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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Author/custodian	Paediatric Infection Specialist			**Review date**	26/08/2022
Supersedes	1.0				
Applicable to	All CHQ Staff				
Authorisation	Executive Director Clinical Services (QCH)				

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.

Guideline: Fever in a child with Central Venous Access Device (CVAD)

1. General Management Principles

- For empiric antibiotic treatment follow flow diagram - Figure 1.

A. Unexplained fever or suspected CVAD infection (≥38.5°C x1 or ≥38°C x2) in a child with a tunnelled central venous line always requires medical review, assessment and rapid empiric antibiotics (Figure 1).

- However, there are specific guidelines for the empiric treatment of Febrile Neutropenia (FN), Febrile Non-neutropenia or Fever in child receiving parenteral nutrition (PN)

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 CVL 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, ECHO and if exit site infection swab MC&S.
- If a catheter suspected to be infected is removed, the tip should be sent for culture.
- Central venous access device (CVAD) tips are NOT routinely cultured in the absence of infection/ symptoms.

D. If Blood cultures (BC) are negative:

- Patient well with no focus identified, apyrexial for more than 24 hours and at least 2 sets of cultures are negative after 48 hours, stop antibiotics.
- If fevers continue for more than 48 hours; repeat BC and continue antibiotics. If no other source apparent consider CVAD removal.

2. Line removal for CVAD infections

A. All CVADs should be removed if no longer required

B. Consider CVAD removal if "<u>Complicated</u>" (after discussion with the treating consultant):

- Obvious rigors and hypotension after flushing line (rather than awaiting culture results)
- Haemodynamically unstable (Heartrate (HR) score ≥ 2 on Child Early Warning Tool (CEWT), systolic blood pressure (SBP) below age standard on CEWT form, cap refill ≥ 3 seconds)
- 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 mycobacterium, *Bacillus cereus*.

C. Assuming the patient is clinically stable ("<u>Uncomplicated</u>"), with none of the above indications, catheter salvage may be successful with the following organisms:

- Coagulase negative staphylococci
- Enterococcus including Vancomycin resistant enterococci (VRE)
- Gram negative bacilli other than Pseudomonas aeruginosa
- Streptococcus viridans species
- Bacillus spp.(non-cereus)

  Systemic antibiotics should be administered through the infected CVAD or Percutaneous inserted central catheter (PICC).

  - If only one lumen is infected the systemic antibiotic and lock should be given through this lumen.
  - If more than one lumen is infected, the lumen through which the systemic antibiotic is given should be alternated daily whilst the other lumen is antibiotic locked for that day.
  - See section 3 below: Antibiotic Lock Therapy

  The only exception is when rigors and/or hypotension occur on accessing CVAD/PICC. In this instance CVC should be removed and systemic antibiotics given peripherally if possible.

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

- Bacillus cereus, Staphylococcus aureus, Pseudomonas aeruginosa and Enterobacter spp.

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 CVAD is removed at commencement of treatment:

- Place temporary intravenous access until bacteraemia resolved (more than 48 hours since first negative 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.
- See table 1 and algorithm (figure 1 and 2) for recommended duration antibiotic therapy

G. Reinsertion of tunnelled catheter following CVAD-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 first negative culture).
- If time permits, re-insertion of a tunnelled CVC is preferably done after the systemic course of antibiotics has been completed.

H. 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 fulfil 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 to 7 days after antibiotics completed.

