

TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Diagnosis and Initial Management of Suspected
Central Line-Associated Bloodstream Infections (CLABSI)
Evidence-Based Guideline

Definition: A child is considered to have a CLABSI when the child has a central line and meets **ONE of the following criteria:**

- presence of a recognized pathogen cultured from one or more blood cultures; or
- signs/symptoms of an infection (i.e., fever, chills, or hypotension, especially when an infusion is running through the catheter) AND common skin commensal[‡] is cultured from two or more blood cultures drawn on separate occasions; or
- if the **child is ≤ 1 year** and has signs/symptoms of an infection (i.e., fever, hypothermia, apnea, or bradycardia) AND common skin commensal[^] is cultured from two or more blood cultures drawn on separate occasions.

Modified from the CDC's surveillance definition of a CLABSI event to appropriately guide clinical care. ⁽¹⁾

[‡]diphtheroids [*Corynebacterium* spp. not *C. diphtheriae*], *Bacillus* spp. [not *B. anthracis*], *Propionibacterium* spp., coagulase-negative staphylococci [including *S. epidermis*], viridians group streptococci, *Aerococcus* spp., *Micrococcus* spp.

Pathophysiology: In the first week following catheter insertion, pathogens may migrate along the external surface of the catheter tubing and colonize it. Contamination of the hub followed by migration of pathogens into the lumen of the catheter may occur, usually more than 10 days after catheter insertion. Hematogenous seeding of the catheter by pathogens from another source also can be seen. Contamination of catheters from a contaminated infusate is rare. Risk factors for CLABSI include: prematurity, young age, emergency insertion, inadequate barriers for insertion, poor skin antisepsis, prolonged duration of use, catheter site, multiple lumens, excessive manipulation, neutropenia, and receipt of total parenteral nutrition. ⁽²⁻⁶⁾

Epidemiology: Coagulase-negative staphylococci are the most common cause of CLABSI but infection with other gram-positive organisms (methicillin-susceptible and methicillin-resistant *Staphylococcus aureus*, enterococci, etc.) also occurs. Gram-negative organisms (*Escherichia coli*, *Klebsiella*, *Pseudomonas*, etc.) should be considered in all patients but especially in those who are neutropenic, severely ill, or known to be colonized with these pathogens. *Candida* species cause CLABSI most often in patients who are critically ill, have been on broad-spectrum antibiotic therapy, are receiving total parenteral nutrition, have a hematologic malignancy, or have received a bone-marrow or solid-organ transplant. Less virulent organisms such as *Bacillus* species, *Corynebacterium*, *Micrococcus* and *Propionibacteria* may also cause CLABSI. Mycobacteria, fungi and molds are less common but important causes of CLABSI in immunocompromised hosts. ^(2,3,7-9)

Inclusion Criteria

- Children with a central line[‡] and signs of infection

Exclusion Criteria

- Children without a central line[‡]

Differential Diagnosis

Fever and neutropenia

Urinary tract infection

Localized infection other than the intravascular catheter (e.g., pneumonia, intra-abdominal)

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Diagnostic Evaluation

History: Assess for

- Presence of central line[‡]
 - Fever (e.g., sudden onset, no other obvious source)
 - Positive blood cultures
 - Local infection
 - High grade bacteremia/fungemia
 - Cluster of unusual Gram-negative bacteremias
 - Patient is a likely candidate for sepsis
 - Endocarditis and other metastatic infections acquired in hospital
 - Rigors, especially with infusion through the central line
- In the neonate, hypothermia, apnea, and bradycardia should be assessed as well.

[‡]Central lines are an intravascular catheter that terminates at or close to the heart or in one of the following vessels: aorta, pulmonary artery, superior vena cava, inferior vena cava, brachiocephalic veins, internal jugular veins, subclavian veins, common iliac veins, femoral veins, and in neonates, the umbilical artery/vein. Central lines are used for infusion, withdrawal of blood or hemodynamic monitoring.

