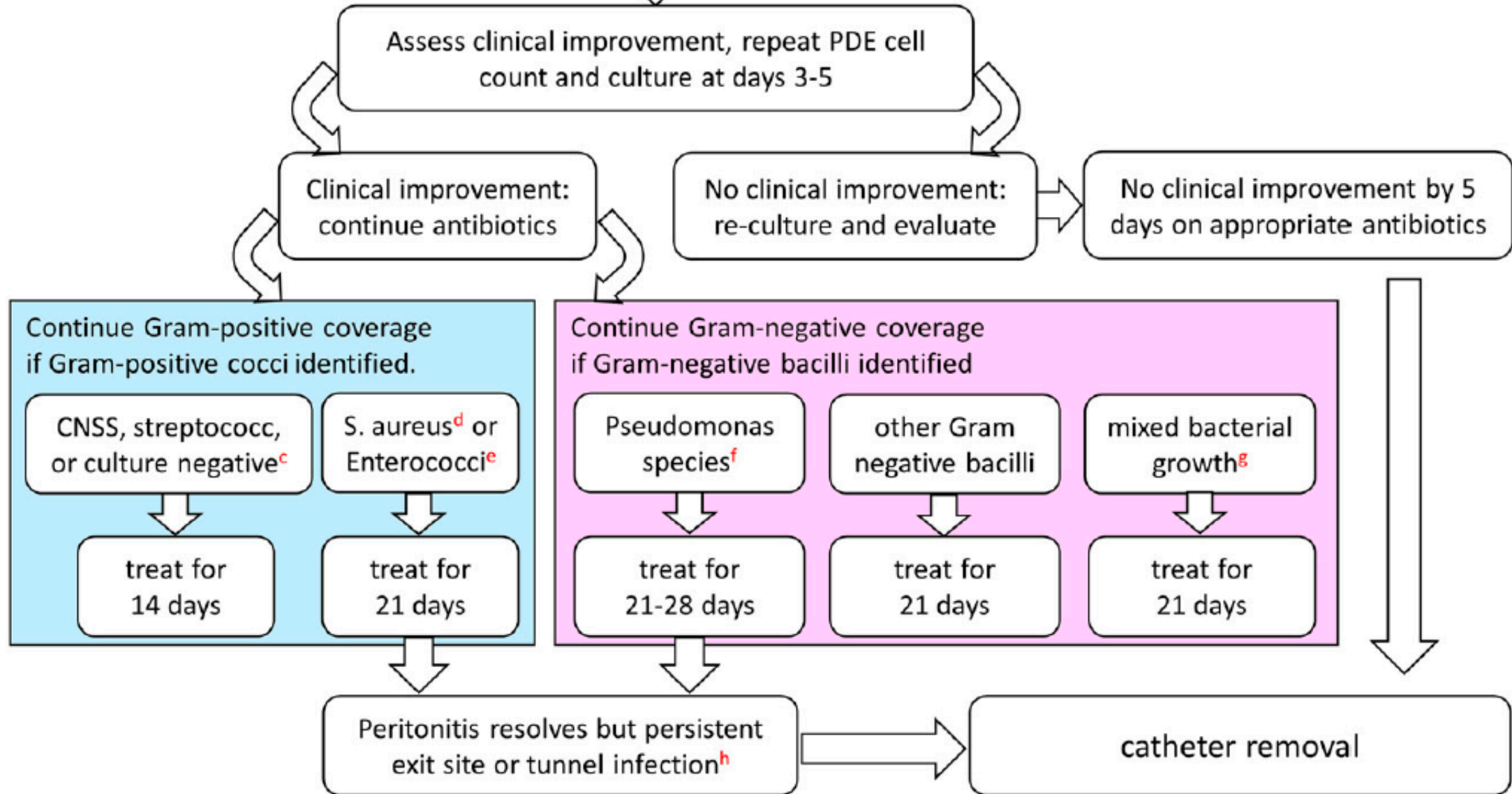
Outcomes of PROMPT study

- Median SC (symptom to contact time) 5.0 hrs
- Median CT (contact to treatment time) 2.3 hrs
- Median ST (symptom to treatment time) 9.0 hrs
- PD failure (24%) patient episodes (28 catheter removals, 10 deaths)
- **Risk of PD failure increased by 5.5% for each hour of delay of administration of antibiotics (odds ratio for CT: 1.055, P=0.032)**
- **Multivariable analysis – only CT for presentation to hospital based facility compared with community PD facility (OR: 1.068, P=0.015) and female sex (OR 2.4; P=0.027) associated with PD failure**
- **EACH HOUR DELAY IN STARTING ANTIBIOTICS FROM PRESENTING TO HOSPITAL FACILITY INCREASED RISK OF PD FAILURE OR DEATH BY 6.8%**

