Peritonitis Management in Children on PD

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Nelson-Atkins Museum of Art
Peritonitis: Signs & Symptoms

Cloudy bag

Infection

Nausea/vomiting

Tummy pain

Diarrhoea

High temperature
Peritonitis
2005-2010

Age

Annualized Rate

0-1  2-5  6-12  >12

NAPRTCS, 2011
Months Between Peritonitis Episodes

International Pediatric Peritoneal Dialysis Network
Infectious hospitalization
Rates in children & adults,
2006 (per patient year)

52% higher

Age 0-19: 0.6
Age 20+: 0.4

USRDS, 2008
Hospitalization Causes in Children on PD

- Inefficient dialysis
- Malnutrition
- Social
- Catheter malfunction
- Fluid imbalance
- Infection

Percent

International Pediatric Peritoneal Dialysis Network
Reasons for Change of Modality

- Infection
- Family Choice
- Access Failure

Patients (%)

PD vs. HD (Data from NAPRTCS, 2011)
Patient Mortality on Dialysis

PD

- Infectious: 22%
- CVD: 21%
- Malignancy: 33%
- Dialysis Complications: 6%
- Other: 15%
- Unknown: 3%

NAPRTCS, 2011
ISPD GUIDELINES/RECOMMENDATIONS

CONSENSUS GUIDELINES FOR THE TREATMENT OF PERITONITIS IN PEDIATRIC PATIENTS RECEIVING PERITONEAL DIALYSIS

Bradley A. Warady, Franz Schaefer,¹ Maggie Holloway,² Steven Alexander,³ Marianne Kandert,¹ Beth Piraino,⁴ Isidro Salusky,² Anders Tranæus,⁵ Jose Divino,⁶ Masataka Honda,⁷ Salim Mujais,⁸ and Enrico Verrina,⁹ for the International Society for Peritoneal Dialysis (ISPD) Advisory Committee on Peritonitis Management in Pediatric Patients

The Children’s Mercy Hospital, Kansas City, Missouri, U.S.A.; University Children’s Hospital,¹ Heidelberg, Germany; U.C.L.A. Hospital,² Los Angeles, California; Stanford University Medical Center,³ Stanford, California; University of Pittsburgh,⁴ Pittsburgh, Pennsylvania, U.S.A.; Baxter Limited, Japan,⁵ Tokyo, Japan; Baxter SA,⁶ Brussels, Belgium; Tokyo Metropolitan Children’s Hospital,⁷ Tokyo, Japan; Renal Division,⁸ Baxter Healthcare Corporation, Deerfield, Illinois, U.S.A.; G. Gaslini Children’s Hospital,⁹ Genoa, Italy
If the patient presents with:
- No fever
- Mild or no abdominal pain
- No risk factors for severe infection

Glycopeptide (vancomycin or teicoplanin) and ceftazidime

If any of the following is present:
- Fever, severe abdominal pain or age <2 years
- History of MRSA infection or carrier
- Recent or current exit site/tunnel infection

Initiate empiric therapy

Peritoneal effluent evaluation
Cell count and differential
Gram stain
Culture

Cloudy effluent

1st generation cephalosporin and ceftazidime

Empiric Therapy
Spectrum of Causative Organisms

International Pediatric Peritonitis Registry; n=501

- Gram negative
- Staph aureus
- Coag.neg. staph
- Streptococci
- Enterococci
- Fungal
- Culture negative

(% of positive cultures)
Peritonitis Episodes: Causative Organisms

- S. epidermidis/other coag. neg. Staph.: 47
- S. aureus, non-MRSA/MRSA: 66
- Other gram-negative: 41
- Enterococci: 31
- Pseudomonas sp.: 28
- Klebsiella sp.: 24
- E. coli: 22
- Enterococci: 20
- Other gram-positive: 18
- Acinetobacter sp.: 16
- Proteus sp.: 2
- Aerobe rods: 1
- Fungus: 10

Warady BA et al, JASN, 2007
<table>
<thead>
<tr>
<th>Outcome</th>
<th>PD Continued</th>
<th>PD Discontinued</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Temporary</td>
<td>Permanent</td>
<td></td>
</tr>
<tr>
<td>Full functional recovery</td>
<td>420</td>
<td>9</td>
<td>429 (89%)</td>
</tr>
<tr>
<td>Ultrafiltration problems</td>
<td>8</td>
<td>1</td>
<td>16 (3.3%)</td>
</tr>
<tr>
<td>Adhesions</td>
<td>3</td>
<td>1</td>
<td>15 (3.1%)</td>
</tr>
<tr>
<td>Uncontrolled infection</td>
<td>0</td>
<td>1</td>
<td>12 (2.5%)</td>
</tr>
<tr>
<td>Secondary fungal peritonitis</td>
<td>0</td>
<td>0</td>
<td>4 (0.8%)</td>
</tr>
<tr>
<td>General therapy failure</td>
<td>0</td>
<td>0</td>
<td>6 (1.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>431 (89%)</td>
<td>12 (2.5%)</td>
<td>39 (8.1%)</td>
</tr>
</tbody>
</table>
ISPD GUIDELINES/RECOMMENDATIONS

CONSENSUS GUIDELINES FOR THE PREVENTION AND TREATMENT OF CATHETER-RELATED INFECTIONS AND PERITONITIS IN PEDIATRIC PATIENTS RECEIVING PERITONEAL DIALYSIS: 2012 UPDATE

