

Guideline

Fever in a Child with Central Venous Access Device

Management of Suspected Central Venous Access Device (CVAD) Infection in Children

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Purpose

This Guideline provides recommendations for the management of suspected CVAD infection in children.

Scope

This Guideline provides information for Children's Health Queensland (CHQ) staff caring for paediatric patients with suspected CVAD infection in children.

Related documents

Policy and Standard(s)

- CHQ procedure 03450 [Intravascular Access Device, Management \(peripheral and Central Venous Access Devices\)](#)
- CHQ nursing standard 03453 [IVAD - Central Venous Catheters: Nursing Care and Management of Tunnelled \(cuffed and non-cuffed\) CVC in Paediatric Patients](#)

- CHQ nursing standard 03454 [IVAD - Venous Port Device: Nursing Care and Management of Totally Implanted Venous Port Device \(Port\) in Paediatric Patients](#)

Procedures, Guidelines, Protocols

- CHQ procedure 01052 [Parenteral Nutrition - emergency management of the child undergoing home PN](#)
- Queensland Paediatric Haematology Oncology Network (QPHON) [Acute management of Fever in the Neutropenic Paediatric Oncology Patient](#)
- Queensland Paediatric Haematology Oncology Network (QPHON) [Management of the Paediatric Non-Neutropenic Oncology Patient with Fever](#)
- CHQ guideline: [Empiric Antibiotic guidelines for Paediatric Intensive care unit \(PICU\)](#)
- CHQ guideline: [Antibiotic Lock therapy for Catheter related blood stream infections](#)
- CHQ guideline: [Use of Taurolidine/Citrate lock solution in the prevention of central venous catheter related bacteraemia](#)
- Paediatric Tobramycin/Gentamicin Therapeutic drug monitoring : <http://qhps.health.qld.gov.au/childrenshealth/resources/clinforms/docs/658202.pdf>
- Paediatric Vancomycin Therapeutic drug monitoring: <http://qhps.health.qld.gov.au/childrenshealth/resources/clinforms/docs/658201.pdf>

List of abbreviations:

ABLT	Antibiotic lock therapy
BC	Blood culture
CHQ	Children's Health Queensland
CoNS	Coagulase Negative Staphylococcus
CRBSI	Catheter related blood stream infection
CrCl	Creatinine clearance
CRP	C-reactive protein
CVAD	Central venous access device
CXR	Chest x-ray
ELFT	Electrolytes and Liver function tests
ESBL	Extended spectrum beta-lactamase
FBC	Full blood count
ID	Infectious Diseases
IMPS	Infection Management and Prevention Service
IV	Intravenous
MC&S	Microscopy
MRSA	Methicillin resistant Staphylococcus aureus
MSSA	Methicillin sensitive Staphylococcus aureus
nmMRSA	Non multi-resistant methicillin resistant Staphylococcus aureus

PICC	PICC line (Percutaneous Inserted Central Catheter)
PCR	Polymerase chain reaction
PN	Parenteral nutrition
TDM	Therapeutic drug monitoring
TPN	Total parenteral nutrition
VRE	Vancomycin resistant enterococci

Guideline: Fever in a Child with Central Venous Access Device

1. General Management Principles

(For empiric antibiotic treatment follow flow diagram - Figure 1)

A. Unexplained fever or suspected CVAD infection ($\geq 38.5^{\circ}\text{C}$ x1 or $\geq 38^{\circ}\text{C}$ x2) in a child with a tunneled central venous line (PORT-a-Catheter and Percutaneous Inserted Central Catheter) always requires medical review, assessment and rapid empiric antibiotics (Figure 1).

