

Guidelines for the Management of Intravascular Catheter–Related Infections

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EXECUTIVE SUMMARY

These guidelines from the Infectious Diseases Society of America (IDSA), the American College of Critical Care Medicine (for the Society of Critical Care Medicine), and the Society for Healthcare Epidemiology of America contain recommendations for the management of adults and children with, and diagnosis of infections related to, peripheral and nontunneled central venous catheters (CVCs), pulmonary artery catheters, tunneled central catheters, and implantable devices. The guidelines, written for clinicians, contain IDSA evidence-based recommendations for assessment of the quality and strength of the data. Recommendations are presented according to the type of catheter, the infecting organism, and the associated complications.

Intravascular catheter–related infections are a major cause of morbidity and mortality in the United States. Coagulase-negative staphylococci, *Staphylococcus aureus*,

aerobic gram-negative bacilli, and *Candida albicans* most commonly cause catheter-related bloodstream infection. Management of catheter-related infection varies according to the type of catheter involved. After appropriate cultures of blood and catheter samples are done, empirical iv antimicrobial therapy should be initiated on the basis of clinical clues, the severity of the patient's acute illness, underlying disease, and the potential pathogen(s) involved. In most cases of nontunneled CVC–related bacteremia and fungemia, the CVC should be removed. For management of bacteremia and fungemia from a tunneled catheter or implantable device, such as a port, the decision to remove the catheter or device should be based on the severity of the patient's illness, documentation that the vascular-access device is infected, assessment of the specific pathogen involved, and presence of complications, such as endocarditis, septic thrombosis, tunnel infection, or metastatic seeding. When a catheter-related infection is documented and a specific pathogen is identified, systemic antimicrobial therapy should be narrowed and consideration given for antibiotic lock therapy, if the CVC or implantable device is not removed.

These guidelines address the issues related to the management of catheter-related bacteremia and associated complications. Separate guidelines will address specific issues related to the prevention of catheter-related infections. Performance indicators for the management of catheter-related infection are included at the end of the document. Because the pathogenesis of catheter-related infections is complicated, the virulence of the pathogens is variable, and the host factors have

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Table 1. Infectious Diseases Society of America–United States Public Health Service Grading System for ranking recommendations in clinical guidelines.

Category, grade	Definition
Strength of recommendation	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use
Quality of evidence	
I	Evidence from ≥ 1 properly randomized, controlled trial
II	Evidence from ≥ 1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

not been well defined, there is a notable absence of compelling clinical data to make firm recommendations for an individual patient. Therefore, the recommendations in these guidelines are intended to support, and not replace, good clinical judgment. Also, a section on selected, unresolved clinical issues that require further study and research has been included. There is an urgent need for large, well-designed clinical studies to delineate management strategies more effectively, which will improve clinical outcomes and save precious health care resources.

INTRODUCTION

These guidelines from the IDSA, the American College of Critical Care Medicine (for the Society of Critical Care Medicine), and the Society for Healthcare Epidemiology of America provide an overview of the epidemiology and pathogenesis of iv catheter-related infections and then focus on issues related to the diagnosis and management of such infections. Specific recommendations are based on the strength of the evidence (denoted by categories A–E) and the quality of the data (denoted by Roman numerals I–III), by use of previously defined IDSA criteria (table 1) [1]. Data to support most of the recommendations in these guidelines have been garnered from small clinical trials in which patients were not randomized, therapy was not blinded, and data analysis was limited. In fact, to date, there have been no published reports of randomized, double-blind, clinical trials with regard to the clinical diagnosis or management of iv catheter-related infections.

EPIDEMIOLOGY AND PATHOGENESIS

Each year in the United States, hospitals and clinics purchase >150 million intravascular devices for the administration of iv

fluids, medications, blood products, and parenteral nutrition fluids; to monitor hemodynamic status; and to provide hemodialysis [2]. The majority of these devices are peripheral venous catheters, but >5 million CVCs are inserted each year. More than 200,000 nosocomial bloodstream infections occur each year in the United States; most of these infections are related to different types of intravascular devices—in particular, the nontunneled CVC (tables 2 and 3) [2, 4]. The risk factors for iv catheter-related infections vary according to the type of catheter; the hospital size, unit, or service; the location of the site of insertion; and the duration of catheter placement [2, 4, 5].

The pathogenesis of nontunneled CVC infection is often related to (1) extraluminal colonization of the catheter, which originates from the skin and, less commonly, from hematogenous seeding of the catheter tip, or (2) intraluminal colonization of the hub and lumen of the CVC [6]. In comparison, for tunneled CVCs or implantable devices, contamination of the catheter hub and intraluminal infection is the most common route of infection [2, 5]. The microorganisms most commonly associated with peripheral vascular and CVC infection are coagulase-negative staphylococci, *S. aureus*, different species of aerobic gram-negative bacilli, and *C. albicans* (table 4) [2].

Infection related to iv devices results in significant increases in hospital costs, duration of hospitalization, and patient morbidity [9]. In a recent meta-analysis of 2573 catheter-related bloodstream infections, the case-fatality rate was 14%, and 19% of these deaths were attributed to the catheter-related infection [10]. The mortality rate attributed to catheter-related *S. aureus* bacteremia (8.2%) significantly exceeded the rates for other pathogens ($P < .001$), whereas the mortality rate attributed to coagulase-negative staphylococcal catheter-related bacteremia

Table 2. Commonly used definitions of intravascular catheter–related infections.

Infection	Definition
Catheter colonization	Significant growth of a microorganism in a quantitative or semiquantitative culture of the catheter tip, subcutaneous catheter segment, or catheter hub (see the Diagnosis section)
Phlebitis	Induration or erythema, warmth, and pain or tenderness around catheter exit site
Exit-site infection	
Microbiological	Exudate at catheter exit site yields a microorganism with or without concomitant bloodstream infection
Clinical	Erythema, induration, and/or tenderness within 2 cm of the catheter exit site; may be associated with other signs and symptoms of infection, such as fever or pus emerging from the exit site, with or without concomitant bloodstream infection ^a
Tunnel infection	Tenderness, erythema, and/or induration >2 cm from the catheter exit site, along the subcutaneous tract of a tunneled catheter (e.g., Hickman or Broviac catheter), with or without concomitant bloodstream infection ^a
Pocket infection	Infected fluid in the subcutaneous pocket of a totally implanted intravascular device; often associated with tenderness, erythema, and/or induration over the pocket; spontaneous rupture and drainage, or necrosis of the overlying skin, with or without concomitant bloodstream infection, may also occur ^a
Bloodstream infection	
Infusate related	Concordant growth of the same organism from infusate and cultures of percutaneously obtained blood samples with no other identifiable source of infection
Catheter related	Bacteremia or fungemia in a patient who has an intravascular device and ≥ 1 positive result of culture of blood samples obtained from the peripheral vein, clinical manifestations of infection (e.g., fever, chills, and/or hypotension), and no apparent source for bloodstream infection (with the exception of the catheter). One of the following should be present: a positive result of semiquantitative (≥ 15 cfu per catheter segment) or quantitative ($\geq 10^2$ cfu per catheter segment) catheter culture, whereby the same organism (species and antibiogram) is isolated from a catheter segment and a peripheral blood sample; simultaneous quantitative cultures of blood samples with a ratio of $\geq 5:1$ (CVC vs. peripheral); differential time to positivity (i.e., a positive result of culture from a CVC is obtained at least 2 h earlier than is a positive result of culture from peripheral blood)

NOTE. Adapted in part from [3].

