

1 BACKGROUND

In Leicester the rate of PD peritonitis is on average 0.4 episodes per patient year. However, this obscures the large variation in rate between different patients. Prevention of a first episode of peritonitis is dependent on careful patient selection, good surgical technique and post operation care, thorough training and continued supervision. This has resulted in a lengthening of the median time to first peritonitis amongst patients on PD in Leicester.

If a patient develops peritonitis 88% will still be alive and on peritoneal dialysis one month after the episode. This has remained unchanged in Leicester over the last six years. This can be improved with attention to accurate diagnosis, correct initial treatment and attentive follow-up of patients who present with suggestive symptoms. These guidelines are designed to help with that process.

2 STANDARDS

The current recommended standards for the incidence of PD peritonitis are contained in the ISPD recommendations for managing PD peritonitis (2022) and the renal standards document of the renal association. In summary the standards are:

- 2.1 Overall peritonitis rate of less than 0.4 episodes per patient-year
- 2.2 Culture negative rate in patients with clinical peritonitis less than 10%
- 2.3 Initial cure rate should be >80% without catheter removal

The renal unit audits performance against these standards on an annual basis. The peritonitis data is available on the renal unit shared M drive.

3 DEFINITION

PD Peritonitis is defined as two out of three of the following

- A. Symptoms and signs of peritoneal inflammation
- B. Cloudy dialysate with total WCC of greater than 100/mm³, of which > 50% neutrophils
- C. Demonstration of organisms by positive gram stain or culture

Other definitions

- **Culture-negative peritonitis** is defined when peritonitis is diagnosed using the criteria above), but no organism is identified on culture of dialysis effluent.
- **Catheter-related peritonitis** is defined as peritonitis that occurs within 3 months of with a catheter infection (either exit-site or tunnel) with the same organism at the exit-site or from a tunnel collection and in the effluent or one site sterile in the context of antibiotic exposure.
- **Enteric peritonitis** is defined as peritonitis arising from an intestinal source involving processes such as inflammation, perforation or ischemia of intraabdominal organs. If a peritonitis episode in this context is culture negative, it should be classified/recorded as enteric peritonitis rather than as culture-negative peritonitis.

4. PREVENTION

4.1 Antimicrobial prophylaxis:

4.1.1 Following contamination:

Antibiotic prophylaxis with a single dose of IP Vancomycin (see section 9 for dosing) is indicated following an episode of 'wet contamination'.

Wet contamination is defined as contamination with an open system, when either dialysis fluid is infused after contamination or if the catheter administration set has been left open for an extended period. Contamination with a closed system (dry contamination) does not require antimicrobial prophylaxis.

Examples include leaks from dialysate bags, leaks or breaks in tubing proximal to the tubing clamp, breach of aseptic technique or touch contamination of the connection during a PD exchange.

Contamination (wet or dry) also requires an extension set change.

4.1.2. Antifungal prophylaxis during systemic antibiotic courses:

A Cochrane meta-analysis of two trials (assessing fluconazole and nystatin respectively) showed that antifungal prophylaxis reduced the risk of fungal peritonitis, but that the evidence was of low quality.

Due to concerns regarding inducing resistance, and of drug interactions with fluconazole, nystatin prophylaxis (500,000 units QDS), is preferred, and may be considered for patients on PD who receives a course of antibiotics. Of note, rates of Candida PD peritonitis in UHL are low (around 1/year), but can have a high mortality.