Diagnosis of CLABSI: Prior to initiating antibiotics, a central and a peripheral blood culture should be obtained simultaneously, when feasible (to assess time to positivity). If an adequate blood volume from a peripheral venipuncture cannot be obtained, the recommended total blood volume should be obtained from the central line. In the cases where equal and optimal blood volume has been obtained, time to positivity may provide useful information in detecting whether or not the central line can be preserved. Growth of microbes from a blood sample drawn from a catheter at least 2 hours before microbial growth is detected in a blood sample obtained from a peripheral vein best defines CLABSI. For children who have multiple lumens, obtaining a sample from each lumen can be considered, providing that obtaining an adequate blood volume is not compromised. It's imperative that an adequate sample is obtained to optimize detection of the microorganism(s). (See Table 1 below.)

Table 1. Blood Volume for Culture by Body Weight

Weight in kg	Optimal total blood volume (ml) [‡]	Volume of blood per bottle (ml)	Number and type of bottles NOTE: Priority should be given to the aerobic blood culture.
≤3	2	1	1 pediatric aerobic blood culture order (central) 1 pediatric aerobic blood culture order (peripheral)
>3-5	3	1.5	1 pediatric aerobic blood culture order (central) 1 pediatric aerobic blood culture order (peripheral)
>5-7	5	2.5	1 pediatric aerobic blood culture order (central) 1 pediatric aerobic blood culture order (peripheral)
>7-12	10	5	1 pediatric aerobic blood culture order (central) 1 pediatric aerobic blood culture order (peripheral)
>12-20	15	5	1 adult blood culture order [^] (central) 1 pediatric aerobic blood culture order (peripheral)
>20-30	30	10	1 adult blood culture order [^] (central) 1 pediatric aerobic blood culture order (peripheral)
>30-45	40	10	1 adult blood culture order [^] (central) 1 adult blood culture order [^] (peripheral)
>45	60	10	2 adult blood culture orders [^] (central) 1 adult blood culture order [^] (peripheral)

[‡] per a 24 h time period

[^]max blood volume/DAY is 3-4 ml/kg of body weight (or 3.8% of total blood volume) ⁽¹⁰⁾

[^]1 adult blood culture order includes, one aerobic bottle and one anaerobic bottle.

NOTE: The volume of blood drawn for culture is the most important variable in detecting bacteremia or fungemia. This observation is based on data published from multiple studies of adults. The recommended volume for an adult blood culture is 20 ml (2 adult bottles - one set) per culture, with a collection of 3 sets per episode.

Critical Points of Evidence*

TCH Evidence-Based Recommendations

Evidence Supports

- Obtain optimal blood volume for blood culture. (11-19) - Strong recommendation, high quality evidence
- In the cases where equal and optimal blood volume has been obtained, time to positivity may provide useful information in detecting whether or not the central line can be preserved. Growth of microbes from a blood sample drawn from a catheter at least 2 h before microbial growth is detected in a blood sample obtained from a peripheral vein best defines CLABSI. (20-26) - Strong recommendation, moderate quality evidence
- An anaerobic bottle should be obtained in addition to the aerobic bottle when volume permits. (18, 27-28) – Strong recommendation, low quality evidence
- Empiric antibiotic therapy should be administered in children with suspected CLABSI. (3,29) - Strong recommendation, moderate quality evidence
- Prompt removal of the central line should be considered when any of the following conditions and/or organisms exist: severe sepsis, suppurative thrombophlebitis, endocarditis, bloodstream infection that continues despite > 72 h of antimicrobial therapy to which the infecting microbes are susceptible, and infections due to *S.aureus*, *P. aeruginosa*, fungi, or mycobacteria, gram-negative bacilli, and enterococci. (3,30-32) - Strong recommendation, moderate quality evidence
- Priority should be given to obtaining the optimal amount of blood. Blood cultures should not be routinely obtained from multiple lumens if blood volume will be significantly impacted. (20, 33-36) - Weak recommendation, low quality evidence.
- Time to positivity or quantitative cultures should be utilized for detecting central line associated blood stream infections (CLABSI). (20-26) – Weak recommendation, low quality evidence
- One peripheral blood culture and one central blood culture should be obtained for work-up of suspected late-onset sepsis in infants with an indwelling central venous catheter. (20,33,37-41) – Strong recommendation, low quality evidence

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

General: Antibiotic therapy for suspected CLABSI should be initiated promptly after appropriate blood cultures are obtained. Blood cultures of optimal volume allow for better detection of pathogens causing CLABSI and, therefore, ensure optimal treatment of infection. The initial choice of antimicrobial therapy depends on the severity of the patient's illness, risk factors for infection including degree of immunosuppression and likely pathogens causing infection.