- (Note: For initial empiric treatment of [Febrile Neutropenia \(FN\)](#), [Febrile Non-neutropenia](#) or [Fever in child receiving parenteral nutrition \(PN\)](#) please follow the specific guidelines)

B. CVAD infection should be suspected if any of the following are present:

- After flushing CVAD any of the following symptoms:
 - Fever, rigors, malaise, hypotension, tachycardia
 - Erythema or pus at exit site or along tunnel tract
- Otherwise unexplained febrile illness with signs of haemodynamic compromise in a child with CVAD
- Otherwise unexplained fever in children receiving total parenteral nutrition (TPN) via CVAD

C. Investigations and diagnosing CVAD infection

- Bloods:
 - Full blood count (FBC), Electrolytes and Liver function tests (ELFT), C-reactive protein (CRP), blood culture (BC) from each lumen and peripherally if possible or according to unit specific protocols.
 - Greater than one set of cultures should be collected prior to starting empiric antibiotics when possible.
- Other investigations as clinically indicated: for example Respiratory viral PCR, chest x-ray (CXR), urine microscopy (MC&S), lumbar puncture, echocardiogram, and if exit site infection swab MC&S.
- If a catheter suspected to be infected is removed, the tip should be sent for culture. Ensure "Suspected CVAD infection" written on Pathology request form.
- CVAD tips are NOT routinely cultured in the absence of infection/ symptoms.

D. If Blood cultures are negative:

- Patient well with no focus identified, afebrile for more than 24 hours and one or more sets of cultures are negative after 48 hours, stop antibiotics.
- If fevers continue for more than 48 hours; repeat BCs and continue antibiotics. If no other source apparent consider CVAD removal.

2. Line removal for CVAD infections

A. All central lines should be removed if no longer required

B. Consider line removal if “Complicated” (after discussion with treating consultant):

- Obvious rigors and hypotension after flushing line (rather than awaiting culture results)
- Haemodynamically unstable and positive CVAD culture. (Heart rate (HR) score ≥ 2 on Child Early Warning Tool (CEWT) form, systolic blood pressure (BP) below age standard on CEWT form, cap refill ≥ 3 seconds). Establish alternate intravenous access before CVAD removal
- Evidence of disseminated infection
- Pus at exit site, erythema along tunnel tract or port abscess
- Positive blood culture persisting 72 hours after starting antibiotics to which the organism is sensitive.
- Difficult to cure organisms are cultured, for example: *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida*, other fungi, multi-resistant bacterial pathogens, non-tuberculous mycobacteria, *Bacillus cereus*, *Micrococcus*, *Propionibacteria*.

C. Assuming the patient is clinically stable (“Uncomplicated”), with none of the above indications, catheter salvage may be attempted with the following organisms:

- Coagulase negative staphylococci
- Enterococcus including Vancomycin resistant enterococci (VRE)
- Gram negative bacilli other than *Pseudomonas aeruginosa*

Systemic antibiotics should be administered through the CVAD or Percutaneous inserted central catheter (PICC). The only exception is when rigors/hypotension occur on accessing CVAD/PICC. In this instance CVAD should be removed and systemic antibiotics given peripherally if possible. If only one lumen is infected the systemic antibiotic and lock should be given through this lumen, if more than one, the lumen through which the systemic antibiotic is given should be alternated daily whilst the other is antibiotic locked for that day. (See section 3 below: Antibiotic Lock Therapy)

D. Catheter salvage may be attempted but is unlikely to be successful for:

- *Bacillus* species, *Micrococcus*, *Propionibacteria*, *Corynebacteria*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

E. Catheter salvage should NOT be attempted with the following organisms:

- Methicillin resistant *Staphylococcus aureus* (MRSA)
- *Mycobacteria*
- *Candida* species

- Fungi
- Management of any of these infections should be discussed with Infectious Diseases.

