

## British Intestinal Failure Alliance (BIFA) Recommendation

### Management of Catheter Related Blood Stream Infections (CRBSIs)

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This document aims to provide the UK standard for the management of CRBSI in patients receiving parenteral support (PS; includes parenteral nutrition and/or fluids). This is written for adult patients but the principles may be appropriate for children.

These should be read in conjunction with the BIFA recommendations for diagnosis of CRBSI.

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#### Background

Central-venous CRBSIs are a significant cause of morbidity and mortality in patients requiring home parenteral support (HPS) (1, 2). While an infection can arise from the infusate, catheter exit site or haematogenous spread from another source, the infection is most commonly derived from the catheter hub. Organisms from the catheter hub spread down the inner surface of the catheter forming an adherent biofilm. When there is flow within the catheter, these organisms enter the circulation. The infected biofilm may be associated with thrombosis at the end of the catheter and the organisms may extend onto the outer side of the catheter within the fibrin sheath. Microorganisms commonly encountered in CRBSI in HPS patients are: coagulase-negative staphylococci, Gram negative bacilli, other Gram positive bacteria (including *Staphylococcus aureus*) and *Candida* species. Around 10% of episodes are due to infections with multiple organisms.

CRBSI is suspected, but not limited to, when a fever and/or rigors occur often within 30-60 min of starting (or occasionally disconnecting) a parenteral support (PS) infusion. Patients can also present with non-specific malaise or as a febrile episode, including (e.g. endocarditis, septic pulmonary emboli, discitis, osteomyelitis (3, 4) etc.), with raised blood inflammatory markers. Traditionally an infected central venous catheter (CVC) is removed and antimicrobial agents are given for 2-3 days before another catheter is inserted. However, there are no data about the efficacy of this approach, which does have the advantage of only 3-5 days in hospital and PS only being discontinued for 2-3 days. It is thought that repeated catheter replacement can damage the central vein, which in turn can lead to a loss of venous access which can be an indication for a small bowel transplant (5, 6).

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Since patients find the catheter insertion procedure unpleasant, there has been an increasing tendency to salvage infected CVCs in patients having long-term PS and this approach is in keeping with the 2016 ESPEN Guidelines (5). The largest and most recent publications to support this practice derive from Salford Royal (7-9) and the Mayo Clinic (10). Their data relates only to the salvage of tunnelled long-term catheters as there is insufficient evidence to recommend salvage of implanted ports or peripherally inserted central catheters (PICCs).

## Recommendations

### **When to consider catheter salvage**

1. CVC salvage can probably be attempted for all bacterial CRBSIs, providing the patient is stable and not critically ill. However, see 3 below.

### **When not to salvage a CVC catheter**

2. Immediate removal is recommended if the patient has septic shock (systemic inflammatory response syndrome (SIRS) with profound circulatory, cellular, and metabolic abnormalities and is associated with a greater risk of mortality than sepsis alone).
3. Some HPS units would not consider CVC salvage for *Staphylococcus aureus* or polymicrobial infections. The general consensus among HPS specialists is that the CVC should be removed and not salvaged if infected with a fungus.

The Infectious Diseases Society of America (IDSA) recommend that long-term catheters should be removed from patients with CRBSI associated with any of the following conditions: severe sepsis; suppurative thrombophlebitis; endocarditis; bloodstream infection that continues despite >72 h of antimicrobial therapy to which the infecting microbes are susceptible; or infections due to *S. aureus*, *Pseudomonas aeruginosa*, fungi, or mycobacteria (6). IDSA also recommend (with a less strong evidence base) that for CRBSI due to less virulent microbes that are difficult to eradicate (e.g. *Bacillus* species, *Micrococcus* species, or Propionibacteria), catheters should generally be removed after blood culture contamination is ruled out on the basis of multiple positive culture results, with at least 1 blood culture sample drawn from a peripheral vein.

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4. Salvage is generally not recommended if patients have a CVC tunnel and/or cuff infection, a metastatic infection (e.g. endocarditis, discitis, osteomyelitis, septic pulmonary emboli etc), a fungal infection, a septic thrombosis associated with the CRBSI or if the infection has returned after a previous salvage attempt. In these circumstances the CVC should generally be removed. However, occasionally CVC salvage is attempted in these circumstances if there is very limited venous access but this therapy will need to be carefully individualised and coordinated through close communication with the microbiology team and other relevant specialists (e.g. cardiology, orthopaedic, etc.).
5. Salvage may be inappropriate if the CVC requires removal for another reason (e.g. a mal-positioned CVC tip as identified on CXR (this should be performed at the point of admission), exposed cuff, or CVC fracture unamenable to repair).
6. A cardiac ECHO (trans-thoracic or trans-oesophageal) should be performed in any patient with a prosthetic heart valve, pacemaker/ICD and persistent bacteraemia and/or pyrexia 72 hour after initiation of appropriate antibiotic therapy and also performed if there is *S aureus* infection. If back pain is present, a spinal MRI should be considered. If there is a fungal infection, a thorough ophthalmological examination must be performed in case of spread to the eye (up to 25% cases) which, if untreated, can cause blindness (12).

