## Inpatient Diagnosis and Treatment of Central Vascular Catheter (CVC) Infections

### Patient population and scope:
This guideline applies to the management of central vascular catheters (CVC) once infection is suspected, in patients of all ages. CVC infections include central line-associated bloodstream infections (CLABSI), but also include infections that do not meet the CLABSI definition (see definitions, page 2). If additional clinical processes are being considered, other treatment guidelines may supersede this guideline (e.g. if a patient presents with fever and neutropenia, please refer to Fever and Neutropenia treatment guidelines).

### Excluded from the scope of the guideline:
- Extracorporeal membrane oxygenation (ECMO) catheters
- Umbilical catheters
- Peripheral catheters, such as midline catheters, peripheral venous or peripheral arterial catheters
- Prevention of central catheter infections (Instead, see Infection Control policy on prevention
  [http://www.med.umich.edu/iice/policies/pdfs/central_lines/central_line_policy.pdf](http://www.med.umich.edu/iice/policies/pdfs/central_lines/central_line_policy.pdf)).

(Note --Michigan Medicine internal access only)

### Objectives:
To improve appropriate early antimicrobial treatment of bloodstream infections, standardize management of CVC infections, and improve patient outcomes associated with CVC infections.

### Key points:
**Diagnosis (Figure 1)**
- In any patient with a CVC and clinical suspicion for line infection, blood cultures should be drawn. Do **not** draw blood cultures routinely via a CVC, unless CVC infection is suspected. [IA]
- Blood cultures should be obtained prior to the initiation of antibiotics, **unless** the patient is unstable or critically ill (necessitating immediate initiation of antimicrobials, regardless of whether blood cultures have been obtained). [IB]
  - When infection is suspected, at least 2 sets of cultures should be drawn (aerobic & anaerobic). [IB]
  - Blood cultures should be drawn from peripheral site and the central line if catheter infection is suspected [IB]. Blood cultures should not be drawn from central catheters routinely. [IIID]

**Treatment**
- Empiric treatment should be initiated after blood cultures are obtained (Figure 2). [IC]
- Definitive antimicrobial therapy should be tailored to the organism identified and the susceptibilities of that organism (Table 1). [IC]
- The preferred management of confirmed CVC infection includes removal of the central vascular catheter in most cases. [ID]
- There are different considerations for short-term and non-tunneled hemodialysis CVC (Figure 3), long-term CVC (Figure 4), and tunneled hemodialysis CVC (Figure 5). [IC]
- Unless there is an urgent need for central vascular access, new central vascular catheter placement should be delayed until after 48 hours after the first negative blood cultures when treating any bacteremia, including CVC-related bacteremia. [IC]
- CVC removal and Infectious Disease consultation is recommended for any of the following situations related to CVC infections: cultures positive for *S. aureus* or *Candida* species; persistent bacteremia with any organism after 72 hours of appropriate antimicrobial therapy; persistence of septic shock; presence of an intravascular prosthetic device (e.g., mechanical valve, pacemaker, or AICD); or development of any complication (e.g., endocarditis, osteomyelitis, suppurrative thrombophlebitis, or others). [IC]

*Strength of recommendation:
I = generally should be performed; II = may be reasonable to perform; III = generally should not be performed.

### Levels of evidence for the most significant recommendations
- A = systematic reviews of randomized controlled trials;
- B = randomized controlled trials;
- C = systematic review of non-randomized controlled trials or observational studies;
- D = individual observation studies (case or case series);
- E = opinion of expert panel.
Definitions

Device Definitions

Central vascular catheter: A catheter placed within a vein or artery whose distal end is intended to be located within a central vein or artery, usually the vena cava (inferior or superior). This includes peripherally inserted central catheters, tunneled and non-tunneled central venous catheters, central and pulmonary arterial catheters, and subcutaneous ports or reservoirs.

Short-term central vascular catheter: Central catheter placed into a central vein or artery without tunneling or cuffs, including non-tunneled hemodialysis catheters. These are generally intended for short-term use (less than 30 days). These include catheters placed at the subclavian, internal jugular or femoral sites, as well as peripherally inserted central catheters.

Peripherally inserted central catheter: Catheter inserted into a peripheral vein (usually basilic or cephalic), with distal tip ending in a central vein, usually the superior vena cava.

Long-term central catheter: Surgically implanted central catheter with a tunneled portion under the skin and a cuff just inside the exit site. These catheters are intended for use longer than 30 days and include Pro-Line®, Powerline®, Hickman®, Broviac® and Groshong® catheters. Tunneled hemodialysis catheters are long-term catheters, but are discussed separately for the purposes of this guideline.

Hemodialysis catheter: A central venous catheter, either non-tunneled or tunneled, temporary or permanent, which is used to dialyze the blood.

Port: Implantable subcutaneous port or reservoir for self-sealing septum tunneled beneath the skin and accessed by a needle through the skin. These are intended for long-term use and managed similarly to long-term catheters.

Infection definitions

Exit site infection: Infection, as indicated by exudate, erythema, induration and/or tenderness, at the catheter exit site.

Tunnel infection: Infection, as indicated by erythema, induration, and/or tenderness, >2cm proximal to the catheter exit site, or anywhere along the tract of the tunneled catheter.

