EXECUTIVE SUMMARY

- Peritonitis is a potentially serious complication of peritoneal dialysis that needs to be managed urgently and well to minimise both early and late morbidity and mortality.
- Antibiotics for peritonitis need to be broad spectrum initially but the spectrum should be rapidly narrowed immediately an organism is known, making a microbiological diagnosis essential.

1. ASSOCIATED MELBOURNE HEALTH POLICY
   MH02. Care Planning and Appropriateness Policy

2. PURPOSE AND SCOPE
   This policy outlines the procedure for treatment of peritonitis for patients undergoing peritoneal dialysis.

3. DEFINITIONS

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>PD qualified- MH Staff</td>
<td>Staff who have successfully completed the relevant RMH Kidney Care PD training program (or a relevant component thereof) and have current knowledge, experience and demonstrated competence in PD. Any MH PD qualified staff member who has not had practical experience in PD for &gt;12 months, will be required to undertake competency assessment or re-training. This can be arranged via the Nephrology Ward or Home Dialysis Services.</td>
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<tr>
<td>Severe, immediate hypersensitivity (allergy) to penicillin</td>
<td>Symptoms/signs including anaphylaxis, urticaria, bronchospasm, drug rash with eosinophilia and systemic symptoms, or Stevens-Johnsons syndrome</td>
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<tr>
<td>Recurrent Peritonitis</td>
<td>An episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism. This should be counted as a separate peritonitis episode.</td>
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<tr>
<td>Relapsing Peritonitis</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. Relapsing episodes should not be counted when calculating peritonitis rates.</td>
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<tr>
<td>Repeat peritonitis</td>
<td>An episode that occurs more than 4 weeks after completion of therapy of a prior episode with the same organism. This should be counted as a separate peritonitis episode.</td>
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<tr>
<td>Refractory Peritonitis:</td>
<td>Failure of the effluent to clear after 5 days of appropriate antibiotics.</td>
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<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>
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4. **RESPONSIBILITIES**

4.1. Director Nephrology, Line Managers, Home Dialysis Service

5. **PROCEDURE**

5.1. On presentation with signs and symptoms of Peritonitis, follow flow chart (appendix 1)

5.2. Obtain dialysate effluent sample within 30 mins of presentation as per policy KCS 010201, do not flush peritoneum unless severe pain (see additional treatment below)

5.3. Send PD fluid for the following samples:
   - EDTA blood tube (Vacutainer®) white blood cell count (WBC) and differential
   - Yellow sterile urine specimen container (at least 30ml – 100ml) (do NOT use this to dipstick)
   - PD fluid in 4 **blood culture bottles** (2 anaerobic and 2 aerobic) – at least 5ml per bottle as per policy KCS00000. Consider fungal culture bottle if high suspicion (eg has been on prolonged antibiotics)
   - Urine Dipstick a separate drop for the presence of leucocytes (a deep purple colour change suggests presence of numerous white cells. A negative result is unhelpful – await formal white count but do not delay antibiotics if the patient is unwell).

5.4. Send blood for **FBE, U&E, LFT, Ca/P0₄, ALP, Glucose, CRP, (and blood culture if diagnosis unclear)**

5.5. Send an exit site swab if there is any doubt over the exit site.

5.6. Initiate Intra-Peritoneal antibiotics as per empirical therapy below.
   a. Add antibiotics to one exchange daily for CAPD (minimum dwell time 4-6 hrs) or in daytime dwell bag for APD.
   b. Antibiotics must be added according to policy KCS020211. Intra-peritoneal (IP) medication administration.
   c. Note: Initial therapy should be IP unless the PD catheter is completely blocked or there is no-one competent to access the PD catheter, in which case antibiotics may be given IV.

