

Central Venous Catheter related Sepsis

Key Points

- Management of dialysis catheter related sepsis
- Guidelines for empirical and specific organism antibiotic therapy
- Indication for line removal

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Abbreviations

BSI	Blood stream infection
CRBSI	Catheter related blood stream infections
CABSI	Catheter associated blood stream infection
CSBSI	Catheter suspected blood stream infection
MSSA	Methicillin Sensitive Staphylococcus Aureus
TOE	Transoesophageal Echocardiogram
TTE	Transthoracic echocardiogram

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Introduction

It has long been recognised that indwelling intravenous devices are at risk of becoming colonised with micro-organisms and that in some cases, infection follows on from colonisation.

Catheter related bloodstream infections (CRBSI) may originate from the insertion site, hub or both. The commonest organisms causing CRBSIs in order of prevalence are; coagulase-negative staphylococci, *Staphylococcus aureus*, candida species and enteric Gram-negative organisms. Various strategies have been put forward to minimise the risk of catheter colonisation developing and include; the use of tunnelled lines, anti-microbial or silver impregnated lines, and the use of anti-microbial lock solutions.

However, despite all these precautions the risk of colonisation can only be minimised, but never removed completely. Thus, line colonisation and infection are clinical scenarios that the renal physician will encounter and this policy aims to provide guidance on the best management of these cases (both empirically and once a causative organism has been identified).

Whilst the majority of intravenous catheters used in the Renal unit will be long term (>14 days duration), there will be occasions when temporary lines have been placed and are in place for less than 14 days, in which case they are termed short term catheters in this policy and are treated slightly differently from long term catheters.

Definitions^{1, 2}:

Catheter colonisation – significant growth of one or more micro-organisms from culture of the catheter tip.

Exit site infection – exudate at exit site, tenderness, erythema and induration at exit site, or along subcutaneous tract of a dialysis catheter (+/- CRBSI).

BSI – (Bloodstream infection)

Presence of one or more recognised pathogens from ≥ 1 blood culture,

OR

If common skin organism, then it should have been cultured from 2 or more blood cultures drawn on separate occasions, or from 1 blood culture from a patient already on anti-microbials.

Patient must also have ≥ 1 of: fever, chills/rigors, hypotension.

CABSI – (Catheter associated bloodstream infection)

BSI in a patient with an intravascular catheter and clinical manifestations of infection, with no apparent source other than the line.

CRBSI – (Catheter related bloodstream infection)

BSI in a patient with an intravascular catheter and clinical manifestations of infection, with no apparent source other than the line

Plus, one of the following MUST be present:

- Positive line tip/CVC blood culture with the same organism as from a peripheral blood culture
- Differential time to positivity (growth in blood culture collected from catheter detected at least 2 hours before growth in a peripheral culture *taken simultaneously*)

CSBSI – (Catheter suspected bloodstream infection)

Negative blood cultures in the presence of systemic anti-microbials and clinical signs of systemic infection with a clinical improvement following line removal in the absence of another source of infection

Where CRBSI is used in the remaining text, it can also refer to CABSI or CSBSI depending upon the clinical circumstances.

Diagnosis of Line Colonisation/Sepsis

There is great variability in the signs and symptoms of line-related infections.

- **Colonisation** of a line with micro-organisms may not yield any clinical signs.
- **Pyrexia** is extremely sensitive, but not specific to line-related infections.
- **Exit site erythema** and discharge may help to indicate the likely source but are not in themselves indicative of CRBSIs.
- **Blood cultures** are the most useful tool available to the physician in confirming the diagnosis of a CRBSI.
- **Laboratory criteria** involving time to positivity of blood cultures taken from the line and a peripheral vein can help diagnose CRBSI.
- **Culture of line tips** will help to confirm the diagnosis, especially if the organism matches that grown in blood cultures.

Do not routinely take blood cultures during day to day dialysis.

False positive blood cultures due to poor technique or contamination may lead to inappropriate investigations and treatment. It should be noted that in some patients the peripheral veins are not suitable for venepuncture due to multiple failed fistulae or grafts, or because of the need to preserve peripheral veins for future fistula formation. In this subset of patients, the only culture that can be obtained is from the line and a positive result should be taken in the context of the clinical condition and treated as a line infection (CABSI) if indicated.

Initial management

If a line infection is suspected, then assess the clinical condition of the patient and review the exit site for signs of infection. Appropriate cultures need to be taken in order to confirm the diagnosis.