Pocket infection: Infection in the subcutaneous pocket of an implanted port site; usually associated with tenderness, erythema, and/or swelling over the pocket/port area.

Complicated infection: An infection is considered complicated if: clinical symptoms or bacteremia persist despite 72 hours of appropriate antimicrobial therapy, persistence of sepsis syndrome, intravascular hardware is in place (e.g., mechanical valve, pacemaker, or AICD); or sites of metastatic disease are present (such as endocarditis, osteomyelitis, or suppurative thrombophlebitis).

Severe sepsis: Life-threatening organ dysfunction caused by a dysregulated host response to infection. Suspected or documented infection and an acute increase of ≥ 2 SOFA points; for more pediatric specific criteria please refer to the Pediatric Sepsis Consensus statement.

Central Vascular Catheter Infection. Primary bloodstream infection in a patient with a central line, without another infectious source. This includes all CLABSI, plus CVC infections not meeting strict CDC definition of CLABSI.

Central line-associated bloodstream infection (CLABSI): Primary bloodstream infection in a patient with a central line, without another infectious source. This is a surveillance definition outlined by the National Healthcare Safety Network (NHSN) at the Centers for Disease Control and Prevention (CDC). CLABSI does not always correlate with clinical infection.
Figure 1. Approach to Diagnosis of Central Vascular Catheter Infections

Suspected CVC Infection
(See Box 1)

Obtain at least 2 sets of blood cultures
(set = aerobic & anaerobic)

Initiate empiric treatment
(See Figure 2)

Blood Culture

Common skin contaminant?
(Box 2)

Yes

Multiple cultures positive?

No

Positive

Yes

- Look for other source of infection
- Stop antibiotics or direct antibiotics at other infection

Treat per Table 1, Figures 2 – 5

Box 1: Clinical features increasing suspicion for central catheter infection. (See Appendix A for definitions of vital signs.)

Any one of the following, in the absence of signs/symptoms of another source of infection:
- Fever (Hyper/Hypothermia
  - Children - Adults: >38.3 C / <36.0 C
  - Infants < 3months: >38.0 C (rectal) / <36.0 C
- Hypotension
- Tachycardia
- Altered perfusion (capillary refill > 2 seconds)
- Vomiting
- Altered mental status
- Chills
- Erythema, tenderness, or purulent discharge at/near the central line site
- CVC malfunction, with another sign of infection as above

Box 2: Common Skin Contaminants*

- Aerococcus species
- Bacillus species
- Coagulase-negative staphylococci
- Diphtheroids
- Micrococcus species
- Propionibacteria
- Viridans group streptococci

*Note: a single positive culture can be a true pathogen in certain populations including: pediatrics, immune compromised patients, and potentially in those where only one blood culture was able to be obtained
Figure 2. Empiric Antimicrobial Therapy for CVC Infections

For dosing recommendations for pediatric and adults patients at Michigan Medicine, see http://ummcpharmweb.med.umich.edu/i/GuidelinesForms/AntimicrobialUseGuidelines/tabid/303/Default.aspx (Note – Michigan Medicine internal access only)

Suspected CVC infection
(See Fig 1, Box 1)
Blood cultures drawn

Box 2. When to use empiric Gram-negative coverage

- Severe sepsis
- Neutropenia
- Hemodialysis CVC present
- Solid organ transplant
- Short gut syndrome
- Femoral CVC present

Risk for Gram-negative infection (Box 3)?

No

Begin vancomycin

Yes

Begin vancomycin + piperacillin / tazobactam or vancomycin + cefepime

Blood positive for Gram negative?

No

Continue vancomycin

Yes

Add piperacillin / tazobactam or cefepime

Risk for candidemia (Box 4)

No

Yes

Begin micafungin

Box 4. When to consider empiric Candida treatment

High risk patients are defined as those in the ICU with:

EITHER
- Recent abdominal surgery with recurrent gastrointestinal perforations/anastomotic leaks (tertiary peritonitis)

OR
- Having 2 or more of the following: in the ICU ≥ 3 days, ventilated, receiving broad spectrum antibiotics, have a central line and have 1 of these additional risk factors: parenteral nutrition, dialysis, major surgery, pancreatitis, receiving steroids or other immunosuppressive agents.

In high risk patients, a Beta-D-Glucan assay should be performed prior to or with the initiation of empiric antifungal therapy.
Figure 3. Catheter Management for Infected Short-term CVCs and Non-Tunneled Hemodialysis CVCs

Infection in short-term catheter or non-tunneled hemodialysis catheter
(See Figure 1, Box 1)

Complicated?  
Complicated  
Remove catheter  
Treat underlying infection  
Consult Infectious Diseases  

Uncomplicated

Complicated Short-term CVC Infections:
- Bacteremia after 72 hr. of appropriate treatment
- Persistence of sepsis syndrome
- Suppurative thrombophlebitis
- Endocarditis
- Osteomyelitis
- Intravascular hardware in place

Coagulase negative staphylococci

Organism

Staphylococcus aureus  
Candida sp.