F. If line is removed at commencement of treatment:

- Place temporary intravenous access until bacteraemia resolved (more than 48 hours since last positive culture).
- Guidewire exchange could be used if haemodynamically stable with no evidence of exit site infection and no other venous access available, and after systemic antibiotics given through the line. Daily cultures should then be performed until negative result is obtained.
- If CVAD guidewire exchanged but cultures remain positive after 72 hours of appropriate antibiotic therapy, attempts at salvage should be abandoned and the catheter removed.
- Treat with at least 1 week of intravenous (IV) antibiotics (longer for specific indications)

H. Reinsertion of tunneled catheter following CVC-related bacteraemia, should be postponed until:

- Appropriate systemic antibiotic antimicrobial therapy has commenced AND
- the patient is afebrile AND
- there are negative blood cultures (more than 48 hours since last positive culture).
- If time permits, re-insertion of a tunneled CVC is preferably done after the systemic course of antibiotics has been completed, and blood cultures taken more than 48 hours after completion are negative.

I. If line is NOT removed at commencement of treatment:

- Repeat BC 24 to 96 hours after the institution of treatment.
- If BC still positive at 48 to 72 hours either remove line, look for alternate focus or if stable repeat daily until negative
- Attempt line preservation unless at any point they fulfill the indications above for line removal or have repeated positive cultures
- Use antibiotic locks in the infected catheter daily or after each dialysis session (see section 3 below: Antibiotic Lock Therapy)
- Consider surveillance blood cultures 5-7 days after antibiotics completed

3.0 Antibiotic Lock therapy (ABLT)

3.1 Gram Positive organism:

- Vancomycin (5mg/mL) and heparinised saline (10 units/mL) antibiotic locks (see CHQ guideline: [“Antibiotic Lock therapy for Catheter related blood stream infections”](#))

OR

- Vancomycin (5mg/mL) and Citrate (4.67%) antibiotic locks (*for haemodialysis patients only*)

Preparation method:

- a. Reconstitute 500mg vial of Vancomycin with 10mL water for injection (to give concentration of 50mg/mL) – draw up 1mL (50mg).
- b. Draw up 1mL of Trisodium Citrate 46.7% and add to 1mL of Vancomycin 50mg/mL and 8mL of Sodium Chloride 0.9% to give a total volume of 10mL.
- c. This gives a final concentration of 5mg/mL Vancomycin and 4.67% Citrate in a total volume of 10mL. Prepare fresh for each lumen.
- d. Instil the required volume for size and type of central venous access device and allow to dwell for up to 24 hours.

3.2 Gram Negative organism:

- Gentamicin (1mg/mL)/heparinised saline (10 units/mL) antibiotic locks (see CHQ guideline: [“Antibiotic Lock therapy for Catheter related blood stream infections”](#))

OR

- Gentamicin (1mg/mL)/Citrate (4.67%) antibiotic locks (*for haemodialysis patients only*)

Preparation method:

- a. Draw up 0.25mL of Gentamicin 40mg/mL (equals 10mg).
- b. Draw up 1mL of Trisodium Citrate 46.7% and add to 0.25mL Gentamicin 40mg/mL and 8.75mL of Sodium Chloride 0.9% to give a total volume of 10mL.
- c. This gives a final concentration of Gentamicin 1mg/mL and Citrate 4.67% in a total volume of 10mL.
- d. Prepare fresh for each lumen.
- e. Instil the required volume for size and type of central venous access device and allow to dwell up to 24 hours.

