Worcestershire NHS
Acute Hospitals NHS Trust

Guideline for the management of long-term catheter-related bacteraemia with antibiotic lock therapy

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

Central venous catheters (CVCs) are commonly used for the management of patients needing long-term treatment e.g. chemotherapy, dialysis or parenteral nutrition.

Catheter related bloodstream infection (CRBSI), exit site infections and tunnel infections are common complications with CVCs.

The risk factors for a CVC related infection include: the type and the material of the CVC, the location of the catheter, the frequency of use, the duration of insertion and the pathogenicity of the infecting pathogen, this includes the ability to attach to the catheter surface and to produce a biofilm.

Antibiotic lock therapy is a technique whereby the catheter lumen is locked with an antibiotic solution up to 1000 times the minimum inhibitory concentration of the infecting pathogen, to eradicate the bacteria in the biofilm and thereby sterilising the catheter lumen. An antibiotic line lock has a specified dwell time due to the stability of the solution. Antibiotic lock therapy may be used when catheter salvage is considered the most desirable course of action.

This guideline is for use by the following staff groups:

Haematology, Oncology, Intensive Care, Surgery, Microbiology, Pharmacy

Lead Clinician(s)

Hugh Morton	Microbiologist
Dr. David Davies	Haematology Consultant
Harriet Cook	Lead Pharmacist - Haematology
Approved by Haematology and Palliative Care Governance on:	18th September, 2024
Approved by Medicines Safety Committee on:	9th October, 2024
This guideline should not be used after end of:	9th October, 2027

Key amendments to this guideline

Date	Amendment	Approved by:
18th September, 2024	New Document Approved	Haematology and Palliative Care Governance
9th October, 2024	Approved at Medicine Safety Committee	Medicine Safety Committee

Core Pathogens (for percutaneously inserted non-cuffed catheters, surgically implanted and peripherally inserted central venous catheters)

Coagulase-negative staphylococci (for example, *Staphylococcus epidermidis*) *Staphylococcus aureus*
Candida species
Enteric Gram-negative bacilli
Pseudomonas aeruginosa and other environmental Gram-negative bacilli e.g. *Stenotrophomonas maltophilia.*

Catheter salvage

The diagnosis and management of catheter-related infection is beyond the scope of this guideline. However, removal of an infected catheter in combination with antimicrobial therapy is the most reliable method of eradicating infection. Retention of the CVC may result in failure to clear the organism from the catheter with subsequent relapse of infection. In some cases, it may nevertheless be desirable to consider catheter salvage, for example:

- High risk of replacing catheter e.g. coagulopathy
- Alternative vascular access sites limited or not available

Whilst a decision to salvage a catheter requires careful consideration of the risks and benefits, catheter salvage should **NOT** be attempted in the following circumstances:

- Organisms known to be difficult to eradicate e.g. *Staphylococcus aureus*, *Candida* spp., *P. aeruginosa*, Mycobacteria and environmental non-fermenting Gram-negative bacilli e.g. *Stenotrophomonas maltophilia*
- Sepsis with haemodynamic instability
- Bacteraemia persisting despite 72 hours of antimicrobial therapy
- Metastatic complications e.g. infective endocarditis, osteomyelitis
- Relapse of infection following a previous course of antimicrobial therapy.

Antibiotic Line Lock Therapy (ALLT)

When catheter salvage is attempted, antibiotic lock therapy may be considered. Discussion with microbiology is required before prescribing.

Antibiotic line locks are only recommended for use <u>in combination with systemic antibiotics</u> and for a total of 7-14 days

Exception: ALLT may be used without systemic therapy when more than one culture from the catheter is positive for coagulase-negative staphylococci but peripheral blood cultures are negative. A decision not to give systemic therapy should take into account the patient's clinical state and the specific microbiology. Discussion with microbiology is advised.

Evidence of benefit

The evidence base to support the use of antibiotic line locks is poor. The majority of the trials are open- label or observational case studies with unclear participant allocation to the control and intervention groups. The trials lacked statistical power and the confidence intervals were too large to allow reliable conclusions to be drawn.