Enterococcus  
Gram negative bacilli

Either:
- Remove catheter and treat per Table 1  
- or
- Treat with systemic antibiotics (per Table 1), and lock therapy*

Remove catheter and treat per Table 1  
Consult Infectious Diseases

*Recommendations for Antibiotic Lock Treatment of Infected Central Venous Catheters/Ports at Michigan Medicine can be found at: https://pharmwebsp.med.umich.edu/AC/SitePages/Antimicrobial%20Use%20GuideLines.aspx
Figure 4. Catheter Management for Infected Long-term CVC

Complicated long-term CVC Infections:
- Tunnel infection except with coagulase-negative staphylococci
- Bacteremia after 72 hr. of appropriate treatment
- Persistence of sepsis syndrome
- Suppurative thrombophlebitis
- Endocarditis
- Osteomyelitis
- Intravascular hardware in place

Infection in long-term catheter
(See Figure 1)

Complicated? Uncomplicated

Complicated?

Coagulase negative staphylococci

Organism

Staphylococcus aureus Candida sp.

Enterococcus

Gram negative bacilli

Tunnel infection?

Yes

Line salvage needed?

Yes

No

Treat with systemic antibiotics (per table 1), and lock therapy*

Remove catheter and treat per Table 1

If clinical deterioration, relapsing or persistent infection, remove catheter

Remove catheter and treat per Table 1

Consult Infectious Diseases

Remove catheter and treat per Table 1

Consult Infectious Diseases

*Recommendations for Antibiotic Lock Treatment of Infected Central Venous Catheters/Ports at Michigan Medicine can be found at: https://pharmwebsp.med.umich.edu/AC/SitePages/Antimicrobial%20Use%20GuideLines.aspx
Figure 5. Catheter Management for Tunneled Hemodialysis CVC

- For extenuating circumstances that make removal not clinically feasible, see text for discussion of salvage.
- Recommendations for antibiotic lock treatment of infected central venous catheters/ports at Michigan Medicine can be found at: https://pharmwebsp.med.umich.edu/AC/SitePages/Antimicrobial%20Use%20GuideLines.aspx
### Table 1. Definitive Treatment of Uncomplicated CVC Infection

<table>
<thead>
<tr>
<th>Organism</th>
<th>Definitive Therapy*</th>
<th>Antibiotic Duration for Infections**</th>
<th>Short-term CVC</th>
<th>Long-term CVC</th>
</tr>
</thead>
</table>
| Coagulase-negative staphylococci | ● vancomycin  
● If sensitive to methicillin, then can use cefazolin or nafcillin              | 5-7 days, if catheter removed  
10-14 days, if catheter retained   |                |               |
| Enterococcus              | ● If VSE – vancomycin; ampicillin if sensitive  
● If VRE – linezolid or daptomycin; ampicillin if sensitive                      | 7-14 days^                            |                |               |
| S. aureus                 | ● Consult Infectious Diseases  
● If MSSA—cefazolin or nafcillin  
● If MRSA—vancomycin               | At least 14 days                      |                |               |
| Gram negative             | Dependent upon species and sensitivities                                            | 7-14 days^                            |                |               |
| Candida                   | ● Consult Infectious Diseases  
● micafungin, then switch to fluconazole if susceptible strain                  | 14 days                               |                |               |

*Allergy Alternatives:

<table>
<thead>
<tr>
<th>Agent causing allergy</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>vancomycin</td>
<td>linezolid or daptomycin</td>
</tr>
<tr>
<td>Penicillins <strong>without</strong> anaphylaxis, angioedema, or urticarial</td>
<td>Cefazolin for MSSA; vancomycin for Enterococcus</td>
</tr>
<tr>
<td>Penicillins <strong>severe</strong> allergy; cephalosporin; ampicillin allergy in the setting of VSE</td>
<td>vancomycin</td>
</tr>
<tr>
<td>Other allergy concerns</td>
<td>Consider consulting Infectious Diseases</td>
</tr>
</tbody>
</table>

** Repeat blood cultures until clearance documented; Antibiotic Duration: day 1 = date of first negative blood culture  
^Seven day treatment preferred for patients with good clinical response after removal of catheter.
Clinical Background

Background and Epidemiology

More than 150 million intravascular devices are used in healthcare settings in the United States every year. Of these devices, central vascular catheters (CVC) significantly increase the risk of healthcare-associated bloodstream infection. The Center for Disease Control and Prevention (CDC) estimated that, in 2009, 18,000 central catheter-associated bloodstream infections (also called central line-associated bloodstream infection [CLABSIs]) occurred in intensive care units in the United States. Another 23,000 CLABSI occurred among patients in inpatient wards and 37,000 CLABSI occurred in patients undergoing outpatient hemodialysis.

CVC infections have a significant impact on patient morbidity, mortality and costs associated with medical care. In a recent analysis, CVC infections were found to be the most costly healthcare-associated infection at $45,814 per infection. CVC infections are also one of the most deadly healthcare-associated infections, with a mortality rate of 12-15%. Implementation of CVC infection management guidelines is intended to improve appropriate early antimicrobial treatment of bloodstream infections, standardize infected CVC management, and improve patient outcomes.