Bradley A. Warady,1 Sevcan Bakkaloglu,2 Jason Newland,1 Michelle Cantwell,3 Enrico Verrina,4 Alicia Neu,5 Vimal Chadha,1 Hui-Kim Yap,6 and Franz Schaefer7

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Pediatric Peritonitis Guidelines
Workgroup Members

Brad Warady  Enrico Verrina
Franz Schaefer  Hui Kim Yap
Vimal Chadha  Michelle Cantwell
Alicia Neu  Jason Newland
Sevcan Bakkaloglu
ISPD GUIDELINES/RECOMMENDATIONS

PERITONEAL DIALYSIS-RELATED INFECTIONS
RECOMMENDATIONS: 2010 UPDATE

Philip Kam-Tao Li,1 Cheuk Chun Szeto,1 Beth Piraino,2 Judith Bernardini,2 Ana E. Figueiredo,3
Amit Gupta,4 David W. Johnson,5 Ed J. Kuijper,6 Wai-Choong Lye,7
William Salzer,8 Franz Schaefer,9 and Dirk G. Struijk10

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Hospital, and School of Medicine, University of Queensland, Brisbane, Australia; Department of Medical
Microbiology,6 Leiden University Medical Center, Leiden, The Netherlands; Centre for Kidney Diseases,7
Mount Elizabeth Medical Centre, Singapore; Section of Infectious Disease,8 Department of Internal Medicine,
University of Missouri-Columbia School of Medicine, Columbia, MO, USA; Pediatric Nephrology
Division,9 University Children’s Hospital, Heidelberg, Germany; Dianet Dialysis Centers,10
Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
### Guidelines

#### Pediatric
1. Training
2. Catheter Placement/Antibiotics and Catheter Type
3. Early Exit-Site Care
4. Chronic Exit-Site Care
5. Connectology
6. Prophylactic Antibiotic Therapy
7. Ostomy Patients
8. Diagnosis of Peritonitis and Culture Technique
9. Empiric Therapy
10. Gram-Positive Peritonitis
11. Gram-Negative Peritonitis
12. Culture Negative Peritonitis
13. Fungal Peritonitis
14. Relapsing Peritonitis
15. Adjunctive Therapy
16. Catheter Removal/Replacement
17. Diagnosis of Catheter Related Infection
18. Treatment of Catheter Related Infection
19. Modification of APD
20. Evaluation of Primary Response
21. Failure to Demonstrate Improvement

#### Adult
1. Initial Presentation and Management
   - Clinical presentation
   - Specimen processing
   - Empiric antibiotic selection
   - Adjunctive treatments

2. Subsequent Management of Peritonitis
   - Refractory peritonitis
   - Relapsing, recurrent and repeat peritonitis
   - Coagulase-negative Staphylococcus
   - Streptococcus and Enterococcus
   - Staphylococcus aureus
   - Corynebacterium peritonitis
   - Culture-negative peritonitis
   - Pseudomonas aeruginosa peritonitis
   - Other single gram-negative micro-organisms
   - Polymicrobial peritonitis
   - Fungal peritonitis
   - Peritonitis due to mycobacteria
   - Catheter removal and reinsertion for peritoneal infection
   - Prevention of further peritonitis
# Rating Guideline Recommendations

<table>
<thead>
<tr>
<th>Grade*</th>
<th>Patients</th>
<th>Implications</th>
<th>Clinicians</th>
<th>Policy</th>
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<tbody>
<tr>
<td>Level 1</td>
<td>'We recommend’</td>
<td>Most people in your situation would want the recommended course of action and only a small proportion would not.</td>
<td>Most patients should receive the recommended course of action.</td>
<td>The recommendation can be adopted as a policy in most situations.</td>
</tr>
<tr>
<td>Level 2</td>
<td>'We suggest’</td>
<td>The majority of people in your situation would want the recommended course of action, but many would not.</td>
<td>Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.</td>
<td>The recommendation is likely to require debate and involvement of stakeholders before policy can be determined.</td>
</tr>
</tbody>
</table>

* The additional category ‘Not Graded’ was used, typically, to provide guidance based on common sense or where the topic does not allow adequate application of evidence.

**A:** High quality of evidence. We are confident that the true effect lies close to that of the estimate of the effect.

**B:** Moderate quality of evidence. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**C:** Low quality of evidence. The true effect may be substantially different from the estimate of the effect.

**D:** Very low quality of evidence. The estimate of effect is very uncertain, and often will be far from the truth.
Guideline 1
Training Recommendations

1.1 We suggest that PD training be performed by an experienced peritoneal dialysis nurse with pediatric training, using a formalized teaching program with clear objectives and criteria and which incorporates adult learning principles (2C).

1.2 We suggest that retraining be provided to all caregivers periodically. We also suggest that re-evaluation of PD technique be conducted following the development of a peritonitis episode (2C).
Training Content and Percent Alloted Time for Pediatric PD

Theory
- Functions of the kidney, pathophysiology of the RF
- Osmosis/diffusion, fluid balance, decision making regarding % dextrose, etc

Practical/technical skills
- Aseptic technique, BP monitoring, exit-site care, performance of CAPD exchanges,
- Set-up and functions of the cycler
- Problem solving alarms, etc

Peritonitis
- Recognition of sign and symptoms,
- Initiating treatment, medicating bags for ongoing treatment

Complications
- Exit-site/tunnel infections
- Hypo/hypertension
- Catheter flow problems

A Survey of Peritonitis Management in Pediatric Patients

Survey completed by 76 centers

597 children <21 years of age

Training time: 8.2±5.5 days and 5.5±1.9 hours/day

Lower peritonitis rates in clinics with more children (>15) in the program with longer training time

Peritonitis rate in pediatric centers 1/17.5; combined center 1/15.7

No correlation between nurse-to-patient ratio and peritonitis rate

How to Handwash?

