



# Update on ISPD Infection Recommendations

**RPN Nephrology Education  
Day**

Jenny Ng, BScPhm, ACPR  
April 8th, 2011



**Sunnybrook**

HEALTH SCIENCES CENTRE

when it matters  
**MOST**



# Objectives

- General overview of Peritonitis
- Highlight changes/updates from 2005 to 2010 guidelines
- Case review



# Peritonitis

- Leading complication of peritoneal dialysis
- 18% of infection related mortality in PD pts is the result of peritonitis

## Factors that may contribute

- technique
- continuous presence of non-physiologic fluid in the peritoneal cavity can impair host defenses



# Case Discussion

Mr. KW is a 56 year old male who has been on peritoneal dialysis for 4 years. His weight is ~100 kg. RRF – 760 mL/day

He presents to the home dialysis office with c/o abdominal pain & cloudy dialysate

Due to hives/rash reaction with cephalosporins, he is empirically treated with:

- Vancomycin 2 g IP x1
- Ciprofloxacin 500 mg po BID
- Nystatin 500,000 units PO QID swish and swallow



# Case Discussion Continued

Initial investigations:

- Dialysate WBC :  $6500 \times 10^6/L$
- Dialysate Neutrophil Count:  $5655 \times 10^6/L$



# Peritonitis – ISPD Clinical Presentation

- Abdominal pain
- +/- Cloudy fluid
- Other
  - Fever
  - Nausea/vomiting
  - diarrhea



# ISPD Peritonitis Diagnosis

- Dialysate effluent
  - Gram stain (checking for yeast)
  - Culture
  - Effluent WBC count  $> 100/\mu\text{L}$  (after a dwell of at least 2 hrs) with  $> 50\%$  polymorphonuclear neutrophils (PMN)
- For APD pts with no day dwell
  - Infuse 1 L of dialysate for 1-2 hrs and then sample effluent



# Source of Infection & Common Organisms

- Exit site infections
  - *S. aureus*
  - *P. aeruginosa*
- Touch Contamination
  - Coagulase –ve staph
  - Streptococcus/enterococcus
  - *S. aureus*





# Empiric Treatment

<b>Gram + Coverage</b>	<b>Gram –ve Coverage</b>
<ul style="list-style-type: none"><li>• cefazolin</li><li>• vancomycin</li></ul>	<ul style="list-style-type: none"><li>• Aminoglycosides</li><li>• Ceftazidime</li><li>• Cefepime</li><li>• Carbapenem</li><li>• Quinolone * only if local sensitivities support such use</li></ul>



## Case Discussion Continued

Day #	1	2
Dialysate WBC (x10 <sup>6</sup> /L)	6500	6850
Dialysate PMN(x10 <sup>6</sup> /L)	5655	5890