Microbiological Etiology

Microorganisms associated with CLABSIs are introduced into the bloodstream from the skin at the catheter insertion site or from the hub of the catheter. Not surprisingly, the most common organisms associated with CLABSIs are: coagulase-negative staphylococcus (20.5%); Staphylococcus aureus (12.3%); Enterococcus faecalis (8.8%); Candida species (8.8%); followed by various gram-negative bacilli. Of note, in U.S. hospitals, over 50% of S. aureus and over 80% of coagulase-negative staphylococci in CLABSI exhibit methicillin resistance. Of the gram-negative organisms, Pseudomonas aeruginosa is associated with 3.8% of CLABSI; extended-spectrum beta-lactamase producing or carbapenem-resistant Enterobacteriaceae are prevalent in some geographic areas. Therefore, it is essential to incorporate the local epidemiology of microorganisms and their resistance patterns into guidelines for empiric treatment of CVC infections.

Clinical Presentation

Clinical suspicion and investigation for CVC infection should occur in the following conditions (Figure 1, Box 1):

1) In any age patient with a CVC and altered temperature (i.e. fever or hypothermia), where there are no other signs or symptoms of another source of infection. Temperature definitions of fever/hypothermia vary but traditionally fever is defined as > 38.3°C in children and adults, > 38.0°C in infants < 3 months of age, and hypothermia is defined as < 36°C.

2) In any age patient with a CVC and any one or more of the following (with or without alteration in body temperature), when there are no other signs or symptoms of another source of infection or explanation of alternative cause:
   - Hypotension (Adult SBP < 90mmHg or SBP decrease > 40 mmHg or < 2 SD below mean) (Infants/children SBP defined by age and < 2 SD below mean [see Appendix A])
   - Tachycardia (defined by age, range > 2 SD above mean [see Appendix A])
   - Altered perfusion (mottling, cool extremities, capillary refill > 2 sec)
   - Tachypnea (defined by age, range > 2 SD above mean [see Appendix A])
   - Altered mental status (ranging from severe lethargy to irritability)

3) In any age patient with a CVC and abnormal skin findings (erythema, pain or discharge) around the CVC exit site.

4) In any patient with a compromised CVC device requiring repair (i.e. broken or leaking line, hub, caps) and any criteria in 1 or 2 above.

5) Patient populations with high-risk conditions, combined with any of the above criteria. High-risk conditions include leukopenia/neutropenia, malignancy, asplenia, steroid dependence, immune-compromise/deficiency/suppression, organ or bone marrow transplantation, and post-transplant lymphoproliferative disease (PTLD).

Diagnostic Procedures and Considerations

Obtaining Blood Cultures

Blood cultures should be drawn in any patient with a CVC and clinical suspicion for a CVC infection. (See Figure 1, Box 1). A blood culture "set" includes 2 bottles, 1 aerobic and 1 anaerobic. A blood culture "site" refers to the location from which the culture is drawn.

Cultures should not be drawn from CVC for surveillance purposes alone [III-D]. If a patient has no clinical signs or symptoms of infection, blood cultures are of little utility and may increase the risk of inappropriate treatment of blood culture contaminants.

As antibiotic administration significantly decreases the sensitivity of blood cultures, blood cultures should be obtained prior to the initiation of antibiotics, unless the patient is unstable or critically ill, in which case antimicrobials should be initiated immediately, regardless of whether blood cultures have been obtained.

In adults with suspected CVC infection, at least 2 sets of cultures should be drawn. Blood cultures drawn from a catheter have higher risk of contamination, but may be more sensitive for catheter infection. Cultures should be drawn from a catheter only when there is suspicion of catheter infection and no other source of infection identified (Figure 1, Box 1). While it is also ideal to obtain 2 sets of blood
cultures in pediatric patients, patient size and blood volume needed may limit the feasibility of doing so. Additionally, for pediatric patients, patient comfort may potentiate the need for blood cultures to be drawn from the catheter, as peripheral draws are more often avoided in this patient population to limit the number of peripheral sticks.

If cultures are drawn from a catheter, it is preferable to draw one set of blood cultures from each lumen of a multi-lumen catheter. In a retrospective study of patients with proven CLABSI in which all lumens of a multi-lumen CVC had been cultured, analysis showed that the false negative rate would have been 16-38% if one or more lumen had not been cultured.

For patient with bacteraemia and CVC, it is standard to repeat serial blood cultures (e.g. daily) until clearance of the bacteremia is demonstrated (blood cultures are negative at 48 hours).

**Differential Time to Positivity (DTTP)**
Differential Time to Positivity (DTTP) of peripheral and CVC drawn cultures best predicts CLABSI and may be useful in some settings. DTTP uses continuous blood culture monitoring. The growth of microbes from a sample drawn from a catheter hub at least 2 hours before growth of the same microbes from a peripheral site is consistent with CLABSI.

**Catheter Tip Cultures**
Catheter tip cultures should be obtained in any CVC removed due to suspicion for, but not prior confirmation of, CVC infection. If CVC infection has been diagnosed by positive blood cultures, culture of the catheter tip has not been shown to alter clinical management. If CVC infection is suspected, but not yet confirmed, a central vascular catheter tip culture may aid in diagnosis. Growth of >15 cfu/plate from a 5 cm segment of catheter tip using the roll-plate technique is suggestive of infection. At Michigan Medicine labs, growth of >15 cfu/plate is reported as “moderate” or “numerous.” In a patient without signs or symptoms of infection, routine catheter tip culture upon removal of a catheter is not recommended as positive cultures most likely indicate colonization rather than true infection.