WASH HANDS WHEN VISIBLY SOILED! OTHERWISE, USE HANDRUB

Duration of the entire procedure: 40-60 seconds

0. Wet hands with water;
1. Apply enough soap to cover all hand surfaces;
2. Rub hands palm to palm;
3. Right palm over left dorsum with interlaced fingers and vice versa;
4. Palm to palm with fingers interlaced;
5. Backs of fingers to opposing palms with fingers interlocked;
6. Rotational rubbing of left thumb clasped in right palm and vice versa;
7. Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa;
8. Rinse hands with water;
9. Dry hands thoroughly with a single use towel;
10. Use towel to turn off faucet;
11. Your hands are now safe.

World Health Organization
Patient Safety
SAVE LIVES
Clean Your Hands
How to Handrub?

RUB HANDS FOR HAND HYGIENE! WASH HANDS WHEN VISIBLY SOILED

Duration of the entire procedure: 20-30 seconds

1. Apply a sufficient amount of the product in a cupped hand, covering all surfaces;
2. Rub hands palm to palm;
3. Right palm over left dorsum with interlaced fingers and vice versa;
4. Palm to palm with fingers interlaced;
5. Backs of fingers to opposing palms with fingers interlocked;
6. Rotational rubbing of left thumb clasped in right palm and vice versa;
7. Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa;
8. Once dry, your hands are safe.

World Health Organization | Patient Safety | SAVE LIVES
A World Alliance for Safer Health Care | Clean Your Hands

May 2010
Retraining

Training Experience

Chow K M et al. CJASN 2007;2:647-652
Guideline 2
Catheter Type and Placement

2.1 We suggest the use of a double-cuff Tenckhoff catheter with a downward or lateral subcutaneous tunnel configuration that is placed by a surgeon or nephrologist experienced in PD catheter placement (2B).

2.2 We recommend that perioperative antibiotic prophylaxis be used within 60 minutes prior to incision for peritoneal dialysis catheter placement to reduce the incidence of early onset peritonitis (1A).
Time to First Peritonitis Infection by Peritoneal Dialysis Access Characteristics

NAPRTCS, 2011
Gram Negative Peritonitis: Risk Factors for Poor Initial Treatment Response

- Intermittent Ceftazidime administration
  Odds Ratio 13.9 (CI 3.1-63, p<0.001)

- Single cuff catheter
  Odds Ratio 12.8 (CI 2.9-55, p<0.001)

- Severe abdominal pain at onset
  Odds Ratio 4.0 (CI 1.8-9.1, p<0.001)

Relapsing Peritonitis


<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RP</th>
<th>Non-RP</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>50</td>
<td>56</td>
<td>0.42</td>
</tr>
<tr>
<td>Age (years; mean ± SD)</td>
<td>12.5 ± 6.0</td>
<td>9.5 ± 5.8</td>
<td>0.0004</td>
</tr>
<tr>
<td>Duration of dialysis (years; mean ± SD)</td>
<td>1.7 ± 1.8</td>
<td>1.7 ± 1.5</td>
<td>0.99</td>
</tr>
<tr>
<td>CAPD/CCPD/NIPD (%)</td>
<td>18 / 64 / 18</td>
<td>26 / 47 / 27</td>
<td>0.08</td>
</tr>
<tr>
<td>Nasal S. aureus carrier (%)</td>
<td>25</td>
<td>15</td>
<td>0.11</td>
</tr>
<tr>
<td>One/two-cuff catheters (%)</td>
<td>25 / 75</td>
<td>13 / 87</td>
<td>0.03</td>
</tr>
<tr>
<td>Gastrostomy present (%)</td>
<td>2</td>
<td>8</td>
<td>0.10</td>
</tr>
</tbody>
</table>
# Intravenous antibiotic prophylaxis versus placebo or no treatment: effects on early peritonitis

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (random)</th>
<th>Weight</th>
<th>RR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>Wikdahl 1997 (Cefuroxime)</td>
<td>0/18</td>
<td>4/20</td>
<td>8.24</td>
<td>0.12 [0.01, 2.13]</td>
<td></td>
</tr>
<tr>
<td>Lye 1992 (Cefazolin, gentamicin)</td>
<td>2/25</td>
<td>1/25</td>
<td>12.14</td>
<td>2.00 [0.19, 20.67]</td>
<td></td>
</tr>
<tr>
<td>Bennett Jones 1988 (Gentamicin)</td>
<td>1/13</td>
<td>6/13</td>
<td>16.73</td>
<td>0.17 [0.02, 1.20]</td>
<td></td>
</tr>
<tr>
<td>Gadallah 2000 (Vancomycin/cefazolin)</td>
<td>7/148</td>
<td>10/73</td>
<td>62.89</td>
<td>0.35 [0.14, 0.87]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>204</td>
<td>131</td>
<td>100.00</td>
<td>0.35 [0.15, 0.80]</td>
<td></td>
</tr>
</tbody>
</table>

Total Events: 10 (Treatment), 21 (Control)

Test for heterogeneity: Chi² = 3.22, df = 3 [P = 0.36], I² = 6.7%

Test for overall effect: Z = 2.49 (P = 0.01)

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**Early peritonitis**

(< 1 month of catheter placement)

Strippoli GFM et al, Cochrane Library, 2007
Prevention of Catheter Related Infection

- No sutures at the exit-site
- Sterile dressing after the procedure
- Catheter anchoring and immobilization
- Dressing changes should be performed weekly until site is healed
- If possible, do not use the catheter at least for two weeks
- No showering and swimming during the initial 6 weeks
Guideline 4
Chronic Exit-Site Care

4.1 We recommend cleansing the exit site with a sterile antiseptic solution and sterile gauze (1C).

4.2 Each program should evaluate the type, frequency, and resistance patterns of organisms causing ESIs and institute a center-specific protocol to diminish such risk (not graded).