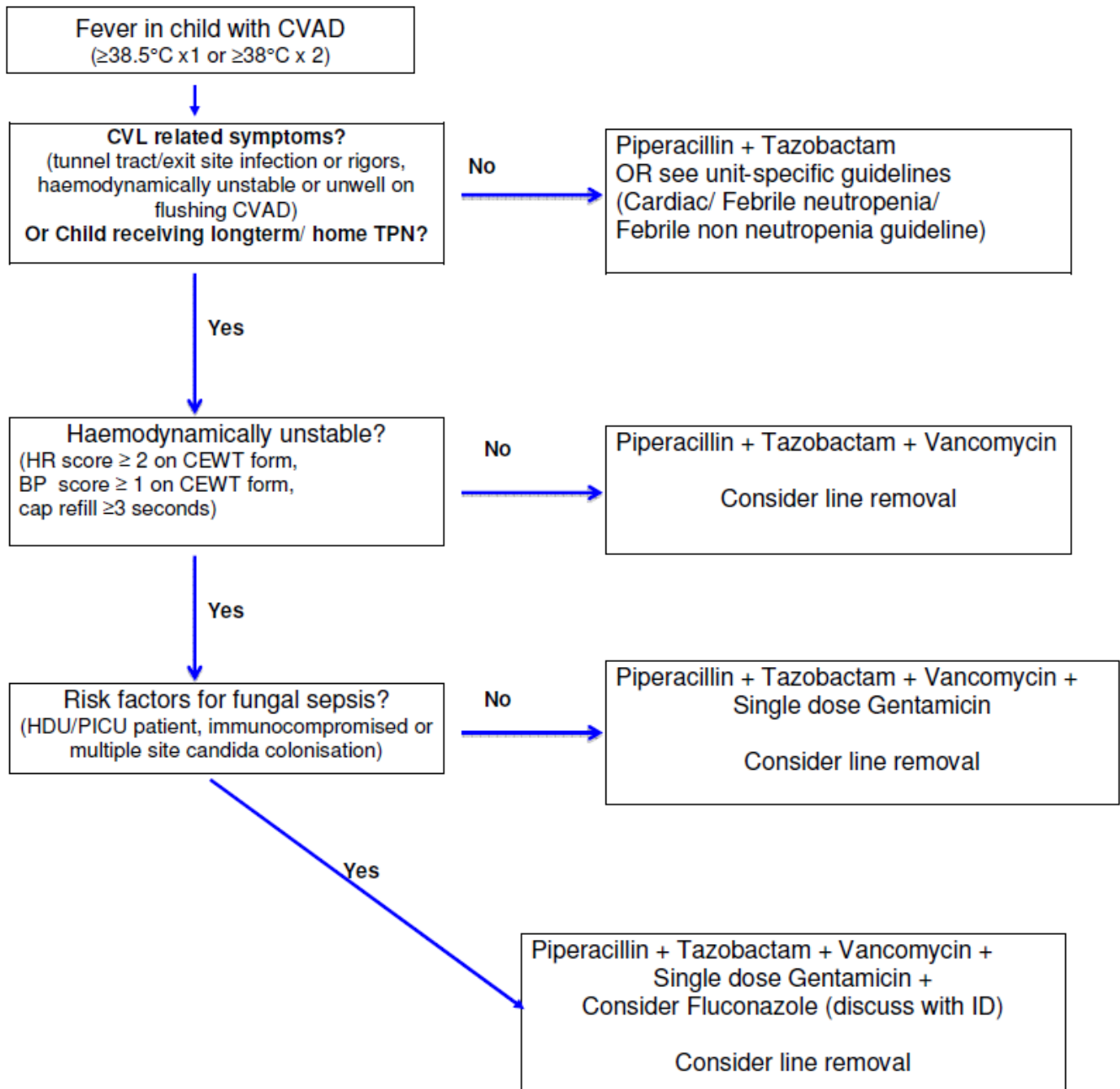
3.3 Long Term Antiseptic Lock therapy

For high risk children (More than 10 episodes of catheter related bloodstream infection (CRBSI) per 1000 catheter days, previous life threatening septic shock, catastrophic implications if that line is lost):

- **Taurolidine (1.35%) / citrate (4%) antiseptic locks**

Instil the required volume of TauroLock® solution for size and type of central venous access device and allow to dwell for up to 7 days or as discussed with ID (see CHQ guideline: [“Use of Taurolidine/Citrate lock solution in the prevention of central venous catheter related bacteraemia”](#)).

Figure 1. Empiric antibiotic therapy in suspected CVAD infection.