In most of the randomised controlled trials, the method of blinding was unclear and none of the trials were done with an intention to treat analysis, increasing the likelihood of 'chance' findings. The definitions of a CRBSI varied between trials and some trials did not perform peripheral blood cultures to confirm a CRBSI. The primary outcome in some trials was a blood stream infection rather than a CRBSI, this may have overestimated the response rate with antibiotic line locks. Most of the randomised controlled trials looked at prevention rather than treatment of a CRBSI. Furthermore, some trials used antibiotic flush solutions rather than antibiotic line locks.

Two controlled trials showed successful treatment with antibiotic line locks in comparison to the control groups, however they lack statistical power. Recurrent bacteraemia was more likely if the catheter was retained.

All trials used different types of antibiotics at different concentrations. However, the majority of the trials used vancomycin antibiotic line locks. One trial reported immediate precipitation of ciprofloxacin with heparin and significant absorbance changes with heparin and the following: Ceftazidime and Gentamicin.

Short-term and long-term adverse effects of antibiotic line locks were not assessed and are unknown.

The Infectious Diseases Society of America (IDSA)[5] recommends the use of antibiotic lock therapy in uncomplicated CRBSI with the use of systemic antibiotics, where catheter salvage is considered the best option for the patient.

Antibiotic lock solutions

Choice of antibiotic line lock will be guided by the isolated organisms and their sensitivities.

There is no urgent clinical need to start line locks at weekends, bank holidays or out of hours in the week.

Please discuss with microbiology in working hours. In this instance, patients can be given systemic antibiotics and may be switched to ALLT in the working week.

Table for Adult ALLT Concentrations

Antibiotic	Final Concentration of the ALLT	Diluent*	Final Volume	Dwell times
Vancomycin	20mg/2ml	0.9% sodium chloride	2 mL	24 HOURS Remove line lock before the next dose by aspirating 2ml from the CVC and then flushing the line with 0.9% sodium chloride.
Gentamicin	10mg/2ml			
Ciprofloxacin	4mg/2ml			

Method for preparation and administration

Antibiotic	**preparation**	**Procedure**	**Dosage**
Vancomycin	500mg vial	Reconstitute 500mg with 10ml water for injection. Take 2ml of this solution and further dilute to 10ml with sodium chloride 0.9%	20mg/2ml
Gentamicin	80mg/2ml ampoule	Further dilute to 16ml with sodium chloride 0.9%	10mg/2ml
Ciprofloxacin	200mg/100ml	Ready diluted	4mg/2ml

*** Heparin should NOT be used as a diluent. There is little evidence it reduces the risk of catheter-associated thrombosis and it may cause antibiotic precipitation.**

Line Volumes

The length of each line is different on a line by line basis due to insertion points and where it is cut. Instilling the full 2ml volume will ensure that the line is completely locked. This will result in some of the 2ml being systemically injected into the patient but the effect this will have is nominal.

Instillation of ALLT into all lumens of multi-lumen catheters is preferred when feasible. It may be necessary to rotate lumens every 12-24 hours in order to administer other fluids or medications. If a significant number of IV therapies are needed, the agents should be reviewed for Y-site compatibility to optimize the ALLT dwell time in the infected catheter.

Prescribing of line lock therapy

ALLT should be prescribed on the antibiotic section of the drug chart. The indication should state “Antibiotic lock therapy for CVC” and a stop/review date should be documented. The words “do not infuse through the line” should be annotated on the prescription.