4.2 We suggest that a topical antibiotic be applied to the peritoneal catheter exit site as a component of chronic exit-site care (2B).
Risk ratios and 95% CIs for mupirocin vs. placebo or no prophylaxis in clinical trials on S. aureus-related infections

- Perez-Fontan, 1993
- MSG, 1996
- Thodis 1, 1998
- Thodis 2, 1998
- Crabtree, 2000
- Casey, 2000

Overall

Mupirocin prophylaxis substantially reduces the rate of SA infection in the dialysis patients.

Peritonitis and ESI were found to be reduced by 66% and 62%, respectively, among PD patients.

Tacconelli et al, CID 2003;37:1629-1638
Risk Factors for Pseudomonas Peritonitis

*Pseudomonas* peritonitis independently associated with

- Exit site care > twice per week (p<0.005)
- Exit site mupirocin (p<0.005)
- Non-sterile (saline or soap) ES cleansing (p<0.001)
Guideline 6
Adjunctive Prophylactic Antibiotic Therapy

6.1 We suggest that the use of oral nystatin or fluconazole be considered at the time of antibiotic administration to PD patients to reduce the risk of fungal peritonitis (2B).

6.2 We suggest prophylactic antibiotic administration after accidental intraluminal contamination. (2B)

6.3 We suggest prophylactic antibiotic administration before invasive dental procedures to lower the risk of peritonitis. (2D)

6.4 We suggest prophylactic antibiotic administration before procedures involving the gastrointestinal or genitourinary tract and associated with a high risk of bacteremia to lower the risk of peritonitis. (2D)
Prophylactic Fluconazole


p <0.05
Touch Contamination

Algorithm for PD contamination

 Clamp on transfer set remained closed

 Patient not to proceed with dialysis
 Call dialysis center immediately
 Sterile tubing change done by PD nurse

 Clamp on transfer set open

 Close clamp

 Patient not to proceed with dialysis
 Call dialysis center immediately
 Sterile tubing change done by PD nurse and prophylactic antibiotics

Bender et al., KI, 2006
# Prophylaxis

<table>
<thead>
<tr>
<th>Indication</th>
<th>Antimicrobial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antifungal Prophylaxis</strong>&lt;br&gt;High baseline rate of FP in PD unit&lt;br&gt;PEG placement</td>
<td>Nystatin 10,000 u/kg/day&lt;br&gt;Fluconazole 3-6 mg/kg IV or PO QOD (maximum 200 mg)</td>
</tr>
<tr>
<td><strong>Touch Contamination</strong>&lt;br&gt;Instillation of PD fluid after disconnection of system&lt;br&gt;Disconnection during PD</td>
<td>Cefazolin (125 mg/L IP), or Vancomycin (25 mg/L IP)&lt;br&gt;if known colonization with MRSA&lt;br&gt;Culture result, if obtained, directs subsequent therapy</td>
</tr>
<tr>
<td><strong>Invasive Dental Procedures</strong>&lt;br&gt;Manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa</td>
<td>Amoxicillin (50 mg/kg PO; maximum: 2g)&lt;br&gt;or Ampicillin (50 mg/kg IV/IM; maximum: 2g)&lt;br&gt;or Cefazolin (25 mg/kg IV; maximum: 1g)&lt;br&gt;or Ceftriaxone (50 mg/kg IV/IM; maximum: 1g)&lt;br&gt;or Clindamycin (20 mg/kg PO; maximum: 600 mg)&lt;br&gt;or Clarithromycin (15 mg/kg PO; maximum: 500 mg)&lt;br&gt;or Azithromycin (15 mg/kg PO; maximum: 500 mg)</td>
</tr>
<tr>
<td><strong>Gastrointestinal Procedures</strong>&lt;br&gt;High risk procedures-esophageal stricture dilation, treatment of varices, ERCP and PEG&lt;br&gt;Other GI or GU procedures</td>
<td>Cefazolin (50 mg/kg IV; maximum: 2g) or Clindamycin (20 mg/kg IV; maximum 600 mg) or, if high risk for MRSA, Vancomycin (15 mg/kg IV; maximum: 1g)&lt;br&gt;Cefoxitin/Cefotetan (30-40 mg/kg IV; maximum: 2g)&lt;br&gt;Alternatives: Cefazolin (25 mg/kg IV; maximum: 2g) plus metronidazole (10 mg/kg IV; maximum: 1g) or Clindamycin (10 mg/kg IV; maximum: 600 mg) plus aztreonam (30 mg/kg IV; maximum: 2g)</td>
</tr>
</tbody>
</table>
Guideline 7

Ostomy Patients

7.1 The PD catheter exit-site should be placed as far as possible from an ostomy site (not graded).

7.2 We recommend that gastrostomy placement should preferentially take place either before or at the time of PD catheter placement (1C).

7.3 We recommend the preferential use of an open surgical procedure for gastrostomy placement in patients who are already receiving PD. In patients not yet receiving PD, gastrostomy placement can be performed by either open surgical technique or laparoscopically (1C).