Treatment Recommendations:

Empiric Therapy (3,29)

- Vancomycin is recommended for empiric therapy due to the increased prevalence of methicillin-resistant staphylococci in our community.
- Empirical coverage for gram-negative bacilli should be based on the drug susceptibility history of child, local antimicrobial susceptibility data and the severity of disease
 - In chronically hospitalized patients who are not severely ill, and in whom repeated exposure to third-generation cephalosporins or broad-spectrum antibiotic therapy is not desirable, initial treatment with an aminoglycoside, such as gentamicin, is reasonable.
 - Patients who are severely ill or immune compromised cared for outside of the Newborn Center should receive empirical therapy with a third- (e.g., cefotaxime or ceftazidime) or fourth-generation (e.g., cefepime[§]) cephalosporin or a beta-lactam/beta-lactamase combination (e.g., piperacillin-tazobactam). Once culture and susceptibility data are available, de-escalation of antibiotic therapy can be performed, if feasible. [§]Cefepime is only available for non-neonatal patients treated at the Pavilion for Women.

- Empirical therapy for suspected catheter-related candidemia should be used for patients with neutropenia and fever lasting > 5 days. ([Fever and Neutropenia Guideline](#))
 - Risk factors for candidemia include:
 - total parental nutrition
 - prolonged use of broad-spectrum antibiotics
 - hematologic malignancy
 - receipt of bone marrow or solid organ transplant
 - femoral catheterization
 - colonization due to *Candida* species at multiple sites

Preserving/Removing the Central Line (3,30-32)

The benefits of catheter removal must be weighed against the difficulty of obtaining alternate venous access for each individual patient.

Prompt removal of the central line should be considered when any of the following conditions and/or organisms exists:

- Severe sepsis
- Endocarditis
- Bloodstream infection that continues despite > 72 h of antimicrobial therapy to which the infecting microbes are susceptible
- Infections due to *S. aureus*, gram-negative bacilli including *P. aeruginosa*, *Bacillus* species, and/or enterococci

Prompt removal of the catheter is necessary in cases of:

- Infections due to mycobacteria and/or fungi
- Tunnel site infection (e.g., redness, inflammation along catheter line, purulent drainage)
- Suppurative thrombophlebitis

Admission Criteria

- Children who are otherwise healthy with a central line and fever.
- Ill-appearing children with short gut who have a central line and fever should be admitted on antibiotics.

For ill-appearing children with hematology/oncology conditions, refer to [Fever and Neutropenia Guideline](#).

Children with septic shock should be admitted to an intensive care unit. Children with suspected central line-associated bacteremia should be admitted to the area that can best address their medical needs given their physiologic status at the time of admission.