References

1. Bestul, M and VandenBussche, H. (2005) Antibiotic lock technique: Review of the Literature. Pharmacotherapy, Vol. no. 25 (2), pg 211-227.
2. Cicalini, S; Palmieri, F and Petrosillo, N. (2004) Clinical review: New technologies for prevention of intravascular catheter-related infections. Critical care, vol. no. 8, pg 157 – 162.
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4. Henrickson, K; Axtell, R; Hoover, S et al (2000) Prevention of Central venous catheter-related infections and thrombotic events in immunocompromised children by the use of vancomycin / ciprofloxacin / heparin flush solution: A Randomised, Multicenter, Double-blind trial. Journal of clinical oncology, Vol. no. 18 (no. 6 / March), pg 1269 – 1278.
5. Mermel, L; Allon, M; Bouza, E et al. (2009) Clinical practice guidelines for the diagnosis and management of intravascular catheter related infection: 2009 update by the infectious disease society of America (IDSA). Clinical infectious diseases, vol. no. 49, pg 1-49.
6. Rijnders, B; Van Wijngaerden, E; Vandecasteele, S et al (2005) Treatment of Long-term intravascular catheter related bacteraemia with antibiotic lock: randomised, placebo-controlled trial. Journal of Antimicrobial chemotherapy, Vol. no. 55, pg 90-94.
7. Robinson, J; Tawfik, G; Saxinger et al. (2005) Stability of heparin and physical compatability of heparin / antibiotic solutions in concentrations appropriate for antibiotic lock therapy. Journal of Antimicrobial Chemotherapy, Vol. no. 56, pg 951 – 953.
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9. Snaterse, M; Ruger,W; Scholte op Reimer, W.J.M et al. (2010) Antibiotic-based catheter lock solutions for prevention of catheter-related bloodstream infection: a systematic review of randomised controlled trials. Journal of Hospital infection, Vol. no 75, pg 1-11.
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12. Verbal communication – NUH PICC practitioner C Hinz; April 2017
13. Lal, S. Chadwick. P, Nightingale, J (2019) Management of catheter related blood stream infections (CRBSI) BAPEN
14. Cesar Justos, Aitziber Aguinaga, Francisco Carmona-Torre, and Jose Luis Del

Pozo. (2014) Long-term catheterisation: Current approaches in the diagnosis and treatment of port-related infections. Infect Drug Resist. 7: 25-35

Acknowledgement

This guideline was reproduced and adapted with the kind permission of Annette Clarkson, Antimicrobial Stewardship Pharmacist, Nottingham University Hospitals NHS Trust

Monitoring Tool

This should include realistic goals, timeframes and measurable outcomes.

How will monitoring be carried out?

Who will monitor compliance with the guideline?

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
	These are the 'key' parts of the process that we are relying on to manage risk. We may not be able to monitor every part of the process, but we MUST monitor the key elements, otherwise we won't know whether we are keeping patients, visitors and/or staff safe.	What are we going to do to make sure the key parts of the process we have identified are being followed? (Some techniques to consider are; audits, spot-checks, analysis of incident trends, monitoring of attendance at training.)	Be realistic. Set achievable frequencies. Use terms such as '10 times a year' instead of 'monthly'.	Who is responsible for the check? Is it listed in the 'duties' section of the policy? Is it in the job description?	Who will receive the monitoring results? Where this is a committee the committee's specific responsibility for monitoring the process must be described within its terms of reference.	Use terms such as '10 times a year' instead of 'monthly'.
ALL	Audit to ensure compliance with guideline	Audits	Every one or two years	Haematology Department	Haematology / Oncology governance meeting	Every 1 – 2 years

Contribution List

This key document has been circulated to the following individuals for consultation;

Designation
Sadiya Hussain (Lead Pharmacist – AMS)
Keith Hinton (Lead Pharmacist – Surgery)

This key document has been circulated to the chair(s) of the following committees / groups for comments;

Committee
Haematology and Palliative Care Governance
Medicines Safety Committee

Supporting Document 1 – Equality Impact Assessment form

To be completed by the key document author and included as an appendix to key document when submitted to the appropriate committee for consideration and approval.