Notes:

In a patient known to be colonised with VRE, substitute vancomycin with teicoplanin

In a patient known to be colonised with ESBL, substitute piperacillin/ tazobactam with meropenem

Figure 2.
Targeted antibiotic therapy, positive catheter blood culture in child with CVAD.

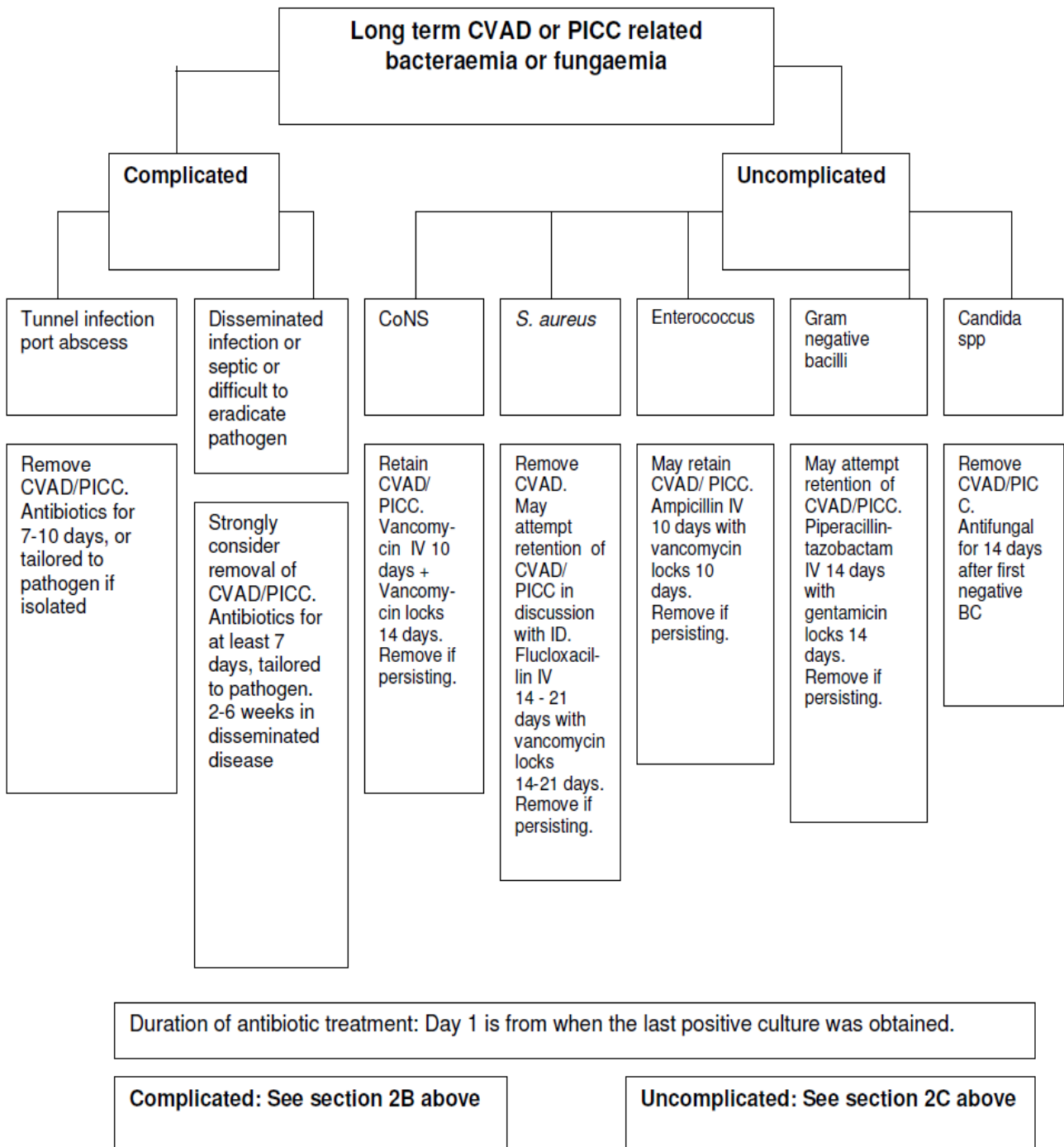


Table 1: Targeted Antibiotic Therapy (Refer to Table 2 for Paediatric Antimicrobial Dosing Recommendations)

