# Joint Trust Protocol for Peritoneal Dialysis Peritonitis and Catheter-Associated Infections

## A Clinical Protocol recommended for use

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|---|---|
| **In:** | NNUH, JPUH |
| **By:** | Medical and Nursing staff in the Renal Department |
| **For:** | Patients receiving peritoneal dialysis |
| **Key words:** | Peritoneal Dialysis, Peritonitis, Exit-Site Infection, Tunnel Infection |
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| **If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?** | N/A |

This protocol has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

The Trust's protocol are made publicly available as part of the collective endeavour to continuously improve the quality of healthcare through sharing medical experience and knowledge. The Trust accepts no responsibility for any misunderstanding or misapplication of this document.

**Version and Document Control:**

| Version Number | Date of Update | Change Description | Author |
|---|---|---|---|
| 2 | 29/12/2021 | Antibiotics to use to PD patients<br>Pre procedure antibiotic cover noted<br>To add an antifungal as part of the treatment of peritonitis | Dr Matt Todd |
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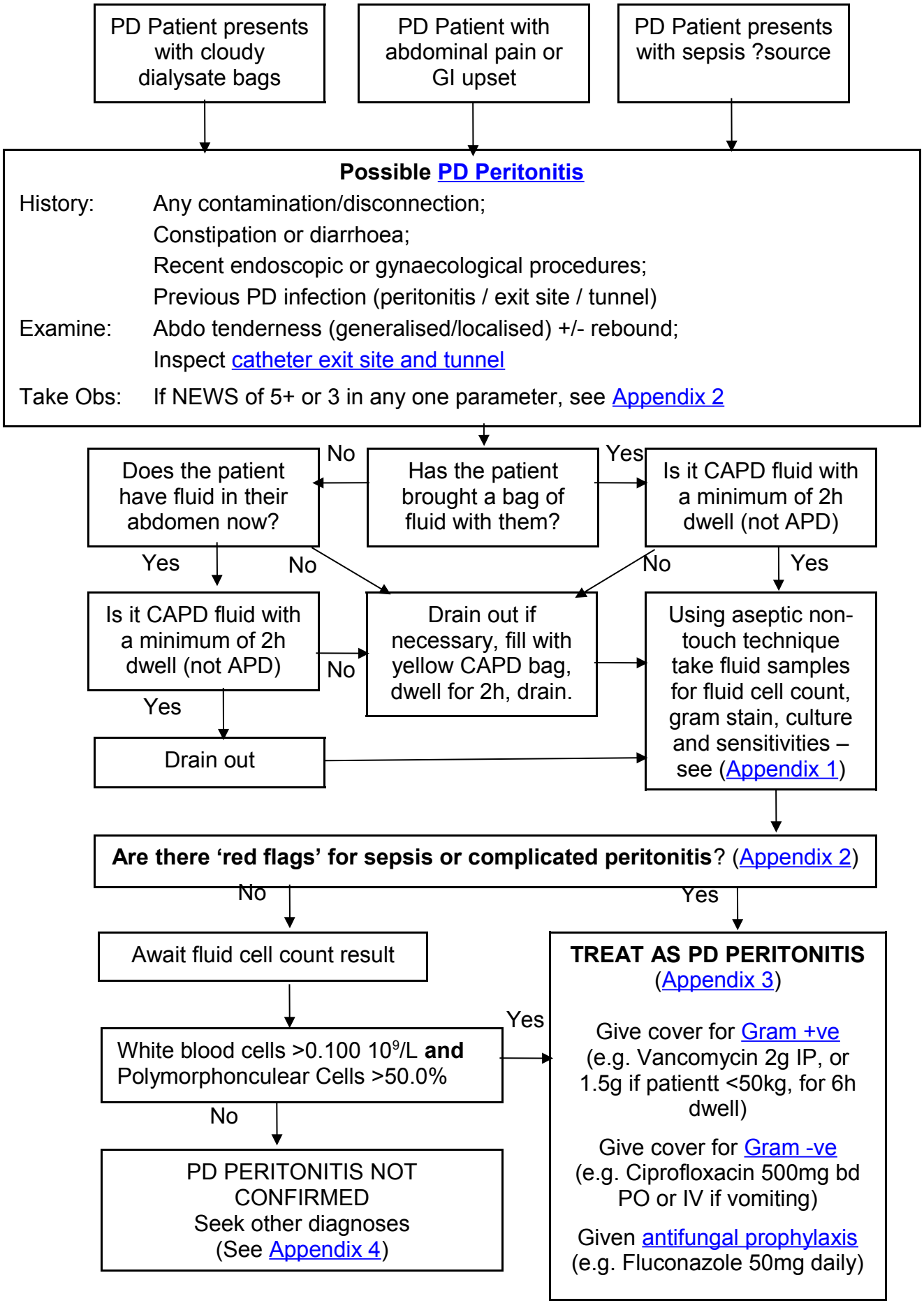
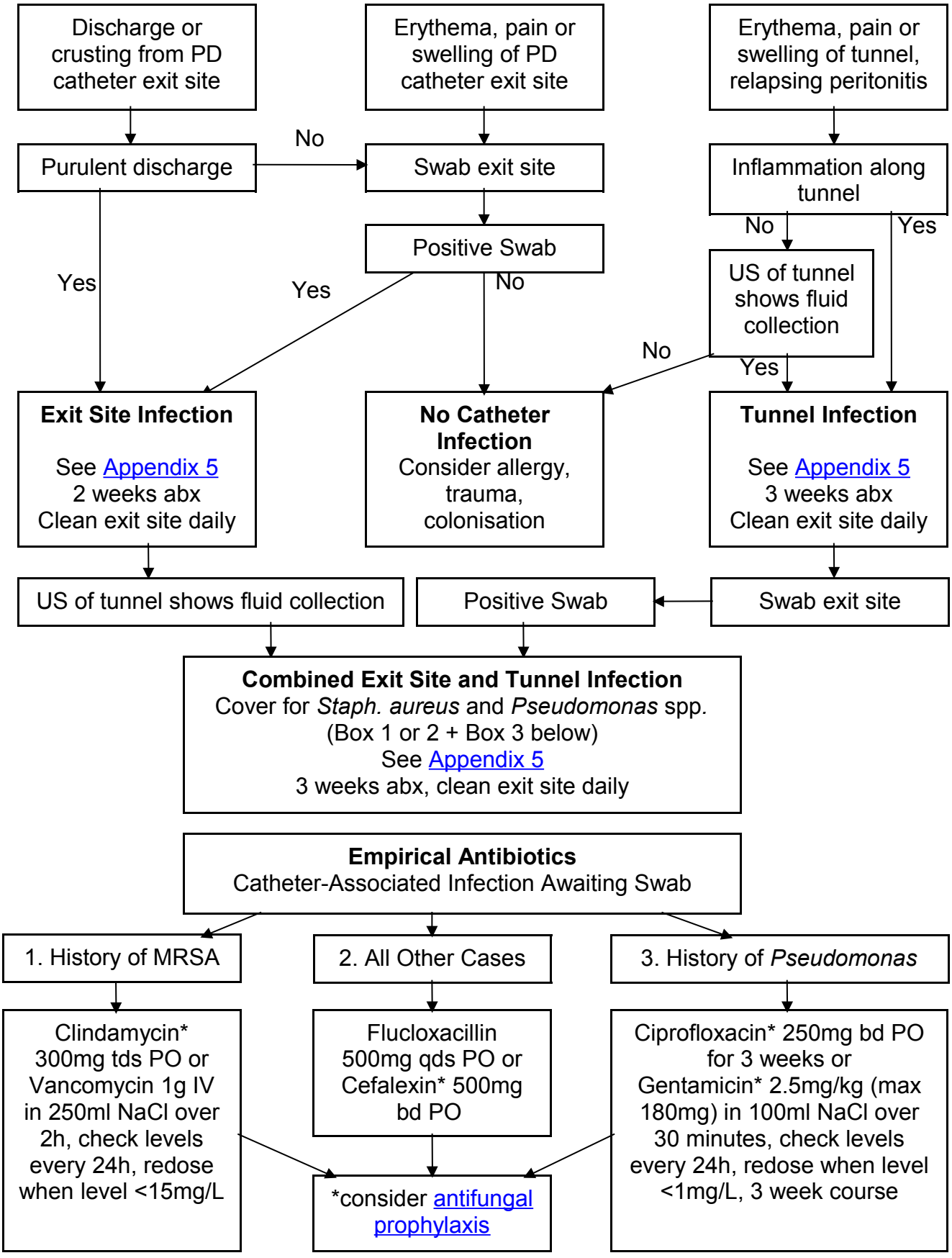
## Quick Reference: Initial Management of Suspected PD Peritonitis