^a For surveillance purposes, patients with positive results of blood culture would be classified as having catheter-related bloodstream infection.

(0.7%) was significantly lower than that for other pathogens [10].

DIAGNOSIS

Clinical diagnosis. Clinical findings are unreliable for establishing a diagnosis of intravascular device–related infection, because of their poor specificity and sensitivity. For example, the most sensitive clinical findings, such as fever with or without chills, have poor specificity, and inflammation or purulence around the intravascular device and bloodstream infection have greater specificity but poor sensitivity [2]. Blood culture results that are positive for *S. aureus*, coagulase-negative staphylococci, or *Candida* species, in the absence of any other identifiable source of infection, should increase the suspicion for catheter-related bloodstream infection [3, 5, 11]. Current evidence-based recommendations for diagnosis are summarized in table 5.

Rapid diagnostic techniques. Gram stain may be helpful for the diagnosis of local infections, but it is significantly less sensitive than are quantitative methods for the diagnosis of

catheter-related infections [55]. In one study, use of acridine orange stains for rapid diagnosis resulted in a positive predictive value of 91% and a negative predictive value of 97% [16].

Cultures of samples of iv catheters. Laboratory criteria for the diagnosis of intravascular catheter–related infections are precise, but differences in the definitions and methodologies used in various studies have made data difficult to compare [2, 3]. Semiquantitative (roll plate) or quantitative (vortex or sonication methods) catheter culture techniques are the most reliable diagnostic methodologies, because they have greater specificity in the identification of catheter-related infection, in comparison with qualitative cultures, in which a single contaminating microbe can result in a positive culture result (table 5) [13, 14]. The predictive value of quantitative or semiquantitative culture methods may vary depending on the type and location of the catheter, the culture methodology used, and the source of catheter colonization [56]. For example, a recently inserted catheter (duration of placement, <1 week) is most commonly colonized by a skin microorganism along the external surface of the catheter, so the roll plate method will be

Table 3. Types of intravascular devices and comments on their use.

Type of intravascular device	Comments
Peripheral venous catheter	Usually inserted into the veins of the forearm or the hand; most commonly used short-term intravascular device; rarely associated with bloodstream infection
Peripheral arterial catheter	For short-term use; commonly used to monitor hemodynamic status and to determine blood gas levels of critically ill patients; risk of bloodstream infection may approach that of CVCs
Midline catheter	Peripheral catheter (size, 7.6–20.3 cm) is inserted via the antecubital fossa into the proximal basilic or cephalic veins, but it does not enter central veins; is associated with lower rates of phlebitis and infection than are CVCs
Nontunneled CVC	Most commonly used CVC; accounts for an estimated 90% of all catheter-related bloodstream infections; increased risk of infection with internal jugular vein site of insertion
Pulmonary artery catheter	Inserted through a Teflon introducer and typically remains in place for an average duration of only 3 days; most catheters are heparin bonded to reduce catheter thrombosis and microbial adherence to the catheter
Pressure-monitoring system	Used in conjunction with arterial catheter; associated with both epidemic and endemic nosocomial bloodstream infections; source is often the fluid column in the tubing between the patient's intravascular catheter and the pressure-monitoring apparatus, contaminated infusate, or nondisposable transducers
Peripherally inserted central catheter	Provides an alternative to subclavian or jugular vein catheterization; is inserted via the peripheral vein into the superior vena cava, usually by way of cephalic and basilar veins; is easier to maintain and is associated with fewer mechanical complications (e.g., hemothorax) than are nontunneled CVCs
Tunneled CVC	Surgically implanted CVC (e.g., Hickman, Broviac, Groshong, or Quinton catheter) with the tunneled portion exiting the skin and a Dacron cuff just inside the exit site; the cuff inhibits migration of organisms into the catheter tract by stimulating growth of surrounding tissue, thus the sealing catheter tract; used to provide vascular access to patients who require prolonged iv chemotherapy, home-infusion therapy, or hemodialysis (figure 4)
Totally implantable device	A subcutaneous port or reservoir with self-sealing septum is tunneled beneath the skin and is accessed by a needle through intact skin; low rates of infection

NOTE. CVC, central venous catheter.

quite sensitive in the identification of such colonization. For longer-dwelling catheters (duration of placement, >1 week), in which intraluminal spread from the hub may be the dominant mechanism for catheter colonization, the roll plate method is less sensitive, and methods that obtain samples of both the internal and external surfaces for culture are more sensitive [56]. As use of antimicrobial-coated catheters becomes more prevalent, the existing definitions of catheter colonization and catheter-related infection may need to be modified, because such coatings may lead to false-negative culture results [57, 58].

The most widely used laboratory technique for the clinical diagnosis of catheter-related infection is the semiquantitative method, in which the catheter segment is rolled across the surface of an agar plate and colony-forming units are counted after overnight incubation [14]. Quantitative culture of the catheter segment requires either flushing the segment with broth, or vortexing, or sonicating it in broth, followed by serial dilutions and surface plating on blood agar [13, 59, 60]. A yield of ≥ 15 cfu from a catheter, by means of semiquantitative culture, or a yield of $\geq 10^2$ cfu from a catheter, by means of quantitative culture, with accompanying signs of local or systemic infection, is indicative of catheter-related infection. In a

prospective study that compared the sonication, flush culture, and roll plate methods, the sonication method was 20% more sensitive for the diagnosis of catheter infection than was the roll plate method, and it was >20% more sensitive than was the method of flushing the individual catheter lumens [6]. If only catheter-related bloodstream infections are considered, the sensitivities of the 3 methods are as follows: sonication, 80%; roll plate method, 60%; and flush culture, 40%–50%.

Summary receiver operating characteristic–curve analysis has been recommended as a potentially more rigorous method for comparing the accuracy of different diagnostic tests for the same condition, because a given test may have one sensitivity at a given specificity and a different sensitivity at another specificity [61]. A meta-analysis confirmed that quantitative cultures of catheter segments were more accurate than were the roll plate and qualitative methods in a receiver operating characteristic–curve analysis ($P = .03$) [12]. At this time, it is unclear whether any of these differences are clinically significant.

Paired cultures of blood drawn through the iv catheter and percutaneously. Patients with suspected iv catheter-related infection should have 2 sets of blood samples drawn for culture, with at least 1 set drawn percutaneously. The clinical usefulness

of cultures of blood samples drawn from an indwelling CVC was assessed in a study of hospitalized patients with cancer [17]. In the study, the positive predictive value of catheter and peripheral blood cultures was 63% and 73%, respectively, and the negative predictive value was 99% and 98%, respectively. Therefore, a positive culture result for a blood sample drawn through a catheter requires clinical interpretation, but a negative result is helpful for excluding catheter-related bloodstream infection.