Organism	Complicated	Uncomplicated
Staphylococcus aureus and Staphylococcus lugdunensis	CVAD/PICC removed: <ul style="list-style-type: none"> ▪ Intravenous (IV) antibiotics for 2 weeks from last positive blood culture ▪ 4 to 6 weeks IV antibiotics if persistent bacteraemia after catheter removal, endocarditis or suppurative thrombophlebitis ▪ 6 to 12 weeks treatment with at least 4 weeks as IV antibiotics if there is an organ based focus 	CVAD/PICC removed: 1 to 2 weeks, all IV antibiotics CVAD/PICC retained: <ul style="list-style-type: none"> ▪ Intravenous antibiotics with vancomycin locks for 2 to 3 weeks from last positive blood culture ▪ 6 weeks IV antibiotics if endocarditis, ▪ 6 to 12 weeks total treatment with at least 4 weeks as IV antibiotics if there is an organ based focus ▪ Systemic antibiotics should be administered through the CVC/P.
<p>Comments: Strongly consider line removal in these patients. Line salvage is successful in only 50% of cases however may be attempted in discussion with ID. If still febrile or positive blood cultures at 48 hours remove line unless risks of removal outweigh risks of retention. If still febrile at 72 hours, screen for disseminated infection; specifically considering CXR, fundoscopy, echocardiogram for endocarditis, bone and joint examination for osteomyelitis and septic arthritis, abdominal ultrasound for organ micro abscesses. Screening for disseminated infection is not required routinely if rapid resolution of symptoms and fever and no focal signs. Important: ECHO may need to be repeated if fevers or positive cultures persist. Antibiotics:</p> <ul style="list-style-type: none"> ▪ MSSA (Methicillin sensitive s. aureus): Flucloxacillin IV. Alternative for haemodialysis catheters: Cefazolin IV after dialysis. (Teicoplanin IV may be considered for treatment via HITH. Discuss with ID team.) ▪ MRSA/nmMRSA (Non-multi-resistant Methicillin Resistant Staphylococcus aureus): As per sensitivities. Discuss with ID team. 		
Coagulase negative Staphylococcus (CoNS)	CVAD/PICC removed: <ul style="list-style-type: none"> ▪ Vancomycin IV or as per sensitivities for 7 days following last positive blood culture 	CVAD/PICC removed: Vancomycin IV or as per sensitivities for 5 days after catheter removal CVAD/PICC retained: <ul style="list-style-type: none"> ▪ Vancomycin IV (tailored to sensitivities) for 10 days with vancomycin antibiotic locks for 14 days. ▪ Systemic antibiotics should be administered through the CVAD/PICC.
<p>Comments: Most CoNS (coagulase negative staphylococcus) infections are uncomplicated, there is a high success rate with CVAD/PICC salvage using systemic antibiotics and ABLT. Line should be removed if persistently or relapsing positive cultures, haemodynamic instability or disseminated disease (complicated infection). Teicoplanin IV may be considered for treatment via HITH. Discuss with ID team.</p>		

Table 1: Targeted Antibiotic Therapy (Refer to Table 2 for Paediatric Antimicrobial dosing recommendations) (continued)