## Quick Reference: Initial Management of Exit-Site or Catheter Tunnel Infection



## Quick Reference: Antibiotic Prophylaxis and Cleaning for Patients with PD Catheters

1. Daily application of antibiotic cream or ointment to the catheter exit site; one of:
    a. Mupirocin 2% Ointment (non-proprietary or as Bactroban®)
    b. Mupirocin 2% Cream (Bactroban® Cream), if ointment poorly tolerated
    c. Gentamicin 0.3% Drops (e.g. Genticin® eye/ear drops – unlicensed indication)
    d. 3% Hypertonic Saline, if none of the above are tolerated

2. Topical cleansing agents for the prevention of catheter-associated infections, when cleaning the exit site at least twice weekly and after showering; one of:
    a. 2% Chlorhexidine/70% Alcohol
    b. Povidone-Iodine
    c. Antibacterial soap and water, if neither of the above is tolerated

3. Prophylaxis before PD Catheter insertion or manipulation; one of:
    a. Vancomycin 1g IV over 1-2h
    b. Teicoplanin 400mg IV over 30 minutes, if known to be tolerant of teicoplanin (there is an unquantified amount of crossover between vancomycin and teicoplanin sensitivity)
    c. Cefuroxime 750mg IV (refer to Medusa for administration), if allergic to vancomycin, and if teicoplanin sensitivity not known
    d. Gentamicin 2.5mg/kg (max 180mg) IV (Refer to Medusa for administration)

4. Prophylaxis prior to colonoscopy or invasive gynaecological procedures, one of:
    a. Ampicillin 1g IV, Gentamicin 2.5mg/kg IV (max 180mg) (Refer to Medusa for administration)
    b. Piperacillin-Tazobactam 4.5g IV (refer to Medusa for administration)
    c. Ciprofloxacin 500mg IV (refer To Medusa for administration)

5. Prophylaxis before extensive dental procedures; one of:
    a. Amoxicillin 500mg PO as a single dose
    b. Clarithromycin 500mg PO as a single dose, if penicillin allergic
    c. Doxycycline 100mg PO as a single dose, if macrolide allergic

6. Prophylaxis following wet contamination, e.g. infusion of non-sterile fluid, opening of catheter to the outside world for an extended period; one of:
    a. Vancomycin 2g IP (1.5g IP if patient weighs <50kg) in 2L with 6h dwell time (1.5L if patient does not tolerate 2L dwells)
    b. Teicoplanin 15mg/kg IP in 2L with 6h dwell time (1.5L if patient does not tolerate 2L dwells)

c. Ceftriaxone 1g IP in 2L with 6h dwell time (1.5L if patient does not tolerate 2L dwells)

d. Intravenous antibiotics as in 3. above

7. Antifungal prophylaxis for patients with PD catheters taking broad-spectrum antibiotics (see Appendix 6); one of:

   a. Nystatin 500 000 international units PO qds

   b. Fluconazole 50mg PO od (care with drug-drug interactions)

   Antifungals should continue until the last dose of antibiotics, or 2d after last dose of gentamicin/amikacin, whichever is the longer.

## Objective/s

- To provide evidence-based recommendations for appropriate diagnosis and management of peritonitis in patients on peritoneal dialysis
- To provide evidence-based recommendations for appropriate diagnosis and management of exit site and tunnel infections in patients on peritoneal dialysis
- To provide clarity on appropriate doses, routes of administration, and durations of therapy for antimicrobial agents when treating peritoneal dialysis-associated infections, including prophylaxis

## Rationale

Catheter-associated infections are common and serious complications of Peritoneal Dialysis (PD). Infections at the catheter exit site (Exit Site Infections), along the tunnel (Tunnel Infections), or intraperitoneally (PD Peritonitis) can lead to cessation of or withdrawal from peritoneal dialysis, hospital admission, morbidity and death. PD Peritonitis is a major cause of technique failure and unplanned conversion from PD to haemodialysis, limiting patient choice and self-care. Infections may occur as a result of contamination during the dialysis procedure, poor technique and hand hygiene, spread of infection from the catheter exit site, and through intra-abdominal sources such as infection with enteric organisms.

There are clear national and international guidelines for the prevention, identification and management of catheter-associated infections. Antimicrobial choices should be based on likely organisms, local patterns of resistance, and the pharmacodynamic properties of these drugs when used in patients with end-stage renal failure on peritoneal dialysis. The clinical features of catheter-associated infections, particularly PD peritonitis, may be different from similar infections in people not on peritoneal dialysis – for example PD peritonitis does not necessarily present with a tender, rigid, guarded abdomen like traditional peritonitis.