5. DIAGNOSIS

- PD peritonitis should be suspected in any patient on PD (or resting with a PD catheter in-situ) who has abdominal pain, cloudy dialysate or unexplained fever.
- Clinicians should remain vigilant to the possibility that although the patient is on PD, they can have an alternative cause of peritonitis or abdominal pain (such as perforated viscera) just as with any other patient.
- Identification of multiple organisms (particularly both gram-positive and gram-negative) is highly suggestive of an enteric/surgical cause for peritonitis;
- Initial clinical assessment must include an assessment of cardiovascular state (shock, volume overload), gastrointestinal symptoms, time of last PD exchange and the current state of the patients PD exit site. The patients' home circumstances should also be considered.
- Visual assessment should be made of the patients spent dialysate. In order to maximize the likelihood of positive culture the PD dialysate sent for microbiology should have spent a minimum of two hours dwell in the peritoneal cavity. Often patient bring their last dialysis bag with them. If this is cloudy on inspection and had dwelted for more than 2 hours, it should be sent promptly for microbiology. If no bag was brought then the patients' current bag should be drained out and inspected.
- If a patient has symptoms of peritonitis, but the bag is clear then allow a further bag to dwell for at least two hours before reassessment. This is particularly important for patients on APD in whom the previous dwell may have been short.
- Once a decision is taken to send a sample for microscopy it should be transported promptly. The likelihood of successful culture declines significantly if the dialysate is delayed more than four hours before it is placed under culture conditions.
- Dialysate which appears clinically transparent is unlikely to contain significant numbers of WCC. Microbiology will not culture any bag which on microscopy contains 5 WCC or fewer. It is generally agreed that any organism cultured in this situation will likely represent contamination and not true peritonitis.
- If there are greater than 5 WCC the bag will go on to be cultured, and the microbiology technical staff will phone back a total WCC and Gram stain. Consider sending sample for cytology if there is clinical uncertainty about whether the patient has bacterial peritonitis or an allergic reaction.
- Patients with significant abdominal pain often derive symptomatic relief with three PD flushes of a 1.36% dialysate drained into and immediately out of the peritoneum. These bags should not be sent for culture however as they have had insufficient dwell time.

- To avoid delay, empirical treatment should be started immediately the samples have been taken, especially in patients who are clinically unwell. In clinically unwell patient's blood cultures should also be taken. In patients with an inflamed PD exit site this should also be swabbed.

6. INITIAL TREATMENT (Day Zero)

Empirical antibiotics should be started as soon as possible, in any patient with suspected PD peritonitis, once the relevant samples have been taken. The diagnosis should be reviewed when the WCC and microbiology results are available to determine whether antibiotic therapy should continue as well as the appropriate choice and duration of treatment. See section 9 for doses of antibiotics.

- Empirical treatment for patients on either APD and CAPD is with intraperitoneal (IP) vancomycin AND regular oral ciprofloxacin
- IP vancomycin AND IP gentamicin OD may be considered as an alternative regime for patients on APD. **IP gentamicin is no longer suitable for patients on CAPD.**
- If using gentamicin, consider prescribing oral N-acetylcysteine 600mg BD to reduce risk of ototoxicity.
- If both gentamicin and ciprofloxacin are contraindicated, IP Ceftazidime is an alternative agent, but this is not stable against ESBL-producing gram negative bacteria and as such second (CAPD) or third line (APD) is a less preferred treatment option.
- If the patient is allergic to vancomycin, discuss alternatives with microbiology
- IP Aminoglycosides have not been shown to accelerate loss of residual kidney function. However repeated courses of aminoglycoside are associated with increased risk of ototoxicity. If repeated antibiotic courses are required, an alternative agent should be considered

7. SUBSEQUENT TREATMENT – ALL PATIENTS

- The culture result and patient clinical condition should guide subsequent management. For outpatients, this should be reviewed at the first follow up visit (typically on day 4).
- The PD effluent should be assessed for cloudiness. If it is still cloudy, a repeat sample should be sent for another white cell count. The case should be discussed with a senior clinician, as the possibility of refractory PD peritonitis will need to be considered.
- Refractory peritonitis is an episode in which the PD effluent fails to clear after 5 days of appropriate antibiotics
- Prolonged attempts to treat refractory or relapsing peritonitis by antibiotics

without catheter removal are associated with extended hospital stay, peritoneal membrane damage, increased risk of fungal peritonitis and excessive mortality.

- If there has been no reduction in PD effluent white cell count by day 5 then catheter removal is recommended. For less virulent organisms, if the PD effluent white cell count is decreasing by day 5, and the patient is clinically improving, then expectant management without catheter removal is reasonable

7.1 Subsequent treatment - Gram positive organisms

7.1.1 Coagulase negative Staphylococcus, Corynebacterium, or viridans group Streptococci:

- Stop gram negative agents (e.g., gentamicin, ciprofloxacin, or ceftazidime)
- Continue IP Vancomycin for 2 weeks. For those on “APD protocol”, this should be with bolus IP vancomycin (see below sections 9 and 9.1.). Those on CAPD should receive IP vancomycin four times per day
- If there is no improvement by day 5, catheter removal is advised, followed by a further 14 days antibiotic treatment.
- Review patients exchange technique, consider re-training
- Consider fibrinolytic therapy or PD catheter exchange for relapsing/recurrent peritonitis (see section 8.1)