- Line and peripheral blood cultures should be taken at the same time using strict aseptic technique. Ensure that the same volume of blood is placed into all blood culture bottles and that the time, site it was taken from and the patient details are clearly written on the form and bottles.
- If a peripheral culture cannot be taken (e.g., no suitable peripheral sites) then line cultures should be taken correctly (as per renal blood culture policy), from each lumen if applicable. Clinicians should be made aware that no peripheral culture has been taken.
- A swab of the exit site is appropriate if the exit site score is equal to or greater than 4.

Initial empirical anti-microbial therapy

Where a CRBSI is suspected, after cultures are taken, anti-microbial therapy should be initiated. The clinician should review any recent microbiology results on the patient to determine whether changes need to be made to empirical anti-microbial therapy.

- Vancomycin and Gentamicin are the mainstay of empirical therapy, in haemodialysis patients and are dosed according to weight, however Microguide should be the source of current prescribing guidelines
- Maintenance doses should be prescribed in conjunction with the Renal Consultant, Microbiologist and using Microguide as a reference.

For inpatient treatment:

Antibiotic levels should be checked daily and the doses adjusted as required.

The risk of multi-resistant organisms are increased in patients who are neutropaenic, have had recent anti-microbial therapy, recent hospital admission (within 6 months), or have had positive microbiology for multi-resistant organisms previously.

In the presence of septic shock, appropriate broad spectrum cover should be given in addition to the above agents and consideration should be made for the inclusion of a carbapenem anti-microbial such as Meropenem 1g every 24 hours.

The risk of catheter related candidaemia is increased in patients who are receiving total parenteral nutrition, broad-spectrum anti-microbial agents, patients who have haematological malignancies, femoral site catheterisation and colonisation with candida species at multiple sites. In these cases consideration should be made for the inclusion of an anti-fungal agent. Discussion with a medical microbiologist is warranted.

Note: With regard to the duration of treatment, day 1 is NOT the first day on which the antibiotics were started, but the first day on which negative blood cultures were obtained.

Thus repeat blood cultures are indicated to assess response to treatment and to determine duration of treatment (see below). In CRBSIs not due to fungi or staphylococcus aureus, the usual duration of treatment is 10 – 14 days in the absence of persisting bacteraemia.

Indications for immediate dialysis line removal

Dialysis line removal as part of initial management should be considered in any patient presenting with signs of line infection and who is seriously ill with:

- hypotension
- signs of multi-organ failure
- evidence of metastatic infection (such as endocarditis)
- Staphylococcus aureus, Pseudomonas aeruginosa, or Candida blood stream infection (see below)

Temporary lines should be inserted in a different anatomical location to provide access for haemodialysis. If there is absolutely no alternative site available then exchange of the catheter over a guide wire should be undertaken, but clinicians should be aware of the increased risk of colonisation of the new line in these circumstances.

Further management

Repeat blood cultures should be obtained 72 hours after initiation of anti-microbials to determine whether there is persistence of bacteraemia which would suggest an ongoing focus and would therefore be an indication for line removal.

If a long-term catheter is being retained, the surveillance blood cultures should be taken 72 hours to one week after completion of an anti-microbial course. If these blood cultures are positive, then the catheter should be removed, and a new long-term catheter placed, but only after further blood cultures are sterile following appropriate further anti-microbial therapy.

Organism Specific management

Staphylococcus aureus

Identification of *Staphylococcus aureus* should prompt immediate line removal in both short and long term catheters (if this is the last dialysis access for the patient, please discuss with medical microbiologist and consultant nephrologist prior to line removal).

A temporary non-tunnelled catheter should be placed at another anatomical site to allow for ongoing dialysis after initiation of appropriate anti-microbial therapy.

Patients should be investigated for metastatic complications such as:

- osteomyelitis/discitis
- septic arthritis
- occult intra-abdominal collections
- infective endocarditis

Note: a trans-oesophageal echo is usually preferable to a trans-thoracic echo. The echo should be performed 5-7 days after onset of bacteraemia to minimise the possibility of a false-negative result. Please liaise with cardiology team regarding indications for a TOE following a TTE.

The agent of choice will depend upon the sensitivity profile of the organism, but in general, methicillin sensitive *Staphylococcus aureus* (MSSA) is best treated with Flucloxacillin rather than glycopeptides (Vancomycin or Teicoplanin).

Therapy should be for four to six weeks.