**Diagnosis of CVC Infection (Figure 1)**
A CVC infection is considered definitive when two blood samples, one from the lumen of the CVC and one from a peripheral site, grow the same organism. Alternatively, if a peripheral blood culture cannot be obtained, then a CVC infection is defined as blood cultures from two or more lumens of a CVC growing the same organism. A CVC infection is presumed when a CVC is in place and there is at least one positive blood culture growing a pathogen from any site, in the setting of clinical signs of infection with no other apparent source for that infection.

The possibility of culture contamination should be considered when determining a treatment course. A single blood culture from any site growing a common skin contaminant likely represents a contaminated blood culture (Figure 1, Box 2).

If an initial single positive blood culture grows coagulase-negative staphylococci, or other common skin contaminants, in a patient with clinical findings of infection, then additional blood cultures from the CVC and peripheral site should be obtained to help rule out contamination.

Occasionally, blood cultures positive with skin flora can represent true infection. In the setting of multiple positive blood cultures from different sites, growing the same organism, one should consider the likelihood of a true infection even if the organism is otherwise considered a commensal organism (common skin contaminant). For example, if a blood culture from the catheter and peripheral site both grow coagulase-negative staphylococci, in the setting of clinical symptoms consistent with a potential CVC infection, the treatment for an infection is warranted. Caution should be used when treating pediatric patients (especially the neonatal population) when clinical reasons do not allow for multiple blood cultures to be obtained prior to the initiation of antibiotics; coagulase-negative staphylococcus is a frequent cause of CVC infection in pediatric patients and a single positive culture may represent a true infection. Additionally, in immunocompromised patients, a single positive blood culture with an organism considered to be skin flora can represent true infection.

**Treatment**

**Empiric Antimicrobial Treatment (Figure 2)**
If a patient exhibits signs and/or symptoms concerning for a CVC infection (see Figure 1, Box 1) and blood cultures have been obtained, then empiric antimicrobial therapy should be initiated pending culture results. Empiric therapy should be dependent upon clinical scenario and local epidemiology.

Many CVC infections are caused by Gram-positive organisms, therefore empiric coverage for Gram-positive organisms should be started after cultures are obtained. Given the prevalence of methicillin-resistant _S. aureus_ in the Michigan Medicine, empiric coverage for Gram-positive organisms should be vancomycin. If the patient has a vancomycin allergy or intolerance, alternative agents should be discussed between the clinical care team and the Antimicrobial Stewardship Team.

Given local epidemiology, empiric coverage for Gram-negative organisms should also be added pending culture results if the patient: shows evidence of septic shock, has a hemodialysis catheter, is neutropenic, has a femoral CVC, has a history of short gut syndrome, or history of a solid organ transplant. Gram-negative coverage can be achieved with a beta-lactam/beta-lactamase combination (such as piperacillin/ tazobactam) or a 4th generation cephalosporin (such as cefepime). In patients with severe sepsis or a history of multi-drug resistant Gram-negative organisms, a second Gram-negative agent should be added to provide expanded coverage in the setting of...
potentially resistant organisms. This broadened coverage can be achieved by adding an aminoglycoside or a fluoroquinolone (fluoroquinolone less preferred) to the piperillin/ tazobactam or cefepime.20–22

Empiric antifungal therapy should be added in patients with unexplained fever or other signs of infection and who are at high risk for invasive candidiasis (Figure 2, Box 4).

When considering empiric antifungal treatment of CVC infection, “high risk” patients in the ICU with a central line are defined as those with:

EITHER
Recent abdominal surgery with recurrent gastrointestinal perforations/anastomotic leaks (tertiary peritonitis)

OR
Having 2 or more of the following: in the ICU ≥ 3 days, ventilated, receiving broad spectrum antibiotics, have a central line and have 1 of these additional risk factors: parenteral nutrition, dialysis, major surgery, pancreatitis, receiving steroids or other immunosuppressive agents.

In such adult patients, a Beta-D-Glucan (BDG) assay should be performed prior to or with the initiation of empiric antifungal therapy. BDG can be found in the cell wall of certain microorganisms, such as Candida. Discontinuation of empirical antifungal therapy is strongly encouraged in adult patients with BDG values that are negative (< 80 pg/mL). If the initial BDG value is >80 pg/mL, a repeat test is recommended as 2 consecutive serum BDG >80 pg/mL are suggestive of invasive candidiasis in high-risk adult patients. However, positive results should not be utilized as the sole evidence for continuation of antifungal therapy, given the poor positive-predictive value of the test. Of note, BDG values have not been well established in pediatric patients and it is not currently recommended that this test be used for clinical management.23

Infectious Diseases should be consulted when two positive BDG results are obtained and/or if continuation of empiric therapy is desired in the absence of positive cultures. Given local epidemiology at Michigan Medicine, in a critically ill patient, first-line treatment choice is an echinocandin. In some clinical scenarios, such as pediatric patients, an azole may be considered instead.24–27

Treatment Based on Microorganism
Definitive antimicrobial therapy should be tailored to the organism identified and the susceptibilities of that organism. Antimicrobial treatment and duration will be determined based on catheter type and organisms identified in cultures (See Table 1). Note that when S. aureus or Candida sp. is the causative pathogen of a CVC infection, consultation with infectious diseases is recommended.