7.1.2 Staphylococcus aureus:

- Stop gram negative agents (e.g. gentamicin, ciprofloxacin, or ceftazidime)
- Continue IP vancomycin for total 21 days
- If patient is allergic to vancomycin, discuss alternatives with microbiology.
- Consider adjuvant PO rifampicin for 5 days, as this may reduce the risk of biofilm formation and subsequent relapse. Rifampicin induces CYP450 enzymes and as such has a number of drug interactions which may preclude its use.
- If there is no improvement by day 5, catheter removal is advised, followed by a further 14 days antibiotic treatment.
- Review for signs of exit site or catheter tunnel infection. If present, continue antibiotics AND consider catheter removal

7.1.3 Enterococcus

- For amoxicillin susceptible Enterococcus: oral amoxicillin for 21 days.
- For Amoxicillin resistant, Vancomycin susceptible Enterococcus, or penicillin allergy: IP vancomycin for 21 days
- Vancomycin resistant Enterococcus: Discuss with microbiology, though usually oral linezolid is used
- If there is no improvement by day 5, catheter removal is advised, followed by a further 14 days antibiotic treatment.

7.2 Subsequent treatment - Gram negative organisms

7.2.1 Enterobacterales (e.g., E coli, Klebsiella, Proteus):

- Stop gram positive agents (e.g., vancomycin, daptomycin)
- Antibiotic treatment will depend on the specific organism and susceptibility; however, PO ciprofloxacin can usually be used for susceptible organisms. 21 days treatment is recommended.
- PD peritonitis caused by Enterobacterales resistant to Ciprofloxacin, or if ciprofloxacin is contra-indicated, should be discussed with a microbiologist
- If there is no improvement by day 5, catheter removal is advised, followed by a further 14 days antibiotic treatment.

7.2.2 Pseudomonas

- Any patient who grows Pseudomonas on PD effluent culture should be recalled the same day for reassessment and senior consultation
- Treatment needs to include two effective anti-Pseudomonal antibiotics. Usually this would be IP Ceftazidime + oral Ciprofloxacin 750mg BD, but should be guided by susceptibilities and in discussion with a microbiologist
- Provided the patient makes clinical improvement this regimen should be continued for 21 days.
- If there is no improvement by day 5, catheter removal is advised, followed by a further 14 days antibiotic treatment.
- Pseudomonas peritonitis is potentially very serious and is extremely difficult to treat without removal of PD catheter. Catheter removal is associated with a lower risk of death after Pseudomonas peritonitis.

7.2.3 Stenotrophomonas

- The isolation of a Stenotrophomonas organism, while infrequent, requires special attention since it displays sensitivity to only a few antimicrobial agents. All cases should be discussed with a microbiologist.
- Stenotrophomonas antibiotic susceptibility testing is extremely difficult. Co-trimoxazole and cefiderocol are the only agents which can be reliably tested in the laboratory.
- Therefore, the recommended treatment is with co-trimoxazole. Treatment with an additional agent such as PO ciprofloxacin or IP ceftazidime may have benefit, but this is based on low quality evidence (case reports).
- At least 21 days of therapy is required, though longer may be needed.
- If there is no improvement by day 5, catheter removal is advised, followed by a further 14 days antibiotic treatment.

7.3 Subsequent treatment: Fungal peritonitis

- Catheter removal is recommended without delay, in all cases of fungal peritonitis due to a very high mortality
- Advice must be sought from microbiology regarding choice of antifungal due to the possibility of resistance to imidazoles. Anti-fungal therapy should continue till catheter removal and then for at least an additional 14 days

7.4 Subsequent treatment: culture-negative Peritonitis

- Culture negative peritonitis may be due to prior antibiotic use, improper culture technique, or due to infection from fastidious organisms.
- Often these are gram positive organisms which respond to vancomycin.
- Therefore, if there is no growth on culture and the patient is improving at the first follow up visit, stop gram negative agents and continue with vancomycin monotherapy for a total of 14 days.
- If the PD effluent white cell count has not improved, continue both gram positive and gram-negative agents, and consider sending repeat samples for fungal and mycobacterial culture.
- If the patient has still not improved by day 5 of treatment, and the cultures are still negative, catheter removal is advised, followed by 14 days of antibiotics.

