Peritoneal dialysis (PD) peritonitis and exit-site infections — diagnosis and treatment

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Diagnosis and management of peritoneal dialysis (PD) Peritonitis

Patients may present with 2 of the following 3 features:-

1. **Signs and symptoms of peritonitis**
   - Abdominal pain or tenderness
   - Constipation or diarrhoea
   - Pyrexia

2. **Cloudy PD fluid**
   - PD fluid white cell count (WCC) >100/μL with >50% polymorphonuclear neutrophils.
   - After a Dwell time of more than 2 hours

3. **Microorganisms in the PD fluid**
   - Confirmed by Gram-stain or culture

Management of suspected PD peritonitis on initial presentation

If a patient contacts the renal unit complaining of a cloudy bag/effluent with or without abdominal pain they must be asked to attend the unit as soon as possible for assessment. Ask the patient to bring the PD fluid that they have drained out to the unit with them (this sample is the best to send for microbiological analysis).

In preparation for their arrival ensure that there is a 2 litre CAPD bag of fluid on the heater plate. (Ask the patient which fluid they usually use, if it is for a night dwell and the patient is usually on APD use Extraneal).

On arrival to the renal unit drain the patient as if they were carrying out a CAPD exchange, observing their effluent. If the fluid is obviously cloudy the patient will require treatment for peritonitis.

All patients should have the following performed:

- MEWs Chart: Blood pressure, pulse rate, temperature, pain assessment, respiratory rate, and oxygen saturations.
- Blood tests: FBC and CRP
- Where clinically appropriate blood cultures

A record of the above assessment should be recorded in the medical notes or cyberren.
The Home Therapies Team MUST be made aware of any patient with a diagnosis or suspected diagnosis of PD peritonitis. The team will liaise with the renal doctors, including the nephrologist of the week. The Home Therapies Team is available 24 hours a day for advice; contact details:

- Home Therapies Team Office ext 8186 (an answerphone service is available)

Any patient attending with suspected PD peritonitis should be reviewed by a renal doctor to assess suitability for treatment as an outpatient. The renal doctors are available via the oncall bleep 0010 from 9am until 8pm daily. Alternatively, outside of these hours the patient should be discussed with the nephrologist of the week. If the patient is systemically unwell (pyrexia, hypotension, rigors) or pain, nausea or vomiting is severe then the patient will require admission to hospital.

**Microbiological testing**

The following samples are to be collected in a patient suspected of having PD peritonitis:

a) 1 x blood culture set i.e 1x aerobic and 1x anaerobic bottle with 10 mL each of the effluent.
b) 2 x universal containers with 30 mL each of effluent
c) Assess exit site/tunnel for any infection: If purulent, send a wound swab from exit site.

The following technique should be adopted to minimise contamination.

1. Gently remove flip caps from top of blood culture bottles with fingers and disinfect rubber septum using 2% Chlorhexidine / 70 % alcohol wipe and allow to air-dry. Using a 20 mL sterile syringe, draw approximately 15-20 mL of the effluent from the dialysis bag. Using a sterile needle, inoculate approximately 5-10 ml each into first the aerobic bottle, then the anaerobic bottle of blood culture set. Gently shake bottles to achieve mixing.

2. Then, use a 50 mL syringe and draw 50-60 mL of effluent from dialysis bag. Inoculate approximately 25-30 mL of effluent into each of 2 sterile universal containers, without touching the inside of the containers. Seal them tightly.

3. Send to the lab for processing as soon as possible – The samples can be sent via the Pod system to Specimen reception at Arrowe Park Hospital.

4. Please inform Microbiology laboratory to expect sample on ext 4511 (during working hours) or the on-call Microbiology BMS via switch (if out of hours). Request both whole cell count and differential count.

