Antibiotic Line-lock therapy for treatment of infected long-term intravascular devices

Introduction
Antibiotic lock therapy (AbLT) is indicated for patients with catheter-related bloodstream infections (CRBSIs) involving long-term catheters with no signs of exit site or tunnel infection, for whom catheter salvage is the goal. Additional systemic antibiotics will be needed to treat any associated bacteraemia.

Please note that:
- Line removal, with systemic antibiotic treatment, is the norm in most cases of proven line-related bacteraemia. On rare occasions, when there are strong grounds for persisting with the current line, this policy may apply.
- This guideline does not refer to the prophylactic use of line locks for the prevention of IV catheter infections.

Antibiotic lock therapy involves instilling a high concentration of an antibiotic to which the causative organism is susceptible, into the catheter lumen. The antibiotic solution is instilled or "locked" into each catheter lumen during periods when the catheter is not being used. The decision to use AbLT should be made by a Medical Microbiologist or Infectious Diseases physician in conjunction with members of the patient’s own medical team and the IV Access team. Antibiotic line locks should not be used other than on the advice of an Infection Specialist, and should not to be used without systemic antibiotics for treating systemic infections. The decision to use AbLT will be influenced by the identity of the causative organism, since lines infected with Candida or other fungi, S. aureus, Pseudomonas, Mycobacteria or multi-resistant organisms are less amenable to this form of therapy.

Diagnosis of catheter-related bloodstream infection (CRBSI)
Symptoms and signs associated with catheter related infection range from mild fever to profound sepsis with or without localised signs of exit site infection. Clinical findings alone may be unreliable for establishing a diagnosis of CRBSI. The overall diagnosis of CRBSI is made by a combination of clinical findings, positive blood cultures, and other microbiological evidence in the absence of other identifiable source of infection.

To facilitate the diagnosis of suspected CRBSI paired blood culture samples, with similar volumes of blood drawn from the catheter and a peripheral vein, should be taken, before commencing antimicrobial therapy, with the bottles and request forms clearly marked to reflect the site from which the samples were obtained.

A diagnosis of CRBSI can be made by the presence of primary bloodstream infection (bacteraemia or fungaemia) in a patient with an intravascular catheter (which has usually been in-situ for at least 48hrs prior to onset of infection), where primary bloodstream infection is defined as:
- Isolation of a pathogen (e.g. Staphylococcus aureus, Escherichia coli, Klebsiella sp etc.) from one or more blood cultures that is unrelated to infection at any other site, or
- Isolation of a common skin contaminant (e.g. coagulase negative staphylococcus, dipheroids, propionibacterium spp) from two or more blood
cultures drawn on separate occasions with at least one systemic manifestation of infection (fever, chills, hypotension) and no other suspected source of infection.

**Systemic antibiotic therapy**

Systemic antimicrobial therapy should be initiated on suspicion of catheter related infection, after blood culture samples have been taken. Empirical therapy should include IV Teicoplanin with IV Piperacillin/tazobactam (Tazocin). Gentamicin may be added if the patient is severely unwell, or used as an alternative to Tazocin in patients with a documented penicillin allergy.

Other factors, e.g. previous microbiology results, may also influence the initial choice of antimicrobial agent, and complicated cases should be discussed with a Medical Microbiologist.

It is important that empirical systemic antimicrobial therapy is modified if possible to specific therapy once the identification and sensitivities of the infecting organism(s) are available.

Repeat blood cultures should be performed 72 hours into effective treatment to demonstrate clearance of the bacteraemia.

It may occasionally be appropriate to treat intraluminally colonised catheters by AbLT alone, without systemic antibiotics, when percutaneous blood cultures are negative.

**Antimicrobial line lock therapy**

This may be introduced, in discussion with a Microbiologist or Infectious Diseases physician, when the diagnosis of CRBSI has been made and the causative organism identified. The choice of agent for AbLT will depend upon the antibiotic susceptibility of the infecting organism.

The following agents may be suitable for use as locks to salvage infected lines. Vancomycin is available from pharmacy in pre-prepared 3mL syringes; Gentamicin locks must be prepared on the ward immediately prior to use, using 20mg/2ml vials.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration</th>
<th>Diluent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin*</td>
<td>10mg/ml</td>
<td>Sodium chloride 0.9%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>10mg/ml (2ml) Paediatric Injection</td>
<td></td>
</tr>
<tr>
<td>Taurolidine</td>
<td>In pre-prepared ampoules</td>
<td></td>
</tr>
</tbody>
</table>

When using lumens for antibiotic locks, it is important to ensure the “locked” lumen is identified by a red label, which contains:
- The date that the line was locked
- The name of the agent and the concentration used
- The date of removal of the lock
- The signature of the operator.
Use the lumen volume as marked on the line. If no lumen volume is marked, use the following as a guide:

<table>
<thead>
<tr>
<th>Type of CVC catheter</th>
<th>Lumen volume (if not marked on lumen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICC</td>
<td>1ml per lumen</td>
</tr>
<tr>
<td>Tunnelled access devices</td>
<td>2ml per lumen</td>
</tr>
<tr>
<td>(e.g. Hickman line, Vascath, portacaths)</td>
<td></td>
</tr>
<tr>
<td>Temporary CVC</td>
<td>0.5ml per lumen</td>
</tr>
<tr>
<td>(e.g. jugular / femoral lines)</td>
<td></td>
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</tbody>
</table>

**Additional comments**

Amongst patients receiving parenteral nutrition, infected PICC or midlines are usually removed. Other infected intravascular devices are usually not used for feed while the infection is treated. Such patients should always be discussed with the Parenteral Nutrition team (extension 3650 Bleeps 4595/4024).