Please complete assessment form on next page;

Herefordshire & Worcestershire STP - Equality Impact Assessment (EIA) Form
Please read EIA guidelines when completing this form

Section 1 - Name of Organisation (please tick)

Herefordshire & Worcestershire STP		Herefordshire Council		Herefordshire CCG	
Worcestershire Acute Hospitals NHS Trust	X	Worcestershire County Council		Worcestershire CCGs	
Worcestershire Health and Care NHS Trust		Wye Valley NHS Trust		Other (please state)	

Name of Lead for Activity	**Dr Hugh Morton, Consultant Microbiologist** **Dr David Davies, Consultant Haematologist**

Details of individuals completing this assessment	**Name**	**Job title**	**e-mail contact**
	Hugh Morton	**Cons. Microbiologist**	**Hugh.morton@nhs.net**
Date assessment completed	**01/11/2024**		

Section 2

Activity being assessed (e.g. policy/procedure, document, service redesign, policy, strategy etc.)	**Title:** Guideline for the management of long-term catheter-related bacteraemia with antibiotic lock therapy			
What is the aim, purpose and/or intended outcomes of this Activity?	Manage infections of central lines in an attempt to salvage such a device			
Who will be affected by the development & implementation of this activity?	❑ X ❑ ❑	Service User Patient Carers Visitors	X ❑ ❑ ❑	Staff Communities Other _____
Is this:	❑ Review of an existing activity X New activity ❑ Planning to withdraw or reduce a service, activity or presence?			
What information and evidence have you reviewed to help inform this assessment? (Please name sources, eg demographic information for patients / services / staff groups affected, complaints etc.	See above document			

Summary of engagement or consultation undertaken (e.g. who and how have you engaged with, or why do you believe this is not required)	Haematology governance group Pharmacy Patient engagement not required; professional document that needs specialist expertise to interpret. Document intended for professional use only
Summary of relevant findings	No objections

Section 3

Please consider the potential impact of this activity (during development & implementation) on each of the equality groups outlined below. **Please tick one or more impact box below for each Equality Group and explain your rationale**. Please note it is possible for the potential impact to be both positive and negative within the same equality group and this should be recorded. Remember to consider the impact on e.g. staff, public, patients, carers etc. in these equality groups.

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Age		X		This guideline will be applied equally to all patients for whom salvage therapy for infected indwelling central lines is considered. There is nothing that would adversely affect groups with protected characteristics.
Disability		X		
Gender Reassignment		X		
Marriage & Civil Partnerships		X		
Pregnancy & Maternity		X		
Race including Traveling Communities		X		
Religion & Belief		X		
Sex		X		
Sexual Orientation		X		
Other Vulnerable and Disadvantaged Groups (e.g. carers; care leavers; homeless; Social/Economic deprivation, travelling communities etc.)		X		
Health Inequalities (any preventable, unfair & unjust differences in health status between groups, populations or individuals that arise from the unequal distribution of social,		X		

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
environmental & economic conditions within societies)				

Section 4

What actions will you take to mitigate any potential negative impacts?	Risk identified	Actions required to reduce / eliminate negative impact	Who will lead on the action?	Timeframe
	None	.		
How will you monitor these actions?	**N/A**			
When will you review this EIA? (e.g in a service redesign, this EIA should be revisited regularly throughout the design & implementation)	**N/A**			

Section 5 - Please read and agree to the following Equality Statement

1. Equality Statement

1.1. All public bodies have a statutory duty under the Equality Act 2010 to set out arrangements to assess and consult on how their policies and functions impact on the 9 protected characteristics: Age; Disability; Gender Reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual Orientation

1.2. Our Organisations will challenge discrimination, promote equality, respect human rights, and aims to design and implement services, policies and measures that meet the diverse needs of our service, and population, ensuring that none are placed at a disadvantage over others.

1.3. All staff are expected to deliver services and provide services and care in a manner which respects the individuality of service users, patients, carer's etc, and as such treat them and members of the workforce respectfully, paying due regard to the 9 protected characteristics.

Signature of person completing EIA	Hugh Morton
Date signed	01/11/2024
Comments:	
Signature of the Leader Person for this activity	Hugh Morton
Date signed	01/11/2024

Comments:	

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	**Yes/No**
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue	No
3.	Does the implementation of this document require additional manpower	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	No
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval