Date of preparation: July 2022

Central London Intestinal Failure Partnership

GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF CATHETER-RELATED BLOODSTREAM INFECTIONS IN ADULT INTESTINAL FAILURE PATIENTS RECEIVING HOME PARENTERAL SUPPORT

Authors: Members of the Intestinal Failure teams at University College London Hospitals NHS Foundation Trust, Guy's & St Thomas' NHS Foundation Trust, and Bart's Health NHS Trust

---

This document aims to provide guidelines for the diagnosis and management of CRSBI in adult patients receiving parenteral support (PS; includes parenteral nutrition and/or fluids).

A. Background

1. These guidelines have been developed to help clinicians to manage suspected catheter-related bloodstream infections (CRBSI) in Intestinal failure patients receiving home parenteral support (1). The risk of CRBSI varies depending on the device used, the insertion site, the experience and training of the individual who inserts the catheter, the number of catheter lumens, the frequency with which the catheter is accessed, the duration of catheter placement, characteristics of the patient and the use of proven preventative procedures (2). CRBSIs independently increase hospital cost and length of stay.
2. Most causative pathogens either migrate along the outer surface of the catheter into deeper tissue and the blood stream, or less commonly they are introduced into the catheter hub and proceed along the lumen. The mechanism of infection varies depending on the intra-vascular device. Endoluminal infection introduced via the hub is the most important route in long- term tunnelled central catheters.
3. The main causative organisms are coagulase negative staphylococci (CNS), *Staphylococcus aureus* (including MRSA), enteric gram-negative bacilli (*E.coli, Enterobacteriaceae*), *Pseudomonas aeruginosa* and, less commonly, *Candida* species.

B. Definition of a confirmed CRBSI

4. Growth of an indistinguishable organism (same species and antibiotic resistance pattern) from at least one peripherally drawn blood culture and the tip of the removed catheter, OR
5. Growth of an indistinguishable organism from at least one peripheral and one centrally drawn blood culture, where the central culture was detected in the automated blood culture machine ≥2 hours before the peripheral culture (differential time to positivity or DTP)

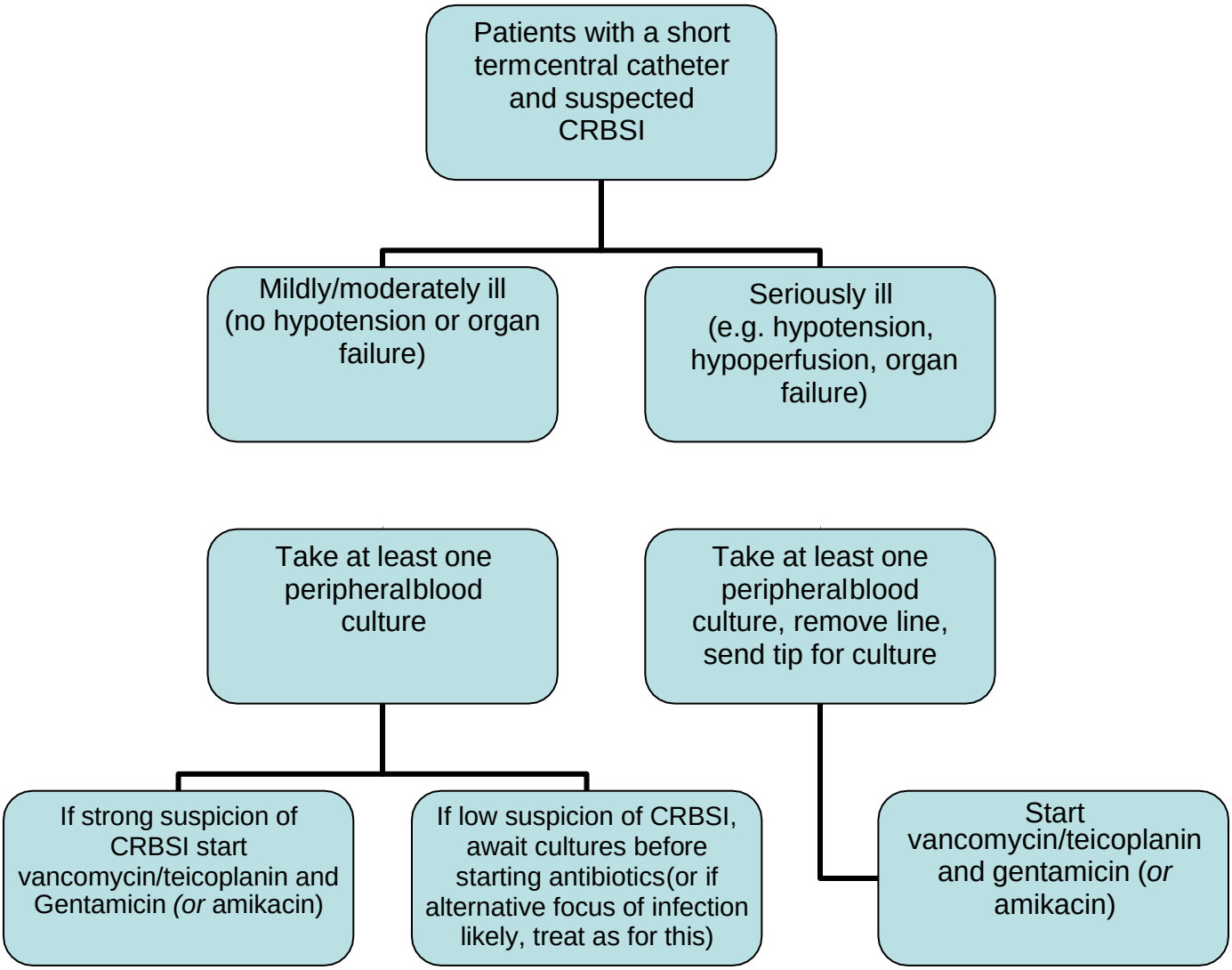
C. When to suspect CRBSI

6. The diagnosis should be considered in all patients who develop fever and/or sepsis in the presence of an intravascular catheter.
   a. CRBSI frequently occurs without clinical evidence of inflammation at the catheter exit site, especially with peripherally inserted central catheters (PICCs) and tunnelled central lines.
   b. Fever and/or sepsis in the presence of significant erythema/purulence at the catheter exit site.
   c. The development of fever and/or rigors after accessing the intravascular catheter.
   d. Blood cultures positive for certain organisms, for example S. aureus, CNS and Candida species, with no other obvious focus of infection should raise the suspicion for CRBSI.

D. Investigations

7. *IMPORTANT NOTE:* It is essential that all blood cultures are collected aseptically and that bottles are optimally filled, especially when drawing peripheral and central cultures where the differential time to positivity criterion is critically dependent on blood volume. The microbiologists routinely consider DTP when advising on interpretation of positive blood cultures.
8. *When and how should samples be collected for microbiological analysis in patients with a suspected CRBSI?*
   a. Blood cultures should be drawn when a CRBSI is suspected. If there is a catheter exit site exudate, swab the drainage for culture
      i. For the diagnosis of CRBSI related to tunnelled central lines or ports, paired catheter and peripheral cultures should be taken.
      ii. For the diagnosis of CRBSI related to peripheral venous/arterial access devices or short term central venous lines, one (or ideally two) peripheral blood cultures should be drawn
   b. If the catheter is removed, the tip should be cut off with sterile scissors, put in a sterile Universal container, and sent to Microbiology for culture
   c. Blood cultures should not be taken from patients who do not have suspected CRBSI (e.g. patients with simple exit site infection without systemic features)
   d. Blood cultures should not be routinely drawn from patients who have been apparently successfully treated for CRBSI with CVC retention, unless recommended by a microbiologist.