Quantitative cultures of peripheral and CVC blood samples. Quantitative blood culturing techniques have been developed as an alternative for the diagnosis of catheter-related bloodstream infection in patients for whom catheter removal is undesirable because of limited vascular access. This technique relies on quantitative culture of paired blood samples, one of which is obtained through the central catheter hub and the other from a peripheral venipuncture site. In most studies, when blood obtained from the CVC yielded a colony count at least 5–10-fold greater than that for blood obtained from a peripheral vein, this was predictive of catheter-related bloodstream infection [19]. Among tunneled catheters, for which the method is most accurate, a quantitative culture of blood from the CVC that yields at least 100 cfu/mL may be diagnostic without a companion culture of a peripheral blood sample [62].

Differential time to positivity for CVC versus peripheral blood cultures. This new method, which correlates well with quantitative blood cultures, makes use of continuous blood-culture monitoring for positivity (e.g., radiometric methods) and compares the differential time to positivity for qualitative cultures of blood samples drawn from the catheter and a peripheral vein. When studied with tunneled catheters, this method has offered accuracy comparable to that of quantitative cultures of blood samples and has had greater cost-effectiveness [20, 21]. In a study of differential time to positivity, a definite diagnosis of catheter-related bacteremia could be made in 16 of the 17 patients who had a positive result of culture of a blood sample from the CVC at least 2 h earlier than they had a positive result of a peripheral blood culture; the overall sensitivity was 91% and specificity was 94% [20]. Most hospitals do not have quantitative blood culture methodologies, but many will be able to use differential time to positivity for diagnosis.

Infusate-related bloodstream infection. Infusate-related bloodstream infection is uncommon and is defined as the isolation of the same organism from both infusate and separate percutaneous blood cultures, with no other source of infection. The sudden onset of symptoms of bloodstream infection soon after the initiation of an infusion, resulting from the administration of contaminated iv fluid, is often diagnostic [2]. When

this diagnosis is suggested, cultures of iv fluid should be part of an investigation of potential sources of infection.

MANAGEMENT OF CATHETER-RELATED INFECTIONS

Antibiotic therapy for catheter-related infection is often initiated empirically. The initial choice of antibiotics will depend on the severity of the patient's clinical disease, the risk factors for infection, and the likely pathogens associated with the specific intravascular device (figure 1; table 4). Although there are no data that support the use of specific empirical antibiotic therapy for device-related bloodstream infection, vancomycin is usually recommended in those hospitals or countries with an increased incidence of methicillin-resistant staphylococci, because of its activity against coagulase-negative staphylococci and *S. aureus*. In the absence of methicillin-resistant *S. aureus*, penicillinase-resistant penicillins, such as nafcillin or oxacillin, should be used. Additional empirical coverage for enteric gram-negative bacilli and *Pseudomonas aeruginosa* with use of a third- or fourth-generation cephalosporin, such as ceftazidime or cefepime, may be needed for severely ill or immunocompromised patients who have suspected catheter-related bloodstream infection. Use of amphotericin B or, for selected patients, iv fluconazole should also be considered for empirical treatment when fungemia is suspected. Initial antimicrobial therapy should be given intravenously, but once the patient's condition has stabilized and antibiotic susceptibilities are known, an oral quinolone, such as ciprofloxacin, trimethoprim-sulfamethoxazole, or linezolid, could be administered because of their excellent oral bioavailability and tissue penetration.

There are no compelling data to support specific recommendations regarding the duration of therapy for device-related infections. Patients with catheter-related bacteremia should be separated into those with complicated infections, in which there is septic thrombosis, endocarditis, osteomyelitis, or possible metastatic seeding, and those with uncomplicated bacteremia, in which there is no evidence of such complications (figures 1–4). If there is a prompt response to initial antibiotic therapy, most patients who are not immunocompromised, without underlying valvular heart disease or an intravascular prosthetic device, should receive 10–14 days of antimicrobial therapy for pathogens other than coagulase-negative staphylococci. A more prolonged course of antibiotic therapy (duration, 4–6 weeks) should be considered if there is persistent bacteremia or fungemia after catheter removal or if there is evidence of endocarditis, or septic thrombosis, and 6–8 weeks of therapy should be considered for the treatment of osteomyelitis (figures 2 and 4). Streptokinase has been used in combination with antimicrobial therapy, but its use has not been shown to be beneficial

Table 4. Intravenous antimicrobial treatment of iv catheter-related bloodstream infection in adults, according to specific pathogen isolated.

Pathogen	Preferred antimicrobial agent	Example, dosage ^a	Alternative antimicrobial agent	Comment
Gram-positive cocci				
<i>S. aureus</i>				
Meth susceptible	Penicillinase-resistant Pen ^b	Naf or Oxa, 2 g q4h	Cfaz or Cfur	Penicillinase-resistant Pen or Csps are preferred to Vm ^c
Meth resistant	Vm	Vm, 1 g q12h	Linezolid; or Quin/Dalf; or Vm + (Rif or Gm); or TMP-SMZ alone (if susceptible)	Strains of <i>S. aureus</i> with reduced susceptibility to Vm have been reported
Vm resistant	Linezolid or Quin/Dalf	Linezolid, 600 mg q12h, or Quin/Dalf, 7.5 mg/kg q8h	Vm	For adults <40 kg, linezolid dose should be 10 mg/kg
Coagulase-negative staphylococci				
Meth susceptible	Penicillinase-resistant Pen	Naf or Oxa, 2 g q4h	First-generation Csp or Vm or TMP-SMZ (if susceptible)	Vm has dosing advantages over Naf and Oxa, but the latter are preferred because of concerns about increasing Vm resistance
Meth resistant	Vm	Vm, 1 g iv q12h	Linezolid or Quin/Dalf	For adults <40 kg, linezolid dose should be 10 mg/kg
<i>E. faecalis/E. faecium</i>				
Amp susceptible	Amp or (Amp or Pen) + aminoglycoside	Amp, 2 g q4h–q6h, or Amp + Gm, 1 mg/kg q8h	Vm	Vm may have dosing advantages over Amp and Gm, but there are concerns about Vm resistance
Amp resistant, Vm susceptible	Vm or Vm + aminoglycoside	Vm, 1 g iv q12h, or Vm + Gm, 1 mg/kg q8h	Linezolid	Quin/Dalf is not effective against <i>E. faecalis</i>
Vm resistant	Linezolid or Quin/Dalf	Linezolid, 600 mg q12h, or Quin/Dalf, 7.5 mg/kg q8h		Susceptibility of VRE isolates varies; Quin/Dalf is not effective against <i>E. faecalis</i>
Gram-negative bacilli ^d				
<i>E. coli</i> and <i>Klebsiella</i> species	Third-generation Csp	Ctri, 1–2 g q.d.	Fluoroquinolone, such as Cpx or Lvfx, or Atm	Susceptibility of strains varies
<i>Enterobacter</i> species and <i>S. marcescens</i>	Carbapenem	Imi, 500 mg q6h, or Mero, 1 g q8h	Cefepime or fluoroquinolone, such as Cpx or Lvfx	Susceptibility of strains varies
<i>Acinetobacter</i> species	Amp/Sulb or carbapenem	Amp/Sulb, 3 g q6h; or Imi, 500 mg q6h; or Mero, 1 g q8h		Susceptibility of strains varies
<i>S. maltophilia</i>	TMP-SMZ	TMP-SMZ, 3–5 mg/kg q8h	Tic and Clv	