Administration of antibiotics

- Vancomycin, aminoglycosides and cephalosporin can be mixed in same dialysis bag
- Recommended dosages of antibiotics summarized in ISPD guideline
 - Based on clinical experience rather than pharmacokinetic studies
- Dosage of many antibiotics need to be adjusted for residual kidney function
- Intermittent dosing possible because many antibiotics have substantial systemic absorption during peritonitis – enables reentry into peritoneal cavity in subsequent PD cycles
- Antibiotic-containing PD solution should dwell for at least 6 hours
- If on APD, give antibiotics in day dwell – higher daily dose often required than on CAPD because of removal during rapid cycles of APD

Algorithm for management of peritonitis



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Specific
microbial
causes of
peritonitis
with poor
outcomes

Staphylococcus
aureus

Pseudomonas

Staphylococcus aureus related peritonitis

- Associated with touch contamination and catheter infections (ESI, tunnel)
- Should be treated with effective antibiotics for 3 weeks
- Vancomycin appropriate whether methicillin-sensitive or resistant; teicoplanin and daptomycin alternatives for methicillin-resistance
- One retrospective study (2007) showed rifampicin for 5-7 days reduced risk of relapse or repeat S Aureus infection from 42% to 21%
 - Rifampicin potent liver enzyme inducer so potential drug interactions
 - High rate of resistance with repeated use
- Consider catheter removal if concomitant exit site or tunnel infection

Pseudomonas related peritonitis

- Generally severe and often associated with catheter infection. Associated with higher frequency of hospitalization, higher rates of catheter removal and permanent HD transfer
- Treat with 2 antibiotics with different mechanisms of action and to which organism is sensitive (e.g. IP gentamicin or oral ciprofloxacin with IP ceftazidime or cefepime) for 3 weeks (Grade 2C)
 - Carbapenems are valid alternatives
- If concomitant exit-site and tunnel infection, catheter should be removed (Grade 2C)

Outcomes of pseudomonas peritonitis in Australia 2003-6

Outcome	<i>Pseudomonas</i> Peritonitis (<i>n</i> = 191 Episodes)	Non- <i>Pseudomonas</i> Peritonitis (<i>n</i> = 3403 Episodes)	<i>P</i>
Relapse (<i>n</i> [%])	17 (9)	485 (14)	0.040
Hospitalization			
<i>n</i> (%)	150 (79)	2354 (69)	0.006
duration (d; median [IQR])	9.00 (5.00 to 20.00)	6.00 (3.00 to 11.00)	<0.001
Catheter removal			
<i>n</i> (%)	84 (44)	691 (20)	<0.001
time to occurrence (d; median [IQR])	5.50 (3.00 to 11.00)	6.00 (3.00 to 13.00)	0.400
Temporary hemodialysis			
<i>n</i> (%)	20 (10)	132 (4)	<0.001
time to occurrence (d; median [IQR])	7.50 (4.25 to 12.50)	6.00 (3.00 to 11.50)	0.500
duration (d; median [IQR])	73.50 (51.00 to 109.50)	67.00 (20.50 to 103.00)	0.300
Permanent hemodialysis			
<i>n</i> (%)	66 (35)	569 (17)	<0.001
time to occurrence (d; median [IQR])	6.00 (4.00 to 11.75)	7.00 (4.00 to 13.00)	0.700
Death			
<i>n</i> (%)	6 (3)	76 (2)	0.400
time to death (d; median [IQR])	19.00 (5.00 to 26.00)	11.00 (3.00 to 22.25)	0.400

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Infectious indications for rapid removal of PD catheter