Patients on Peritoneal Dialysis can also be at risk of more traditional forms of peritonitis, such as a perforated abdominal viscus. This guideline includes identifying patients with systemic sepsis or complicated/secondary peritonitis, and the approach to their management, but the full management of such patients is outside its scope and should include the involvement of the general surgical team.

This protocol sets out the standardised approach to PD catheter-associated infections in line with best practice guidelines, local patterns of infection and resistance, and formulary-appropriate antimicrobials suitable for use in patients on PD.

## Scope

This protocol is for use in all patients with PD catheters in situ, whether or not actively receiving treatment with continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD). It applies to patients of the Renal Home Therapies Team (RHTT) across Norfolk and Waveney, under the care of NNUH and/or JPUH, as well as visiting patients not already known to the service.

It is essential that the protocol is routinely followed, and that any necessary deviations are discussed with a senior member of the Renal and Microbiology team, and PD nursing staff.

## Processes To Be Followed

### A) Exit Site and Tunnel Infections

In patients with a peritoneal dialysis catheter in situ:

Investigate for a potential exit site infection in a patient with any of:

- Known or suspected PD peritonitis
- Pain at the catheter exit site
- Redness at the exit site
- Swelling, oedema or induration at the exit site
- Crusting at the exit site
- Discharge (serous / bloody / purulent) from the exit site

1. Swab the exit site
2. Examine the tunnel for any evidence of tunnel infection (see below)
3. If there is purulent discharge, start empirical treatment
4. If there is no purulent discharge, await swab results before initiating treatment
5. A positive swab in the absence of any of the above features indicated exit site colonisation, not clinical infection
6. For the empirical management of exit site infections or colonisation, see Appendix 5
7. Treatment of uncomplicated exit site infection (i.e. no associated tunnel infection) should be for a minimum of 2 weeks

Investigate for a potential tunnel infection in a patient with any of:

- Proven exit site infection
- Discharge (serous / bloody / purulent) from the exit site
- Pain along the tunnel
- Redness along the tunnel
- Swelling, oedema or induration at the exit site

1. Swab the exit site (if not already performed)
2. If there is pain, erythema, swelling, oedema or induration of the tunnel proximal to the external cuff, start empirical treatment – see Appendix 5
3. Otherwise, contact the RHTT to arrange for an ultrasound examination of the tunnel
4. If ultrasound shows a tunnel collection of >1mm thickness then start empirical treatment – see Appendix 5
5. Treatment of tunnel infections, whether associated with a proven exit site infection or nor, should be for a minimum of 3 weeks

Following treatment for an exit site or tunnel infection the exit site should be swabbed by the RHTT to ensure no colonisation. Following treatment for a tunnel infection with ultrasound evidence of a collection >1mm thick the RHTT should arrange for a repeat ultrasound examination to ensure that there is no residual collection.

## B) PD Peritonitis

Investigate for potential PD peritonitis in a patient with any of:

- Turbid or discoloured PD effluent ('cloudy bags')
- Abdominal pain
- GI upset (diarrhoea, vomiting, nausea)
- Unexplained fever
- Systemic sepsis of unclear source

Take a full set of clinical observations and calculate a NEWS-2 score. If the NEWS-2 score is greater than 5 in total, or scores 3 in any individual parameter, arrange for an urgent medical review (See Appendix 2).

The patient should be reviewed by a clinician experienced in history taking and physical examination (e.g. doctor, advanced nurse practitioner).

Take a history, specifically asking about:

1. Any history of accidental contamination, disconnection, or trauma to the catheter
2. Nausea and/or vomiting
3. Constipation and/or diarrhoea, including stool frequency and consistency
4. Fever, chills, rigors, shakes or sweats
5. Abdominal pain or tenderness
6. Any recent invasive procedures, including endoscopic or gynaecological investigations
7. Any recent or previous episodes of catheter-associated infections (exit site, tunnel or peritonitis)
8. If there are cloudy bags, when were they noted to become cloudy
9. If there are GI or septic symptoms, when did they begin

Examine the patient, in particular:

1. Swab the exit site and examine the exit site and tunnel for any evidence of infection / inflammation
2. Examine the abdomen for pain, focal or diffuse tenderness, rebound, guarding, and bowel sounds

Send an urgent sample of PD effluent for fluid cell count, gram stain and MC&S – see Appendix 1. Send bloods for FBC, U&Es, CRP, LFTs, and bone profile.

If the patient has a high NEWS-2 score (5+ in total or 3+ in any parameter), a history of >12h of cloudy bags/symptoms, severe abdominal pain with guarding/rebound tenderness, diarrhoea and/or vomiting, fever ≥ 38°C, or new/worsened confusion then they should be treated as complicated peritonitis and potentially systemic sepsis – see Appendix 2 and initiate empirical treatment immediately, before fluid cell count results are back.

If there are no signs of complicated peritonitis or sepsis, await fluid cell count results. A diagnosis of PD peritonitis is made, and empirical treatment started, if the fluid cell count shows WCC >0.100 x$10^9$/L **and** Polymorphs >50%. In other circumstances do not diagnose PD peritonitis,but see Appendix 4 for other potential causes.

Treatment should continue for a **minimum of 2 weeks**. Subsequent antibiotic changes/ deviations will be dependent on microbiological culture and sensitivities (see below for 'deviations from standard treatment' and 'directed microbiological treatment')

## Empirical antimicrobial treatment

Administer vancomycin and ciprofloxacin immediately as below until culture results are known (unless known allergy to either agent). This is in keeping with expert recommendations that initial antibiotic regimes should cover Gram positive and Gram negative organisms including Pseudomonas species.

### *Vancomycin*

Given as a single intraperitoneal (IP) loading dose, dependent on weight (see below)
This should be given in a volume of 2 litres dialysate for a minimum six hour dwell. However, it may be given in 1.5 litres of dialysate if larger volumes are not tolerated.

***Patients > 50kg***
Give a 2g dose of vancomycin as above

***Patients < 50kg***
Give a 1.5g dose of vancomycin as above

### *Ciprofloxacin*

500mg 12-hourly (BD) orally

If there is concern about absorption of oral ciprofloxacin (e.g. ileus or vomiting), patients should receive intravenous ciprofloxacin 200 mg 12-hourly.

Absorption of ciprofloxacin is reduced by sevelamer, calcium compounds, oral iron, zinc, magnesium and milk. It should therefore be given at least 2 hours before any of these medications.

## Deviations from Standard Treatment

If a patient is allergic or intolerant to Vancomycin or Ciprofloxacin, see the alternative regimes listed in Appendix 3. Empirical treatment should include cover for Gram positive and Gram negative organisms.