Antibiotic Lock Therapy
Antibiotic lock treatment may be considered for treatment of infected catheters with no signs of exit site or tunnel infection for which catheter salvage is the goal (Figures 3-5). For patients with multiple positive catheter-drawn blood cultures that grow coagulase-negative staphylococci and concurrent negative peripheral blood cultures, antibiotic lock therapy can be given without systemic therapy for 10–14 days. For all other situations, antibiotic locks should not be used alone and should be used in conjunction with systemic antimicrobial therapy, both administered for 7–14 days.

Catheter removal is recommended for CLABSI due to S. aureus and Candida species, instead of treatment with antibiotic lock and catheter retention, unless there are unusual extenuating circumstances (See Removal vs Salvage below).28,29

In scenarios where the catheter is retained, it is often difficult to clear the infection with systemic antimicrobial treatment alone, due to the likely development of an intraluminal biofilm, resulting in high recurrence rates. By instilling a high concentration of antibiotic into the intraluminal space and allowing the antibiotic to dwell for an extended period of time, the rate of successful infection clearance is increased. The antibiotic selected for lock therapy should be comparable to the systemic antibiotic chosen, providing adequate coverage for the organism causing infection.

For directions for antibiotic locks treatment of CVC infections at Michigan Medicine, see institutional guidelines (https://pharmwebsp.med.umich.edu/AC/SitePages/Antimicrobial%20Use%20Guidelines.aspx). Infectious Disease consult should be considered. Use of antibiotic locks in the treatment of CVC infections in pediatric patients should be guided by the Pediatric Infectious Diseases Consult Service. At this time, there are insufficient data to recommend ethanol locks for the treatment of CVC infections.

Removal versus Salvage of Infected CVC
The preferred management of a confirmed CVC infection includes removal of the central vascular catheter in most cases (Figures 3–5). However, there are some circumstances in which the removal of the infected catheter may not be possible. These are usually circumstances in which either (a) replacing the CVC in another location is not possible (e.g. multiple areas of thrombosis or stenosis or the patient is pediatric with limited access opportunities) or (b) removing the catheter carries prohibitive risk and the benefits of salvage may outweigh the risks of removal.

In cases where removal is not possible, the CVC may be left in place during initial antibiotic treatment. In such cases, the clinician must carefully evaluate the risks and benefits of alternative treatments on an individual basis and with the benefit of additional expert guidance. Published literature on attempted salvage of an infected CVC is limited to case series and definitive recommendations are not possible. However, when S. aureus, P. aeruginosa, fungus or mycobacteria are present, rates of treatment failure with
catheters left in place are high, and in those catheters that fail salvage there is a high incidence of complications stemming from the infection.

If a CVC infection is treated without CVC removal, then the following steps are recommended:

1) Document (in medical record) the risk of removing the infected CVC and the rationale for leaving it in place. This will permit tracking of outcomes. Also document that the risks and benefits were discussed with patient and/or family.

2) Review the appropriateness of antibiotic lock therapy (see above).

3) Reevaluate the need for CVC removal on a daily basis, at a minimum. CVC removal should strongly be considered in the presence of persistently positive blood cultures after 72 hours of appropriate antimicrobial therapy, or evidence of endocarditis, persistence of septic shock or development of suppurative thrombophlebitis.

Guidewire exchange may be considered if catheter removal is not feasible, there is no other site for new catheter placement, bacteremia has resolved, and there are no metastatic sites of infection. Data supporting the practice of changing CVCs over a wire are weak. In such cases, the clinician must carefully evaluate the risks and benefits of guidewire exchange on an individual basis and with the benefit of additional expert guidance. Exchanging a CVC over a guidewire should always be accompanied by full antibiotic therapy. The same consideration of risk and benefit of guidewire exchange should also be applied to hemodialysis catheters.

**Consideration for Hemodialysis Catheters**

The management of tunneled dialysis catheter related bacteremia with and without associated tunnel infection is detailed in Figure 5.

In tunneled dialysis catheter-related CVC infection, when tunnel inflammation and/or infection (if present) does not extend to the venotomy, as determined by the nephrology team, a guidewire catheter exchange with the creation of a new tunnel that does not course through the inflamed area is both safe and efficacious. This is most appropriate when the current catheter sits in the most desired location.

**Additional Considerations**

**When to Place a New Central Vascular Catheter after Bloodstream Infection**

Unless there is an urgent need for central vascular access, new CVC placement should be delayed until at least 48 hours after the first negative blood culture when treating a bloodstream infection, including CLABSI. Insertion of a central vascular catheter in the presence of an active bloodstream infection may result in colonization and infection of the new catheter, resulting in relapse of bacteremia after treatment. A recent small study showed that PICCs placed within two days of documented bacteremia had an increased risk of relapse of bacteremia (6.5%) when compared to PICCs placed at least three days after documentation of negative blood culture (0.3%). In clinical scenarios where there is ongoing need for central vascular access, clinicians must weigh the risk/benefit of placing a new CVC in the setting of active bacteremia.