Measures

Process

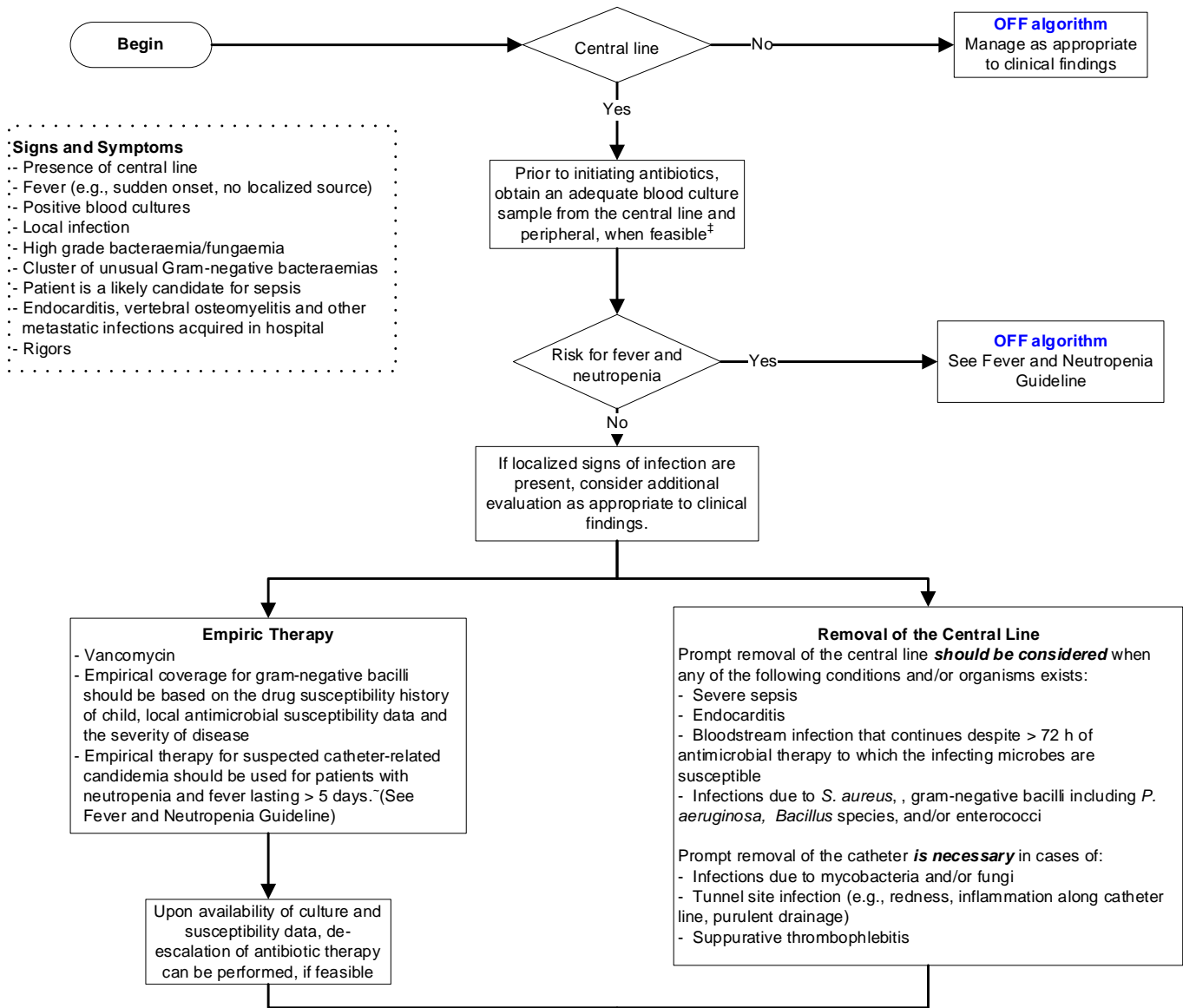
- Utilization of the order set(s)
- Rate of contamination
- Rate of optimal blood volume obtained
- Rate of optimal blood volume obtained prior to initiation of antibiotics
- Rate of paired cultures (central and peripheral)

Outcome

- Length of stay
- Mortality rate
- Rate of admissions
- Time to positivity
- Rate of central line removals after CLABSI diagnosis

TCH Evidence-Based Outcomes Center

Clinical Algorithm for Diagnosis and Initial Management of Suspected Central Line Associated Bloodstream Infections (CLABSI)



- Signs and Symptoms**
- Presence of central line
 - Fever (e.g., sudden onset, no localized source)
 - Positive blood cultures
 - Local infection
 - High grade bacteraemia/fungaemia
 - Cluster of unusual Gram-negative bacteraemias
 - Patient is a likely candidate for sepsis
 - Endocarditis, vertebral osteomyelitis and other metastatic infections acquired in hospital
 - Rigors