AbLT should be used for 7 days and then reviewed. The usual duration of line lock therapy will be 10-14 days; the duration of systemic antibiotic therapy depends upon the infecting organism.

Repeat blood cultures after an antibiotic-free period of at least 48 hours following completion of AbLT therapy, may be indicated in some cases.

Failure to respond to treatment, or persistently positive blood cultures despite AbLT therapy should prompt referral for echocardiography and reconsideration of the diagnosis of CRBSI.
Establish diagnosis:
- Examine patient carefully for source & assess clinical status
- Collect (and clearly label) at least 2 sets of blood cultures (peripheral & each lumen of line)

Suspected CRBSI with systemic upset due to sepsis?
- Remove line promptly if patient is in septic shock due to suspected CRBSI
- Commence empirical systemic antimicrobial therapy (systemic antibiotics may not be necessary if the patient is systemically well and stable)
- Consider line removal if no longer needed

<table>
<thead>
<tr>
<th>First line</th>
<th>Penicillin allergic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teicoplanin 1.2g loading dose, then 800mg OD IV plus Piperacillin/tazobactam 4.5g TDS IV</td>
<td>Teicoplanin 1.2g loading dose, then 800mg OD IV plus Gentamicin 5mg/kg OD (maximum 450mg) IV</td>
</tr>
</tbody>
</table>

If blood cultures positive:
- Modify systemic therapy according to culture results and clinical progress.
- Consider suitability for adjunctive antimicrobial line lock therapy:

Consider adjunctive antimicrobial line lock therapy to salvage line if:
- Uncomplicated intraluminal CRBSI where line salvage is required with no signs of extra-luminal infection
- Blood cultures yield; CoNS, diphtheroids, Corynebacterium spp, Enterococcus spp, E coli, Klebsiella spp
- Absence of all contraindications to lock therapy

Line removal is recommended if:
- Signs of /suspected extraluminal infection e.g. tunnel or pocket infection, port abscess
- Evidence of 2° septic complications, e.g. septic thrombophlebitis, endocarditis, osteomyelitis etc
- Unsuitable organism: Candida spp, fungaemia, S aureus, MRSA, atypical mycobacterium spp, Pseudomonas aeruginosa, multi resistant organisms
- Severe sepsis / haemodynamic instability due to suspected line-related sepsis

Repeat blood cultures should be performed 72 hours into treatment to demonstrate clearance of the bacteraemia

Indications for discontinuation of antimicrobial lock therapy and line removal:
- Clinical deterioration despite treatment, with the onset of severe sepsis / haemodynamic instability
- Development of secondary septic complications or signs of extraluminal infection
- Persistent / relapsing bacteraemia despite 72hrs of antimicrobial treatment with antibiotics to which the organism is susceptible, particularly if the infecting organism is Candida spp or other fungus, S aureus (including MRSA), Pseudomonas aeruginosa, Mycobacterium spp., or multiply-resistant

Algorithm for management of suspected Catheter-associated bloodstream infection
Procedure for installation of Antibiotic locks

1. Manage the vascular access device (VAD) with an aseptic non-touch technique (ANTT), in accordance with, 'RLBUHT ANTT Practice Guideline for Preparation & Administration of IV Medication'.

2. If TPN is being or to be administered the VAD should be managed with an aseptic technique. In such cases the, 'IV Access Care and Maintenance for the patient at hospital and home' policy is applicable.

3. Remove the needle free device (bionector) and decontaminate the hub with a Sanicloth CHG wipe, for 30 seconds using different parts of the cloth. Allow to dry. Apply a new needle free system (Bionector).

4. Obtain a blood return by observing a flash back of blood into the intended saline flush. Flush the catheter lumen using 10ml of Sodium Chloride 0.9%.

5. Specific catheter lumen lock volumes are dependent on each device used. The volumes indicated above are intended as a guide, and the volume to be used should be confirmed with a member of the Team responsible for inserting the VAD:
   IV Access Team – extension 3342/3 Bleeps 4522/4781/4778
   Dialysis Catheters – Ward 6B extension 3603/2368
   Nutritional Team for patients receiving TPN – extension 3650 Bleeps 4595/4024

6. Instil the antibiotic solution into the VAD, injecting slowly (over 5-10 seconds). 10ml is the smallest syringe size which may be used to administer IV therapy into VADs.

7. The solution should ideally remain in the line lumen for 24 hours. “Dwell times” of between 12 and 48 hours may be suitable however, depending on circumstances and the need to access the line for other purposes.

8. When the VAD is next accessed 3-5mls if blood should be aspirated and discarded, prior to administering any further therapy or flushing. If this is not possible please contact a member of the Team responsible for inserting the VAD:
   IV Access Team – extension 3342/3 Bleeps 4522/4781/4778
   Patients receiving dialysis – Ward 6B extension 3603/2368
   Nutritional Team for patients receiving TPN – extension 3650 Bleeps 4595/4024

Central venous catheters with more than one lumen should have each lumen treated as per the above administration guidelines.
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