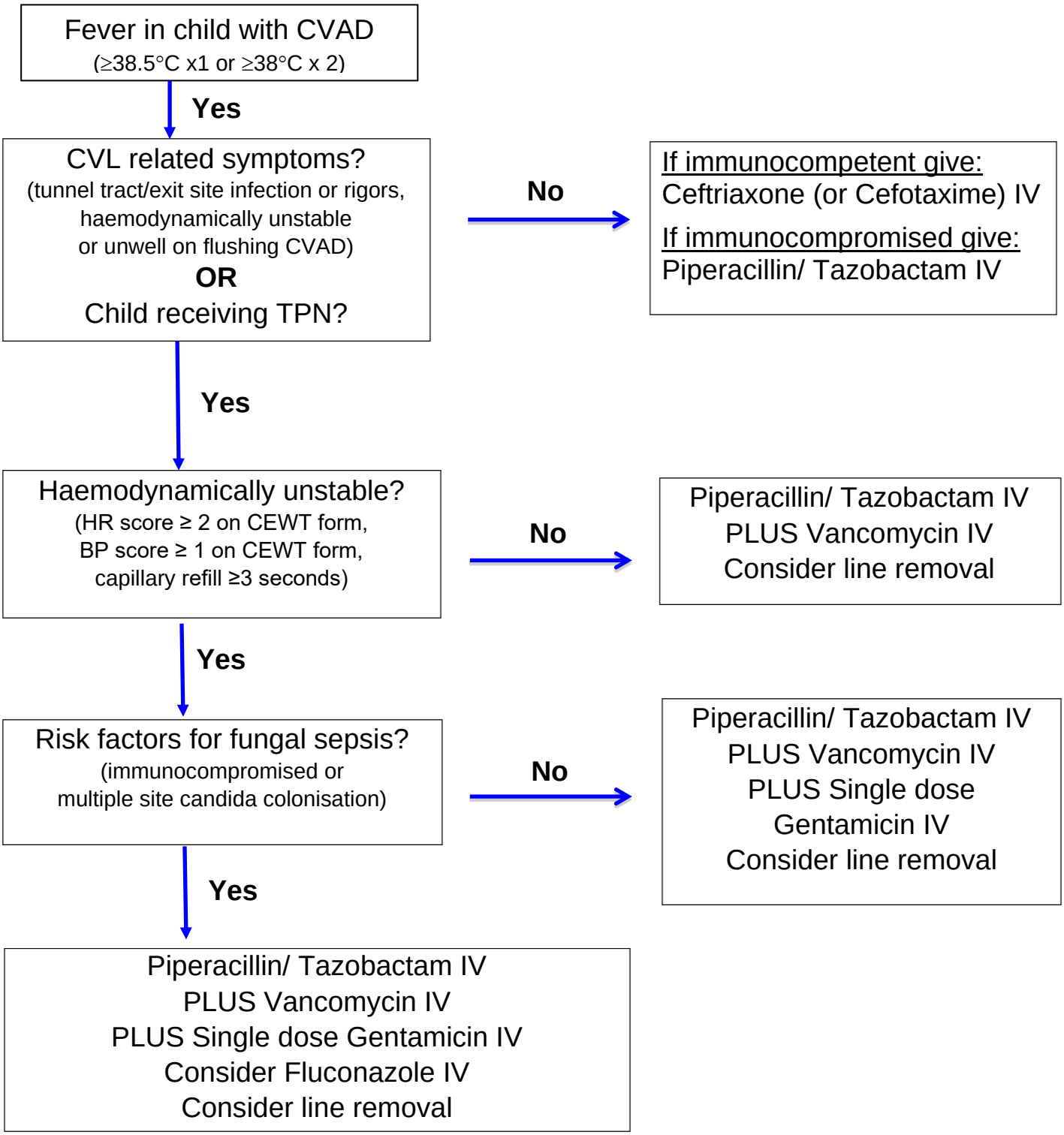
3. Antibiotic Lock therapy (ABLT)

- Antibiotic Lock therapy is indicated for patients with catheter related blood stream infections involving long-term catheters with no signs of exit site or tunnel infection, where catheter salvage is the goal.
- ABLT is most commonly undertaken with vancomycin or gentamicin but is feasible with a number of different antibiotics including cefazolin, ciprofloxacin, linezolid, teicoplanin or ampicillin. ID advice and approval required.
    - Gram positive organisms: Vancomycin locks
    - Gram negative organisms: Gentamicin locks
    - Minimum dwell time: 6 to 8 hours (to make an impact on biofilm formation)
    - Maximum dwell time: CHQ-GDL-01065 Antibiotic Lock Therapy for Catheter Related Blood Stream Infections
    - For preparation and administration advice, CHQ-GDL-01065 Antibiotic Lock Therapy for Catheter Related Blood Stream Infections