5.7. Patients do not necessarily need admission if they are well but have a cloudy bag.

5.8. **Notify home dialysis of peritonitis episode as soon as you are aware of it and the cell count** (tel ext 8387 2097, fax 8387 2095, email: RMH-KCSHomeTraining@mh.org.au, after hours support 8387 2096)

5.9. Do not diagnose peritonitis if PD WBC<100 cells/mm look for other causes and repeat WBC even if you started empirical antibiotics. Patients who have a dry abdomen during the day or have just had their catheter inserted may have more cells in the peritoneum.

5.10. Antibiotic choice after the first 24-48 hours should be guided by culture and sensitivities.

5.11. In order to monitor an episode of peritonitis, two further samples should routinely be taken.

5.12. Mid–peritonitis PD fluid sample – on the third to fifth day of treatment. White cell count should be considerably reduced.

5.13. Post–peritonitis PD fluid sample – two days after completion of antibiotics to detect early relapse, white cell count should be <20 and culture sterile.

5.14. Admitted unwell patients should have daily PD WBC to monitor response to therapy
5.15. DO NOT KEEP THE PATIENT IN HOSPITAL IF THEY ARE IMPROVED FOLLOWING ANTIBIOTICS

5.16. Empirical therapy is selected to cover a wide G+ve and G-ve spectrum

5.17. Standard treatment is with vancomycin IP and ceftazidime IP.

5.18. It is vital to revise the antibiotic regime to narrow the antibiotic spectrum as soon as possible when culture results are known. This often means stopping ceftazidime but see appendix 2 and refer to home dialysis.
### Standard treatment

<table>
<thead>
<tr>
<th>Ceftazidime 20mg/kg (max 2g) IP once daily.</th>
<th>Plus</th>
<th>Vancomycin 30 mg/kg IP (max 2g) stat. Repeat dose when serum level falls below 20mg/L.</th>
<th>Plus</th>
<th>Nystatin tablets 500,000 units orally four times a day for the duration of the antibiotic therapy Continue oral nystatin for 7 days post cessation of antibiotics</th>
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<tbody>
<tr>
<td>If pd catheter not working or no competent person to use PD catheter give</td>
<td>give Ceftazidime 1g IV daily.</td>
<td>give Vancomycin 25mg/kg IV (actual body weight) (max 1.5 g)</td>
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<td>Nystatin PO as above</td>
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#### If allergic

- If cephalosporin allergic, or immediate hypersensitivity (life threatening) reaction to penicillin (see definitions page 3) consult Infectious Diseases Unit and consider aztreonam IP (note still small risk of cross reaction) or ciprofloxacin PO (or IV only if NBM)
- If vancomycin allergic consider IV linezolid following consultation with Infectious Diseases Unit. (note teicoplanin IP or IV may be an option but still small risk of cross reaction as it is a glycopeptide)

<table>
<thead>
<tr>
<th>Nystatin tablets 500,000 units orally four times a day for the duration of the antibiotic therapy</th>
<th>Continue oral nystatin for 7 days post cessation of antibiotics</th>
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#### Additional treatment

**Severe pain:** appropriately trained PD staff flush peritoneum with 1-2l of 1.5% dextrose dialysate +/- heparin 500iu/l +/-5-10ml 1% lignocaine. Do not do this unless severe pain – as washes out useful white cells.

**Cloudy effluent:** If the effluent looks very cloudy and there are drain problems or obvious fibrin strands then consider adding heparin 500 units/L IP.

**Pain:** For short term pain relief administration of 5-10ml of 1% lignocaine IP prior to the antibiotics.

**Antibiotic monitoring**

**Vancomycin**

**Target level** Aim for therapeutic levels >20mg/L.

An initial ‘spot’ level is recommended on the 2nd day following the initial dose, and a repeat dose given if level is ≤ 20mg/L. Timing of subsequent levels may vary between 3-7 days, and will be guided by the rate of decline of serum levels following the initial dose. Levels should not be allowed to fall below 15 mg/L.
Apart from hypersensitivity reactions, ototoxicity is the main concern and this is very rare with concentrations below 30 mg/L.