### Day 2

- Admitted to hospital, Vancomycin + Cipro 400 mg IV BID
- gram –ve bacilli

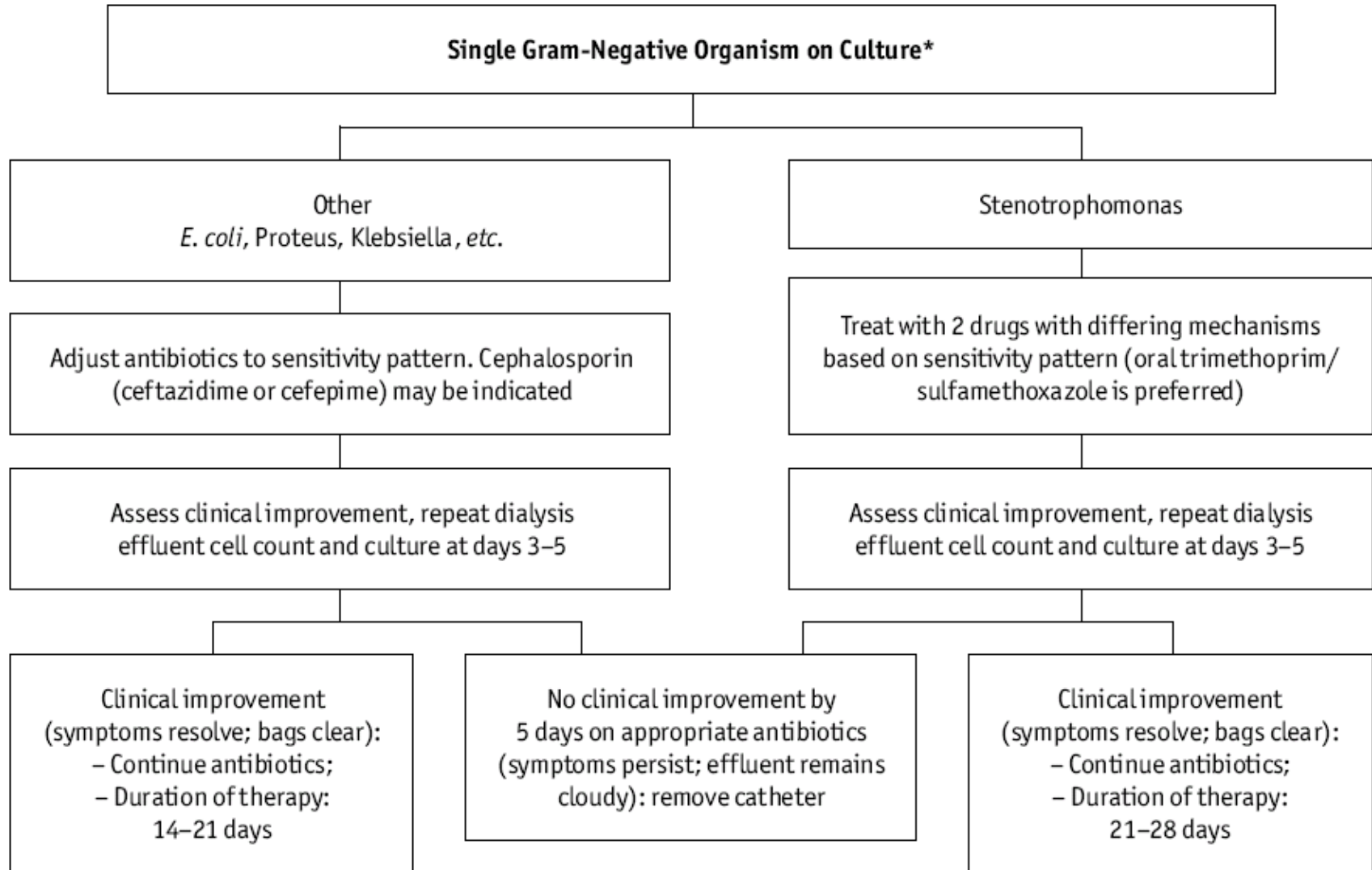


Figure 7 — Other single gram-negative organism peritonitis: \*Choice of therapy should always be guided by sensitivity patterns.



## Case Discussion Continued

Day #	1	2	3
Dialysate WBC (x10 <sup>6</sup> /L)	6500	6850	7000
Dialysate PMN(x10 <sup>6</sup> /L)	5655	5890	

### Day 3

- E.Coli resistant to Cipro, sensitive to cefazolin, gentamicin and co-trimoxazole
- Klebsiella cultured as organism #2
- Tobramycin 80 mg IP x 1 dose and cefazolin 2 g IP OD



# Situations to consider double coverage

- In slowly resolving or particularly severe *S. aureus* exit-site infection (ESI) – rifampin 600 mg po OD may be added (for peritonitis ISPD indicates use x 1 week)
- *P. aeruginosa* ESI – FQ first line (especially if slow resolving or if recurrent *P. aeruginosa* ESI)
- \* SPICE organisms (*Serratia*, *Pseudomonas*, *Providencia*, *Citrobacter* and *Enterobacter*)
- *Stenotrophomonas*



## Case Discussion Continued

Day #	1	2	3	4
Dialysate WBC (x10 <sup>6</sup> /L)	6500	6850	7000	8000
Dialysate PMN(x10 <sup>6</sup> /L)	5655	5890		

### Day 4

- Klebsiella is sensitive to cefazolin, gentamicin, ciprofloxacin
- Continues on cefazolin 2 g IP OD



## Case Discussion Continued

Day #	1	2	3	4	5	6
Dialysate WBC (x10 <sup>6</sup> /L)	6500	6850	7000	8000	2650	36160
Dialysate PMN(x10 <sup>6</sup> /L)	5655	5890			1801	30228

### Day 6

- Dialysate effluent is described as cloudy/milky
- PD catheter to be removed



# Indications for Catheter Removal

- Refractory peritonitis (failure of effluent to clear in 5 days of appropriate Abx)
- Refractory exit-site and tunnel infection
- Tunnel infection
- P. Aeruginosa
- Fungal peritonitis
- Relapsing peritonitis
  
- Catheter removal may also be considered for
  - Repeat peritonitis
  - Mycobacterial peritonitis
  - Multiple enteric organisms
  - Exit-site infection that progresses to/ presents with peritonitis with same organism





# Case Conclusion

- PD catheter removed
- Started on IHD 3x/week
- CT abdomen to r/o abscess
  - Diverticulitis?
  - Enteric source of infection?
- Antibiotics:
  - Ceftazidime 2 g IV qhemodialysis
  - Vancomycin 1 g IV qhemodialysis
  - Metronidazole 500 mg po BID



# NEW - Adjunctive Treatments: Fungal Prophylaxis

- Fungal peritonitis accounts for 3-15% of all peritonitis episodes
- Mortality rate ranges from 5-25%
- Majority of fungal peritonitis episodes are preceded by courses of Antibiotics
- Use of fungal prophylaxis may prevent some cases of Candida peritonitis in programs that have high rates of fungal peritonitis