Figure 1: Management of suspected CRBSI in patients with non-tunnelled (short term) central catheters



Blood cultures positive – liaise with microbiologists regarding management

Blood cultures negative – CRBSI unlikely. Consider alternative source(s) of infection

E. Management of suspected CRBSI

Short term CVC-related infection

9. If there is a low suspicion of CRBSI and the patient is not seriously ill:
   a. Send peripheral blood cultures and manage according to most likely source of infection
10. If there is a strong suspicion of CRBSI and/or the patient is seriously ill (hypotension, signs and symptoms of organ failure):
   a. Send peripheral blood cultures
   b. Remove CVC and send tip for culture
   c. Start empirical antimicrobials:
      i. Vancomycin/teicoplanin (dose according to Antibiotic Guideline), plus
      ii. Gentamicin or Amikacin (dose according to Antibiotic Guideline)
      Note: Amikacin (dose according to Antibiotic Guideline) should be used instead of gentamicin in patients known to be colonised with gentamicin resistant/amikacin susceptible Gram negative organisms

PICC or tunnelled central catheter/port-related infection

11. The management of these CRBSI is more complex as vascular access options may be limited. In addition, there may be an ongoing need for central access. For these reasons, establishing an accurate diagnosis of CRBSI is particularly important. It is therefore critical to take appropriate central and peripheral blood cultures immediately after the diagnosis of CRBSI is suspected. Antibiotic line lock therapy may be considered for salvage of tunnelled catheters/Port-A-Caths; PICC lines should usually be removed, but antibiotic lock therapy may be appropriate in selected cases (i.e. known compromised central venous access) if agreed with the microbiologists.
12. Details of how to administer antibiotic lock therapy are described below. The principle of this approach is to deliver very high antibiotic concentrations to the lumen of the catheter for prolonged periods of time. It is important to appreciate that infusing therapeutic doses of an antibiotic through the catheter is NOT the same as antibiotic lock therapy.
13. If the subcutaneous tunnel of the catheter, or the subcutaneous reservoir (e.g. of a Port-A-Cath), is overtly erythematous with or without purulent exudate, catheter salvage is not feasible and the catheter should be removed as soon as possible.
14. **The catheter should also be removed if a CRBSI is complicated by septic thrombophlebitis, endocarditis or other metastatic septic manifestations (e.g. lung, liver abscesses, osteomyelitis/discitis).**
15. Outline of management:
   a. Send peripheral blood cultures together with blood cultures drawn from all lumens of the catheter. Ensure careful documentation of the site of each blood culture
   b. **If the catheter is being used for parenteral nutrition (PN):**
      i. stop the PN infusion immediately and await results of blood cultures before recommencing the feed
      ii. If *all* blood cultures are negative after 48-72 hours incubation, and CRBSI not still strongly suspected, PN may be recommenced
      iii. If CRBSI confirmed and catheter removed, wait at least 48-72 hours before placing a new catheter; new catheter should be placed at a different site to the infected catheter

c. If the patient is not seriously ill (no hypotension/organ involvement):
   i. await cultures before starting antibiotics
   ii. the implicated line may still be used (apart from for parenteral nutrition)
   iii. consider repeating blood cultures at 24-48 hours if there is ongoing clinical suspicion of CRBSI but negative blood cultures
d. If the patient is seriously ill start empirical antimicrobials:
   i. Vancomycin/teicoplanin (dose according to Antibiotic Guideline), plus
   ii. Gentamicin (dose according to Antibiotic Guideline)
   iii. Note: Amikacin (dose according to Antibiotic Guideline) should be used instead of gentamicin in patients known to be colonised with gentamicin resistant/amikacin susceptible Gram negative organisms
   iv. Antibiotics can be administered through the implicated intravenous catheter
   v. **In patients who do not respond promptly to fluid resuscitation and antibiotic therapy, consider urgent removal of catheter** (if strong suspicion it is the source of infection). Administer antibiotics through a separate venous access device after catheter removal.