**Complications of a CVC Infection**

In adults, a transthoracic echocardiogram (TTE) to rule out endocarditis should be performed in any patient with CVC infection who has a prosthetic heart valve, pacemaker or ICD, or persistent bacteremia greater than 72 hours after initiation of appropriate antimicrobials and removal of central catheter; in pediatric patients a transthoracic echocardiogram (TTE) is generally sufficient. In addition, a TTE should be performed in any adult patient with *S. aureus* bacteremia, since secondary infections are common and duration of treatment will be significantly impacted (at Michigan Medicine, see institutional guideline). In pediatric patients TTE is recommended for patients with a history of congenital heart disease, bacteremia for greater than 2-3 days, or with any clinical findings concerning for endocarditis. In patients with confirmed or suspected endocarditis, from any organism, treatment for 4-6 weeks with intravenous antibiotics is required to effectively treat infection.

In patients with persistent bacteremia due to a CVC infection, suppurative thrombophlebitis should be considered if neck, chest or upper extremity swelling is present. Diagnosis is confirmed with venous Doppler studies of the upper extremity or computed tomography of the chest. There are few studies to guide duration of the therapy, but generally longer durations of antibiotics are recommended for complicated CVC infections and should be aided by Infectious Diseases consultation. Anticoagulation with heparin should be considered for suppurative thrombophlebitis of a great vessel.

A search for other metastatic foci should be undertaken in any patient with persistent bacteremia (e.g., joint infection, vertebral osteomyelitis, splenic abscess, and secondary infection of prosthetic material should be considered). This is especially true for patients with *S. aureus* bacteremia (see Guideline for Vertebral Osteomyelitis), as *S. aureus* is the most common bacteremia associated with vertebral osteomyelitis. In pediatric patients, particularly in neonates, bacteremia can lead to seeding of the central nervous system and a lumbar puncture may be considered if there is concern for meningitis. A Pediatric Infectious Diseases consultation is recommended in these circumstances.

**When to Consult Infectious Diseases Service**

Several studies have shown that ID consultation for patients with *S. aureus* bacteremia is associated with improved adherence to evidence-based therapies and up to 56% decrease in mortality. ID consultation is recommended for all patients with *S. aureus* bacteremia because of the high
risk for secondary sites of infection, including vertebral osteomyelitis or endocarditis. There are also studies showing improved outcome in patients with candidemia. Therefore, at Michigan Medicine, Infectious Disease consultation is recommended for all patients with *S. aureus* bacteremia or candidemia, including those related to central vascular catheters.

There are no studies to support Infectious Diseases consultation in other CVC infections. However, Infectious Diseases consult should be considered for any patient with a complicated CVC infection (Figures 3-5).

**Related National Guidelines**

While there are a number of guidelines related to prevention of central venous catheters infection, few focus on treatment of infections in inpatient populations. The current guideline is generally consistent with the IDSA guideline:


**Related National Performance Measures**

There are numerous national measures related to the central line infection rates, most notably CMS Hospital Acquired Conditions (HAC), which includes Central Venous Catheter Bloodstream Infection (PSI 07 in the AHRQ PSI 90 Composite measure, which is part of Domain 1), and Central-line Associated Bloodstream Infection (CLABSI) (part of Domain 2). However, this guideline’s scope is the treatment of existing CVC infections, not prevention of new infections. CLABSI rates are included in the Value-Based Purchasing measures.

**Guideline Development Methodology**

**Funding**

The development of this guideline was funded by Michigan Medicine.

**Guideline Development Team and Disclosures**

The multidisciplinary guideline development team consisted of:

- Primary care physicians: Megan R Mack, MD, Internal Medicine, Jennifer L Vredevelt, MD, Pediatric Medicine, David H Wesorick, MD, Internal Medicine.
- Specialists: Carol E Chenoweth, MD, Infectious Diseases, Marcus D Jarboe, MD, Pediatric Surgery, Matthew A Leavitt, MD, Internal Medicine, Michele M Nypaver, MD, Pediatric Emergency Medicine, Pauline K Park, MD, Surgery, Terri L Stillwell, MD, Pediatric Infectious Disease.
- A guideline development methodologist: F. Jacob Seagull, PhD, Learning Health Sciences.
- Literature search services were provided by informationists at the Taubman Health Sciences Library, University of Michigan Medical School.

The Michigan Medicine endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

No relevant personal financial relationships with commercial entities: Carol E Chenoweth, MD, Marcus D Jarboe, MD, Megan Mack, MD, Michele M Nypaver, MD, Pauline K Park, MD, F Jacob Seagull, PhD, Terri L. Stillwell, MD, and Jennifer L Vredevelt, MD, David Wesorick, MD.

Relevant personal financial relationships with commercial entities: Matthew A Leavitt, MD, a consultant for Teleflex Medical.

**Strategy for Literature Search**

Within the Medline (Ovid) database, the following search strategy was used for most of the search topics, except for the searches on suppurative thrombosis, endocarditis, and vascular infection. The search below is identified as Main in the search strategies document. Because the appropriate indexing terms either do not exist or were applied inconsistently, the main search uses keywords in addition to MeSH terms to arrive at the following main strategy.