A two-week course of therapy can be considered if the following apply:

- Patient is not diabetic
- Patient is not immunosuppressed
- The catheter is removed
- No prosthetic intravascular device is left in-situ
- There is no evidence of metastatic infection
- There is no evidence of endocarditis or suppurative thrombophlebitis
- Fever and bacteraemia have resolved within 72 hours of initiation of appropriate anti-microbials

Persisting bacteraemia at 72 hours despite appropriate anti-microbial therapy is a strong indicator for complicated infections such as endocarditis or musculo-skeletal involvement.

A new long-term haemodialysis catheter can be placed once blood cultures with negative results are obtained.

Coagulase-negative Staphylococci

In the majority of cases of uncomplicated CRBSIs where the catheter is removed, a treatment course of 5-7 days is sufficient. If the catheter is retained, a treatment course of 10-14 days is required with post-therapy surveillance blood cultures taken 72 hours to one week after cessation of anti-microbials.

Complicated CRBSIs with evidence of metastatic infection should be managed in the same way as *Staphylococcus aureus* infections as outlined above.

CRBSI due to *Staphylococcus lugdunensis* should be managed in the same way as *Staphylococcus aureus* infections.

Treatment depends upon sensitivity of the isolate, but normally will be with Vancomycin dosed as for empirical therapy.

Pseudomonas aeruginosa

Isolation of pseudomonas species should always prompt removal of the catheter and insertion of a temporary catheter into a different anatomical site (if this is the last dialysis access for the patient, please discuss with medical microbiologist and consultant nephrologist prior to line removal).

If a patient is critically ill with suspected CRBSI and has a history of previous pseudomonas colonisation or infection, the patient should receive two agents with activity against pseudomonas (normally Gentamicin and Meropenem). Discussion with the medical microbiologist is warranted in these cases. Once sensitivity data are available for the organism, then de-escalation of initial therapy can be considered, but this should be discussed with the medical microbiologist.

The duration of therapy will be 10-14 days assuming the line is removed and there is no evidence of metastatic spread. Evaluation for endovascular infection and metastatic spread should be rigorously pursued and if identified, consultation with the medical microbiologist is required as the patient will require a prolonged anti-microbial course.

Enterococcus species

Short-term catheters should be removed. Long-term catheters should be removed if there is evidence of the following:

- Insertion site infection
- Suppurative thrombophlebitis
- Sepsis
- Endocarditis
- Persistent bacteraemia
- Metastatic infection

Therapy is dependent upon sensitivities, but generally Amoxicillin would be the preferred choice if the enterococcus is sensitive, with Vancomycin used if the patient is penicillin allergic, or if resistance to Amoxicillin is present.

As with *Staphylococcus aureus*, investigations should be undertaken to exclude metastatic infection and endocarditis.

A two-week course of treatment is appropriate for uncomplicated CRBSIs due to enterococci in which the catheter is retained. Follow up blood cultures are required after 72 hours to assess response to treatment and if these are positive, it should prompt line removal.

A surveillance blood culture should be taken 72 hours to one week following completion of treatment for a CRBSI to ensure ongoing sterility has been achieved.

Gram negative bacilli (other than *Pseudomonas*)

As mentioned previously, where previous anti-microbial use is documented, or the patient is known to have had a multi-resistant organism, and/or is critically ill, then consideration should be made for empirical addition of another broad spectrum anti-microbial agent such as a carbapenem.

The isolation of a non-pseudomonas enteric organism should prompt the clinician to ensure that there is no evidence of gastro-intestinal tract or urinary tract infection (especially occult intra-abdominal collections).

The dialysis catheter should be removed if there is persisting symptomatology, persisting bacteraemia or evidence of metastatic infection.

Where the dialysis catheter is retained, treatment should be for 10-14 days with a surveillance culture taken 72 hours to one week after treatment has been completed.

Candida species

The presence of candidaemia should always lead to prompt removal of the catheter with a temporary line inserted at another anatomical site if necessary.

Candidaemia should be treated with a broad spectrum anti-fungal agent until sensitivities are known (Amphotericin B or Caspofungin initially).

All patients with candidaemia should be investigated to exclude metastatic infection (including, but not limited to, hepato-splenic imaging, renal imaging, ophthalmic review and an echocardiogram).

Treatment should be for a minimum of 14 days from the first negative culture in the absence of any evidence of metastatic infection. Specialist advice should be sought in the event of confirmed metastatic spread.