4. Long Term Antiseptic Lock therapy: Taurolidine (1.35%) / citrate (4%) antiseptic locks

- For use in high risk children (more than 10 episodes of catheter related bloodstream infection (CRBSI) per 1000 catheter days (approximately one episode per 3 months), previous life-threatening septic shock or catastrophic implications if that line is lost).
    - ID advice and approval required.
    - Minimum dwell time: 6 to 8 hours (to make an impact on biofilm formation)
    - Maximum dwell time: 28 days
- For preparation and administration advice, CHQ-GDL-01060 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, add gentamicin IV to piperacillin/ tazobactam
- In a patient with severe redman syndrome to Vancomycin, substitute vancomycin with teicoplanin

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

Notes:

- Duration of antibiotic treatment: Day 1 is from when the first negative culture was obtained.
- For definition of complicated and uncomplicated, see Notes 2 b) and c) above

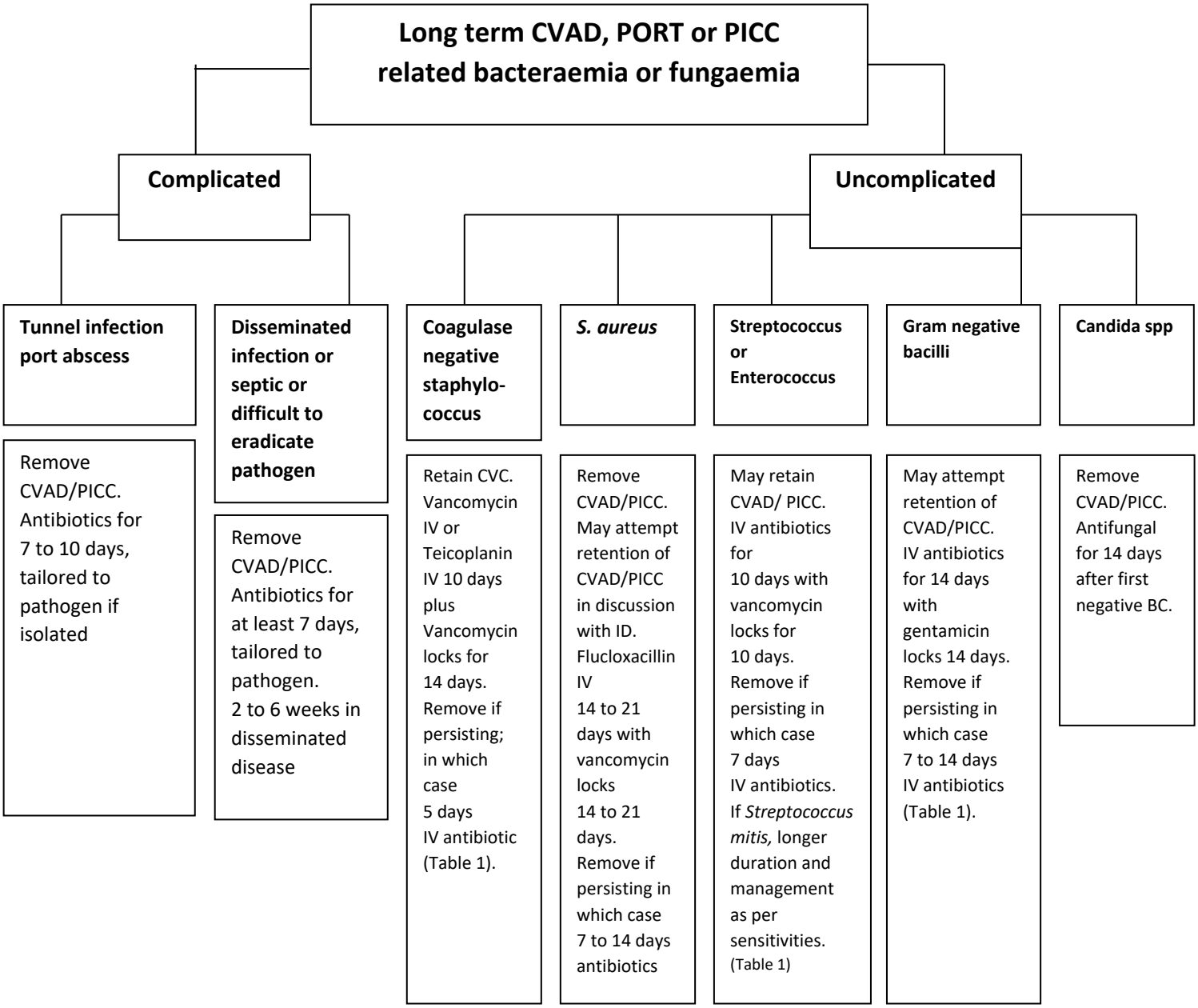


Table 1: Targeted Antibiotic Therapy

(Refer to Table 2 for Paediatric Antimicrobial dosing recommendations)

<table>
<tr><th>Organism</th><th>Complicated</th><th>Uncomplicated</th></tr>
<tr><td rowspan="2">Staphylococcus aureus and Staphylococcus lugdunensis</td><td>CVAD/PICC removed:
Intravenous (IV) antibiotics for 2 weeks from first negative blood culture
4 to 6 weeks IV antibiotics if endocarditis or suppurative thrombophlebitis</td><td>CVAD/PICC removed:
1 to 2 weeks antibiotics; at least one week via IV route

CVAD/PICC retained:
Intravenous antibiotics with vancomycin locks for 2 to 3 weeks from first negative blood culture</td></tr>
<tr><td colspan="2">Comments: Strongly consider line removal in these patients.
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:

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.</td></tr>
<tr><td rowspan="2">Coagulase negative Staphylococcus (CoNS)</td><td>CVAD/PICC removed:
Vancomycin or Teicoplanin IV or as per sensitivities for 7 days following first negative blood culture</td><td>CVAD/PICC removed:
Vancomycin/teicoplanin IV or as per sensitivities for 5 days after catheter removal. If not immunocompromised and prompt response, 48 hours may suffice.

CVAD/PICC retained:
Vancomycin/teicoplanin IV (tailored to sensitivities) for 10 days with vancomycin antibiotic locks for 14 days.
Systemic antibiotics should be administered through the CVAD/PICC.</td></tr>