7.4 We suggest administration of prophylactic antibiotic and antifungal therapy during gastrostomy placement (2C).

7.5 We suggest holding peritoneal dialysis for 1 or more days following gastrostomy placement (2D).
# Prophylaxis for PEG Insertion

<table>
<thead>
<tr>
<th>Pts (n)</th>
<th>Sub-group</th>
<th>Anti-fungal + anti-biotic</th>
<th>Only anti-biotic</th>
<th>None</th>
<th>None</th>
<th>Early peritonitis</th>
<th>Fungal peritonitis</th>
<th>PD catheter replacement</th>
<th>PEG-associated HD</th>
<th>PEG-associated death</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td></td>
<td>8</td>
<td>13</td>
<td>6</td>
<td>14</td>
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<td>7</td>
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# Prophylaxis for PEG Insertion

<table>
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<th>Pts (n)</th>
<th>Sub-group</th>
<th>Anti-fungal + antibiotic</th>
<th>Only antibiotic</th>
<th>None</th>
<th>None</th>
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<th>PD catheter replacement</th>
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<td>6</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Empiric Therapy

Adults

Start intraperitoneal antibiotics as soon as possible
Allow to dwell for at least 6 hours
Ensure gram-positive and gram-negative coverage
Base selection on historical patient and center sensitivity patterns as available

0-6 hours

Gram-positive coverage:
Either first-generation Cephalosporin or vancomycin

Gram-negative coverage:
Either third-generation Cephalosporin or aminoglycoside

6-8 hours

Determine and prescribe ongoing antibiotic treatment
Ensure follow-up arrangements are clear or patient admitted
Await sensitivity results

Kam-Tao Li, P. PDI, 2010
**In vitro Susceptibilities**

Warady BA et al, JASN, 2007

---

**% susceptibilities**

- **gram pos**
- **gram neg**

Bar chart showing the in vitro susceptibilities of various antibiotics against gram-positive and gram-negative bacterial strains. The antibiotics include Cefazolin, Vanco/Teico, Ceftazidime, Aminoglycoside, Cefazolin/Ceftazidime, Glycopeptide/Ceftazidime, Cefazolin/Aminoglycoside, Glycopeptide/Aminoglycoside, Imipenem, and Ciprofloxacin.
10.1 We suggest that the center-specific antibiotic susceptibility pattern should help guide the selection of empiric antibiotic therapy (2B).

10.2 We suggest intraperitoneal cefepime monotherapy for the empiric treatment of peritonitis in centers in which this antibiotic is available and affordable (2C).

10.3 We recommend intraperitoneal administration of a first generation cephalosporin, combined with ceftazidime or an aminoglycoside if cefepime is not available (1C).

10.4 We suggest the addition of an intraperitoneal glycopeptide to cefepime, or the replacement of a first generation cephalosporin with an intraperitoneal glycopeptide, if the center-specific resistance rate of \textit{S. aureus} isolates to methicillin or oxacillin exceeds 10% or if the patient has a history of MRSA (2B).
Cefepime

- 4th generation cephalosporin
- Excellent coverage of methicillin-sensitive gram positive and gram negative spectrum
- Superior coverage of enterobacteriaceae, comparable pseudomonas coverage as ceftazidime (80%); 50% ESBL sensitivity
- Mainly renal elimination, half-life 12 hours
- Excellent systemic absorption upon ip administration; good penetration from circulation into peritoneal cavity
Start intraperitoneal antibiotics as soon as possible
Allow to dwell for 3-6 hours
Ensure gram-positive and gram-negative coverage
Base selection on historical patient and center susceptibility patterns as available

Monotherapy with cefepime*

If cefepime is not available

Gram-positive coverage: Either first-generation cephalosporin or glycopeptide
Gram-negative coverage: Either ceftazidime or aminoglycoside

* If the center’s MRSA rate exceeds 10% or patient has history of MRSA colonization, glycopeptide should be added to cefepime or should replace the first generation cephalosporin for gram-positive coverage.
Regional Distribution of Culture Results

In vitro Resistance Rates

Regional Variation of Staphylococcal Methicillin Resistance

Gram-positive bacteria on culture

Stop gram-negative coverage

**Enterococcus sp. Streptococcus sp.**
- Discontinue initial antibiotics
- Start ampicillin
- Consider adding aminoglycoside for *Enterococcus*
- If resistant to ampicillin, start vancomycin
- For VRE consider daptomycin or linezolid

**MRSA**
- Discontinue cefazolin or cefepime
- Continue or substitute vancomycin or teicoplanin
- Consider clindamycin if allergic to glycopeptide
- Consider adding rifampin in case of poor response

**MSSA**
- Discontinue vancomycin
- Treat with cefazolin or cefepime

**Other gram-positive bacteria**
- Treat based on susceptibilities
Gram-negative bacteria on culture

Stop vancomycin or teicoplanin

- **Pseudomonas sp.**
  - Continue cefepime or ceftazidime
  - Add second agent

- **E.coli, Proteus sp., or Klebsiella sp.**
  - Continue cefepime, ceftazidime or cefazolin if susceptible

- **E.coli, Proteus sp., or Klebsiella sp. resistant to 3rd generation cephalosporins**
  - Discontinue ceftazidime
  - Treat with cefepime, imipenem or fluoroquinolone

- **Other single gram-negative bacteria**
  - Treat based on susceptibilities
# Antibiotic Dosing Recommendations for the Treatment of Peritonitis

