PD-Related Infections Recommendations

Beth Piraino, MD
Professor of Medicine at University of Pittsburgh
Introduction

- Peritonitis remains a major complication in PD
- Peritonitis contributes to mortality
- Peritonitis contributes to peritoneal membrane failure
- Continues to be a leading cause of technique failure
This talk is based on ISPD Guidelines:

Learning objectives

- Learn to recognize and diagnose exit site infections, tunnel infections and peritonitis
- Learn the initial management of peritonitis and choices
- Learn subsequent management.
- Understand terminology for peritonitis
- Know how to calculate rates of infections.
Every program should regularly monitor infection rates, at a minimum on a yearly basis.

- Both exit site and peritonitis rates
- Causative organisms
- Antibiotic sensitivity
- Presumed etiology
There are several ways to examine peritonitis within a program:

- As a rate either
  - Months of at risk divided by # episodes
  - # infections divided by dialysis years at risk
- As % of patients who are peritonitis free for a period of time
- As median peritonitis rate for the program
Example of calculations:

RATE: # peritonitis episodes ÷ time at risk in group

7 episodes in 6 patients in a program with 70 patients over the year with 44 years at risk

RATE: One episode per 75 months
Or 0.16 episodes per year at risk

PD Registry Data--DCI Oakland
For this year only 9% of the patients (6/70) had a peritonitis episode. Since most patients did NOT have peritonitis (individual rate 0), the median rate for the program was zero.
Exit site and tunnel infections

Normal looking exit site:
Normal skin color
No drainage
No crusting
No tenderness or swelling

Chronic exit site infection
Crusting, dark erythema
Purulent drainage from the exit site indicates the presence of infection.

Erythema may or may not represent infection.
Tunnel infection

- Erythema, edema or tenderness along the subcutaneous pathway but often occult
- Almost always in conjunction with exit site infection but rarely occurs alone.
- *S. aureus* and *P. aeruginosa* often causes of tunnel infection
Rx for exit site/tunnel infections

- The most serious and common exit site pathogens are S aureus and P aeruginosa and must be treated aggressively.
- Oral antibiotic therapy is recommended, with the exception of MR S aureus.
Therapy for exit site and tunnel infections

- Empiric therapy should cover S aureus
- A penicillinase-resistant penicillin or first generation cephalosporin can be used
- Avoid vancomycin unless MR
- Rifampin 600 mg each day can be added if S aureus and slow to resolve---but drug interactions
Pseudomonas aeruginosa exit site and tunnel infections

- Pseudomonas aeruginosa hard to treat
- Often require prolonged rx
- Can start with a quinolone
- Add second drug as needed
  - Ceftazidime
  - Cefepime
  - Piperacillin
  - etc
Therapy for exit site and tunnel infections

- Sonography of the tunnel may be useful to assess response to treatment
- Catheter removal should be considered
  - If more than 3 weeks fails to resolve the infection
  - If P. aeruginosa is present consider early catheter removal
  - Or if peritonitis develops
Initial Presentation and Management of Peritonitis

Cloudy fluid: you cannot read print through the bag
A PD patient presenting with cloudy effluent should be presumed to have peritonitis.

This is confirmed with a cell count, 100 or more WBC per mcl, 50% or more polymorphonuclear white cells.
Differential diagnosis of cloudy effluent

- Culture positive infectious peritonitis
- Infectious peritonitis with sterile cultures
- Chemical peritonitis
- Eosinophilia of the effluent
- Hemoperitoneum
- Malignancy (rare)
- Chylous effluent (rare)
- Specimen taken from ‘dry’ abdomen
Peritonitis

PD patients presenting with abdominal pain with no clear cause should also be presumed to have peritonitis until proven otherwise.
Interpreting the cell count

This is dependent on dwell time and amount of effluent in the abdomen.

- APD without a daytime exchange—infuse 1 liter and wait 1-2 hours, use differential
- APD presenting at night will have short dwells, use differential
Gram stain

- Generally negative
- However, may indicate yeast, which allows for rapid catheter removal
- Otherwise, don’t rely on Gram stain for initial antibiotic coverage.
Other points

- Question the patient about causality
- Check on recent procedures
- Check exit site carefully

- Abdominal pain usually generalized
  - Abdominal film/other imaging if bowel source suspected
  - Free air suggests perforation
Specimen processing

- Culture negative peritonitis should not exceed 20% of cases
- Standard approach: inject 5-10 cc in each blood culture bottle
- Centrifuging 50 ml effluent and culturing sediment will increase the yield.
Specimen processing

- Rapid blood culture techniques (BACTEC, Septi-Check, BacT/Alert, Becton Dickinson) may speed up isolation and are the best approach.

- >75% of cases diagnosis is established in less than 3 days.
Empiric antibiotic selection: *2005 guidelines recommended a center directed approach. No change in 2010 guidelines.*

- Cephalosporin or vancomycin
- AND
- 3rd generation cephalosporin or aminoglycoside
Method of delivery

- Intraperitoneal administration is superior to IV dosing for treating peritonitis

- Intermittent and continuous dosing are equally efficacious
Adjunctive treatments

- Most fungal peritonitis follows course of antibiotics
- Use of anti-fungal prophylaxis during antibiotic rx may lead to less antibiotic related fungal peritonitis
- Each program will need to decide as to whether to give anti-fungal rx during rx of bacterial peritonitis.
Subsequent management of peritonitis

Electron micrograph of peritoneum in patient with peritonitis

Normal peritoneum for comparison
Once culture results and sensitivities available, adjust antibiotic therapy.