<tr><td colspan="2">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.</td></tr>
</table>

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

Organism	Complicated	Uncomplicated
Streptococcus	**CVAD/PICC removed:** IV antibiotic as per sensitivities for 7 to 10 days following first negative blood culture. If *S.mitis,* IV antibiotics for 10 to 14 days.	**CVAD/PICC removed:** IV antibiotic per sensitivities for 7 days after catheter removal; 10 days if *S.mitis* **CVAD/PICC retained:** IV antibiotics (tailored to sensitivities) with vancomycin locks for 10 to 14 days. Systemic antibiotics should be administered through the CVAD/PICC.
Enterococcus	**CVAD/PICC removed:** IV antibiotic as per sensitivities for 7 days following first negative blood culture	**CVAD/PICC removed:** IV antibiotic per sensitivities for 5 days after catheter removal **CVAD/PICC retained:** • IV antibiotic with vancomycin antibiotic locks for 10 days. • Systemic antibiotics should be administered through the CVAD/PICC.
	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.	
Bacillus sp.	Where only one BC is positive, with a subsequent negative BC, the significance is uncertain and unlikely to be pathogenic. If systemically well, repeat BC and observe If febrile and no other cause for fever or 2 or more BCs positive, options include: 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 CVAD/PICC) with vancomycin antibiotic locks for 14 days. Although uncommon, true 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.	

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

Organism	Complicated	Uncomplicated
Gram negatives	**CVAD/PICC removed:** IV antibiotic per sensitivities for 10 to 14 days following first negative blood culture Consider at least 14 days therapy if *Pseudomonas aeruginosa*	**CVC/PICC removed:** IV antibiotics per sensitivities for 7 to 10 days after catheter removal; 10 days if immunocompromised **CVAD/PICC retained:** IV antibiotics per sensitivities with gentamicin antibiotic locks for 14 days. Systemic antibiotics should be administered through the CVAD/PICC.
	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.	
Candida	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 Liposomal Amphotericin IV may be used in disseminated or persistent disease, or if other candida species isolated, after discussion with ID team. Initial treatment should be IV, with consideration of oral stepdown therapy if rapid clinical and microbiological response.	