<i>P. aeruginosa</i>	Third- or fourth-generation Csp or carbapenem or antipseudomonal β -lactam (Tic, Pip, Mez) + aminoglycoside	Czid, 2 g q8h; or cefepime, 2 g q12h; or Imi, 500 mg q6h; or Mero, 1 g q8h; or (Tic, 3 g q4h, + Amik, 15 mg/kg q24h); or Tm, 5–6 mg/kg q24h		Susceptibility of strains varies
Fungi				
<i>C. albicans</i> or <i>Candida</i> species	AmB or fluconazole (if organism is susceptible)	AmB, 0.3–1 mg/kg/d, or fluconazole, 400–600 mg q.d.	Lipid AmB preparations	AmB should be used to treat critically ill patients until fungal isolate is identified
Uncommon pathogens				
<i>Corynebacterium</i> species (JK-1)	Vm	Vm, 1 g q12h	PenG + aminoglycoside	Check susceptibilities for other corynebacteria
<i>B. cepacia</i>	TMP-SMZ or carbapenem	TMP-SMZ, 3–5 mg/kg q8h; or Imi, 500 mg q6h; or Mero, 1 g q8h		Other species, such as <i>Burkholderia acidovorans</i> and <i>Burkholderia picketii</i> , may be susceptible to same antimicrobial agents
<i>Flavobacterium</i> species	Vm	Vm, 1 g q12h	TMP-SMZ or Imi or Mero	
<i>O. anthropi</i>	TMP-SMZ or fluoroquinolone	TMP-SMZ, 3–5 mg/kg q8h, or Cpx, 400 mg q12h	Imi or Mero + aminoglycoside	
<i>T. beigeli</i>	Ket	Ket, 200 mg p.o. q.d.		Numerous drug interactions of note; gastric acid required for absorption; may be enhanced by use of cola
<i>M. furfur</i>	AmB			Intravenous lipids should be discontinued; some experts recommend removal of catheter
<i>Mycobacterium</i> species	Susceptibility varies by species			Different species have wide spectra of susceptibility to antimicrobials; see [7, 8]

NOTE. AmB, amphotericin B; Amp, ampicillin; Atm, aztreonam; *B. cepacia*, *Burkholderia cepacia*; Cfaz, cefazolin; Cfur, cefuroxime; Clv, clavulanate; Cpx, ciprofloxacin; Csp, cephalosporin; Ctri, ceftriaxone; Czid, ceftazidime; *E. coli*, *Escherichia coli*; *E. faecalis/E. faecium*, *Enterococcus faecalis/Enterococcus faecium*; Gm, gentamicin; Imi, Imipenem; Ket, ketoconazole; Lvfx, levofloxacin; *M. furfur*, *Malassezia furfur*; Mero, meropenem; Meth, methicillin; Mez, mezlocillin; Naf, nafcillin; *O. anthropi*, *Ochrobacterium anthropi*; Oxa, oxacillin; *P. aeruginosa*, *Pseudomonas aeruginosa*; Pen, penicillin; PenG, penicillin G; p.o., by mouth; Pip, piperacillin; Quin/Dalf, quinupristin/dalfopristin; Rif, rifampin; *S. aureus*, *Staphylococcus aureus*; *S. maltophilia*, *Stenotrophomonas maltophilia*; *S. marcescens*, *Serratia marcescens*; Sulb, sulbactam; *T. beigeli*, *Trichophyton beigeli*; Tic, ticarcillin; Tm, tobramycin; TMP-SMZ, trimethoprim-sulfamethoxazole; Vm, vancomycin.

^a Initial antibiotic dosages for adult patients with normal renal and hepatic function and no known drug interactions. Fluoroquinolones should not be used for patients <18 years of age (see the Pediatric Infections section and [7, 8]).

^b Pen, if strain is susceptible.

^c Some clinicians will add an aminoglycoside for the first 5 days of therapy.

^d Pending susceptibility results for isolate.

Table 5. Current evidence-based recommendations for the diagnosis and management of catheter-related infections.

General recommendations

Culture of catheters

Culture of catheters should be done only when catheter-related bloodstream infection is suspected (B-II) [2, 12]

Quantitative or semiquantitative cultures of catheters are recommended (A-II) [6, 12]

Qualitative broth cultures of catheters are not recommended (E-II) [12–14]

When culturing a CVC segment, either the catheter tip or a subcutaneous segment should be submitted for culture (B-III) [6]

For suspected pulmonary artery catheter infection, culture of the introducer tip should be done because it provides a higher yield, in comparison with the pulmonary artery catheter tip (A-II) [15]

If available, acridine orange leukocyte cytospin should be considered for rapid diagnosis of CVC infection (B-II) [16]

Culture of blood samples

Two sets of blood samples for culture, with at least 1 drawn percutaneously, should be obtained from all patients with a new episode of suspected CVC-related bloodstream infection (A-II) [12, 15, 17–21]

Paired quantitative blood cultures or paired qualitative blood cultures with a continuously monitored differential time to positivity are recommended for the diagnosis of catheter-related infection, especially when the long-term catheter cannot be removed (A-II) [12, 17, 19–21]

Specific recommendations

Peripheral venous catheters

If there is suspicion of short-term peripheral catheter infection, the catheter should be removed, the tip should be cultured by use of a semiquantitative method, and 2 separate blood samples should be obtained for culture before starting antibiotic therapy (A-II) [14]

If there are signs of local infection, any exudate at the exit site should be submitted for Gram stain and culture (A-II) [2]

Nontunneled CVCs

CVCs in patients with fever and mild to moderate disease should not routinely be removed (D-III) [22]

CVC should be removed and cultured if the patient has erythema or purulence overlying the catheter exit site, or clinical signs of sepsis (B, III) [15, 23]; if blood culture results are positive or if the CVC is exchanged over the guidewire and has significant colonization according to results of quantitative or semiquantitative cultures, the catheter should be removed and placed into a new site (B-III) [24, 25]

In some patients without evidence of persistent bloodstream infection, or if the infecting organism is a coagulase-negative staphylococcus, and if there is no suspicion of local or metastatic complications, the CVC may be retained (C-III) [26]

If not contraindicated, TEE should be done to rule out vegetations in patients with catheter-related *Staphylococcus aureus* bloodstream infection because of recently reported high rates of complicating endocarditis (B-II) [27–30]; if TEE is not available and results of transthoracic echocardiography are negative, the duration of therapy should be decided clinically for each patient

After removal of a colonized catheter associated with bloodstream infection, if there is persistent bacteremia or fungemia, or a lack of clinical improvement (especially if it is >3 days after catheter withdrawal and initiation of appropriate antimicrobial therapy), aggressive evaluation for septic thrombosis, infective endocarditis, and other metastatic infections should ensue (B-III) [31]

Febrile patients with valvular heart disease or those patients with neutropenia whose catheter tip culture reveals significant growth of *S. aureus* or *Candida* species on semiquantitative or quantitative culture in the absence of bloodstream infection, should be followed closely for development of infection, and samples of blood for culture should be obtained accordingly (B-II) [6, 32, 33]

After catheters have been removed from patients with catheter-related bloodstream infection, nontunneled catheters may be reinserted after appropriate systemic antimicrobial therapy is begun (C-II)

Tunneled CVCs and IDs

Clinical assessment is recommended to determine that the CVC or the ID is the source of infection or bloodstream infection (B-III; figure 3) [5, 34, 35]