**Continuous Therapy**

<table>
<thead>
<tr>
<th>Antibiotic Class (IP)</th>
<th>Loading Dose</th>
<th>Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aminoglycosides (IP)</strong></td>
<td>8 mg/L</td>
<td>4 mg/L</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>8 mg/L</td>
<td>4 mg/L</td>
</tr>
<tr>
<td>Netilmycin</td>
<td>8 mg/L</td>
<td>4 mg/L</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>25 mg/L</td>
<td>12 mg/L</td>
</tr>
<tr>
<td>Amikacin</td>
<td>12 mg/L</td>
<td></td>
</tr>
<tr>
<td><strong>Cephalosporins (IP)</strong></td>
<td>500 mg/L</td>
<td>125 mg/L</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>500 mg/L</td>
<td>125 mg/L</td>
</tr>
<tr>
<td>Cefepime</td>
<td>500 mg/L</td>
<td>250 mg/L</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>500 mg/L</td>
<td>125 mg/L</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>20 mg/kg</td>
<td></td>
</tr>
<tr>
<td><strong>Glycopeptides (IP)</strong></td>
<td>1000 mg/L</td>
<td>25 mg/L</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>400 mg/L</td>
<td>20 mg/L</td>
</tr>
<tr>
<td>Teicoplanin</td>
<td>15 mg/kg</td>
<td></td>
</tr>
<tr>
<td><strong>Penicillins (IP)</strong></td>
<td>--</td>
<td>125 mg/L</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td><strong>Quinolones (IP)</strong></td>
<td>50 mg/L</td>
<td>25 mg/L</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>--</td>
<td></td>
</tr>
</tbody>
</table>

**Intermittent Therapy**

- **Aminoglycosides (IP)**
  - anuric: 0.6 mg/kg
  - non-anuric: 0.75 mg/kg
- **Cephalosporins (IP)**
  - 20 mg/kg
  - 15 mg/kg
  - 30 mg/kg
  - 20 mg/kg
- **Glycopeptides (IP)**
  - 30 mg/kg;
  - Repeat dosing:
    - 15 mg/kg every 3-5 days
    - 15 mg/kg every 5-7 days

---

Consensus Guidelines, Perit Dial Int, 2012
Antibiotic Dosing Recommendations for the Treatment of Peritonitis (continued)

<table>
<thead>
<tr>
<th></th>
<th>Continuous Therapy</th>
<th>Intermittent Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Loading Dose</td>
<td>Maintenance Dose</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aztreonam (IP)</td>
<td>1000 mg/L</td>
<td>250 mg/L</td>
</tr>
<tr>
<td>Clindamycin (IP)</td>
<td>300 mg/L</td>
<td>150 mg/L</td>
</tr>
<tr>
<td>Imipenem/Cilastin (IP)</td>
<td>250 mg/L</td>
<td>50 mg/L</td>
</tr>
<tr>
<td>Linezolid</td>
<td>&lt; 5 Years: 30 mg/kg daily, divided into 3 doses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-11 Years: 20 mg/kg daily, divided into 2 doses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 12 Years: 600 mg/dose, twice daily</td>
<td></td>
</tr>
<tr>
<td>Metronidazole (PO)</td>
<td>30 mg/kg daily, divided into 3 doses (maximum: 1.2 g daily)</td>
<td></td>
</tr>
<tr>
<td>Rifampin (PO)</td>
<td>10-20 mg/kg daily, divided into 2 doses (maximum: 600 mg daily)</td>
<td></td>
</tr>
<tr>
<td>Antifungals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole (IP, IV or PO) only</td>
<td>6 – 12 mg/kg every 24-48 h (maximum dose: 400 mg daily)</td>
<td></td>
</tr>
<tr>
<td>Caspofungin (IV only)</td>
<td>70 mg/m² on day 1 (maximum: 70 mg daily)</td>
<td>50 mg/m² daily (maximum: 50 mg daily)</td>
</tr>
</tbody>
</table>

Consensus Guidelines, Perit Dial Int, 2012
Guideline 13
Modification of Therapy for Culture-Negative Peritonitis

13.1 If the initial cultures remain sterile at 72 hours and signs and symptoms of peritonitis are improved, we suggest that empiric antibiotic therapy consisting of cefepime, ceftazidime, cefazolin, or a glycopeptide be continued for 2 weeks (2B).

13.2 We suggest that the administration of an aminoglycoside be discontinued at 72 hours in patients with a sterile culture and clinical improvement (2B).
Rationale for Discontinuing Aminoglycoside Therapy

- 97% of 151 culture-negative episodes had good response to empiric therapy at 72 hours
- Treatment with ceftazidime and glycopeptide/cefazolin continued for 14 days in 91% of patients
- 97% of patients experienced full functional recovery
- Gram-negative peritonitis is associated with a severe clinical course and the PD culture is typically positive
- Aminoglycoside associated ototoxicity/nephrotoxicity
# Terminology for Peritonitis

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent</td>
<td>An episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism</td>
</tr>
<tr>
<td>Relapsing</td>
<td>An episode that occurs within 4 weeks of completion of therapy of a prior episode with the same organism or 1 sterile episode</td>
</tr>
<tr>
<td>Repeat</td>
<td>An episode that occurs more than 4 weeks after completion of therapy of a prior episode with the same organism</td>
</tr>
<tr>
<td>Refractory</td>
<td>Failure of the effluent to clear after 5 days of appropriate antibiotics</td>
</tr>
<tr>
<td>Catheter-related peritonitis</td>
<td>Peritonitis in conjunction with an exit-site or tunnel infection with the same organism or 1 site sterile</td>
</tr>
</tbody>
</table>
Guideline 15
Relapsing Peritonitis

15.1 We recommend that the diagnosis of relapsing peritonitis be made if peritonitis recurs with the same organism as in the preceding episode, according to antibiotic susceptibilities, within 4 weeks of completion of antibiotic treatment (1A).