# Fungal Prophylaxis – What is the evidence?

**Table 2. Studies of Antifungal Prophylaxis**

Study	Study Design	Years of Study	Intervention	Number of Patients per Group: Control Versus Treated	Follow-Up Time: Control Versus Treated, Patient-Months	Result of Intervention
Lo et al <sup>92</sup>	Randomized trial	1991-1993	Nystatin with each course of antibiotics versus no prophylaxis	199 versus 198	16.6 months versus 18 months	Benefit
Restrepo et al <sup>93</sup>	Randomized trial	2004-2007	Fluconazole with each course of antibiotics versus no prophylaxis	608 PD-related infections requiring antibiotics	150 days after each antibiotic administration	Benefit
Zaruba et al <sup>94</sup>	Observational	1979-1982 versus 1983-1989	No prophylaxis versus nystatin	38 versus 93	415 versus 2,102	Benefit
Robitaille et al <sup>95</sup>	Observational	1989-1991 versus 1991-1993	No prophylaxis versus nystatin or ketoconazole	25 children overall	361 (total)	Benefit
Wadhwa et al <sup>96</sup>	Observational	1991-1993 versus 1993-1995	No prophylaxis versus fluconazole	122 versus 112	1,832 versus 1,705	Benefit
Wong et al <sup>97</sup>	Observational	1995-1999 versus 1999-2005	No prophylaxis versus nystatin	320 versus 481	8,875 versus 13,725	Benefit
Thodis et al <sup>98</sup>	Observational	1996 versus 1997	No prophylaxis versus nystatin	240 versus 240	2,400 versus 2,400	No benefit
Williams et al <sup>99</sup>	Observational	1997-1999	No prophylaxis versus nystatin	N/A	3,911 versus 2,124	No benefit

Abbreviation: N/A, data not available.



# What is recommended?

- ISPD

“Each PD program must examine its history of fungal peritonitis and decide whether such a protocol might be beneficial”

- Nessim 2011

“Given significant morbidity and mortality associated with fungal peritonitis, the potential for benefit based on the available evidence and the low risk of the intervention, use of fungal prophylaxis with either nystatin or fluconazole at time of antibiotic use is recommended to prevent antibiotic related fungal peritonitis”



# Summary

- Peritonitis remains a leading complication in peritoneal dialysis
- Proper management and focus on prevention of peritonitis is necessary to avoid treatment failure
- Further research with properly conducted studies are required for new antibiotics, stability in newer dialysis solutions and prevention techniques to aid in our management of people on peritoneal dialysis



## References

- Peritoneal Dialysis - related infections recommendations: 2005 Update. PDI 2005; 25: 107-31
- Peritoneal Dialysis – related infections recommendations 2010 Update. PDI 2010; 30: 393-423
- [www.ispd.org](http://www.ispd.org)

**TABLE 3**  
 Summary of Studies Using Antifungal Prophylaxis During Antibiotic Therapy to Prevent Fungal Peritonitis (FP) in Patients Receiving Peritoneal Dialysis

Study (Ref.)	Antifungal agents used for prophylaxis	Total follow-up of study group (patient-months)	AR-FP (episodes/patient-year) (All FP) (episodes/patient-year)		Effect
			Without prophylaxis	With prophylaxis	
Zaruba <i>et al.</i> , 1991 (4)	Nystatin 0.5 MU t.d.s.	2102	0.29 (0.29)	0.02 (0.023)	+ (+)
Robitaille <i>et al.</i> , 1995 (5) <sup>a</sup>	Nystatin 0.01 MU/kg or ketoconazole	361	0.14 (0.14)	0 (0)	+ (+)
Wadhwa <i>et al.</i> , 1996 (6)	Fluconazole q.o.d.	1705	0.08 (0.098)	0.01 (0.028)	+ (+)
Lo <i>et al.</i> , 1996 (7)	Nystatin 0.5 MU q.i.d.	3576	0.02 (0.044)	0.01 (0.013)	- (+)
Thodis <i>et al.</i> , 1998 (8)	Nystatin 0.5 MU q.i.d.	2400	0.02 (0.03)	0.02 (0.06)	- (-)
Williams <i>et al.</i> , 2000 (9)	Nystatin 0.5 MU q.i.d.	2124	0.01 (0.01)	0.01 (0.017)	- (-)
Current study	Nystatin 0.5 MU q.i.d.	13725	0.014 (0.019)	0.003 (0.011)	+ (-)

MU = mega units; t.d.s. = three times per day; q.o.d. = once on alternate days; q.i.d. = four times per day; AR = antibiotic-related; + = positive effect; - = negative effect.

<sup>a</sup> Pediatric patients.