For complicated infections, the CVC or the ID should be removed (B-II) [36]

For salvage of the CVC or the ID in patients with uncomplicated infections, antibiotic lock therapy should be used for 2 weeks with standard systemic therapy for treatment of catheter-related bacteremia due to *S. aureus*, coagulase-negative staphylococci, and gram-negative bacilli for suspected intraluminal infection in the absence of tunnel or pocket infection (B-II) [37–45]

Tunneled catheter pocket infections or port abscess require removal of catheter and usually 7–10 days of appropriate antibiotic therapy (C-III)

Reinsertion of tunneled intravascular devices should be postponed until after appropriate systemic antimicrobial therapy is begun, based on susceptibilities of the bloodstream isolate, and after repeat cultures of blood samples yield negative results (B-III); if time permits, insertion of a tunneled intravascular catheter in a stable patient ideally should be done after a systemic antibiotic course of therapy is completed and repeat blood samples drawn 5–10 days later yield negative results (C-III)

Hemodialysis catheters

Vancomycin use for methicillin-susceptible *S. aureus* bloodstream infections is not recommended because of the risk of selecting out vancomycin-resistant organisms; antistaphylococcal penicillinase-resistant penicillin (nafcillin or oxacillin) is recommended; furthermore, glycopeptides are inferior to antistaphylococcal penicillins (B-III) [46–49]

Antibiotic lock therapy is recommended for treatment when the catheter is retained (B-III; table 7)

Catheter-related, coagulase-negative staphylococcal bloodstream infection can be treated without removal of the catheter, but this may require longer duration of therapy (B-II) [46, 47, 49, 50]

In addition to iv antimicrobial therapy and catheter removal for catheter-related bloodstream infection, culture of the nares for *S. aureus* and treatment of carriers with mupirocin ointment (2%) are recommended for those patients who will need iv access (B-II) [51–54]

NOTE. CVC, central venous catheter; ID, implantable device; TEE, transesophageal echocardiography. The letter and Roman numeral shown in parentheses after each recommendation represent Infectious Diseases Society of America evidence-based criteria that reflect the strength and quality of evidence (table 1) [1].

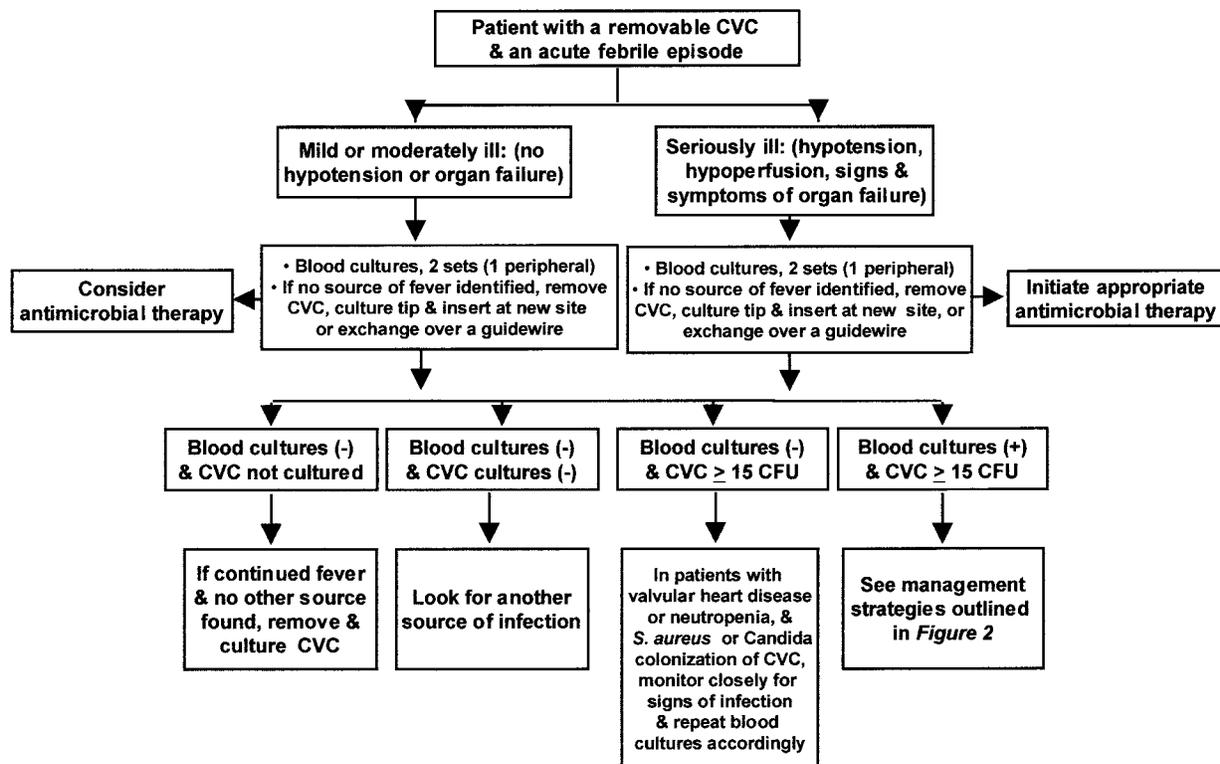


Figure 1. Methods for the diagnosis of acute fever in a patient suspected of having nontunneled central venous catheter (CVC) infection. The patient should be assessed for severity of illness, and 2 blood samples should be obtained (at least 1 peripherally and 1 via a catheter) for culture. If a catheter is the suspected source of infection in a patient who has mild to moderate illness, antimicrobial therapy should be considered, and the catheter either should be removed and cultured, or exchanged over a guidewire and cultured. Patients with severe disease due to catheter-related infection should be given appropriate antimicrobial therapy, and the CVC should be removed, cultured, and inserted into a different site. Results of catheter and blood cultures help to establish the presence of infection and the infecting organism, which may allow for adjustment in antibiotic coverage and catheter management. +, positive; -, negative.

as adjunctive therapy to antibiotic treatment among patients with CVC-related bloodstream infection when the catheter is not removed [63, 64].

Short-term peripheral venous catheters. If a patient has infection of a short-term peripheral catheter, the catheter should be removed, the tip should be cultured semiquantitatively, and at least 2 separate cultures of blood samples, one of which is drawn percutaneously, should be obtained before initiation of antibiotic therapy (table 5) [2].

Nontunneled CVCs. The diagnosis and management points for patients with a nontunneled CVC and unexplained fever are summarized in table 4 and in figures 1 and 2 [15, 65]. CVCs in patients with fever and mild to moderate disease (figure 1) should not routinely be removed; in 1 series [22], 71% of catheters from patients with suspected catheter-related infections were sterile. The CVC should be removed and cultured if the patient has severe disease or erythema overlying the catheter exit site, purulence at the catheter exit site, or clinical signs of unexplained sepsis [2]. If the blood culture results are positive, or if the CVC is exchanged over a guidewire

and has significant colonization by quantitative or semiquantitative cultures, the catheter should be removed and a new catheter should be placed in a new site [24].