15.2 (a) We recommend that empiric therapy in accordance with guideline 9 be reinitiated for relapsing peritonitis with consideration of the susceptibilities of the original bacteria (1C).

15.2 (b) We suggest that post-empiric antibiotic therapy of relapsing peritonitis be guided by in vitro susceptibility results, choosing an antibiotic other than cefazolin (2B).

15.3 We suggest intraluminal instillation of a fibrinolytic agent be considered after diagnosis of a first peritonitis relapse that is not by extraluminal pathology such as a tunnel infection or intra-abdominal abscess (2C).

15.4 We recommend removal of the PD catheter as soon as peritonitis is controlled by antibiotic therapy in the setting of relapsing peritonitis associated with persistent or recurrent tunnel infection, or a second peritonitis relapse (1C).
**Use and Duration of Monotherapies with \textit{in vitro} Efficacy and Risk of Relapse**

<table>
<thead>
<tr>
<th>Administered antibiotic with documented \textit{in vitro} efficacy</th>
<th>Number of episodes</th>
<th>Total duration of administration (days)</th>
<th>% followed by relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-generation cephalosporin</td>
<td>26</td>
<td>15 ± 7 (p=0.47)</td>
<td>23% (p=0.02)</td>
</tr>
<tr>
<td>Glycopeptide</td>
<td>44</td>
<td>16 ± 5 (p=0.25)</td>
<td>9% (p=0.77)</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>45</td>
<td>14 ± 5 (p=0.78)</td>
<td>4% (p=0.73)</td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>5</td>
<td>19 ± 3</td>
<td>0% (p=0.44)</td>
</tr>
</tbody>
</table>

Lane J. et al., CJASN, 2010
# Relapsing Peritonitis: Impact on Final Clinical Outcome

<table>
<thead>
<tr>
<th></th>
<th>Non-relapsing</th>
<th>Relapsing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full functional recovery</strong></td>
<td>391/430 (90.9%)</td>
<td>38/52 (73.1%)**</td>
</tr>
<tr>
<td><strong>Ultrafiltration problems</strong></td>
<td>9/430 (2.1%)</td>
<td>7/52 (13.5%)**</td>
</tr>
<tr>
<td><strong>Adhesions</strong></td>
<td>11/430 (2.6%)</td>
<td>4/52 (7.7%)</td>
</tr>
<tr>
<td><strong>Technique failure (PD discontinued)</strong></td>
<td>30/430 (6.9%)</td>
<td>9/52 (17.3%)*</td>
</tr>
</tbody>
</table>

Lane J. et al., CJASN, 2010
Guideline 17
Catheter Removal and Replacement

17.1 We recommend removal of the peritoneal catheter for refractory bacterial peritonitis (1C).

17.2 We recommend removal of the peritoneal catheter when a diagnosis of fungal peritonitis is established (1B).

17.3 We recommend catheter removal in patients with an exit-site or tunnel infection in conjunction with peritonitis with the same bacteria (particularly *S. aureus* and *P. aeruginosa*), except CNS (1C).

17.4 We suggest simultaneous catheter removal and replacement for a refractory exit-site or tunnel infection (2C).

17.5 We suggest simultaneous removal and replacement of the peritoneal catheter after clearing of the peritoneal effluent (white blood cells < 100/mm³) in repeated relapsing bacterial peritonitis (2C).

17.6 We suggest a minimum period of 2 – 3 weeks between catheter removal and insertion of a new catheter for fungal, enteric, and refractory bacterial peritonitis (2C).
# Indications for Catheter Removal for PD Associated Infections

<table>
<thead>
<tr>
<th>Approach to catheter</th>
<th>Indication</th>
<th>Reinsertion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definite removal</strong></td>
<td>Refractory bacterial peritonitis</td>
<td>After 2-3 weeks</td>
</tr>
<tr>
<td></td>
<td>Fungal peritonitis</td>
<td>After &gt; 3 weeks</td>
</tr>
<tr>
<td></td>
<td>ESI/TI in conjunction with peritonitis with the same organism (mainly, <em>S. aureus</em> and <em>P. aeruginosa</em>; except CNS)</td>
<td>After 2-3 weeks</td>
</tr>
<tr>
<td><strong>Simultaneous removal and replacement</strong></td>
<td>Repeatedly relapsing or refractory ESI/TI (including <em>P. aeruginosa</em>)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Relapsing peritonitis</td>
<td></td>
</tr>
<tr>
<td><strong>Relative removal</strong></td>
<td>Repeat peritonitis</td>
<td>After 2-3 weeks</td>
</tr>
<tr>
<td></td>
<td>Mycobacterial peritonitis</td>
<td>After 6 weeks</td>
</tr>
<tr>
<td></td>
<td>Peritonitis with multiple enteric organisms because of an intra-abdominal pathology or abscess; so-called surgical peritonitis</td>
<td>Depends on the clinical course of the patient; at least 2-3 weeks</td>
</tr>
</tbody>
</table>
Simultaneous Catheter Removal and Replacement

Italian Registry of Pediatric CPD

Infectious Causes For Catheter Removal

- Exit-Site/Tunnel Infections: 71%
- Without Peritonitis: 78%
- With Peritonitis: 22%
- Refractory Peritonitis: 29%

Rinaldi S, et al. PDI, 2004
Guideline 18
Diagnosis of Catheter-Related Infection

18.1 We suggest that an objective scoring system be used to monitor the status of the PD catheter exit-site (2B).

18.2 We suggest that a diagnosis of a catheter exit-site infection be made in the presence of pericatheter swelling, redness, and tenderness (exit-site score of 2 or greater in the presence of a pathogenic organism and 4 or greater regardless of culture results) (2B).