Other organisms

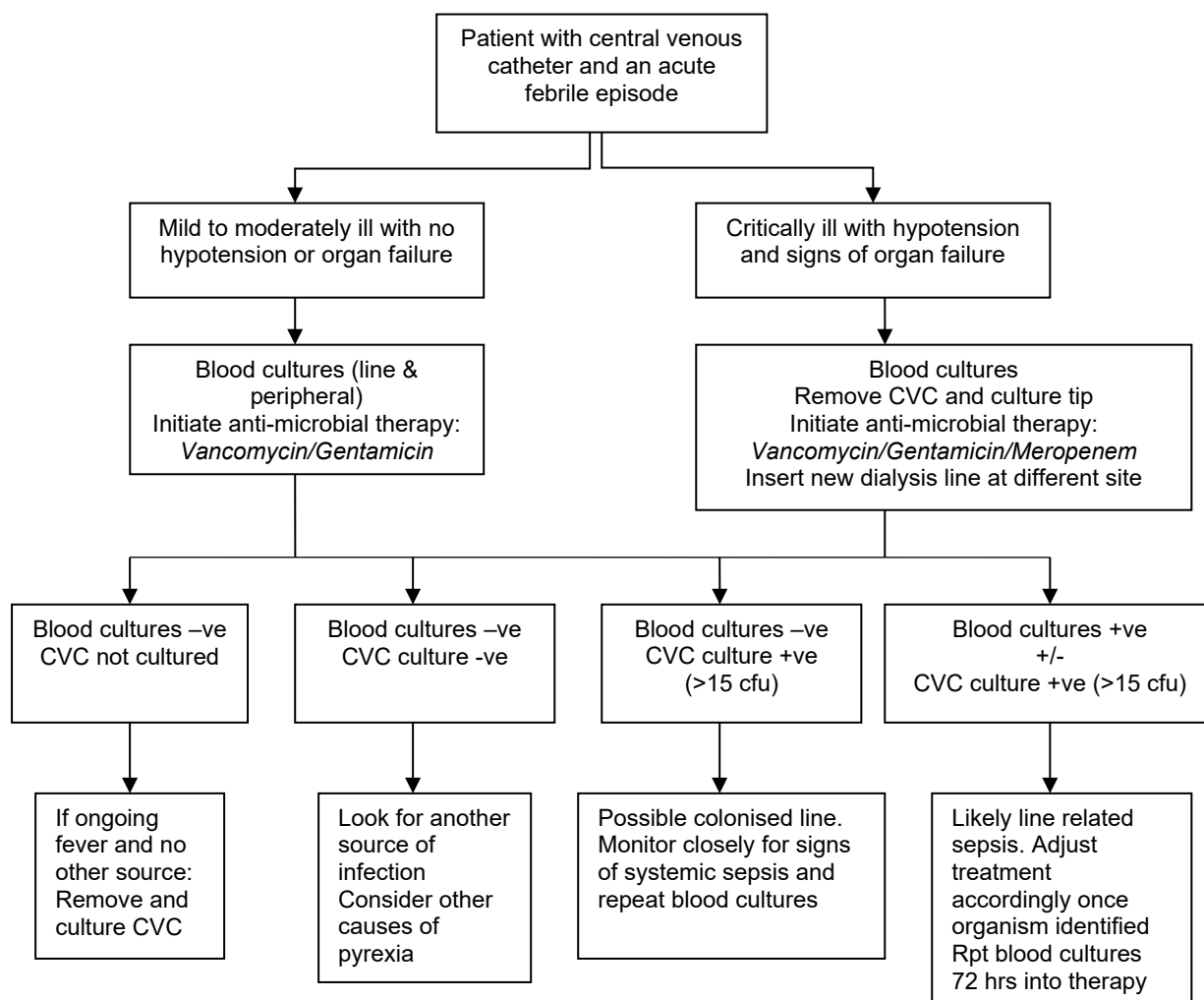
CRBSIs due to *Corynebacterium* species, *Bacillus* species, and *Micrococcus* species usually require at least two sets of blood cultures to be positive with the same organism to attain significance.

Catheters should be removed if there is evidence of infection as there is poor clinical response to treatment if the catheter is retained. Blood cultures should be repeated at 72 hours to assess response to treatment.

References

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Appendix: Initial treatment algorithm



(Adapted from IDSA Guidelines for Intravascular Catheter-Related Infection 2009)

Full version control record

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