For some patients without evidence of persistent bloodstream infection, or if the infecting organism is a coagulase-negative staphylococcus and there is no suspicion of local or metastatic complications, the CVC may be retained [26]. If available, transesophageal echocardiography (TEE) should be used to rule out vegetations in patients with *S. aureus* catheter-related bloodstream infection [27–29]. The ideal time to perform TEE in this setting has not been defined. If there is persistent bacteremia or fungemia, or a lack of clinical improvement, especially if it is >3 days after catheter withdrawal and initiation of appropriate antimicrobial therapy has not been effective, then an aggressive workup for septic thrombosis, infective endocarditis, and other metastatic infections should ensue [65].

There are no data in the literature to guide clinicians regarding the use of antimicrobial therapy for patients whose catheter tip cultures reveal significant growth in the absence of culture-proven bacteremia or fungemia. In this setting, a febrile

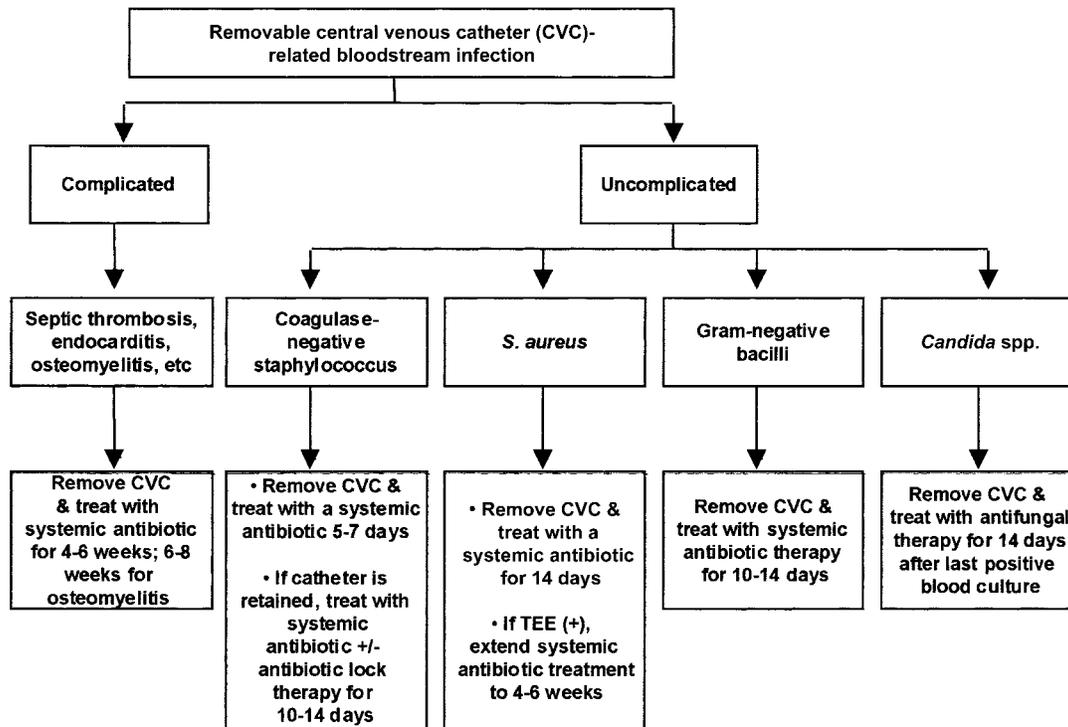


Figure 2. Approach to the management of patients with nontunneled central venous catheter (CVC)-related bloodstream infection. Duration of treatment will depend on whether the infection is complicated or uncomplicated. The catheter should be removed and systemic antimicrobial therapy should be initiated, except in some cases of uncomplicated catheter-related infection due to coagulase-negative staphylococci. For infections due to *Staphylococcus aureus*, transesophageal echocardiography (TEE) may reveal the presence of endocarditis and help to determine the duration of treatment. +, positive; -, negative.

patient with valvular heart disease or a patient with neutropenia (absolute neutrophil count, <1000 cells/mL), whose catheter tip culture reveals significant growth of *S. aureus* or *C. albicans* by means of semiquantitative (≥ 15 cfu) or quantitative ($\geq 10^2$ cfu) culture should be followed closely for signs of infection, and some experts would administer a short course (5–7 days) of antibiotics. This is based on the fact that *S. aureus* and *Candida* organisms are more likely than enterococci or gram-negative bacilli to be associated with catheter-related bloodstream infection and complications [6, 32, 33, 66].

Tunneled CVCs or implantable devices. Surgically implantable vascular devices consist of either a surgically implantable catheter, such as a tunneled silicone catheter (e.g., a Hickman, Broviac, or Groshong catheter), or implantable devices, such as a Portacath [5]. Because removal of a surgically implantable vascular device is often a management challenge, it is important to be sure that one is dealing with a true catheter-related bloodstream infection, rather than skin contamination, catheter colonization, or infection from another source (table 5; figure 3). For example, for a patient who has a tunneled CVC and a single blood culture result that is positive for coagulase-negative staphylococci, it is recommended that the clinician repeat the blood cultures and not hastily remove the

catheter or initiate antimicrobial therapy before it is determined that the positive result reflects a true bloodstream infection and that the catheter is the source of the bloodstream infection [13, 67]. Microbiological data suggestive of bloodstream infection caused by coagulase-negative staphylococci, rather than contamination, include the following: multiple positive blood culture results, quantitative cultures of blood samples drawn from a catheter with ≥ 100 cfu/mL, and isolation of the same organism from quantitative catheter cultures and percutaneous blood cultures [68]. A differential growth time of >2 h for cultures of blood samples obtained through the CVC, compared with cultures of peripheral blood samples, is also predictive of catheter-related bloodstream infection.

Management of CVC-related bloodstream infections in patients with tunneled CVCs or implantable devices, such as ports, is summarized in tables 4–7 and in figure 4. Patients with complicated device infections, such as tunnel infection or port abscess, require removal of the catheter and 7–10 days of antibiotic therapy; patients with septic thrombosis or endocarditis require removal of the catheter or device and antibiotic treatment for 4–6 weeks; and patients with osteomyelitis require removal of the catheter and antibiotic treatment for 6–8 weeks [5]. For the management of uncomplicated infection, see rec-

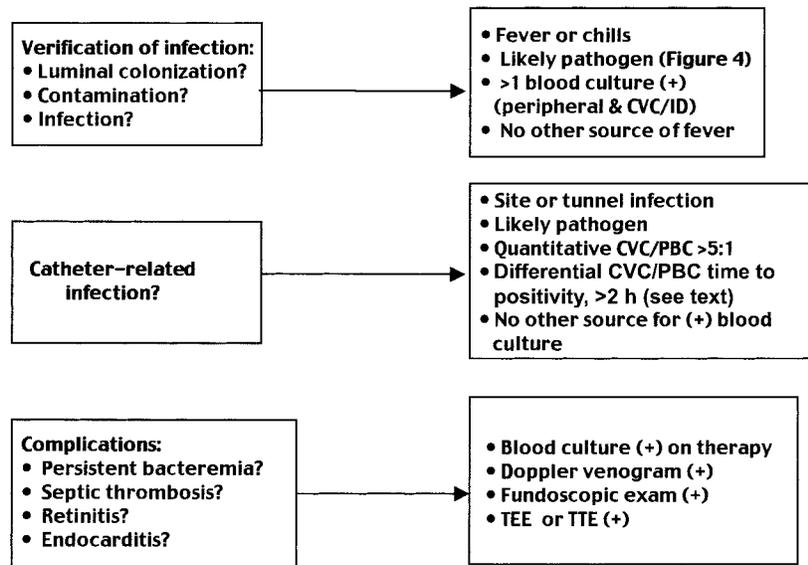


Figure 3. Management points for a patient with bloodstream infection and a tunneled central venous catheter (CVC) or an implantable device (ID). It is important (1) to verify that the CVC or the ID is infected and that it is the source of bloodstream infection, and (2) to carefully assess the patient for possible complications, such as septic thrombosis, metastatic seeding, endocarditis, or osteomyelitis. PBC, peripheral blood culture; TEE, transthoracic echocardiogram; TTE, transthoracic echocardiogram; +, positive.