### **Treatment**

7. Once a CRBSI is suspected and while blood cultures results are awaited, therapy should be commenced empirically with a CVC lock (high concentration of antibiotic put into catheter for 12-24 hours and subsequently flushed into the circulation) plus a systemic antimicrobial agent, typically given via a peripheral catheter or PICC, depending upon local microbiological guidance. The initial choice of antibiotics will depend on the severity of the patient's clinical disease, the risk factors for infection, and the likely pathogens associated with the specific intravascular device (5-7). It is important to provide cover for both Gram positive bacteria (including coagulase-negative staphylococci) and Gram negative bacteria empirically. It is therefore appropriate to consider a combination of IV agents initially, such as a glycopeptide (vancomycin or teicoplanin) or daptomycin for Gram positive cover plus piperacillin-tazobactam (or a carbapenem or an extended-spectrum cephalosporin , fluoroquinolone or aminoglycoside) for Gram negative cover, depending on local susceptibility patterns and allergy status. IDSA also recommend adding empirical cover for *Candida* species in patients receiving 'total parenteral nutrition' (6), although this is not routine practice in all IF/HPS units unless patients are critically ill. For some antimicrobial agents, monitoring of serum levels is needed.

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Sometimes, the systemic treatment has to be given via the infected CVC, particularly if there is poor venous access; in this instance the systemic antimicrobial agents should then be used as a CVC lock and remain in the catheter for 12 hours. If the patient needs a large volume of parenteral support that cannot be given peripherally, then the lock agent may only have a dwell time of 10-12 hours.

8. Once CRBSI blood culture results are available, CVC salvage should involve the administration of systemic antimicrobial agents of appropriate microbial activity based on blood culture and susceptibility results; alongside targeted CVC lock therapy.
9. Some units use thrombolytic locks (urokinase) during salvage therapy (6-8) as it may dissolve the fibrin sheath. 5,000 units are left in the CVC for 4-12 hours after the antibiotic lock then removed daily during the salvage period. However, the use of urokinase locks may depend on local protocols and is not currently recommended by the IDSA.
10. Although various guidelines recommend 7-14 days of antibiotic therapy (5, 6) for uncomplicated CRBSIs, the duration of therapy may vary according to local protocols and the organism isolated.
11. The CVC should be removed during salvage therapy if the patient becomes or remains febrile, continues to have raised inflammatory markers or has positive blood cultures (IDSA recommends 2 sets are routinely taken at 72 hours after starting appropriate therapy) as a result of the CRBSI.

### ***Parenteral nutrition during salvage***

12. The largest published U.K. outcome data for CRBSI management (7-9) suggest that the CVC should not be used for parenteral support while salvage is attempted (because parenteral nutrition may provide an infective milieu for organism growth). However, this will depend on the availability of other peripheral access routes and local protocols. If peripheral access is limited, then intravenous fluid and electrolytes rather than parenteral nutrition can be administered via the CVC during the salvage, with continuation of the CVC antibiotic lock during this period.

### ***After the salvage treatment***

13. A re-feeding regimen may be required following successful CRBSI treatment if the patient has not received parenteral nutrition during the salvage period (and if little energy has been absorbed orally/enterally).

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14. Central blood cultures may be done at least 48 hours after treatment finishes as per local microbiology guidance; if negative it is likely that the infection has been eradicated based on data of one-year follow-up (7-9). The CVC may be used for parenteral support while culture results are awaited unless there is clinical suspicion of unsuccessful salvage. If the cultures are positive the CVC should be removed (occasionally a more prolonged course of anti-biotics may be given).

### **Long-term aftercare**

15. Once a CVC is removed following a CRBSI (salvage not attempted or failed), reinsertion of any long term CVC should not take place until after completion of a course of appropriate systemic antimicrobial therapy and, thereafter, once repeat blood cultures are negative (6-8). Generally the new CVC is inserted on the opposite side from the previous one.
16. If a patient has recurrent infections, it is important to check for other sites of infection, particularly UTI, discitis and infective endocarditis and check the condition of the teeth (11). An ECHO or venogram may be needed to determine if there is a thrombus remaining in the central vein. If a thrombus associated with the catheter is infected, it can infect any new catheter that abuts it. Any spinal pain/tenderness should raise the possibility of discitis (3, 4). Consideration should be made to replacement of any other indwelling medical devices (e.g. urinary catheter or venting gastrostomy).
17. It is important to check with the patient/carers the aseptic technique in handling catheters, and any lifestyle related considerations, (for example pets, gardening), which may be implicated in the development of a CRBSI with a particular organism.
18. For recurrent infections consider the prophylactic use of an antimicrobial lock, (for example taurolidine). ESPEN guidelines do not recommend catheter locking with 70% ethanol to prevent central venous catheter-related infections, because its use is associated with systemic toxicity, catheter occlusion and catheter damage.
19. If there is a cluster of cases of CRBSI with the same organism then the infusate and its preparation may need to be investigated.

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***Where should salvage be done?***

20. Patients are usually admitted to an HPN or Integrated IF Centre for CRBSI management. If this is not possible, then the admitting hospital should be advised to manage the CRBSI according to these guidelines. Some patients may be managed in the community by Outpatient Parenteral Antimicrobial Therapy (OPAT) teams.

***Data collection***

21. Data on CRBSI management outcomes (including organism, duration of therapy, success, CVC use during salvage, urokinase locks etc.) should be collected by all HPN and Integrated IF Centres to inform future practice.

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Table. Antimicrobial agent concentrations used for line locks

<b>Antimicrobial agent</b>	<b>Concentration</b>
Vancomycin	4 mg/mL
Gentamicin	4 mg/mL
Teicoplanin	2mg/mL
Ciprofloxacin	2mg/mL
Fluconazole	2mg/mL

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