## Fungal Prophylaxis

The ISPD guidelines recommend antifungal prophylaxis whenever patients on PD receive broad-spectrum antibiotics (evidence grade 1B)

### Interpretation of PD effluent analysis

An elevated dialysate WCC of > 0.100 white cells x $10^9$/litre of which at least 50% are neutrophils is supportive of the diagnosis of peritonitis and the need for immediate initiation of antibiotic treatment. This is the universally agreed diagnostic criteria for diagnosis of PD peritonitis.

The following should also be noted;

- The same diagnostic criteria apply to diagnosis of APD and CAPD peritonitis
- Fluid from short (overnight) cycles may have misleadingly low WCCs. In equivocal cases a further exchange of (minimum) 2 hour dwell is adequate to obtain further samples for diagnostic white cell counts and Microbiology
- Initial drainage of fluid after a period of a dry peritoneal cavity may have an elevated WCC, but predominantly comprised of monocytes. If in doubt a second dialysate sample should be sent after a further 2 hour dwell
- Fungal and mycobacterial peritonitis may result in a predominance of lymphocytes. However the dialysate WCC is typically very high and will also demonstrate a significant number of neutrophils

### Monitoring fluid white cell counts

Patient review and monitoring of PD WCC must be carried out if;

- on day 3 if patient remains unwell or deteriorates despite treatment
- every 3 days if bags remain cloudy or PD WCC is not settling on treatment
- Peritonitis is slow to respond (clinical decision depending on symptoms and rate of decline of PD fluid WCC).

A final dialysate sample, for fluid cell count only, should be sent 1 week after stopping antibiotics.

## Non-antimicrobial treatment

### Recommendation for use of heparin

- Heparin 500 units/litre is added to an exchange if visible fibrin is present in the dialysate, or if there is haemoperitonium
- Consider HIT (Heparin Induced Thrombocytopenia) if the platelet count drops following the introduction of IP heparin

### Recommendations regarding PD regime

- Patients usually remain on their usual PD modality (CAPD or APD)
- It may be necessary to interrupt or delay night cycles of APD in order to administer the 6 hour dwell containing vancomycin
- The use of rapid short cycles for initial treatment of peritonitis to “clear turbid effluent” is not beneficial to clearance of infection. However it may occasionally be of use if there is poor dialysate drainage
- In the case of loss of ultrafiltration, more frequent, shorter duration glucose fluid may be considered as alternatives to using more hypertonic glucose solutions
- Set change is not routinely required in a patient presenting with peritonitis (unless there is definite recent contamination of set line)

### PD catheter removal or exchange in peritonitis

- If infection is severe or unresponsive to appropriate antibiotics
- Fungal peritonitis should result in urgent tube removal with a delay of at least 6 weeks before considering the placement of another PD tube.
- Should be considered if there is failure of PD effluent to clear within 5 days of treatment with appropriate antibiotics. This is important to prevent morbidity and to protect the peritoneal membrane, increasing the chance of a successful subsequent return to PD

PD catheter removal or exchange is indicated to prevent further episodes in:

- Relapsing peritonitis (an episode of peritonitis within 4 weeks of completion of treatment of a prior episode with the same organism)
- Catheter-related peritonitis (peritonitis with an exit-site or tunnel infection with the same organism)

It may be appropriate to perform simultaneous removal and insertion of a new catheter on the contralateral side of the abdomen. This must only be performed after the dialysate WCC has normalised and the procedure must be performed with cover by an antibiotic active against the infecting organism (such as continuation of the course of antibiotics for the episode of peritonitis).

If the catheter is removed, rather than replaced, the patient may require temporary haemodialysis. It is sometimes possible to hold off dialysis, with careful biochemical and clinical monitoring, if the patient has sufficient residual renal function. PD should ideally be withheld for 7-10 days to allow catheter healing.

## Directed antimicrobial treatment

Antimicrobial therapy should be reviewed and amended as necessary when microbiology results are available

### *No bacterial growth:*

In most cases this will be due to Gram positive organisms arising from touch contamination and will respond to appropriate antibiotics. If patient is responding to initiation regime, continue vancomycin as for coagulase negative staphylococci and discontinue ciprofloxacin.

If culture-negative infection not responding to antibiotics:

- Consider non-infective causes
- Consider altering antibiotics suggested by recent positive exit-site culture or recent peritonitis (where possibility this is a relapse)
- Additional microbiological testing, following discussion with microbiology e.g. mycobacterial culture
- Otherwise may require catheter removal

### *Coagulase negative staphylococci*

Continue intermittent intraperitoneal (IP) vancomycin dwells according to blood levels at 3 day intervals (see Appendix 3) and stop oral ciprofloxacin

### *Staphylococcus aureus (methicillin susceptible, MSSA)*

Continue vancomycin (as in coagulase negative staphylococci regime) and consider adding oral rifampicin (300mg 12-hourly) orally after confirming sensitivity with results server or microbiology if systemically unwell or slow to respond

### *Staphylococcus aureus (methicillin resistant, MRSA)*

Continue vancomycin (as in coagulase negative staph regime) and add oral rifampicin (300mg 12-hourly) after confirming sensitivity with results server or Microbiology

### *Gram negative infection (other than Pseudomonas)*

If patient is responding, continue oral ciprofloxacin and give no further vancomycin.
If unsatisfactory response, change to other IP antibiotic according to sensitivities (and discuss with seniors)

### *Pseudomonas*

Should be treated with two agents with activity against the cultured organism, usually oral ciprofloxacin + IP gentamicin

### *Fungal infections*

- The PD catheter should be removed promptly
- A minimum of 2 weeks of appropriate anti-fungal treatment is required **from the time of catheter removal**. Initial anti-fungal regime recommendations are based on review of sensitivities of infections and after discussion with microbiology

## Contacts/ Useful numbers

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|---|---|
| **Home dialysis team** 01603 287070 (Ext 3070) | 08.00 - 17.00 Monday - Friday |
| **Langley co-ordinator (Sister)** Ext 6639 | 24/7 (Use evenings/ weekends) |
| **Langley ward** Ext 3069 | 24/7 (Use evenings/ weekends) |
| **Renal Dect phone (Registrar)** Ext 4922 | 09.00 - 17.00 Monday - Friday |
| **JPU co-ordinator (Sister)** Ext 6020 | 08.00 – 21.00 Monday - Saturday |
| **Renal Consultant on-call** | Mobile via switchboard |

## Clinical audit standards

To ensure that this document is compliant with the above standards the following monitoring processes will be undertaken:

The unit's peritonitis data will be audited on an annual basis. Key audit measures are:

- Peritonitis rate (guidelines suggest that a rate of less than 1 episode / 18 patient treatment months is obtained)
- Rate of culture negative infections (guidelines suggest that inability to culture the responsible organism should occur in less than 20% of episodes)
- Cure rate of peritonitis with preservation of catheter and continuation of PD
- Relapse / recurrence rate
- Antibiotic sensitivity / resistance

The results will be sent to the home dialysis team who will ensure that these are discussed at relevant governance meetings to review the results and make recommendations for further action.