ommendations for specific organisms in tables 5 and 6 and in figure 4. In the presence of uncomplicated infection due to coagulase-negative staphylococci, the CVC may be retained if there is no evidence of persisting or relapsing bacteremia [26]. For catheter-related bacteremia caused by organisms other than coagulase-negative staphylococci, some investigators would retain the CVC, depending on the patient's clinical status, and would use systemic and antibiotic lock therapy.

Infections associated with hemodialysis catheters. A hemodialysis catheter is a unique type of long-term catheter that requires special attention. Catheter-related colonization not associated with clinical manifestations of infection has been found to occur in 10%–55% of hemodialysis catheters [123–125]. Hemodialysis catheter-related bloodstream infections have also been reported to be complicated by deep-seated infections, such as bacterial endocarditis, septic pulmonary emboli, and septic thrombosis (table 7) [126–129].

The risk of infection associated with internal jugular catheters, compared with subclavian vein hemodialysis catheters, has varied in different studies [50, 123, 130]. For long-term catheters, the effect of tunneling, with or without a cuff, on infection rates remains controversial [123, 131, 132]. Because each dialysis treatment requires 4 tubing connections, there is a high risk for the introduction of organisms through the hub and the lumen of the hemodialysis catheter.

In several studies, *S. aureus* has been reported to be the organism that is the leading cause of hemodialysis catheter-related bloodstream infections, contributing 33%–80% of the organisms cultured from blood samples [46, 124, 125, 131].

The prevalence of nasal carriage of *S. aureus* among patients undergoing hemodialysis has ranged from 30% to 60% [133–137]. Reduction of nasal carriage of *S. aureus* has resulted in a decrease in yearly bloodstream infections due to *S. aureus* [51]. Management of the infected hemodialysis catheter and the use of antimicrobial therapy are similar to the management of and therapy for other CVCs, and specific recommendations are included in table 5 and in figures 2–4.

ANTIBIOTIC LOCK THERAPY

Fourteen open trials of standard parenteral therapy for the treatment of catheter-related bloodstream infection and the salvage of tunneled catheters resulted in salvage in 342 (66.5%) of 514 episodes [36, 84, 138–149]. The likelihood of clinical response and catheter salvage has varied according to the site of infection (e.g., exit-site infection has been more likely to respond than has tunnel or pocket infection) and with the type of microbe that is causing the infection (e.g., coagulase-negative staphylococci have been more likely to respond than have *S. aureus* and *P. aeruginosa*) [36, 84]. Nevertheless, even a microbe that is more likely to respond to therapy, such as *Staphylococcus epidermidis*, has been shown to cause recurrent bacteremia within 12 weeks of standard parenteral therapy in 20% of patients whose catheters were not removed, compared with only 3% of patients whose catheters were removed [26].

One reason for treatment failure with regard to vascular catheter infections is the inability of most antibiotics to kill microorganisms growing in a biofilm in therapeutically achiev-

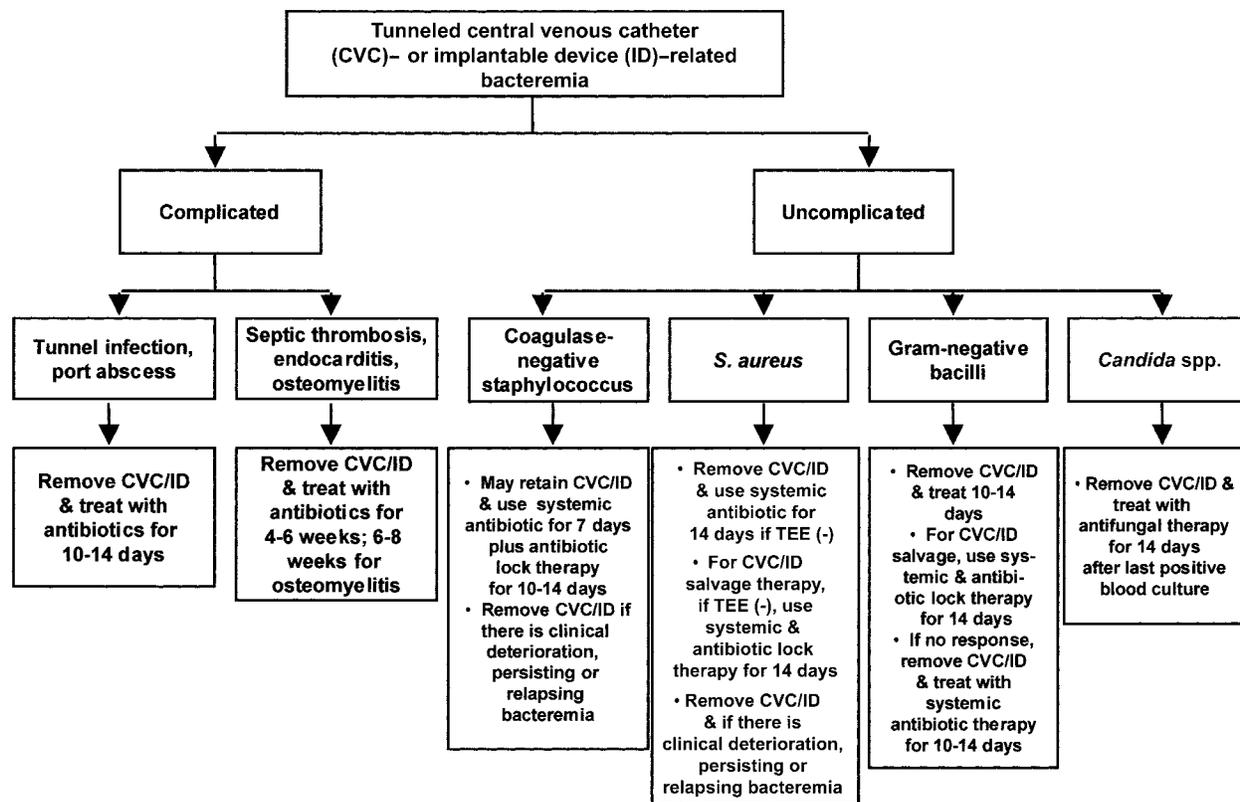


Figure 4. Approach to the management of a patient with a tunneled central venous catheter (CVC)– or a surgically implanted device (ID)–related bloodstream infection. It is important to assess the patient for complications and to identify the specific pathogen. Complicated infections invariably require antimicrobial therapy for 4–8 weeks and removal of the CVC or the ID, depending on the site of metastatic infection. All patients with infection due to *Candida* species should have the device removed and should receive antifungal therapy for 14 days after fungemia has cleared. If tunneled CVC- or ID-related bacteremia is uncomplicated and the CVC or port is not be removed, infections due to coagulase-negative staphylococci, *Staphylococcus aureus*, or gram-negative bacilli should be treated with systemic and antimicrobial lock therapy for 14 days. If a patient has *S. aureus* bacteremia and transesophageal echocardiography (TEE) has demonstrated vegetations, systemic treatment should be extended to 4–6 weeks. –, negative.

able concentrations [37, 150–154]. Recent studies have demonstrated that antibiotic concentrations must be 100–1000 times greater to kill sessile (biofilm) bacteria than to kill planktonic (in solution) bacteria [37, 150–154]. A potential solution to this problem is based on the fact that the majority of infections in tunneled catheters originate in the catheter hub and spread to the catheter lumen [155]. This fact has prompted several investigators to try filling the catheter lumen with pharmacological concentrations of antibiotics and leaving them there for hours or days, the so-called “antibiotic lock” technique [37, 156, 157].