8 SPECIAL SITUATIONS

8.1 Relapsing/recurrent peritonitis:

- Relapsing peritonitis is defined as an episode of peritonitis which occurs within 4 weeks of completion of therapy. The two episodes must either be the same organism, or one of the episodes may be culture negative.
- Recurrent peritonitis is an episode which occurs within 4 weeks of completion of therapy but with a different organism.
- Recurrent gram-positive peritonitis should prompt a review of the patient's technique, and assessment for tunnel infection/abscess.
- Recurrent gram-negative peritonitis should prompt a review for intra-abdominal abscess in addition to review of technique and assessment for tunnel infection.
- Both relapsing and recurrent peritonitis are associated with worse outcomes than non-relapsing/recurrent episodes. Therefore, catheter removal should be considered for episodes of relapsing, recurrent or repeat peritonitis. This is particularly relevant for Staph aureus or Pseudomonas peritonitis due to their propensity for biofilm formation.
- For recurrent/relapsing peritonitis due to Coagulase negative Staphylococci, simultaneous PD catheter removal and reinsertion might be considered. This would avoid the need to interrupt PD, but should only be decided by a senior clinician, and should only be performed once the PD effluent cultures are negative, the effluent WCC has fallen to <100uL, and under antibiotic coverage.
- Another potential treatment for relapsing/recurrent peritonitis due to Coagulase negative Staphylococci is the addition of rifampicin and use of urokinase.
- Patients should be given a flush PD catheter with UROKINASE 5000units in 5 ml left in catheter for 2 hours on 4th and either the 7th or 8th days of antibiotic course. For the urokinase flush procedure, see UHL guidance on "non-infectious complications of peritoneal dialysis" on SharePoint

8.2 Patients who are resting off PD

- A first flush in any patient who has been resting off PD will often appear hazy. In the absence of symptoms or signs of peritonitis this initial bag does not need to be sent for microscopy or culture. If subsequent bags remain cloudy, or the patient has symptoms or signs of clinical peritonitis then the bag should be sent for examination in the normal manner.

9 DOSES

PO Ciprofloxacin

APD or CAPD (not CCPD): 750mg OD

CCPD (overnight APD + day dwell): 750mg BD

For treatment of Pseudomonas, 750mg BD is used for APD, CAPD and CCPD

IP Vancomycin - requires serum trough levels (see section 9.1)

APD – single bolus, with further doses guided by day 4 trough levels.

Patient weight of 20-40 kg = 1 g

Patient weight of 40-70 kg = 1.5 g

Patient weight greater than 70 kg = 2 g (can be up to 2.5 g)

Historical concern regarding rapid infusion of fluid containing vancomycin precipitating allergic reactions have not been borne out in extensive experience in surrounding dialysis units. The PD bag with vancomycin should be drained in with roller clamp fully open and the bag allowed to dwell for six hours [Keane et al 1993]. It should NOT dwell overnight.

CAPD – loading dose then maintenance dose with every dialysis bag

Loading dose: 25mg/kg (maximum dose 2.5 g)

Maintenance dose: vancomycin at 25mg/L per dialysis bag. For patients with 2L and 2.5L bags use 50mg per bag, and those few patients using 3L bags use 75mg per bag.

IP Gentamicin

APD: 0.6mg/Kg OD

CAPD: not recommended

IP Ceftazidime

APD: 1500mg OD (for long dwell) OR 20mg/kg OD (for short dwell)

CAPD: Loading dose: 500mg/L; Maintenance dose: 125mg/L

(Consider 25% dose increase for patients with residual urine volumes of >100ml/day)

IP Daptomycin

APD: 300mg OD

CAPD: Loading dose 100mg/L, Maintenance dose: 20mg/L

PO Amoxicillin

APD and CAPD: 500mg TDS

PO Rifampicin:

APD and CAPD: Body weight <50kg 450mg daily, Body weight >50kg 600mg daily

PO Co-trimoxazole:

APD and CAPD: 960 mg BD

9.1 Vancomycin trough levels:

- It is clear that patients with significant residual renal function are able to clear vancomycin relatively quickly, and some patients will require re-dosing with vancomycin at day four.
- All patients treated using “APD protocol” will have a plasma vancomycin level taken at day 4. It is anticipated that this will occur in either the Renal Planned Care Hub, or a suitably staffed satellite unit first thing in the morning. If day 4 is a Sunday it is acceptable to perform this step on day 5 (Monday).

- Patient requires a clinical assessment. If peritonitis resolving and able to inject own bag then patient to be sent home with pre-filled syringe of vancomycin according to body weight (section 9). If unable to inject patient must stay in unit to wait vancomycin level known.
- Vancomycin level must be chased up once assayed at approximately 2pm daily.
- Serum vancomycin levels of <10.1mg/L at day 5 have been associated with worse outcomes. If the levels are <10mg/L, it may be appropriate to adjust the dose or frequency of vancomycin. Discuss with a senior clinician or renal pharmacist.
- Serum vancomycin levels between 10 and 15mg/ml should prompt redosing, with subsequent doses on days 8 and 12 according to levels. This pattern should continue for those requiring > 2 weeks treatment.
- If level > 15mg/ml: Defer second bolus of vancomycin to day 7. If patient at home they can be instructed to add the pre-filled syringe of vancomycin to the next PD bag. If patient unable to self-inject patient must return to unit on day 7 for vancomycin.