## Summary of development and consultation process undertaken before registration and dissemination

Dr Todd drafted this document on behalf of the Renal Home Therapies Team who have agreed the final content. During its development it has been circulated for comment to: Renal consultants: Dr Mark Andrews (Renal SD), Dr Calum Ross, Dr Mahzuz Karim, Dr Ravi Varma, Dr Anya Friedla, Dr Mahdi Althaf, Dr Jean Patrick (JPUH), Home Dialysis Team: Sr Len O'Driscoll, Jayne Scothern, Karen Emerson, Sara Otty JPU: Matron Owen Brooks Microbiology:

It was reviewed to current practice in 2021.

This version is endorsed by the Clinical Guidelines Assessment Panel

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## Appendix 1

## Specimen Collection Method for Peritoneal Dialysis Fluid in Suspected PD Peritonitis

PD Fluid should be drained from the first cloudy bag which has had a dwell time of at least 2h:

1. If the patient has brought a cloudy bag with them, and is on CAPD with a minimum 2h dwell, samples should be taken from that bag
2. If the patient has not brought a cloudy bag with them, but has fluid in their abdomen, they should drain out after a minimum of 2h from instillation and that fluid should be used for the sample.
3. If the patient is on APD or arrives without fluid in their abdomen they should drain out, then have a 1.5-2L 1.5% Glucose (Yellow) CAPD bag instilled and left to dwell for 2h, then drained out, and that fluid should be used for the sample.

Fluid should be sent for microbiological analysis before the first dose of antibiotics is administered unless the patient is systemically unwell and septic (e.g. patients admitted as an emergency through the Emergency Department or Acute Medical Unit with suspected sepsis).

### Method of Collection

1. Collect the necessary equipment: Blood Culture Collection set, 20ml luer-lock syringe, EDTA (purple) vacutainer, white-topped universal container, 2% chlorhexidine/70% alcohol wipes x3.
2. Print ICE request forms:
    a. Urgent Fluid cell count (in Laboratory Medicine → Urines/Fluids)
    b. Gram stain ('C.A.P.D.' in Microbiology → Swabs/Fluids)
    c. Culture and sensitivities ('C.A.P.D. in blood culture bottle' on the same tab)
3. Clean hands and apply non-sterile gloves.
4. Clean the medication/sample port of the dialysis drainage bag with a 2% chlorhexidine/70% alcohol wipe.
5. Take the blood culture bottle caps off and scrub each bottle port for 15s with a 2% chlorhexidine/70% alcohol wipe. Use a new wipe for each bottle. Leave to dry by evaporation.
6. Using aseptic non-touch technique, and using the butterfly collecting set from the blood culture collection set, first inoculate the aerobic (blue) blood culture bottle with 10ml of fluid, using the label gauge as a guide. Inoculate the anaerobic (red) blood culture bottle in the same way.
7. Do not remove bottle barcodes.
8. Attach the EDTA (purple) vacutainer and allow to fill under vacuum pressure.
9. Detach the blood culture collection hub from the butterfly tubing and attach the 20ml luer-lock syringe.

10. Take a 20ml sample and inoculate into a white-topped universal container.
11. Label all samples and send to lab, with EDTA vacutainer for fluid cell count marked as ‘urgent’.

## Appendix 2

## Sepsis 'Red Flags' and Signs of Complicated Peritonitis

If patient's National Early Warning Score (NEWS-2) is 5 or more, or 3 in any one parameter, or the patient looks systemically unwell ('sick'), then investigate for possible sepsis **immediately**.

Blood tests should include FBC, U&Es, CRP, LFTs, a coagulation screen, and a venous blood gas

Is **ONE OR MORE** of the following Red Flags present?

Responding only to Voice or Pain, or Unresponsive

Acute confusion – new or a change from the patient's baseline

Systolic BP ≤ 90 mmHg, or a drop of more than 40 mmHg from normal for them

Heart rate > 130 beats per minute

Respiratory rate ≥ 25 breaths per minute

New requirement for supplementary oxygen to keep $SpO_2$ ≥ 92%

Non-blanching rash, mottled or ashen or cyanotic

Not passed urine in last 18h or urine output <0.5ml/kg/hr (unless normal for them)

Venous lactate ≥2 mmol/L on venous blood gas

If so, **treatment must not be delayed**. If unable to send immediate samples of peritoneal fluid (e.g. if patient does not have a CAPD bag or fluid in the abdomen with a minimum of 2h dwell time) then consider systemic (intravenous) antibiotics while awaiting a fluid sample.

Administer the '**Sepsis 6**' as soon as possible. All 6 actions must be complete within **1 hour**.

1. **Administer Oxygen** – target $SpO_2$ >94% (88-92% if at risk of $CO_2$ retention)
2. **Take Blood Cultures**, urine and sputum cultures, urine dipstick and CXR
3. **Give Broad-Spectrum IV Antibiotics**, e.g. Piperacillin-Tazobactam 4.5g IV bd if not penicillin-allergic, ??? as second-line
4. **Give IV Fluids**. If hypotensive or raised lactate, give 500ml of crystalloid (0.9% Saline or Hartmann's). Caution if patient is usually oligo-anuric.
5. **Check Serial Lactates**. Confirm high lactate on a venous sample with an arterial blood gas. If lactate is excessively high (>4 mmol/L) or not improving to <2 mmol/L after initial management, consider Critical Care.
6. **Measure Urine Output**. Remember that anuric patients can still get bladder infections; consider bladder scanning. Start hourly input-output chart.

If **any** of the following features are present then the patient may have **complicated peritonitis**, i.e. they are more likely to have an aggressive bug (e.g. gram-negative), an intra-abdominal source (e.g. diverticulitis, perforation), or to have systemic bacteraemia.

Signs of complicated peritonitis:

- >12h of cloudy bags
- Severe abdominal pain
- Rebound tenderness / guarding
- Pyrexia ≥ 38°C
- New confusion
- Diarrhoea and vomiting

Patients with complicated peritonitis should be managed as **inpatients** and require admission. They should also be reviewed by the general surgeons to ensure that there is not secondary cause for peritonism such as a perforated abdominal viscus – consider urgent CT Abdomen.