Fungal peritonitis

Peritonitis associated with exit site or tunnel infection, same organism

Mycobacteria catheter infection or peritonitis

Multiple enteric organisms causing peritonitis

Peritonitis associated with intra-abdominal pathology

Failure of effluent to clear by day 4-5 of appropriate antibiotics

Refractory peritonitis

- Refractory peritonitis defined as failure of PD effluent to clear up after 5 days of appropriate antibiotics
 - PD catheter should be removed promptly (Grade 1C)
 - Earlier removal appropriate if clinical condition deteriorating
- After catheter removal, antibiotics should be continued for further 2 weeks
- Monitoring of WBC count in PD effluent may predict treatment response
 - Retrospective study showed $WBC \geq 1090/mm^3$ on day 3 was independent prognostic marker for treatment failure
- Prolonged attempts to treat refractory peritonitis without catheter removal are associated with extended hospital stay, peritoneal membrane damage, increased risk of fungal peritonitis and excessive mortality

Predictors of peritonitis treatment failure

Parameter	Adjusted OR	95% CI	β , Standardized Coefficient	P
Peritoneal dialysis modality				
intermittent peritoneal dialysis (break-in period)	Reference	—	—	—
continuous ambulatory peritoneal dialysis	0.48	0.001 to 3.50	-3.06	0.17
automated peritoneal dialysis	0.23	0.04 to 1.46	-1.46	0.12
Causative organisms				
Gram-positive only	Reference	—	—	—
Gram-negative only ^b	2.86	1.24 to 6.58	1.05	0.014
<i>Pseudomonas</i> or <i>Xanthomonas</i>	34.7	4.31 to 280	3.55	0.001
polymicrobial	2.47	0.57 to 10.7	0.90	0.23
mycobacterial	5.08	2.14 to 12.1	1.62	<0.0001
fungal	657	71.4 to 6043	6.49	<0.0001
culture negative	1.98	0.57 to 6.95	0.68	0.28
Diabetes	3.34	1.23 to 9.02	1.20	0.018
Duration of peritoneal dialysis (vintage yr)	1.15	1.05 to 1.26	0.14	0.004
Peritoneal dialysate white count $\geq 1090/\text{mm}^3$ on day 3	9.03	4.40 to 18.6	2.20	<0.0001

- Data from Hong Kong
- Based on 565 episodes peritonitis

Poorer outcomes with delays in catheter removal

	Hospitalization > 10 d	Hospitalization < 10 d	<i>P</i> *
Age (y)	64 ± 12.7 (34-87)	58 ± 13.8 (35-79)	0.028
Race (%)			
Caucasian	39	44	NS
Asian	32	44	NS
Afro-Caribbean	17	8	NS
Other	0	8	NS
Organism			
No growth	1	9	0.0038
Gram-positive	11	13	NS
Gram-negative	5	8	NS
<i>Candida</i> species	1	2	NS
Duration of peritonitis (d)	7.9 (5.9), 2-30	5.3 (3.8), 1-15	0.027

- Data from CXH
- Based on 490 episodes peritonitis
- 64 episodes catheter removal

Choi P,.....Levy J, Brown E. AJKD 2004

Cause of death within 30 days after peritonitis onset

Cause	Patients (N=301)	
	N	%
Cardiac	74	24.6
Myocardial ischaemia and infarction	31	10.3
Cardiac arrest (uncertain cause)	34	11.3
Social reasons	70	23.3
Vascular	28	9.3
Cerebrovascular accident	9	3.0
Bowel infarction	14	4.7
Peritonitis	80	26.6
Bacterial	61	20.3
Fungal	18	6.0
Other infection	24	7.9
Septicaemia (site unknown)	15	5.0

ANZDATA 2003-8

6639 patients; 6229 peritonitis episodes; 301 deaths

Ghali JR et al. PDI 2011

Conclusion: Key factors to improve peritonitis outcomes



Awareness of diagnosis and appropriate microbiological techniques for dialysis effluent



Urgent administration of empiric INTRAPERITONEAL antibiotics



Monitoring cell count of dialysis effluent



Use of appropriate antibiotics for culture results



Review at day 4 whether patient in high risk group for failure



Prompt removal of PD catheter once decision made (will depend on overall prognosis of patient)