5. On receipt at Specimen Reception, the blood cultures bottles are to be placed in the incubator at 37 °C and the universal containers are to be stored in the refrigerator until transport to the Microbiology lab. The sample should not be stored at Room Temperature.
Empirical antibiotic therapy:

<table>
<thead>
<tr>
<th>Day</th>
<th>Antibiotic</th>
<th>Route</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>vancomycin</td>
<td>intraperitoneal (IP) dwell time ≥6hours</td>
<td>if weight &lt;60kg STAT 1.5g if weight &gt;60kg STAT 2g</td>
</tr>
<tr>
<td></td>
<td>gentamicin</td>
<td>Intraperitoneal (IP) dwell time ≥6hours</td>
<td>STAT 32mg (regardless of weight)</td>
</tr>
<tr>
<td>2</td>
<td>ciprofloxacin</td>
<td>Oral</td>
<td>250mg TWICE a day</td>
</tr>
</tbody>
</table>

**First Choice**
- Day 1
  - Vancomycin intraperitoneal (IP) dwell time ≥6 hours
    - if weight <60kg STAT 1.5g
    - if weight >60kg STAT 2g
  - Gentamicin Intraperitoneal (IP) dwell time ≥6 hours
    - STAT 32mg (regardless of weight)
  - Ciprofloxacin Oral
    - 250mg TWICE a day

**Second Choice**
- Day 1
  - Vancomycin Intraperitoneal (IP) dwell time ≥6 hours
    - 1.5g if weight <60kg
    - 2g if weight >60kg
  - Ceftazidime Intraperitoneal (IP) dwell time ≥6 hours
    - STAT 1g–1.5g
    - For patients with residual renal function (>100mL/day urine output) - start at higher end of dosing range (1.5g).

**Third Choice**
- Patients unable to receive vancomycin or ceftazidime must be discussed with a renal doctor and microbiologist.
- A proportion of penicillin-sensitive patients will also be allergic to cephalosporins: patients with a history of hypersensitivity to penicillin should not receive ceftazidime.
- Patients with a history of an infection alert (e.g. VRE/CPE) - contact a microbiologist

After the initial stat of empirical antibiotic, the choice of drug will be rationalized depending on peritoneal fluid culture result and relevant antibiotic therapy continued. See culture tables on pages 7-9.

Patients will require at least 14 days in total of antibiotics.

Vancomycin, gentamicin and ceftazidime can be added in the same dialysis solution bag without loss of bioactivity, however separate syringes must be used to make the additions.

A prescription for intraperitoneal antibiotics should be written on the relevant prescription chart and must state for intraperitoneal use on the prescription.

Ciprofloxacin should be prescribed on a green FP10HP prescription for outpatients, on PCIS for inpatients.
Intraperitoneal antibiotic administration

- **Patients on CAPD**
  Once the sample has been taken, move to the next stage of the CAPD exchange 'flush before fill'.
  ALWAYS TAKE SAMPLE PRIOR TO FLUSH.
  During the ‘flush’ phase ensure that the fill volume left in the bag is the correct amount for that patient. i.e. if patient only fills 1500mLs, flush 500mLs out of the 2L fill bag into the drain bag.
  Once the patient’s fill volume is left in the fill bag, add the antibiotics to the dialysis fluid via the additive port using sterile technique. Gently shake the bag to ensure antibiotics are mixed in, and then continue with the fill phase of exchange. Disconnect once fill completed as normal and advise the patient to leave the fluid in for a minimum of 6 hours. If patient is normally on CAPD, they can carry on with their usual regime after 6 hours.

- **Patients on APD**
  In intermittent IP dosing regimes, the antibiotic-containing dialysis solution must be allowed to dwell for at least 6 hours to allow adequate absorption of the antibiotic into the systemic circulation.
  The empirical antibiotic regime described above can be used in patients on CAPD and APD, however for patients on APD the six-hour antibiotic dwell is done in the “day bag”. The patient can have APD exchanges overnight as usual.
  Temporary conversion to CAPD may be required if the patient is being treated with IP ceftazidime, as APD may result in higher peritoneal clearances than CAPD, resulting in reduced dialysate concentrations, reduced serum concentrations and the possibility of prolonged intervals when dialysate concentrations are less than the MIC for susceptible organisms\(^2\).