Pathogen specific treatment

16. The Infectious Diseases/Microbiology service provides 24/7 advice regarding management of suspected/confimred CRBSI. As bespoke clinical advice is provided for every patient, details of antibiotic therapy and duration for all organisms are not covered in this guideline. However, some broad principles are outlined below and in the figure:

Coagulase negative staphylococci (CNS)

17. These organisms are the commonest cause of CRBSI, but also the commonest organisms to contaminate blood cultures. Therefore, careful liaison with Microbiology is required to determine clinical significance. They rarely cause severe infections so salvage of a long-term catheter with antibiotic line lock therapy (as well as systemic therapy) is usually feasible.

Staphylococcus aureus (including MRSA)

18. Due to the virulence of this bacterium, prompt CVC removal is recommended wherever possible. Antibiotic line lock therapy only has an approximately 50% success rate (3) and should only be attempted in exceptional circumstances and with careful multi-disciplinary discussion. Due to the risk of metastatic infection antibiotic treatment is recommended for a minimum of 2 weeks. An echocardiogram may be indicated – advice regarding this will be provided by the Infectious Diseases/Microbiology team.

Gram negative bacilli

19. CVC removal should occur promptly for non-tunnelled catheters. Antibiotic lock therapy may be considered for some tunnelled lines in patients without clinically complicated infections. The appropriate duration of systemic antibiotic therapy infection with these organisms is quite variable – advice will be provided by the Microbiology team.

Candida species

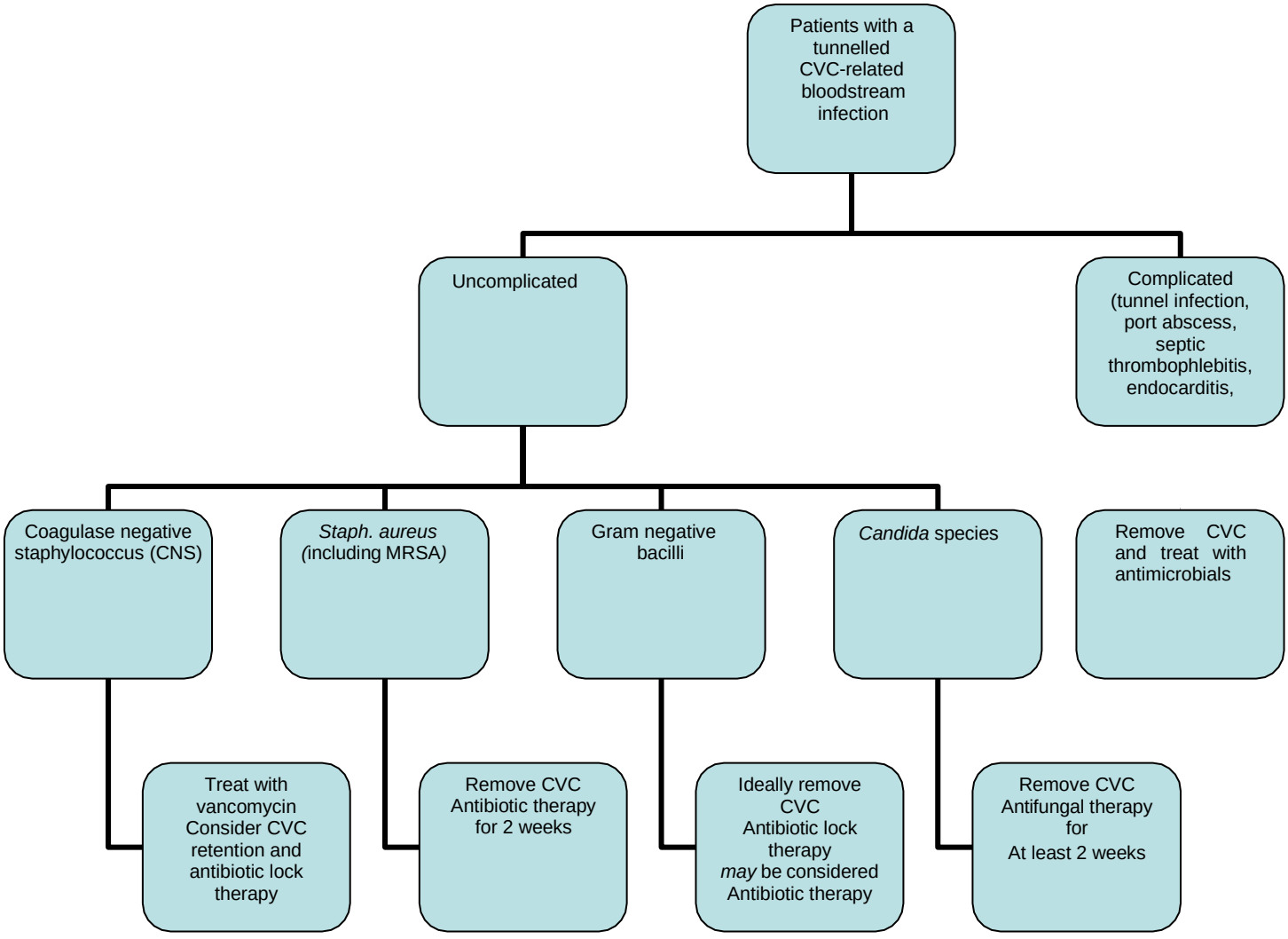
20. Immediate CVC removal is necessary for these infections: delay in removing catheters is

