

1. Introduction

Catheter related blood stream infection (CR-BSI) is a common complication in patients receiving dialysis through either a non-tunnelled (temporary; 'vascath') or tunnelled (semi-permanent; 'permcath') haemodialysis central venous catheter (HD-CVC). Rapid diagnosis and effective treatment are essential to reduce morbidity and mortality and prevent secondary complications (e.g. discitis, endocarditis, osteomyelitis, etc). These guidelines outline the initial approach to diagnosis and management.

2. Scope

These guidelines are applicable to haemodialysis patients directly under the care of University Hospitals of Leicester NHS Trust. Local guidance (for example for the inpatient care of kidney patients not in a Leicester hospital) may also exist and should take precedence.

Clinical guidelines are 'guidelines' only. The interpretation and application of clinical guidelines will remain the responsibility of the individual practitioner. If in doubt, consult a senior colleague or expert.

3. Recommendations, Standards and Procedural Statements

3.1 Diagnosis of CR-BSI

A high index of suspicion for CR-BSI should be maintained in all haemodialysis patients with indwelling HD-CVCs. The diagnosis should be suspected in haemodialysis patients with a dialysis catheter with any of the following symptoms:-

- Fever $>37.5^{\circ}\text{C}$
- Rigors
- Unexplained systemic symptoms (e.g. hypotension, diarrhoea, prostration)
- EWS score 3 or greater – if present, a SEPSIS 6 assessment chart must be completed

The diagnosis will only be confirmed in retrospect by the finding of positive blood cultures taken from both a peripheral vein and through the catheter lumen.

Positive blood cultures taken from a patient with a catheter and symptoms/signs of sepsis should be sufficient to make the diagnosis. If only the catheter blood sample is positive, this may represent colonisation rather than systemic sepsis but the approach will generally be the same. Differential time to positivity will be used increasingly to determine that bacteraemias are related to the catheter.

3.2 Investigation

Blood samples for blood cultures should be drawn from both the HD-CVC and from a peripheral site. Paired blood cultures may be helpful for the diagnosis of CR-BSI by the method of differential time to positivity. Particular care should be taken to use an aseptic technique to avoid false positive samples.

FBC and C-reactive protein should also be checked. The latter is often useful in determining disease severity and monitoring response to therapy.

3.3 Initial treatment of suspected catheter related blood stream infection

Empirical treatment is often necessary pending blood culture results but should not be routinely given to all patients. Patients with minor fever (<37.5°C) or other symptoms which settle during dialysis and who are otherwise well may be observed and given advice to seek help if any further problems develop rather than overusing antibiotics. Such cases should be discussed with medical team before making this decision.

If patients are systemically unwell or EWS 3 or more, antibiotics should be administered within 1 hour as per sepsis guidelines and not delayed till last hour or end of dialysis.

3.3.1 Temporary non-tunneled, non-cuffed HD-CVCs ('Vascaths')

In the majority of cases, the catheter should be removed and empirical antibiotic treatment commenced. The majority of infections are due to gram positive cocci (usually staphylococcal species) and can be covered initially by VANCOMYCIN 1000-1500mg IV (see section 3.5 and appendix). If the patient is:-

- very unwell with high fever
- EWS 3 or greater
- haemodynamically compromised
- immunosuppressed

then gram negative antibiotic cover should also be given with either gentamicin or ciprofloxacin. Continuing therapy should be based on microbiological results but a minimum of two weeks treatment should be given post catheter removal (see below).

3.3.2 Semi-permanent, tunneled, cuffed HD-CVCs ('Permcaths')

These catheters are more difficult to insert and remove. If the patient is stable and there is no evidence of purulent discharge at the exit site, tunnel infection or secondary infections, an initial attempt may be made to treat without catheter removal using the antibiotic approach laid out in 3.3.1. However, if the patient is very unwell with any haemodynamic upset or symptoms/fever persist over 48hours, the catheter must be removed.

Particular care should be taken with endovascular prosthesis (e.g. heart valves, vascular grafts). These patients should have early removal of any source of intravascular sepsis.

Outpatient dialysis patients who have fever <38°C but no other symptoms may not require hospital admission. However, it is important to ensure the patient and the results of investigations (blood cultures, C-reactive protein) are actively reviewed at the next haemodialysis session. Such cases should be discussed with medical team before making this decision.

3.4 Further management following confirmation of blood culture results

Following empiric treatment, further treatment should be determined by the results of blood cultures. The majority of infections are caused by gram +ve cocci but gram -ve and fungal infections also occur.

3.4.1 Methicillin sensitive staph aureus species (MSSA)

If positive blood culture for MSSA, give **FLUCLOXACILLIN 1.0 g qds IV** daily for at least 48hours or until fever settles followed **by oral flucloxacillin for a minimum of two weeks**. If patient is definitely allergic to penicillin, continue treatment with vancomycin as for MRSA (see below). There should be a low threshold for removing tunnelled catheters. All MSSA bacteraemias must be reported to the Infection Prevention Team and have a post infection review undertaken.