If the patient is normally on APD and they have attended during the night, advise them to miss that night's therapy and ask them to drain out in the morning. They will then be able to carry on as normal the next night. (Remind them that they may have to 'by pass' initial drain, if they usually have a day dwell.)

If in doubt, discuss this with the PD nurses, renal doctors or renal pharmacists.
Indications for catheter removal

Refractory peritonitis (defined as failure of effluent to clear / or failure to respond clinically to appropriate antibiotics within 3-5 days) should be managed by catheter removal to protect the peritoneal membrane for future use².

Relapsing peritonitis: (defined as an episode of PD peritonitis occurring within 4 weeks of completion of therapy of a prior episode with the same organism or one sterile episode) catheter removal should be considered especially for MSSA/MRSA or Pseudomonas spp.

Repeat peritonitis (episode of PD peritonitis occurring within 4 weeks of completion of therapy of a prior episode with a different organism) will need surgical intervention either in the form of acute removal of their PD catheter or an elective tube change (removal and re-insertion). This will be dependant on the type of organism.

Recurrent peritonitis (Episode of peritonitis occurring with a different organism within 4 weeks of prior episode): catheter removal should be actively considered.

Fungal peritonitis: will require urgent catheter removal. Refer to consultant nephrologist and surgical team for urgent catheter removal and contact microbiology for advice on antifungal treatment.

Refractory exit site and tunnel infection: Actively consider catheter removal especially if infection is caused by MSSA/MRSA or Pseudomonas.

Further antibiotic therapy

Further antibiotic therapy should be reviewed once culture results and sensitivities are available. The guidelines for therapy below are suggestions only and close liaison with microbiology is important. In particular, patients who are not responding to antibiotic therapy should be reviewed surgically with a view to laparotomy and catheter removal.

Pseudomonas infections have a high morbidity and mortality and all patients should be admitted and reviewed by the surgical team within 24 hours. In general these patients need early catheter removal if not improving after 24-48 hours treatment.
Gram-positive organism identified on culture

**STOP** ciprofloxacin/ceftazidime
Assess exit site / tunnel
Rule out intra-abdominal pathology for Streptococcus / Enterococcus

**Gram-positive organism on culture**
(Result usually available after 48-72 hours)

**Staphylococcus epidermidis**
(coagulase-negative staphylococcus) or other gram-positive organisms except VRE

- Continue IP vancomycin
- Check random serum vancomycin assay on day 3-4 and re-dose as per levels (see Appendix 1)

- Complete 14 days of treatment

**Staphylococcus aureus**

- Methicillin-sensitive (MSSA)
- Methicillin resistant (MRSA)

- Consider adding rifampicin 300mg po BD-AC (counsel patient on orange secretions & PD fluid) & check for interactions with other medicines.
- For MSSA/MRSA patients – also follow trust decolonisation regime
- Remove catheter, if evidence of exit site / tunnel infection

- Continue IP vancomycin
- Check random serum vancomycin assay on day 3-4 and re-dose as per levels (see Appendix 1)

- Complete 4 weeks of treatment

If no improvement by day 3 or 4, send PD fluid for cell count and discuss case with renal consultant and microbiologist.