**Ceftazidime:** Does not need therapeutic drug monitoring

Whenever a patient is commenced on a drug requiring monitoring, the renal pharmacist should be informed. This includes vancomycin, gentamicin, teicoplanin or flucytosine.

**Treatment Duration**

Routine treatment should be for a minimum of **14 days** from commencement of antibiotics

*Staphylococcus aureus, Enterococcus and Pseudomonas* should be treated for **21 days** from commencement of antibiotics.

**Catheter Removal**

If bags fail to clear after 72 hours and culture results indicate the organism is sensitive to the current treatment protocol, the PD catheter should be removed and the patient temporarily transferred to haemodialysis. In general, this should NOT be delayed.

Indications for catheter removal
- Refractory peritonitis
- Relapsing peritonitis
- Refractory exit-site and tunnel infection
- Fungal peritonitis

Catheter removal should also be considered for
- Recurrent episodes of peritonitis
- Mycobacterial peritonitis
- Multiple enteric organisms

Any proposed departure from this policy should be discussed with the consultant in charge of the renal ward or PD consultant.

On rare occasions when the suppliers of ceftazidime have changed the pH of the solution it has precipitated when added to the PD bag – if this happens use another injectable second/third generation cephalosporin antibiotic or use a different brand of ceftazidime. Please inform the renal pharmacist. This is only usually a problem outside RMH.

**ASSOCIATED POLICIES / PROCEDURES**

5.19. KCS02.02.11 Intra peritoneal medication administration

5.20. KCS 02.02.14 Peritoneal Dialysis Effluent Specimen Collection Procedure For Microscopy, Culture and Sensitivities (MC&S)

5.21. KCS 02.02.07 Unblocking of Tenckhoff Catheter- Manual Syringing

**REFERENCES**


7. FURTHER INFORMATION

7.1. Contact person, group or documents that can provide further information or assistance

8. DOCUMENTATION

8.1. PD Peritonitis flow chart

9. REVISION AND APPROVAL HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Rev No</th>
<th>Author and approval</th>
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<td>List all approvers by name and position title prior to submission for approval.</td>
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Appendix 1 - Peritonitis flow chart

Suspected Peritonitis
Abdominal pain
Cloudy bag
Unexplained fever

Take samples
- Blood: FBE, U&E, LFT, Ca, P0₄, ALP, Glucose, CRP, (Blood culture if diagnosis not clear)
- PD fluid: Urgent WBC and Gram stain + 4 blood culture bottles (2 aerobic and 2 anaerobic)
- Swab: Exit site if score > 0

• PD fluid
  o obviously cloudy
  o >100 wbc/mm³
• Patient very unwell
• No sample possible
  o Refer to blocked catheter

Is the patient is very symptomatic or yeasts*

Adverse Drug Reactions?

NO

Await culture. Consider other diagnoses: e.g. cardiac, constipation, pancreatitis, surgical abdomen, bowel, gastroenteritis

YES

Flush with PD fluid 1-1.5 litres.
Repeat up to x3

IP vancomycin 30mg/kg (max 2g) stat (then when level <20mg/L)
+ IP Ceftazidime 20mg/kg (max 2g) IP daily
+ Nystatin 500,000 units QDS

Cephalosporin hypersensitivity or immediate penicillin hypersensitivity: consider aztreonam in addition to vancomycin
Appendix 2

Directed therapy for peritonitis

Once culture results are known treat according to the following guidelines:

Gram Positive organisms

Coagulase negative staphylococci (CNS)
Stop ceftazidime, continue vancomycin for 14 days.
If Methicillin Sensitive CNS, consider management as for MSSA

Staphylococcus aureus (MSSA)
Stop ceftazidime and vancomycin.
Start cephazolin (20mg/kg IP [max 2g] daily) for a total of 14 days providing sensitive.
Use vancomycin instead of cephazolin in patients with severe, immediate hypersensitivity (allergy) to penicillin (see Definitions page 3, and Antibiotics for allergic patients, page 8).