3.4.2 MRSA

If MRSA is grown from blood, appropriate infection control precautions should be taken and the patient should be given a course of vancomycin (section 3.5 and appendix) for a minimum of two weeks. In most cases, the catheter should be removed (if not already done). Decolonization with stellisept and mupirocin should be commenced in accordance with UHL guidance. All MRSA bacteraemias must be reported to the Infection Prevention Team and have a post infection review undertaken.

3.4.3 Coagulase negative staphylococci

The patient should be carefully assessed to determine whether this culture result represents contamination, colonisation or true CR-BSI. This will involve assessment of inflammatory markers, previous blood cultures results etc. If in doubt, patients should be treated as for MRSA.

3.4.4 Other organisms

Gram negative bacteria, streptococci, Enterococci and other organisms should be treated according to sensitivities in conjunction with microbiological advice.

3.5 Use of vancomycin for HD CR-BSI

THERE ARE MAJOR CONCERNS ABOUT THE USE OF VANCOMYCIN IN HD PATIENTS.

The drug is often prescribed unnecessarily and, when correctly prescribed, may not be given in adequate doses or for long enough. The overuse of vancomycin has led to the rise of vancomycin resistant Enterococci (**VRE**) and may lead to vancomycin resistant or insensitive Staph. aureus (**VISA**). Therefore, vancomycin use should be limited to the indications given in section 3.4.

The dosing of vancomycin in HD patients is not easy as a number of factors affect the pharmacokinetics of the drug i.e.

- Body weight
- Residual renal function
- Clearance via high flux membranes or by haemodiafiltration (particularly when given during dialysis although this remains the preferred method for logistic reasons even though 20% or more of dose may be lost)

In addition, there may be problems with the accuracy of vancomycin assays due to cross reactivity with breakdown products which are retained in patients with renal impairment.

Once a decision has been made to prescribe a course of vancomycin for haemodialysis CR-BSI, it is essential that a full course is given – clinical incidents have occurred with serious consequences due to a failure to communicate this prescription to outpatient haemodialysis units. Previously, a simplified low dose regime was recommended (2). However, local experience of high flux dialysis and haemodiafiltration has shown that few, if any, patients achieve the target bloods levels. Therefore, a higher dose regime is recommended with careful monitoring of blood levels – see table below

3.5.1 Give 750-1500mg vancomycin IV initially depending on body size – see table below. For guidance on administration see appendix 1.

Target weight	Loading dose	Maintenance dose
<50kg	750mg	500mg
50-100kg	1000mg	750mg
>100kg	1500mg	1000mg

3.5.2 Prescribe 6 x 500-1000mg vancomycin over next 6 dialysis sessions – this will ensure >2weeks of antibiotic therapy.

3.5.3 Vancomycin concentrations pre-haemodialysis should be checked on each subsequent dialysis to ensure dose does not need to be adjusted (aim for trough concentration ~15 – 20mg/L). The post dialysis dosage should be adjusted within the range 500-1500mg according to these results but dosing should not be withheld if blood level is not going to be available during the time the patient is on dialysis; occasionally additional blood concentrations may be necessary if very high levels are recorded and a dose has to be omitted.

3.5.4 The prescribing doctor should enter this prescription on PROTON database and either write up the prescription in the dialysis unit or ward or send a fully completed prescription chart to the relevant dialysis unit ensuring this is received. The nursing staff at the dialysis unit and relevant consultant (or deputy) should also be informed by telephone or email.

3.5.5 Contraindications to vancomycin include a patient with a history of allergy to vancomycin and where there is documented VRE infection. In such cases, advice on alternative drug recommendations should be sought from microbiology.

3.6 Secondary complications

Patients with CR-BSI are at risk of secondary complications (e.g. endocarditis, discitis, osteomyelitis, septic arthritis, and abscesses in lung, liver, kidney and brain) and should be monitored to ensure all signs of sepsis, particularly fever and C-RP, have returned to normal. Any symptoms (e.g. back pain) or signs suggesting persistent infection should lead to a careful search for these complications.

In 2011, root cause analyses of bacteraemias showed that three patients with recurrent MRSA bacteraemias all had spinal abscesses even without symptoms. It is therefore recommended that all patients with recurrent MRSA/MSSA bacteraemia should have MRI scanning of the spine [as well as other relevant investigations (e.g. echocardiography)] even in the absence of specific back symptoms.