**For VRE**, contact microbiologist - options include Oral Linezolid or IP daptomycin.
Gram-negative organism identified on culture

(result usually available after 48-72 hours)

STOP Vancomycin
Assess exit site and tunnel. Rule out intra-abdominal pathology

Pseudomonas

Use 2 antipseudomonal agents:
- Continue ciprofloxacin 250mg po BD
- PLUS ceftazidime 1g -1.5g* IP daily (minimum 6-hour dwell)

If patient has an allergy or contraindication to either of these agents, consider the use of IP gentamicin 0.6mg/kg daily (minimum 6-hour dwell time). Contact pharmacy for advice on monitoring serum concentrations.
If exit / tunnel infected, remove catheter

Complete minimum 21 days of treatment

Stenotrophomonas

Options may include oral Septrin or moxifloxacin. Will need 3-4 weeks

Complete minimum 21 days of treatment

Other gram-negative organism

Continue monotherapy according to sensitivities:
- Continue ciprofloxacin 250mg po BD
- OR ceftazidime 1g -1.5g* IP daily (minimum 6-hour dwell)
  if unable to have quinolones

If no improvement by day 4 on ciprofloxacin monotherapy send PD fluid for cell count and change to ceftazidime 1g -1.5g* IP daily (minimum 6-hour dwell).
If no response by day 4 on ceftazidime monotherapy discuss case with renal consultant and microbiologist. Consider catheter removal

Complete minimum 14-21 days of treatment
“Culture-negative” peritonitis

The patient should always be asked about recent use of antibiotics for any reason, as this is a known cause of culture-negative peritonitis.

**“Culture-negative” peritonitis**

Continue IP vancomycin AND ORAL ciprofloxacin OR IP ceftazidime

Check random serum vancomycin assay on day 3-4 and re-dose as per levels (see Appendix 1)

If no improvement by day 3, send PD fluid for cell count and repeat cultures in blood culture bottles.

**AND add** ceftazidime 1g -1.5g* IP daily (minimum 6-hour dwell)

Stop Ciprofloxacin

If patient is already on ceftazidime or is unable to receive it, discuss options for management with microbiology.

If no improvement by day 5 discuss case with renal consultant and microbiologist and consider catheter removal

Complete **minimum** 14 days of treatment
**Fungal peritonitis**

Catheter should be removed urgently.
Start IV Micafungin
Rule out intra-abdominal pathology e.g. abscess/ diverticulitis

**Prophylactic antibiotics following accidental touch contamination**
Following a break in sterile technique, the patient should be advised not to continue with the exchange and attend the renal unit for a stat dose of IP vancomycin (1.5g if weight <60kg; 2g if weight >60kg) and a change of catheter extension set.

**Exit site and tunnel infections**
An exit site infection is defined by the presence of purulent drainage with or without erythema of the skin at the catheter-epidermal interface. A positive culture from the exit site in the absence of inflammation is indicative of colonisation rather than infection. A tunnel infection may present as erythema, oedema or tenderness over the subcutaneous pathway but is often clinically occult².

When determining presence or severity of exit site infection consider:

- a) erythema > 4 cm or < 4 cm across
- b) purulent discharge
- c) serous/sero-sanguinous discharge
- d) induration > 4cm or < 4 cm
- e) Crusting

PD catheter removal should be considered for patients with exit site and tunnel infections.
Exit site or tunnel infection
Send exit site swab for culture and sensitivity

Commence empirical antibiotic therapy:
- Flucloxacillin 500mg oral QDS

If penicillin allergic:
- Doxycycline 200mg oral STAT followed by doxycycline 100mg-200mg oral daily (depending on severity). Counsel patient on increased skin sensitivity to sunlight.

Consider adding rifampicin 300mg oral BD-AC to above regimes for severe infections. Counsel patient on orange secretions/PD fluid & check for drug interactions.

Gram positive organism identified:
Continue empirical therapy or adjust according to sensitivities.

If MRSA isolated, consider IP vancomycin if any indication of subclinical peritonitis (see peritonitis treatment algorithm). Also, follow trust MRSA decolonisation regime
Consider catheter removal.

Gram negative organism identified:
Stop empirical therapy. Start ciprofloxacin 250mg oral BD. Counsel patient on tendonitis. If allergy or previous adverse reaction to quinolones, or history of epilepsy, discuss with microbiology.

If Pseudomonas identified, consider catheter removal and discuss with microbiology.