**If a patient has any Red Flags for Sepsis or any features of Complicated Peritonitis then treatment for PD peritonitis should be started as soon as peritoneal fluid cultures have been taken, and not await fluid cell count.**

## Appendix 3

## Initial Treatment for Peritoneal Dialysis Peritonitis

1. Investigate for possible PD peritonitis in the following situations:
    - PD Patient has cloudy PD effluent in their bags
    - PD Patient presents with sepsis of unclear source
    - PD Patient presents with abdominal pain, GI upset, or unexplained fever
    - Follow-up after completion of treatment for PD peritonitis
2. Take a full set of clinical observations and calculate a NEWS-2 score
    - If the patient scores 5+, or 3 in any single parameter, send immediate investigations for possible sepsis and request medical review
    - See Appendix 2 for sepsis investigations and red flags
3. Check for signs of complicated peritonitis
    - Severe abdominal pain, with rebound tenderness and/or guarding
    - Fever ≥ 38°C
    - Vomiting and/or diarrhoea
    - New confusion or altered mental state from the patient's baseline
    - Cloudy bags for >12h duration
4. If there are sepsis red flags or signs of complicated peritonitis the patient will require admission and should initiate treatment immediately, even if PD fluid samples and cell count have not yet been sent – request medical review
5. Collect PD fluid samples and send for fluid cell count, gram stain, and MC&S using the process outlines in Appendix 1
6. If there are no sepsis red flags or signs of complicated peritonitis then await fluid cell count results before initiating treatment
7. Fluid cell count is positive for PD peritonitis if **both** the following features are present:
    - Total white cell count ≥ 0.100 x $10^9$/L
    - Polymorphonuclear cells ≥ 50%
8. If fluid cell count is not positive do not diagnose PD peritonitis, but consider other causes for cloudy bags, abdominal symptoms, or monocytotic PD fluid (see Appendix 4)
9. Start empirical treatment for PD peritonitis before culture results are known:
    - Intraperitoneal antibiotics should be given in 2L of the patient's usual PD fluid (1.5L if the patient is intolerant of 2L dwells), and given over a minimum dwell-time of 6h. For both CAPD and APD patients the first dose should be given at the time of diagnosis and the patient instructed to drain out after at least 6h and then continue their usual dialysis.
    - Using the regimens overleaf, ensure the patient has Gram positive **and** Gram negative cover, and antifungal prophylaxis if needed

10. If the patient's PD fluid contains fibrin or clots, administer heparin 500 units/L to each bag until fibrin and clots are no longer seen.
11. If the patient has uncomplicated peritonitis they may be suitable for outpatient treatment.
    - They will need to return to the Renal Home Therapies Team at the Jack Pryor Unit on Day 3 of treatment for antibiotic monitoring and clinical review.
    - Give the patient the advice leaflet 'Outpatient Treatment for PD Peritonitis', and ensure that they understand the advice.
    - If out of hours, leave a message on the RHTT answerphone at ext. 3070 with the patient's details. Ensure that the medical team put the patient on the handover list.
12. RHTT must record all suspected PD-associated peritonitis on the record sheet

## Antibiotic Therapy for PD Peritonitis: Gram +ve Cover

1. No known Vancomycin sensitivity

Vancomycin 2g (1.5g if patient weighs <50kg) intraperitoneally at start of treatment, for a minimum 6h dwell in 2L of PD fluid (or 1.5L if the patient cannot tolerate 2L dwells). Blood vancomycin levels should be checked every 3 days while on treatment, and a further dose given if the vancomycin level is <20mg/L.

2. No known Teicoplanin sensitivity and inpatient treatment / Previously tolerated Teicoplanin

Teicoplanin 15mg/kg intraperitoneally at start of treatment, for a minimum 6h dwell in 2L of PD fluid (or 1.5L if the patient cannot tolerate 2L dwells), repeated every 5 days. There is an unquantified crossover in sensitivity to vancomycin and teicoplanin, so it should not be used for outpatient therapy in patients without a known history of tolerating teicoplanin.

3. Vancomycin/Teicoplanin sensitivity and no known Penicillin/Cefalosporin allergy

Ceftriaxone 1g intraperitoneally once per day, for a minimum 6h dwell in 2L of PD fluid (or 1.5L if the patient cannot tolerate 2L dwells), with antifungal prophylaxis. Ceftriaxone is not active against MRSA; if the patient has a history of MRSA positivity or culture results come back with MRSA growth, add Clindamycin 300mg orally or intravenously three times per day.

4. Vancomycin/Teicoplanin/Penicillin/Cefalosporin sensitivity

Linezolid 600mg orally or intravenously twice per day. Do not use oral dosing if the patient is vomiting.

5. Fifth-line alternative

Flucloxacillin 1g orally or intravenously four times per day AND Rifampicin 600mg (45mg if patient weighs <50kg) orally or intravenously once per day. Flucloxacillin is not active against MRSA; if the patient has a history of MRSA positivity or culture results come back with MRSA growth, replace Flucloxacillin with Clindamycin 300mg orally or intravenously three times per day. Do not use oral dosing if the patient is vomiting. Warn the patient that Rifampicin can colour their PD fluid and other body fluids orange. Give antifungal prophylaxis if using Clindamycin.

6. Sixth-line alternative

Co-Trimoxazole 960mg orally or intravenously twice per day, with antifungal prophylaxis. Do not use oral dosing if the patient is vomiting.

## Antibiotic Therapy for PD Peritonitis: Gram -ve Cover

For patients being treated with daily intraperitoneal antibiotics as an outpatient, they should have their PD fluid bags made up by the nursing staff or shown how to administer the antibiotics doses using an autoinjector. If the patient is on APD, they will need to add a daytime dwell of a minimum of 6h. If the patient is on CAPD, they can extend one of their usual dwells or 6h or add an overnight dwell.

1. First-line

Ciprofloxacin 500mg orally or 200mg intravenously twice per day, with antifungal prophylaxis. Do not use oral dosing if the patient is vomiting. Ciprofloxacin should be taken 2 hours away from any doses of Sevelamer, calcium, magnesium, iron or zinc preparations, or large volumes of milk.

2. Sensitivity to Ciprofloxacin/Quinolones, previous Ciprofloxacin-resistant organisms

Gentamicin 0.6mg/kg intraperitoneally once per day for a minimum 6h dwell in 2L of PD fluid (or 1.5L if the patient cannot tolerate 2L dwells), with antifungal prophylaxis. Blood gentamicin levels should be checked every 3 days while on treatment, and the same dose given if the gentamicin level is <2mg/L. If the gentamicin level is ≥2mg/L the dose should be reduced by 0.2mg/kg but doses should still be given. It is not necessary to achieve 'therapeutic' systemic levels and the regular dose should not be increased if gentamicin levels are 'sub-therapeutic'.