3.7 Further considerations

3.7.1 Recurrent CR-BSI

If further bacteraemic episodes occur with the same permcath, the catheter should be removed. Temporary access should be used and a new catheter inserted when the sepsis has settled. Certain organisms are more likely to recur (e.g. staphylococci, pseudomonas, stenotrophomonas and Candida species) and therefore earlier removal should be considered

3.7.2 Colonisation v. contamination

When blood cultures grow gram positive, coagulase negative gram positive cocci from the catheter blood sample only, it is very difficult to decide if this represents bacteraemia, colonisation or contamination of blood samples. Assuming the patient is well and C-RP is normal, further blood samples may be taken to decide if catheter removal is necessary. Repeated positive blood cultures with the same organism suggest catheter colonisation. Decisions on catheter removal should be

made on an individual patient basis depending on alternative sites for access, maturing AVF or PD catheters, patient preference etc. In general, the catheter should be removed if possible.

4. Education and Training

All new medical staff and nurses working with haemodialysis patients should become familiar with this guideline.

5. Monitoring and Audit Criteria

Key Performance Indicator	Method of Assessment	Frequency	Lead
Quarterly audit of Staph aureus bacteraemia	NHS England dashboard for renal dialysis	Quarterly	Beverley Pearce
Post infection review analysis of MSSA/MRSA bacteraemia	post infection review	Ad hoc	Lead consultant / matron

6. Legal Liability Guideline Statement

See section 6.4 of the UHL Policy for Policies for details of the Trust Legal Liability statement for Guidance documents

7. Supporting Documents and Key References

- Management guidelines for catheter infections. Mermel LA, et al. CID 2001;32
- Vancomycin use in patients requiring haemodialysis: a literature review. Pallotta KE, Manley HJ. Seminars in Dialysis 2008;21:63–70
- Diagnosis of catheter-related bacteraemia: a prospective comparison of the time to positivity of hub-blood versus peripheral-blood cultures. Blot F, Nitenberg G, Chachaty E, et al. Lancet 1999;354:1071-1077

8. Key Words

Haemodialysis, CR-BSI, catheters, Staphylococci, sepsis, antibiotics, vancomycin

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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APPENDIX 1 – ADMINISTRATION OF INTRAVENOUS VANCOMYCIN DURING HAEMODIALYSIS

Vancomycin is removed to some degree by high flux haemodialysis or haemodiafiltration. However, it is convenient for both patients and staff as it may be given during haemodialysis. Concerns have been expressed previously about the rate of administration of vancomycin and possible incompatibility with heparin administered on dialysis. When high concentrations of heparin and vancomycin are mixed in 5% dextrose, they immediately precipitate. However, when diluted and mixed in 0.9% saline, this does not occur. Furthermore, during haemodialysis any intravenous heparin is rapidly diluted within the extracorporeal circuit. The current procedure has been in use in all haemodialysis practice within UHL over a number of years.

Although some vancomycin will be dialysed out using high flux dialysis membranes or haemodiafiltration, the inconvenience and practical problems of administering post dialysis have led to a pragmatic decision to stick with above policy. Vancomycin is used to treat proven or suspected catheter related bacteraemia in patients on haemodialysis. Practitioners administering IV vancomycin via this route must possess competency in the haemodialysis technique and intravenous drug administration.

Vancomycin is diluted in sodium chloride 0.9% for administration during dialysis because vancomycin diluted in glucose 5% is incompatible with heparin and will precipitate out. Vancomycin should be administered at a maximum rate of 10mg/minute to minimise adverse events.

The practical steps involved in the administration of the vancomycin are:-

- Reconstitute vancomycin in water for injections.
- Add 10mls to 500mg vial and 20mls to 1g vial.
- This must be further diluted before administration.

The recommended dilution and infusion rates are given below:-

Dose	Size of saline bag for infusion	Total volume to be infused	Rate	Time
500mg	50 ml bag	60 mls	60 mls/hour	60 minutes (1 hour)
750mg	100 ml bag	115 mls	92 mls/hour	75 minutes (1 hour 15 mins)
1000mg	100 ml bag	120 mls	72 mls/hour	100 minutes (1 hour 40 minutes)
1250mg	250 ml bag	275 mls	132 mls/hour	125 Minutes (2 hours 5 minutes)
1500mg	250 ml bag	280 mls	112 mls/hour	150 minutes (2 hours 30 mins)
1750mg	250 ml bag	285 mls	97 mls/ hour	175 minutes (2 hours 55 minutes)
2000mg (exceptional - review dose)	250 ml bag	290 mls	87 mls/hour	200 minutes (3 hours 20 minutes)

Additional points to note:-

- Intravenous heparin infusion can be continued through the heparin port as per the patient's prescription
- Monitor patient for documented side-effects of IV vancomycin (i.e. flushing, hypotension, wheezing).
- If side-effects observed, discontinue infusion, take appropriate action and document appropriately in patient's record.
- Ensure clear arrangements are in place for further dosing or check on blood levels according to prescriber's instructions