Methicillin Resistant Staphylococcus aureus (MRSA)
Stop ceftazidime continue vancomycin and consult Infectious Diseases. In total 21 days treatment is required.

Enterococcus (vancomycin sensitive)
Continue vancomycin and consider early removal of PD catheter if not resolving, requires 21 days treatment minimum.
Ampicillin may be suggested but the stability is an issue in PD fluid and needs to be injected freshly so is not preferred in PD

Vancomycin resistant enterococcus (VRE)
Discuss with renal consultant and Infectious Disease (ID) unit.
Requires 21 days treatment

Gram negative organisms

Coliforms (Non-Pseudomonas /Stenotrophomonas)
Stop vancomycin. Continue ceftazidime IP, or give gentamicin (0.6mg/kg [max 50mg] IP daily depending on levels) then be guided by susceptibilities.
If isolate of species likely to carry beta lactamase (e.g. Enterobacter, Serratia, Citrobacter, Acinetobacter, Morganella) use meropenem IV or gentamicin IP until susceptibilities are known. If the patient has recently travelled be aware of risks of multi-resistant gram negatives and discuss with ID unit.

Pseudomonas
Stop vancomycin. Continue ceftazidime IP (or gentamicin 0.6mg/kg [max 50mg] IP daily depending on levels) if sensitive. If susceptible, add oral ciprofloxacin 500mg daily (or 250mg bd) for the duration of antibiotic treatment. Ensure oral ciprofloxacin is separated from phosphate binders by a minimum of 2 hours. If resistant to ceftazidime, consider meropenem IV or gentamicin IP

Consider catheter removal early if not resolving.

Stenotrophomonas
Trimethoprim/sulphamethoxazole 800mg/160mg orally daily (monitor for toxicity).

Consider catheter removal early if not resolving.

Anaerobic organisms
Stop Vancomycin.
Consider perforation. Continue ceftazidime IP and add metronidazole 400mg orally BD (or 500mg IV bd).
Liaise immediately with the surgical team and arrange urgent imaging (often an erect chest X-ray and or a CT abdomen).

**Mixed Growth**
Where the gram stain or culture shows mixed organisms, especially with gram negatives, or if anaerobes are grown on culture, then a perforation should be assumed.
A surgical opinion needs to be requested urgently, and consider switching to IV antibiotics (eg ceftriaxone plus metronidazole or alternatively piperacillin-tazobactam alone).
If ceftazidime is continued IP then metronidazole orally or IV should be added. Remove the catheter if the patient is not improving rapidly.

**Culture negative**
Continue vancomycin for 14 days and stop ceftazidime.
If not improving repeat culture and discuss with Infectious Diseases Unit. Consider unusual organisms such as fungi or mycobacterium. Catheter removal should be considered.

**Fungal Peritonitis**
This is a very rare but serious complication which may be fatal if not treated early. Expect to admit the patient and remove the catheter. Discuss with Infectious Diseases Unit promptly, and inform the consultant nephrologist ‘on call’. In contrast to bacterial peritonitis frequent peritoneal lavage may be required. If it is possible, lavage the abdomen until the PD effluent runs clear before removing the catheter as this reduces adhesions. Surgical removal of the PD catheter should not be delayed if there has been no improvement within 24hrs. Where fungal peritonitis is confirmed, and the patient remains symptomatic at 24hrs without any obvious improvement, the catheter MUST be removed within the following 12 hrs.

If Candida albicans, Start
Fluconazole 400mg orally or IV daily for 2 days, then 200 mg orally daily, thereafter or IP 200mg daily.
If patient is very unwell and showing no signs of improvement within 24hrs the catheter must be removed AS SOON AS POSSIBLE on the next available emergency surgical list or under local anaesthetic, if it was inserted under local.
For non albicans candida, fluconazole resistance more likely, discuss with Infectious Diseases unit but consider systemic therapy with Anidulafungin 200mg IV on day 1 then 100mg IV daily thereafter.