Table 2: Paediatric Antimicrobial Dosing Recommendations

Antimicrobial	Dosing recommendations (for paediatric patients over 1 month of age)		
	Normal renal function (CrCl >20mL/min/1.73m2)	**Severe renal impairment (CrCl ≤ 20mL/min/1.73m2 or patients receiving haemodialysis)**	**Haemodialysis Comments**
Amphotericin (Liposomal)	3 mg/kg/dose to 5 mg/kg/dose IV once daily	3 mg/kg/dose to 5 mg/kg/dose IV once daily	No dose adjustment in renal impairment/ haemodialysis required. Monitor renal function and potassium levels.
Ampicillin	50 mg/kg/dose (Max 2 g/dose) IV every 6 hours	50 mg/kg/dose (Max 1 g/dose) IV every 6 hours	Dose after haemodialysis
Caspofungin	Loading dose: 70 mg/m^2/dose (Max 70 mg/day) IV once daily Maintenance dose: 50 mg/m^2/dose (Max 50 mg/day) IV once daily	Loading dose: 70 mg/m^2/dose (Max 70 mg/day) IV once daily Maintenance dose: 50 mg/m^2/dose (Max 50 mg/day) IV once daily	No dose adjustment in renal impairment/ haemodialysis required
Cefazolin	50 mg/kg/dose (Max 2 g/dose) IV every 8 hours	Loading dose: 50mg/kg (Max 2 g) as a single dose, then 25 mg/kg/dose (Max 1 g/dose) IV once daily as maintenance dose	Dose after haemodialysis
Flucloxacillin	50 mg/kg/dose (Max 2 g/dose) IV every 6 hours	50 mg/kg/dose (Max 1 g/dose) IV every 6 hours	Not dialysed

Table 2: Paediatric Antimicrobial Dosing Recommendations (continued)

Antimicrobial	Dosing recommendations (for paediatric patients over 1 month of age)		
	Normal renal function (CrCl >20mL/min/1.73m2)	**Severe renal impairment (CrCl ≤ 20mL/min or patients receiving haemodialysis)**	**Haemodialysis Comments**
Fluconazole	Loading dose: Day 1: 12 mg/kg (Max 400 mg) IV as a single dose Maintenance: Day 2 onwards: 6 mg/kg (Max 200 mg) IV 24-hourly If critically ill or disseminated disease, seek ID specialist and Senior clinical pharmacist advice on dosing.	Seek pharmacist/ID advice on dosing	Dose after haemodialysis TDM - Seek ID advice
Gentamicin	**If more than 1 month to 10 years old**: 7.5 mg/kg (Max 320 mg) IV once daily, then adjust dose/interval according to therapeutic drug monitoring (TDM). **If more than 10 years old**: 6 mg/kg (Max 560 mg) IV once daily, then adjust dose/interval according to TDM. **If more than 10 years old and septic shock:** 7 mg/kg (Max 640 mg) IV once daily, then adjust dose/interval according to TDM.	**If more than 1 month of age to 10 years old**: 7.5 mg/kg (Max 320 mg) IV as a **single dose**, then adjust dosing interval according to TDM **If more than 10 years old**: 6 mg/kg (Max 560 mg) IV as a **single dose**, then adjust dosing interval according to TDM. Refer to CHQ guideline Tobramycin Gentamicin Therapeutic Drug Monitoring for advice on TDM targets.	Dose based on Ideal body weight. Administer single dose only, then perform Gentamicin 2 and 6 hour post dose levels (to calculate AUC). In severe renal impairment or haemodialysis, if ongoing treatment is required, check true trough level daily (24 hours post dose) and only re-dose gentamicin if level <0.5 mg/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/1.73m2)	**Severe renal impairment (CrCl ≤ 20mL/min or patients receiving haemodialysis)**	**Haemodialysis Comments**
Meropenem	20 mg/kg/dose to 40 mg/kg/dose (Max 2 g/dose) IV every 8 hours	20 mg/kg/dose (Max 1 g/dose) IV every 8 hours	Dose after haemodialysis
Piperacillin/ Tazobactam	100 mg/kg/dose (Max 4 gram/dose Piperacillin component) IV every 6 hours	100 mg/kg/dose (Max 4 gram/dose Piperacillin component) IV every 12 hours	Dose after haemodialysis
Teicoplanin	**Loading dose**: 10 mg/kg (Max 800 mg/dose) IV every 12 hours for 3 doses, **Maintenance dose**: 10 mg/kg (Max 400 mg) IV once daily	**Loading dose**: 10 mg/kg (Max 800 mg) IV as a **single dose** **Maintenance dose**: 10 mg/kg (Max 400mg) IV every 72 hours	Dose after haemodialysis. TDM - Seek ID advice
Vancomycin	15 mg/kg/dose (Max 750 mg/dose as starting dose) IV every 6 hours, then adjust dosing according to TDM. Refer to CHQ guideline Paediatric Vancomycin Therapeutic Drug Monitoring for advice on timing of levels and TDM targets.	15 mg/kg/dose (Max 500 mg/dose) IV as a single dose. Refer to CHQ guideline Paediatric Vancomycin Therapeutic Drug Monitoring for advice on timing of levels and TDM targets.	Dose after haemodialysis Check Vancomycin level 24 hours post dose: If level <15mg/L, re-dose at 15 mg/kg (Max 500 mg) as a single dose. If level >15mg/L, withhold dose and recheck level 24 hours later.