3. Previous Ciprofloxacin- and Gentamicin-resistant organisms

Amikacin 2mg/kg kg intraperitoneally once per day for a minimum 6h dwell in 2L of PD fluid (or 1.5L if the patient cannot tolerate 2L dwells), with antifungal prophylaxis. Blood amikacin levels should be checked every 3 days while on treatment, and the same dose given if the amikacin level is <5mg/L. If the amikacin level is ≥5mg/L the dose should be reduced by 0.5mg/kg but doses should still be given. It is not necessary to achieve 'therapeutic' systemic levels and the regular dose should not be increased if amikacin levels are 'sub-therapeutic'.

4. Treatment with Aminoglycosides (Gentamicin, Amikacin) within previous 3 months

Meropenem 1g intraperitoneally once per day for a minimum 6h dwell in 2L of PD fluid (or 1.5L if the patient cannot tolerate 2L dwells), with antifungal prophylaxis.

5. Meropenem or Penicillin sensitivity

Ceftazidime 1g intraperitoneally once per day for a minimum 6h dwell in 2L of PD fluid (or 1.5L if the patient cannot tolerate 2L dwells), with antifungal prophylaxis.

6. Cefalosporin sensitivity

Co-Trimoxazole 960mg orally or intravenously twice per day, with antifungal prophylaxis. Do not use oral dosing if the patient is vomiting.

## Antibiotic Therapy for PD Peritonitis: Antifungal Prophylaxis and Treatment

### Prophylaxis

1. Antifungal prophylaxis: First-line

Nystatin 500 000 international units orally four times per day. Do not use oral dosing if the patient is vomiting. Antifungal prophylaxis should continue while on broad-spectrum antibiotics, and for 2 days after the last dose of Gentamicin/Amikacin, whichever is the longer.

2. Antifungal prophylaxis: Nystatin intolerance or intractable vomiting

Fluconazole 100mg orally or intravenously once per day. Do not use oral dosing if the patient is vomiting. Check the BNF for drug interactions with fluconazole, increases risk of Long QT syndrome and hypokalaemia. Antifungal prophylaxis should continue while on broad-spectrum antibiotics, and for 2 days after the last dose of Gentamicin/Amikacin, whichever is the longer.

### Treatment

1. Antifungal treatment: First-line

Arrange for urgent catheter removal if culture-proven fungal peritonitis. Fluconazole 200mg intraperitoneally once per day for a minimum 6h dwell in 2L of PD fluid (or 1.5L if the patient cannot tolerate 2L dwells). Check the BNF for drug interactions with fluconazole, increases risk of Long QT syndrome and hypokalaemia.

2. Antifungal treatment after catheter removal

Fluconazole 200mg orally or intravenously once per day. Do not use oral dosing if the patient is vomiting. Check the BNF for drug interactions with fluconazole, increases risk of Long QT syndrome and hypokalaemia. Use a loading dose of 400mg if catheter was removed before full intraperitoneal treatment could be given. Continue therapy for at least 14 days after catheter removal.

3. Antifungal treatment: Fluconazole contraindicated

Arrange for urgent catheter removal if culture-proven fungal peritonitis. Caspofungin 70mg intravenously stat then 50mg once per day. Continue therapy for at least 14 days after catheter removal.

## Appendix 4

## Differential Diagnosis for Possible PD Peritonitis with Negative Fluid Cell Count

1. Poor sampling technique

Specimens taken from a 'dry' abdomen, with insufficient fluid volume, may be cloudy and show monocytes or epithelioid cells on fluid cell count. Drain out fully, then drain in the patient's normal fill volume, leave to dwell of a minimum of 2h, then retake the fluid cell count sample.

2. Chemical peritonitis

Sterile biological chemicals, e.g. bile salts, porphyrins etc. can translocate from inflamed or abnormal bowel mucosa – for example, in inflammatory bowel disease, diverticulitis, etc. These can discolour the PD fluid and act as irritants even in the absence of bowel bacteria translocating into the peritoneal fluid. This may be a sign of a non-PD-related intra-abdominal problem, and an increased risk of future peritonitis.

Rarely, manufacturing problems with PD fluid have led to an accumulation of acids and advanced glycation end-products which have caused neutrophil-poor, culture-negative chemical peritonitis.

3. Calcium channel blocker usage

Dihydropyridine calcium channel blockers (e.g. Amlodipine, Lercanidipine, Nifedipine etc.) are associated with chylous or lymphogenous peritonitis, often with few or no clinical symptoms of peritonitis. If the drugs are stopped the cloudiness should rapidly resolve.

4. Eosinophilic reactions

Eosinophilic peritonitis is thought to be due to allergic-type reactions to one or more components of the PD system (catheter, cuff, fluids, etc.) and is most common in the first few weeks following catheter insertion or starting dialysis. Many cases are self-limiting, some have been successfully treated with antihistamines or intraperitoneal corticosteroids, and a few have been persistent and associated with symptoms requiring cessation of PD.

5. Haemoperitoneum

Very dilute blood in the PD fluid may not look especially red, and can also include some white cells. The commonest causes are menstruation or endometriosis in ovulating women, or anticoagulation/antiplatelet therapy. However, some causes are serious and significant – consider bowel and urinary tract malignancies and peritoneal fibrosis/sclerosis.

6. Malignancy

Solid organ tumours can present with haemoperitoneum, and haematological malignancies can present with chylous peritoneal fluid or a very lymphocytic fluid.

## Appendix 5

## Management of PD Catheter Exit Site and Tunnel Infections

1. Investigate for possible catheter-associated infection in the following situations:
    - Exit site has pain, swelling, redness, crust or discharge
    - Tunnel has pain, swelling, redness, or there is a proven exit site infection
    - Patients being managed for known or suspected PD peritonitis
    - Follow-up after treatment for an exit site, tunnel or peritoneal infection
2. Investigations should include sending an exit-site swab, and an ultrasound scan of the tunnel if there are any tunnel pain, swelling, or redness.
3. If there is purulent discharge from the exit site then treatment should be started empirically while awaiting culture results (see point 7.)
4. A positive exit site culture in the absence of any of the features in 1. above should be treated as colonisation
    - Ensure that the patient is educated on exit site care and cleaning
    - Ensure that an appropriate topical antibiotic is being used
    - Mupirocin 2% ointment is suitable for most Gram +ve infections, such as staphylococci, streptococci
    - Gentamicin 0.3% eye/ear drops are suitable for most Gram -ve infections, such as pseudomonas
    - If neither gentamicin or mupirocin are tolerated, other preparations with evidence for treating PD catheter infections include ciprofloxacin ear drops and hydrocortisone/polymyxin/neomycin (otosporin) ear drops
5. A positive diagnosis of an exit-site infection is made if:
    - Purulent exit-site discharge, even if swab negative OR
    - Positive swab with exit-site pain, swelling, redness, crust or discharge
6. A positive diagnosis of a tunnel infection is made if:
    - Pain, swelling or redness along the tunnel OR
    - Ultrasound evidence of fluid collection along the tunnel (>1mm thick)
7. General treatment for catheter-associated infections:
    - Daily exit-site cleaning and application of topical antibiotics
8. Empirical antibiotics prior to any positive culture and sensitivities:
    - If the patient has a history of positive exit-site swabs for MRSA, either with previous infection or colonisation, use:
        - Clindamycin 300mg PO tds for 2 weeks and consider antifungal cover.
        - If intolerant of Clindamycin, use Vancomycin 1g IV in 250ml 0.9% Sodium Chloride given peripherally over 2 hours, check blood vancomycin levels every 3 days, and re-dose when Vancomycin level <15mg/L, for a total of 2 weeks