associated with a worse outcome in most studies (4,5). Therapy the microbiologists will advise on the appropriate agent) is given for a minimum of two weeks. Ophthalmological examination (to assess for endophthalmitis) is mandatory for all cases and echocardiography should be considered.

Note

21. Antibiotic line lock therapy is NOT usually used for any of the following organisms except on the advice of Microbiology or Infectious Diseases for individual cases, because line salvage in the face of infection with these organisms is usually unsuccessful.
    a. Staphylococcus aureus
    b. Pseudomonas aeruginosa (Klebsiella species)
    c. Mycobacterium species
    d. Fungi

Figure 2 Summary of management of confirmed CRBSI in patients with tunnelled central catheters



F. References

1. Mermel LA et al. Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Relaeted Infection: 2009 Update by the Infectious Diseases Society ofAmerica. Clin Infect Dis. 2009;49:1-45
2. Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies.Mayo Clin Proc. 2006;81(9):1159-71.
3. Fernandez-Hidalgo N et al. Antibiotic-lock therapy for long-term intravascular catheter-related bacteraemia: results of an open, non-comparative study. J AntimicrobChemother 2006;57:1172-1180
4. Lorente L, Martín MM, Vidal P, Rebollo S, Ostabal MI, Solé-Violán J, et al. Should centralvenous catheter be systematically removed in patients with suspected catheter related infection? Crit Care. 2014;18(5):564.
5. Nucci M, Colombo AL, Silveira F, Richtmann R, Salomão R, Branchini ML, et al. Riskfactors for death in patients with candidemia. Infect Control Hosp Epidemiol. 1998;19(11):846-50.
6. Lal, S., Chadwick, P., Nightingale, J., BIFA Committee (2018). Intestinal Failure Alliance (BIFA) Recommendations for Catheter Related Blood Stream Infections (CRBSI) Diagnosis. Available: https://www.bapen.org.uk/pdfs/bifa/recommendations-for-crbsi-diagnosis.pdf
7. Lal, S., Chadwick, P., Nightingale, J., BIFA Committee (2019). British Intestinal Failure Alliance (BIFA) Recommendation: Management of Catheter Related Blood Stream Infections (CRBSIs). Available: https://www.bapen.org.uk/pdfs/bifa/recommendations-on-management-of-crbsi.pdf