Organism	Complicated	Uncomplicated
Enterococcus	<p>CVAD/PICC removed: Ampicillin IV or as per sensitivities for 7 days following last positive blood culture For vancomycin resistant enterococci (VRE): substitute Teicoplanin IV or as per sensitivities. Discuss with ID Team.</p>	<p>CVAD/PICC removed: Ampicillin IV or as per sensitivities for 5 days after catheter removal CVAD/PICC retained:</p> <ul style="list-style-type: none"> • Ampicillin IV (tailored to sensitivities) with vancomycin antibiotic locks for 10 days. • Systemic antibiotics should be administered through the CVAD/PICC.
<p>Comments: Most enterococcus infections are uncomplicated. There is high success rate with CVAD/PICC salvage using systemic antibiotics and ABLT. Line should be removed if persistently or relapsing positive cultures, haemodynamic instability or disseminated disease.</p>		
Bacillus, Micrococcus, Propionibacteria.	<p>Although usually not systemically severe, infection of a CVAD/PICC with these organisms can be very difficult to eradicate. If 2 or more BCs are positive, line removal is strongly recommended. Where only one BC is positive, with a subsequent negative BC, the significance is uncertain. If systemically well options include:</p> <ul style="list-style-type: none"> ▪ observe and repeat cultures if febrile ▪ CVAD/PICC removed: Vancomycin IV or as per sensitivities for 5 days after catheter removal ▪ CVAD/PICC retained: Vancomycin IV or as per sensitivities (administered through the CVC/PICC) with vancomycin antibiotic locks for 14 days. 	
Gram negatives	<ul style="list-style-type: none"> ▪ CVAD/PICC removed: Piperacillin/Tazobactam IV or as per sensitivities for 7 to 14 days following last positive blood culture 	<p>CVAD/PICC removed: Piperacillin/Tazobactam IV or as per sensitivities for 7 days after catheter removal CVAD/PICC retained: Piperacillin/Tazobactam IV (tailored to sensitivities) with gentamicin antibiotic locks for 14 days. Systemic antibiotics should be administered through the CVAD/PICC.</p>
<p>Comments: Increasing experience has indicated success with line retention and systemic antibiotics and ABLT. However a low threshold for line removal should be maintained, especially where pseudomonas aeruginosa (high biofilm production) is isolated. If still febrile or positive blood cultures at 48 hours remove line unless risks of retention outweigh risk of removal. Line should be removed if persistent or relapsing positive cultures, haemodynamic instability or disseminated disease. If still febrile at 72 hours, screen for disseminated infection specifically considering CXR, fundoscopy, echo cardiogram for endocarditis, abdominal ultrasound for organ micro abscesses, suppurative thrombophlebitis.</p>		
Candida	<p>Removal of catheter recommended in all cases of candida CRBSI. CVAD retention worsens outcomes. Fluconazole IV for 14 days is the treatment of choice for Candida albicans. Caspofungin IV or Amphotericin (liposomal) IV may be used in disseminated or persistent disease, or if other candida species isolated, after discussion with ID team.</p>	