**Ongoing therapy**
Further modification of antibiotic regimens may occur on an individual basis and guided by Infectious Diseases Unit advice, and the practicality of administration in PD.
Options include
Anidulafungin 200mg IV on day 1 then 100mg IV daily thereafter or
Fluconazole 200mg IP daily
Or
Amphotericin IV NB: DO NOT use amphotericin intra-peritoneally as it causes chemical peritonitis and pain, and may be poorly bioavailable to the peritoneum.

**Allergies**

**Antibiotics for patients with immediate hypersensitivity to penicillin or hypersensitivity to cephalosporins.**
Cephalosporins should not be administered to patients with immediate hypersensitivity to penicillin (i.e. life threatening penicillin allergy – see definition box). Cephalosporins may be used in patients with other forms of penicillin hypersensitivity.

For patients with severe, immediate hypersensitivity (allergy) to penicillin (see Definitions). The following is a list of alternative antibiotics to use in PD peritonitis. The use of these alternatives should be discussed with Infectious Diseases Unit, the peritoneal dialysis consultant, and pharmacy prior to use.
**Aztreonam:** 1000mg/L loading dose IP, followed by 250mg/L in every exchange for CAPD only. Note that there is a small risk of cross-reactivity in patients with immediate penicillin hypersensitivity. Also, there may be an increased risk of immediate hypersensitivity reactions to aztreonam in patients hypersensitive to ceftazidime, due to their similar side chains.

**Teicoplanin:** Teicoplanin doses are difficult and cannot be recommended unless no other antibiotic will suffice then empirical therapy might bet 400mg bd for 3 doses then 400mg every 72 hours aiming to maintain teicoplanin levels 15-20mcg/ml - but levels are difficult to obtain so may not be available.

**Linezolid:** Cannot be given IP. Prescribe 600mg bd orally. If unable to tolerate oral administration consider IV after consultation with the Infectious Diseases Unit. Fluid volume may be a problem with IV linezolid as it is only available in 600mg/300mL premixed infusion bags. It is very expensive and is associated with several toxicities including bone marrow suppression and peripheral neuropathy. Linezolid is a reversible monoamine oxidase inhibitor. Serotonin syndrome has been reported and co-administration with serotonergic drugs should be avoided where possible (monitor patient closely if concomitant serotonergic drugs are used).

**Gentamicin**
Give gentamicin 0.6mg/kg [max 50mg] IP daily then according to blood levels. Gentamicin distributes relatively poorly into adipose tissue, so slightly reduce the dose per kg in the obese. Severe and poorly reversible vestibulotoxicity as well as ototoxicity (hearing loss) are the main concerns when using gentamicin. Ensure blood levels are taken and avoid if possible in patients on high dose loop diuretics. Nephrotoxicity has not proved to be the major worry it was in the past provided levels are monitored. Through blood levels should be <1mg/L.

**Ciprofloxacin**
Has high oral bioavailability and is usually given orally, but doses must be administered separated by at least ~2hrs from phosphate binders - sevelamer, lanthanum, calcium as these all reduce the absorption of ciprofloxacin by around 50%. There are compatibility / stability issues with ciprofloxacin in PD bags - PD fluid contains calcium & magnesium plus has a pH of around 5.5 and ciprofloxacin is incompatible in solutions with a pH of above 5. Do not use IP.

**Metronidazole**
Give metronidazole orally wherever possible. Doses are 400 mg orally bd. In rare cases it may need to be given IV (500mg bd).Metronidazole is added to provide anaerobic cover when ceftazidime is being used.

**Recurrent Infection**
Follow the same protocol as outlined previously, but ensure that antibiotics cover the previous bacterial or fungal species. If more than two recurrences are seen then catheter should probably be removed.

**PD peritonitis with tunnel infection**
Arrange to remove the PD catheter as soon as possible as well as instituting IP antibiotics. Continue antibiotics for at least 10 days after catheter removal (IV or orally).