- If the patient has a history of positive exit-site swabs for *Pseudomonas* species, either with previous infection or colonisation, use:
    - Ciprofloxacin 250mg PO bd for 3 weeks and consider antifungal cover. Ciprofloxacin should be taken 2 hours away from any doses of Sevelamer, calcium, iron or zinc preparations.
    - If intolerant of Ciprofloxacin, use Gentamicin 2.5mg/kg (max 180mg) IV in 100ml 0.9% Sodium Chloride given peripherally over 30 minutes, check blood gentamicin levels daily, and re-dose when Gentamicin level <1mg/L, for a total of 3 weeks; consider antifungal prophylaxis
    - If there is associated tunnel infection consider catheter removal and replacement as described in point 10. below
- If there is no history of MRSA or *Pseudomonas* infection or colonisation, use:
    - Flucloxacillin 500mg PO qds for 2 weeks.
    - If intolerant of Flucloxacillin use Cefalexin 500mg PO bd for 2 weeks and consider antifungal prophylaxis.

9. Additional antibiotic considerations
    - For slow-resolving, recurrent or severe infection consider combination antibacterial therapy:
        - For *Stapylococcus aureus* consider adding Rifampicin 600mg PO od (450mg if body weight <50kg), Doxycycline 100mg PO od, or Trimethoprim/Sulfamethoxazole 480mg PO od; consider antifungal prophylaxis
        - For *Pseudomonas spp.* consider combination treatment with Ciprofloxacin and Gentamicin as outlined above, or adding intraperitoneal Ceftazidime 1g IP od for a minimum 6h dwell
        - For other organisms be guided by culture & sensitivities and discuss with Microbiology
    - If there is any associated tunnel infection then the duration of antibiotics should be a minimum of 3 weeks regardless of organism
    - Antibiotics should be continued until the minimum duration is reached or the exit-site and tunnel appear normal, whichever is the latest.
10. Diagnose refractory catheter-associated infection if there is failure to respond after 3 weeks of appropriate antibiotics, including combination therapy if indicated
    - Consider simultaneous removal of the current catheter and reinsertion of a new catheter, with prophylactic antibiotic cover
    - Consider removal and later reinsertion of a new catheter, at least 2 weeks after complete resolution of symptoms, for patients with catheter-associated infections which progress to or occur simultaneously with peritonitis, or tunnel infections or peritonitis with *Pseudomonas spp.*
11. RHTT must record all suspected catheter-associated infections on the record sheet

## Appendix 6

## Broad-Spectrum Antibiotics Requiring Antifungal Prophylaxis

Use antifungal prophylaxis with oral nystatin (500 000 international units four times per day) or oral fluconazole (100mg once per day) when a patient with a PD catheter receives oral, intravenous or intraperitoneal administration of any of the following drugs:

| | |
|---|---|
| AMINOGLYCOSIDES | Gentamicin, Amikacin, Neomycin, Tobramycin, Streptomycin |
| PENICILLINS (most) | Ampicillin, Amoxicillin, Co-Amoxiclav, Co-Fluampicil |
| ANTI-PSEUDOMONALS | Piperacillin-Tazobactam, Ticarcillin-Clavulanic Acid |
| MECILLINAMS | Pivmecillinam |
| CARBAPENEMS | Meropenem, Ertapenem, Imipenem-Cilastatin, Doripenem |
| CEFALOSPORINS (most) | Cefaclor, Cefuroxime, Cefixime, Cefotaxime, Cefpodoxime, Cefradine, Ceftazidime, Ceftriaxone |
| FLUOROQUINOLONES | Ciprofloxacin, Levofloxacin, Moxifloxacin, Ofloxacin, Norfloxacin |
| TETRACYCLINES | Doxycycline, Tetracycline, Demeclocycline, Lymecycline, Minocycline, Oxytetracycline, Tigecycline |
| SULPHONAMIDES | Co-Trimoxazole/Septrin, Sulfadiazine |
| OTHERS | Clindamycin, Daptomycin |

The following antibiotics, if used as monotherapy, do not require antifungal prophylaxis routinely. However, note that some of these drugs (e.g. nitrofurantoin, methenamine hippurate) and contraindicated in renal impairment and should not be used in any case. Also consider that combinations of narrow-spectrum drugs may give overall broad-spectrum coverage.

| | |
|---|---|
| SIMPLE PENICILLINS | Benzylpenicillin (Pen G), Phenoxymethylpenicillin (Pen V) |
| ANTI-STAPHYLOCOCCAL | Flucloxacillin, Temocillin |
| 1st GEN CEFALOSPORINS | Cefalexin, Cefazolin, Cefadroxil |
| MONOBACTAMS | Aztreonam |
| MACROLIDES | Azithromycin, Clarithromycin, Erythromycin, Telithromycin |
| GLYCOPEPTIDES | Vancomycin, Teicoplanin |
| METRONIDAZOLE | Metronidazole, Tinidazole |
| URINARY ANTIBIOTICS | Trimethoprim, Nitrofurantoin, Methenamine Hippurate |
| FUSIDIC ACID | Sodium Fusidate/Fucidin |
| OXAZOLIDINONES | Linezolid |
| POLYMIXINS | Colistin |
| ANTI-TUBERCULOUS | Rifampicin, Rifabutin, Cycloserine, Ethambutol, Isoniazid, Pyrazinamide |
| ANTI-LEPROTIC | Dapsone, Clofazimine |

Oral Nystatin is preferred as Fluconazole is a potent inhibitor of Cytochrome P450 isoenzymes (CYP2C19, CYP3A4, CYP2C9) and can cause toxicity or increased side-effects with many drugs including: antiepileptics, calcium-channel blockers, diuretics, sulphonylureas, quinine, immunosuppressants, statins, amiodarone, clopidogrel, warfarin, ivabradine, ranolazine, sotalol, psychoactive medications and many more. Check the BNF.