Table 2: Paediatric Antimicrobial Dosing Recommendations

Antimicrobial	Dosing recommendations (for paediatric patients over 1 month of age)		
	Normal renal function (CrCl >20mL/min/1.73m ²)	Severe renal impairment (CrCl ≤ 20mL/min or patients receiving haemodialysis)	Haemodialysis Comments
Amphotericin (Liposomal)	3mg/kg/dose to 5mg/kg/dose IV once daily	3mg/kg/dose to 5mg/kg/dose IV once daily	No dose adjustment in renal impairment/haemodialysis required. Monitor renal function and potassium levels.
Ampicillin	50mg/kg/dose (Max 2 gram/dose) IV every 6 hours	50mg/kg/dose (Max 1gram/dose) IV every 6 hours	Dose after haemodialysis
Caspofungin	Loading dose: 70mg/m ² /dose (Max 70mg/day) on day 1, then 50mg/m ² /dose (Max 50mg/day) IV once daily	Loading dose: 70mg/m ² /dose (Max 70mg/day) on day 1, then 50mg/m ² /dose (Max 50mg/day) IV once daily	No dose adjustment in renal impairment/haemodialysis required
Cefazolin	25mg/kg/dose to 37.5mg/kg/dose (Max 2 gram/dose) IV every 6 hours	25mg/kg/dose (Max 1 gram/dose) IV once daily	Dose after haemodialysis
Flucloxacillin	50mg/kg/dose (Max 2 gram/dose) IV every 6 hours	50mg/kg/dose (Max 1gram/dose) IV every 6 hours	Not dialysed
Fluconazole	Loading dose: 12mg/kg/day (Max 400mg/day) IV on day 1, then 6mg/kg/day (Max 200mg/day) IV as maintenance dose	6mg/kg/dose (Max 400mg/dose) IV once daily	Dose after haemodialysis
Gentamicin	For <10 years old: 7.5mg/kg (Max 320mg/day) IV once daily, then adjust dose/interval according to therapeutic drug monitoring (TDM) For >10 years old: 6mg/kg (Max 560mg/day) IV once daily, then adjust dose/interval according to TDM Note: In septic shock – 7mg/kg IV (max 640mg/day) once daily as a starting dose, then adjust dose/ interval according to TDM	For <10 years old: 7.5mg/kg (Max 320mg/day) IV as a single dose, then adjust dosing interval according to TDM For >10 years old: 6mg/kg (Max 560mg/day) IV as a single dose, then adjust dosing interval according to TDM	Administer single dose only, then perform Gentamicin 2 and 6 hour post dose levels (to calculate AUC). Adjust dosing interval according to TDM results. If ongoing treatment is required, check level daily and redose gentamicin if serum level <1mg/L.

Table 2: Paediatric Antimicrobial Dosing Recommendations (continued)

Antimicrobial	Dosing recommendations (for paediatric patients over 1 month of age)		
	Normal renal function (CrCl >20mL/min/1.73m ²)	Severe renal impairment (CrCl ≤ 20mL/min or patients receiving haemodialysis)	Haemodialysis Comments
Meropenem	20mg/kg/dose to 40mg/kg/dose (Max 2gram/dose) IV every 8 hours	20mg/kg/dose (Max 1gram/dose) IV every 12 hours	Dose after haemodialysis
Piperacillin/ Tazobactam	100mg/kg/dose (Max 4gram/dose Piperacillin component) IV every 6 hours	50mg/kg/dose (Max 2gram/dose Piperacillin component) IV every 8 hours	Dose after haemodialysis
Teicoplanin	Loading dose: 10mg/kg/dose (Max 800mg/dose) IV every 12 hours for 2 doses, Maintenance dose: 10mg/kg/dose (Max 400mg/dose) once daily	Loading dose: 10mg/kg/dose (Max 800mg/dose) IV every 12 hours for 2 doses, Maintenance dose: 10mg/kg/dose (Max 400mg/dose) every 48hours	Dose after haemodialysis
Vancomycin	15mg/kg/dose (Max 500mg/dose as starting dose) IV every 6 hours, then adjust dosing according to TDM. Check Vanc trough (pre-dose) level before the 4 th or 5 th dose (aim for trough level 15-20mg/L or as advised by ID team/pharmacy)	20mg/kg/dose (Max 1gram/dose) IV as a single dose, then adjust dosing according to TDM	Dose after haemodialysis Check Vancomycin level 24hours post dose: If level <15mg/L, re-dose at 20mg/kg as a single dose If level >15mg/L, withhold dose and recheck level at 48hours post original dose

Consultation

Key stakeholders who reviewed this version:

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Guideline revision and approval history

Version No.	Modified by	Amendments authorised by	Approved by
1.0	Infectious Diseases Consultant (IMPS)	Medicines Advisory Committee (CHQ)	General Manager Operations
Keywords	CVAD, central venous access device, infection, antibiotic lock therapy, Central line associated bloodstream infection, parenteral nutrition, PN, haemodialysis		
Accreditation references	EQIP National Standards: 1 – Governance for Safety & Quality in Health Service Organisations; 3 - Preventing and Controlling Healthcare Associated Infections; 12: Provision of Care		