Empiric Therapy

- Vancomycin
- Empirical coverage for gram-negative bacilli should be based on the drug susceptibility history of child, local antimicrobial susceptibility data and the severity of disease
- Empirical therapy for suspected catheter-related candidemia should be used for patients with neutropenia and fever lasting > 5 days. (See Fever and Neutropenia Guideline)

Removal of the Central Line

Prompt removal of the central line **should be considered** when any of the following conditions and/or organisms exists:

- Severe sepsis
- Endocarditis
- Bloodstream infection that continues despite > 72 h of antimicrobial therapy to which the infecting microbes are susceptible
- Infections due to *S. aureus*, gram-negative bacilli including *P. aeruginosa*, *Bacillus* species, and/or enterococci

Prompt removal of the catheter **is necessary** in cases of:

- Infections due to mycobacteria and/or fungi
- Tunnel site infection (e.g., redness, inflammation along catheter line, purulent drainage)
- Suppurative thrombophlebitis

Upon availability of culture and susceptibility data, de-escalation of antibiotic therapy can be performed, if feasible

Manage as appropriate to clinical findings

- Risk factors for candidemia include:**
- total parental nutrition
 - prolonged use of broad-spectrum antibiotics
 - hematologic malignancy
 - receipt of bone marrow or solid organ transplant
 - femoral catheterization
 - colonization due to *Candida* species at multiple sites

Weight in kg	Optimal total blood volume (ml) [†]	Volume of blood per bottle (ml)	Number and type of bottles NOTE: Priority should be given to the aerobic blood culture.
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> 7-12	10	5	1 pediatric aerobic blood culture order (central) 1 pediatric aerobic blood culture order (peripheral)
> 12-20	15	5	1 adult blood culture order [‡] (central) 1 pediatric aerobic blood culture order (peripheral)
> 20-30	30	10	1 adult blood culture order [‡] (central) 1 pediatric aerobic blood culture order (peripheral)
> 30-45	40	10	1 adult blood culture order [‡] (central) 1 adult blood culture order [‡] (peripheral)
> 45	60	10	2 adult blood culture orders [‡] (central) 1 adult blood culture order [‡] (peripheral)

[†] per a 24 h time period
[‡] max blood volume/DAY is 3-4 ml/kg of body weight (or 3.8% of total blood volume) ⁽¹⁸⁾
[§] 1 adult blood culture order includes, one aerobic bottle and one anaerobic bottle.
 NOTE: The volume of blood drawn for culture is the most important variable in detecting bacteremia or fungemia. This observation is based on data published from multiple studies of adults. The recommended volume for an adult blood culture is 20 ml (2 adult bottles - one set) per culture, with a collection of 3 sets per episode.

Clinical standards are developed for 80% of the patient population with a particular disease. Each practitioner must use his/her clinical judgment in the management of any specific patient.

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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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EBOC Team

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
 - PICO questions established
 - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
 - Infectious Disease Society of America (IDSA), Clinical Practice Guideline for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Disease Society of America, 2009; Seattle Children's Hospital, Diagnosis and Management of Central Line Associated Bloodstream Infections v.2.0, 2015; American Academy of Pediatrics, Report of the Committee of Infectious Diseases, 2015
3. Literature Review of Relevant Evidence
 - Searched: PubMed, Cochrane Database of Systematic Reviews, SumSearch, TripDatabase, Google Scholar, Infectious Disease Society of America (IDSA), AHRQ National Guideline Clearing House
4. Critically Analyze the Evidence
 - 5 meta-analyses and 26 nonrandomized studies

5. Summarize the Evidence

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- Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Diagnosis and Management of Suspected Central Line-Associated Bloodstream Infections (CLABSI) evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions. **"Evidence Supports"** provides evidence to support an intervention. **"Evidence Against"** provides evidence against an intervention. **"Evidence Lacking/Inconclusive"** indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence*.

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	Type of Evidence
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis and management of suspected central line-associated bloodstream infections in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner should use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

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Version History

Date	Comments
Jan 2013	Originally Completed
July 2021	Reaffirmed; PICO Question 1 and 4 archived