1. *Central Venous Catheters/ or *Catheterization, Central Venous/ or (central line or central lines or ("central venous" and (catheter* or line or lines)) or "central line associated" or "catheter related").ti.
2. ("peripherally inserted central" and (line or lines or port or ports or catheter*).mp. or (PICC or PICCS).ti,ab. or *catheters, indwelling/.
3. 1 or 2
4. Cross Infection/ or exp *Sepsis/ or exp *Catheter-Related Infections/ or exp *Bacterial Infections/ or *infection/ or *Prosthesis-Related Infections/.
5. 3 and 4
6. (CLABSI* or CRBSI* or CR-BSI*).ti,ab.
7. 5 or 6

The searches on suppurative thrombosis, endocarditis, and vascular infection used the first 3 searches of the main search strategy. The MEDLINE In-Process search was based entirely on keywords.
Results were limited to: Humans, English, and 2008 to current. The Main search retrieved 391 references. When the search hedges for Guidelines, Clinical Trials, and Cohort Studies were added, the base results are as follow:
- Central Line Infection -Guidelines, total results were 28
- Central Line Infection -Clinical Trials, total results were 187
- Central Line Infection -Cohort Studies, total results were 402

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

Level of evidence supporting a diagnostic method or an intervention:
- A= systematic reviews of randomized controlled trials
- B= randomized controlled trials
- C= systematic review of non-randomized controlled trials or observational studies, non-randomized controlled trials, group observation studies (e.g., cohort, cross-sectional, case control)
- D= individual observation studies (case or case series)
- E = opinion of expert panel.


**Recommendations**

Guideline recommendations were based on prospective randomized controlled trials if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size. The “strength of recommendation” for key aspects of care was determined by expert opinion.

The strength of recommendations regarding care were categorized as:
- I = Generally should be performed
- II = May be reasonable to perform
- III = Generally should not be performed

**Review and Endorsement**

Internal review: Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the Michigan Medicine to which the content is most relevant: Internal Medicine, Infectious Diseases, Pediatrics, Pediatric Emergency Medicine, Pediatric Infectious Diseases.

External review: After internal review, the final document was distributed for external review by a full spectrum of medical specialties and other organizational stakeholders though the Clinical Practice Committee of the Michigan Medicine, as well as the Executive Committee for Clinical Affairs of Michigan Medicine.

**References**


intensive chemotherapy. *Bone Marrow Transplant.* 1999;23(1):41-44.


Appendix A: Normal vital signs for pediatric patients
(Source: American Heart Association, Inc., by permission)

Normal Respiratory Rates by Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Breaths/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant (&lt;1 year)</td>
<td>30 to 60</td>
</tr>
<tr>
<td>Toddler (1 to 3 years)</td>
<td>24 to 40</td>
</tr>
<tr>
<td>Preschooler (4 to 5 years)</td>
<td>22 to 34</td>
</tr>
<tr>
<td>School age (6 to 12 years)</td>
<td>18 to 30</td>
</tr>
<tr>
<td>Adolescent (12-18 years)</td>
<td>12 to 16</td>
</tr>
</tbody>
</table>

Normal Heart Rates (per Minute) by Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Awake Rate</th>
<th>Mean</th>
<th>Sleeping Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn to 3 months</td>
<td>85 to 205</td>
<td>140</td>
<td>80 to 160</td>
</tr>
<tr>
<td>3 months to 2 years</td>
<td>100 to 190</td>
<td>130</td>
<td>75 to 160</td>
</tr>
<tr>
<td>2 years to 10 years</td>
<td>60 to 140</td>
<td>80</td>
<td>60 to 90</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>60 to 100</td>
<td>75</td>
<td>50 to 90</td>
</tr>
</tbody>
</table>

Blood Pressure in Children by Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Systolic Blood Pressure (mm Hg)</th>
<th>Diastolic Blood Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Neonate to 6 months: ranges from 1 standard dev. below to 1 standard dev. above the mean *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonate (1 day)</td>
<td>60 to 76</td>
<td>60 to 74</td>
</tr>
<tr>
<td>Neonate (4 days)</td>
<td>67 to 83</td>
<td>68 to 84</td>
</tr>
<tr>
<td>Infant (1 month)</td>
<td>73 to 91</td>
<td>74 to 94</td>
</tr>
<tr>
<td>Infant (3 months)</td>
<td>78 to 100</td>
<td>81 to 103</td>
</tr>
<tr>
<td>Infant (6 months)</td>
<td>82 to 102</td>
<td>87 to 105</td>
</tr>
<tr>
<td>1 year to adolescent: ranges from 50th to 95th percentile, assuming median height; data do not include pressures below 50th percentile**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infant (1 year)</td>
<td>86 to 104</td>
<td>85 to 103</td>
</tr>
<tr>
<td>Child (2 years)</td>
<td>88 to 105</td>
<td>88 to 106</td>
</tr>
<tr>
<td>Child (7 years)</td>
<td>96 to 113</td>
<td>97 to 115</td>
</tr>
<tr>
<td>Adolescent (15 years)</td>
<td>110 to 127</td>
<td>113 to 131</td>
</tr>
</tbody>
</table>


Definition of hypotension by Systolic Blood Pressure and Age.

<table>
<thead>
<tr>
<th>Age</th>
<th>Systolic Blood Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term neonates (0 to 28 days)</td>
<td>&lt;60</td>
</tr>
<tr>
<td>Infants (1 to 12 months)</td>
<td>&lt;70</td>
</tr>
<tr>
<td>Children 1 to 10 years (5th blood pressure percentile)</td>
<td>&lt;70 + (age in years x 2)</td>
</tr>
<tr>
<td>Children &gt;10 years</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>