Continue treatment for 10-14 days and then review

Resolution
Stop treatment

Improvement
Re-swab, continue treatment for a further 2 weeks

No improvement
Discuss with renal consultant and microbiology
Doses of antibiotics used for PD peritonitis and exit site/tunnel infections

<table>
<thead>
<tr>
<th>Drug</th>
<th>IP dose; intermittent (per exchange, once daily)</th>
<th>Oral dose</th>
<th>Special considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftazidime*</td>
<td>1g – 1.5g&lt;sup&gt;(3)&lt;/sup&gt;</td>
<td>Doses may be empirically increased by 25% in patients with residual renal function (&gt;100mL/day urine output) - start at higher end of dosing range for these patients and consider increasing the dose by 25% if not improving.</td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>200mg oral STAT followed by 100mg-200mg oral daily&lt;sup&gt;1,3&lt;/sup&gt; depending on severity of infection.</td>
<td>Counsel patient on increased skin sensitivity to sunlight.</td>
<td></td>
</tr>
<tr>
<td>Flucloxacillin</td>
<td>500mg oral QDS&lt;sup&gt;(3)&lt;/sup&gt;</td>
<td>Monitor LFTs</td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>0.6mg/kg&lt;sup&gt;(2)&lt;/sup&gt;</td>
<td>Requires serum concentration monitoring, contact pharmacy for advice</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>250mg oral BD&lt;sup&gt;(3)&lt;/sup&gt;</td>
<td>Avoid in epilepsy. Counsel on the possibility of tendonitis as a side effect. Advise the patient take 2 hours before or after any phosphate binders or iron preparations.</td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td>300mg oral BD-AC&lt;sup&gt;(3)&lt;/sup&gt;</td>
<td>Counsel patient on orange body secretions and PD fluid. Check for interactions with other medications (enzyme inducer). &lt;br&gt; <strong>Rifampicin must never be used as monotherapy due to the development of resistance.</strong></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>STAT dose (dwell time ≥6 hours)</td>
<td>Frequency of further doses dependant on serum concentration monitoring. Aim to keep “trough” vancomycin concentration above 15mg/L. See <strong>Appendix 1</strong></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 1. Monitoring of serum vancomycin concentrations.

Vancomycin is administered IP as a stat dose depending on weight.

1.5g if weight <60kg
2g if weight ≥60kg
(dwell time ≥6 hours)

The dosing interval is dependent on residual renal function. Ideally, the timing of repetitive dosing should be based on trough levels.

Intraperitoneal levels of vancomycin after the initial dose will always be lower than serum levels of vancomycin; therefore, the serum levels need to be kept higher than would be otherwise indicated.

Patients should receive another stat dose of vancomycin once trough serum levels have fallen to ≤20 mg/L.¹²

Check serum vancomycin concentration every 3rd to 4th day after initiation of vancomycin.

- If the serum concentration is <15mg/L the patient should receive another stat dose of IP vancomycin the same day. Consider increasing the dose by 500mg, especially if <72hours since last stat dose.²
- If the serum concentration is ≤20mg/L the patient should receive another stat dose of IP vancomycin the same day – the same dose as previous.
- If the serum concentration is 20-22mg/L the patient should receive another stat dose of IP vancomycin in the next 24-48hours – the same dose as previous.
- If the serum concentration is >22mg/L another concentration should be checked in 48hours and the patient re-dosed with IP vancomycin once concentration is <20mg/L. Consider reducing the dose by 500mg if >96hours since the last stat dose and serum concentration is >20mg/L.

When a patient has received antibiotics for a past occurrence of peritonitis take into account the antibiotic dose and dosing frequency which was previously required when making a decision on antibiotic therapy.

The renal pharmacists can provide further dosing and monitoring advice based on the patient's dosing history and serum concentrations.

Renal pharmacist: Bleep 2459, Monday – Friday 9am-5pm.
References.


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Protocol reviewed in and re-agreed May 2014