Definition of terms

Term	Definition
ABLT	Antibiotic lock therapy
BC	Blood culture
CEWT	Child Early Warning Tool
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
CVC	Central venous catheter
CVL	Central venous line
CXR	Chest x-ray
ELFT	Electrolytes and Liver function tests
ESBL	Extended spectrum beta-lactamase
FBC	Full blood count
ID	Infectious Diseases
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
SBP	Systolic blood pressure
TDM	Therapeutic drug monitoring
TPN	Total parenteral nutrition
VRE	Vancomycin resistant enterococci

Consultation

Key stakeholders (position and business area) who reviewed this version are:

- Director IMPS, Immunology and Rheumatology
- Paediatric Infection Management Specialist Team (IMPS, QCH)
- Paediatric Infection Management Fellows (IMPS, QCH)
- Pharmacist Advanced - Antimicrobial Stewardship (QCH)

Related documents

- CHQ-PROC-03455 Management of Compromised Central Venous Access Device (CVAD)
- CHQ-PROC-01052 Parenteral Nutrition - emergency management of the child undergoing home parenteral nutrition (PN)
- CHQ-GDL-01249 Management of fever in a Paediatric Oncology Patient: Febrile neutropenia and febrile non- neutropenia
- CHQ-GDL-01066 Empiric Antimicrobial guidelines for Paediatric Intensive care unit (PICU)
- CHQ-GDL-01065 Antibiotic Lock therapy for Catheter related blood stream infections
- CHQ-GDL-01060 Use of Taurolidine/Citrate lock solution in the prevention of central venous catheter related bacteraemia
- CHQ Paediatric Tobramycin/Gentamicin Therapeutic drug monitoring guideline
- CHQ Paediatric Vancomycin Therapeutic drug monitoring guideline
- CHQ-GDL-01075 Antifungal Prophylaxis and Treatment in Paediatric Oncology Patients and other Immunocompromised Children

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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
2.0 26/08/2020	Paediatric Infection Management Specialists (IMPS) Pharmacist Advanced – Antimicrobial Stewardship	Medicines Advisory Committee (CHQ) – endorsed 17/09/2020	Executive Director Clinical Services (QCH)

Keywords	CVAD, central venous access device, infection, antibiotic lock therapy, Central line associated bloodstream infection, parenteral nutrition, PN, haemodialysis, 01069
Accreditation references	National Safety and Quality Health Service Standards (1-8) 3: Preventing and Controlling Healthcare-Associated Infection, 4: Medication Safety ISO 9001:2015 Quality Management Systems: (4-10)