18.3 We suggest that a tunnel infection be defined by the presence of redness, edema, and tenderness along the subcutaneous portion of the catheter, with or without purulent drainage from the exit site (exit-site score of 6 or greater (2B).
## Exit-Site Scoring System*

<table>
<thead>
<tr>
<th>Indication</th>
<th>0 Points</th>
<th>1 Point</th>
<th>2 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swelling</td>
<td>No</td>
<td>Exit only (&lt; 0.5cm)</td>
<td>Including part of or the entire tunnel</td>
</tr>
<tr>
<td>Crust</td>
<td>No</td>
<td>&lt; 0.5cm</td>
<td>&gt; 0.5cm</td>
</tr>
<tr>
<td>Redness</td>
<td>No</td>
<td>&lt; 0.5cm</td>
<td>&gt; 0.5cm</td>
</tr>
<tr>
<td>Pain on pressure</td>
<td>No</td>
<td>Slight</td>
<td>Severe</td>
</tr>
<tr>
<td>Secretion</td>
<td>No</td>
<td>Serous</td>
<td>Purulent</td>
</tr>
</tbody>
</table>

* Infection should be assumed with a cumulative exit-site score of 4 or greater
## Oral Antibiotics Used in Exit-Site and Tunnel Infection

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Dose</th>
<th>Frequency</th>
<th>Max dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>10-20 mg/kg/day</td>
<td>Daily</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>10-20 mg/kg/day</td>
<td>Daily or 2 times daily</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>10-15 mg/kg/day</td>
<td>Daily</td>
<td>500 mg</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>7.5 mg/kg/day</td>
<td>Daily or 2 times daily</td>
<td>500 mg</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>30 mg/kg/day</td>
<td>3 times daily</td>
<td>600 mg</td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>&lt;40 kg 25-50 mg/kg/day &gt; 40 kg 125-500 mg/dose</td>
<td>4 times daily</td>
<td>500 mg</td>
</tr>
<tr>
<td>Erythromycin (as base)</td>
<td>30-50 mg/kg/day</td>
<td>3 or 4 times daily</td>
<td>500 mg</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>6 mg/kg/day</td>
<td>Every 24-48 hours</td>
<td>400 mg</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>10 mg/kg</td>
<td>Every 48 hours</td>
<td>Day 1 500 mg, then 250 mg</td>
</tr>
<tr>
<td>Linezolid</td>
<td>&lt; 5 years 10 mg/kg/dose 5-11 years 10 mg/kg/dose ≥ 12 years 600 mg/dose</td>
<td>3 times daily 2 times daily 2 times daily</td>
<td>600 mg</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>30 mg/kg/day</td>
<td>3 times daily</td>
<td>500 mg</td>
</tr>
<tr>
<td>Rifampin</td>
<td>10-20 mg/kg/day</td>
<td>2 times daily</td>
<td>600 mg</td>
</tr>
<tr>
<td>Trimethoprim/Sulfamethoxazole (based on TMP)</td>
<td>5-10 mg/kg/day</td>
<td>Daily</td>
<td>80 mg</td>
</tr>
</tbody>
</table>
Continuous Quality Improvement

- Track infection rates by organism and overall
- Monthly meetings to evaluate root causes of each infection and subsequent plan for interventions to prevent recurrence
- Chart trends and reevaluate protocols of PD program
- Involve all members of the PD team

Bender et al., KI, 2006
ISPD GUIDELINES/RECOMMENDATIONS

CONSENSUS GUIDELINES FOR THE PREVENTION AND TREATMENT OF CATHETER-RELATED INFECTIONS AND PERITONITIS IN PEDIATRIC PATIENTS RECEIVING PERITONEAL DIALYSIS: 2012 UPDATE

Bradley A. Warady,1 Sevcan Bakkaloglu,2 Jason Newland,1 Michelle Cantwell,3 Enrico Verrina,4 Alicia Neu,5 Vimal Chadha,1 Hui-Kim Yap,6 and Franz Schaefer7

Department of Pediatric Nephrology,1 Children’s Mercy Hospitals and Clinics, Kansas City, Missouri, USA; Gazi University,2 Ankara, Turkey; Great Ormond Street Hospital,3 London, England; G. Gaslini Children’s Hospital,4 Genoa, Italy; Johns Hopkins University School of Medicine,5 Baltimore, Maryland, USA; Department of Pediatrics,6 National University of Singapore, Singapore; and University Children’s Hospital,7 Heidelberg, Germany
Thank You,
Peritonitis Guidelines
Workgroup Members
Causative Organisms at Exit-Site

% of 413 episodes

- *S. epidermidis*: 5%
- *S. aureus* non-MRSA/MRSA: 30%
- *Corynebacteria*: 5%
- Other gram positive: 5%
- *Pseudomonas*: 15%
- Other negative: 5%
- No organism: 20%

International Pediatric Peritonitis Dialysis Network
Risk Factors for Pseudomonas Peritonitis

*Pseudomonas* peritonitis independently associated with

- Exit site care > twice per week (p<0.005)
- Exit site mupirocin (p<0.005)
- Non-sterile (saline or soap) ES cleansing (p<0.001)