See table for dosing at ispd.org

Increase dosing for those drugs excreted through kidney if RKF present (defined as >100 cc/d)
Management of peritonitis---refractory peritonitis

- Defined as failure to respond to appropriate antibiotics within 5 days

- Manage by removing peritoneal catheter.

- Replace PD catheter when appropriate based on patient’s clinical condition
Other terminology for peritonitis

- **Recurrent**: episodes within 4 wk of completion of therapy of prior episodes with a different organism
- **Relapsing**: an episode within 4 wk of completion of therapy of prior episode with the same or 1 sterile episode
- **Repeat**: a episode that occurs more than 4 wk after completion of therapy of a prior episode with the same organism

Infectious indications for catheter removal

- Refractory peritonitis
- Fungal peritonitis
- Relapsing peritonitis
- Chronic exit site infection

Remove and wait to replace

Simultaneous replacement
Consider catheter removal for:

- Repeat peritonitis
- Mycobacterial peritonitis
- Multiple enteric organisms
Coagulase negative Staphylococcus

- Due primarily to contamination
- Review patient’s technique
- Mild; responds quickly to antibiotics
- However, may lead to relapsing peritonitis or repeat peritonitis due to biofilm. In such cases replace catheter
Streptococcus and enterococcus

- Usually curable with antibiotics but severe
- Best treated with IP ampicillin if sensitive
- Vancomycin-resistant: rx with ampicillin if sensitive, otherwise linezolid or quinupristin/dalfopristin
Staphylococcus aureus

- Usually severe peritonitis
- Often related to catheter infection and if so often requires catheter removal
- Associated with colonization of the patient with S. aureus (nares, skin, etc)
- Rifampicin can be used as adjunct for prevention of relapse or repeat S aureus peritonitis
Pseudomonas aeruginosa

- Often related to catheter infection; catheter infection may be rather subtle (drainage that cultures positive)
- In such cases catheter removal required
- Two antibiotics should be used to treat
Single Gram negative peritonitis

- May be from contamination, exit site infection, transmural migration across bowel wall (constipation, diverticulitis, colitis)
- SPICE (Serratia, Pseudomonas, and indole positive organisms such as Providencia, Citrobacter and Enterobacter) have high risk of relapse
- Two antibiotics may be better than one.
Polymicrobial peritonitis

- If multiple enteric organisms, especially with anaerobes, risk of death is increased and surgical consultation is needed.

- If multiple Gram positive, usually responds to antibiotics. Possibly contamination.
Fungal peritonitis

- Serious
- Catheter removal should be immediate.
- Can often be picked up on presentation through Gram stain showing hyphae.
- Candida is most common fungal peritonitis
- Often follows antibiotic therapy
Mycobacteria causing peritonitis

- Infrequent but may be difficult to diagnose DNA PCR may be helpful
- Treat M. tuberculosis peritonitis with 4 drugs: rifampicin (IP), isoniazid, pyrazinamide and ofloxacin with pyridoxine.
Summary: PD related infections recommendations

- All programs should monitor rates.
- Assess quickly, institute treatment covering both Gram + and Gram negative organisms.
- Subsequent therapy should be tailored to organism and sensitivity.
- Don’t hesitate to remove the PD catheter if refractory or relapsing. Consider in repeat peritonitis, mycobacterial, and enteric peritonitis.
Your center had 7 patients on PD for entire year, 3 patients started during the year and had total of 18 months, and 3 left the program at 3 months, 6 months and 9 months. During the year two patients had peritonitis--- one had S aureus and one had two episodes CNS peritonitis. Which of the following is correct:
1. Your center’s peritonitis rate is 0.2 episodes per year at risk. This is great, nothing to worry about, no intervention needed.

2. Your center’s peritonitis rate is 0.3 episodes per year at risk. This is fine, no intervention needed.

3. Your center’s peritonitis rate is 0.2 episodes per year at risk. The patient with two episodes of CNS peritonitis should have his catheter replaced and this could be done safely as simultaneous procedure.

4. Your center’s peritonitis rate is 0.3 episodes per year at risk. The patient with two episodes of CNS peritonitis should have his catheter replaced and this could be done safely as simultaneous procedure.
Question #1: Correct answer is - 4

- Time in the program is 10 years. 3 episodes peritonitis so 3/10 = 0.3 episodes per year at risk
- The patient with two episodes of CNS peritonitis within one year might well have infected biofilm on catheter so worth trying catheter replacement to prevent further episodes. Patient should also be re-trained.
A 28 year old woman on APD for 7 years presents with severe abdominal pain and cloudy effluent. She has never previously had peritonitis. Her cell count confirms peritonitis. Gram stain shows hyphae (yeast). The catheter exit site looks fine. The correct answer is:
1. Start anti-fungal therapy with fluconazole. Her PD catheter should be removed immediately without waiting for culture results.

2. Start anti-fungal therapy with fluconazole as well as vancomycin and gentamicin to cover Gram positive and Gram negative organisms. Remove PD catheter immediately.

3. Start anti-fungal therapy with fluconazole as well as vancomycin and gentamicin to cover Gram positive and Gram negative organisms. Wait for the culture result before considering removing catheter.

4. Start anti-fungal therapy with fluconazole as well as vancomycin and gentamicin to cover Gram positive and Gram negative organisms. Wait for the culture result before considering removing catheter. Obtain a CT scan of the abdomen.
This is fungal peritonitis which has very high mortality so catheter removal should be done immediately. Broad spectrum coverage needed because there may be enteric organisms as well as fungus.