10 PROCEDURE FOR ADDITION OF VANCOMYCIN TO PD BAG

Dose: Vancomycin 25mg/litre

Vancomycin

- Add 10mls of water for injection to a vial of vancomycin 500mg.
- Mix gently to dissolve the powder.
- Attach a label with details of the date prepared, patient name and the expiry time. (Expiry: - 24 hours after preparation)
- Withdraw 1ml (50mg) from the vial and add to the peritoneal dialysis fluid.
- Store the reconstituted vancomycin in the refrigerator and use for the next exchanges.

4 MONITORING AND AUDIT

Key Performance Indicator	Method of Assessment	Frequency	Lead
PD peritonitis rate, relapse and recurrence rates	UKRR quarterly audit data	Quarterly	J Medcalf

5 LEGAL LIABILITY GUIDELINE STATEMENT

Guidelines issued and approved by the Trust are considered to represent best practice. Staff may only exceptionally depart from any relevant Trust guidelines and always only providing that such departure is confined to the specific needs of individual circumstances. In healthcare delivery such departure shall only be undertaken where, in the judgement of the responsible healthcare professional' it is fully appropriate and justifiable - such decision to be fully recorded in the patient's notes

6 REFERENCES

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- 6.5 Ninth Renal Registry annual report 2006. <http://www.renalreg.com/>
- 6.6 Leeds Hospitals PD Peritonitis treatment guidelines. Dr Graham Woodrow.
- 6.7 Sheffield Hospitals PD Peritonitis treatment guidelines. Dr Martin Wilkie.
- 6.8 Stoke Hospitals PD Peritonitis treatment guidelines. Dr Simon Davies.
- 6.9 Li PKT et al. ISPD peritonitis recommendations 2016 update on prevention and treatment. Peritoneal Dialysis International 2016 (5) 36:481-508.
- 6.10 Li PKT et al. ISPD peritonitis recommendations 2022 update on prevention and treatment

KEYWORDS (up to six)

Peritoneal dialysis, PD, peritonitis, ERF, ESRF

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT		
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REVIEW RECORD		

Date	Issue Number	Reviewed By	Description Of Changes (If Any)
Jun 2007	1	Dr J Medcalf	No changes.
Feb 2008	2	Dr J Medcalf	Change to Outpatients using entirely "APD protocol" with withdrawal of routine pre-filled syringes Change to day 4 vancomycin level with 1.5g and 2g vanc pre-filled syringes.
Feb 2008	2.1	Dr J Medcalf	Added Procedure for adding vanc and gent to bags from Gill Hartley (Senior Renal Pharmacist).
Mar 2008	2.2	Dr J Medcalf	Altered urokinase flushes if recurrent coag negative to days 4 and 7or8 of the episode to fit with vanc level and re-dosing.
May 2008	2.3	Dr J Medcalf	Added "prompt chart" from Anil Permessur - Senior Staff Nurse. Added advice on fungal peritonitis. Clarified that presentation is day 0 in the timescale. Allowed vancomycin level and redosing on Monday if day 4 is Sunday.
April 2010	3	J Medcalf S Bukhari	5.2.3.5 Antibiotic changed from Rifampicin to Doxycycline 7.2.2 Antibiotic changed from Rifampicin to Doxycycline.
Mar 2013	4	J Medcalf	Section on the treatment of fungal peritonitis (deleted in version 3) re-instated. Empirical treatment of both inpatients and outpatients is now with bolus Vancomycin and oral ciprofloxacin (x4 day IP vanc and gent now uncommon). Section added on length of treatment course different depending on severity and organism. New paragraph in introduction to highlight these changes and rationale.
Sep 2015	5	J Medcalf	New guideline template. Added treatment for Stenotrophomonas.
Dec 2018	6	O Iyasere	Section on delaying starting treatment until WCC and gram stain available, edited. Minor grammatical errors corrected.
Aug 2022	7	O Iyasere and J Veater	Update on definitions, targets, antibiotic and antifungal prophylaxis sections added, update to empirical and subsequent treatment sections, doses updated