Several open trials of antibiotic lock therapy of tunneled catheter-related bacteremia, with or without concomitant parenteral therapy, have reported a response and catheter salvage without relapse in 138 (82.6%) of 167 episodes [38–43, 76, 85, 100, 156, 157]. Compared with parenteral therapy used in the 14 aforementioned open trials, therapy including antibiotic lock was significantly more likely to result in catheter salvage (RR, 1.24; 95% CI, 1.13–1.36; $P = .0001$). Some pathogens may be

more difficult to eradicate by use of antibiotic lock therapy, however, because 7 of 10 attempts to salvage catheters with fungal infections reportedly failed (RR of failure to salvage with fungi vs. bacteria, 5.0; 95% CI, 2.9–8.8; $P = .0002$) [43, 76, 100, 101]. One study group reported continuing use of a catheter for 8 months, despite the relapse of *Candida glabrata* fungemia, by administering 3 days of parenteral antifungal therapy and then continuing daily suppressive antibiotic lock therapy with amphotericin B [76].

An in vitro study that used an experimental model of catheter-related infection with a slime-producing strain of *S. epidermidis* found that infusion of vancomycin alone q8h sterilized 0 of 5 catheters, whereas antibiotic lock therapy resulted in sterilization of all 5 catheters [37]. Another in vitro study that involved 7 days of experimental therapy confirmed that antibiotic lock therapy could sterilize catheters with some microbial-antimicrobial combinations while significantly reducing microbial concentrations with others [44]. Antibiotic lock therapy for catheter-related bloodstream infection is often used in

conjunction with systemic antibiotic therapy and involves instilling a high concentration of an antibiotic to which the causative microbe is susceptible in the catheter lumen. Antibiotic solutions that contain the desired antimicrobial agent in a concentration of 1–5 mg/mL are usually mixed with 50–100 U of heparin (or normal saline) in sufficient volume to fill the catheter lumen (usually 2–5 mL) and are installed or “locked” into the catheter lumen during periods when the catheter is not being used (e.g., for a 12-h period each night) [37, 40, 101, 156–161]. For example, vancomycin has been used at a concentration of 1–5 mg/mL; gentamicin and amikacin, at 1–2 mg/mL; and ciprofloxacin, at 1–2 mg/mL; the volume of installed antibiotic is removed before infusion of the next dose of antibiotic or iv medication or solution.

Although the duration of antibiotic lock therapy has varied among different studies, it most often is 2 weeks. The study with the lowest salvage rate reported that a mean of 8 days of therapy was provided [43]. Vancomycin remains stable when kept in heparin or saline solutions at room temperature for days; this allows for antibiotic lock therapy with heparin overnight or longer if indicated. A recent study found that incubation with heparin (final concentration, 10,000 U/mL) for 72 h at body temperature showed a time-dependent loss of antimicrobial activity of 7 antibiotics, but the greatest decrement (a 64.6% decrease in the activity of meropenem against gram-positive microbes) still resulted in a favorable ratio of antibiotic concentration to MIC [162].

Because the purpose of antibiotic lock therapy is to sterilize the lumen of the catheter, patients should be selected to receive such treatment on the basis of a high likelihood of intraluminal infection. Two studies have suggested that 2 weeks of antibiotic lock therapy alone may be as effective for intraluminal infection as a few days of systemic therapy followed by 2 weeks of antibiotic lock therapy [39, 156]. However, with some pathogens (e.g., *S. aureus*) or situations (e.g., bloodstream infection in a patient with neutropenia or moderately severe infection with any pathogen-host combination), most clinicians would not feel comfortable providing antibiotic lock therapy without a full course of parenteral therapy [38].

The importance of patient selection for antibiotic lock therapy was supported by the results of 2 studies in which 15 of 17 patients were treated for 20 episodes of catheter-related bloodstream infection with no relapse of the same species [43, 156]. One of the studies noted that this relapse-free period after salvage allowed for continued catheter use for a mean of 777 days (range, 210–1610 days) [43]. The 2 remaining patients who received parenteral nutrition had a total of 17 episodes of bloodstream infection; 1 patient had 7 episodes that involved various combinations of 3 different species of gram-negative bacilli, and the other patient, who underwent 4 abdominal ostomies, had 10 episodes that involved various combinations

of 8 different species that infected 3 different catheters over a period of 14 months [43, 156].

Catheters that have been in place for <2 weeks are most often infected extraluminally, and some patients who have had catheters in place for longer periods also may have evidence of extraluminal infection (e.g., inflammation over the tunnel or exit site or pocket of a totally implanted port) [56]. With extraluminal infection, antibiotic lock therapy alone will obviously be inadequate, and parenteral therapy plus antibiotic lock therapy would not be much better than parenteral therapy alone (unless there is a combination of intraluminal and extraluminal infection). By contrast, a recent study, in which parenteral antibiotic therapy administered through the catheter was used in addition to antibiotic lock therapy for apparent intraluminal infection, reported cures in 40 of 40 patients with catheter-related bacteremia; each of these patients had salvage of the tunneled catheter, with a mean follow-up of 20.5 months [40, 41]. These cases included 12 episodes of *S. aureus* bloodstream infection. The approach was not as effective in another study that involved subcutaneous ports, in which <50% of the catheters were salvaged [160]. It was not made clear what proportion involved chamber versus pocket infections. A subsequent study found that ports in patients with AIDS and chamber infections with or without associated bacteremia were significantly more likely to be salvaged when antibiotic lock therapy with or without parenteral therapy was used (22 [80%] of 27) than when standard parenteral therapy without antibiotic lock therapy was used (1 [16%] of 6; $P = .005$) [45].

SPECIFIC PATHOGENS

Coagulase-negative staphylococci. Coagulase-negative staphylococci, such as *S. epidermidis*, are the most common cause of catheter-related infections [163–166]. Catheter-related infections due to coagulase-negative staphylococci predominantly manifest with fever alone or fever with inflammation at the catheter exit site. Most patients have a benign clinical course, but rarely do patients develop frank sepsis with a poor outcome [163–165, 167].

To date, there have been no randomized trials that have evaluated any treatment modality for catheter-related infections due to coagulase-negative staphylococci. Coagulase-negative staphylococcal catheter-related bloodstream infection may resolve with removal of the catheter and no antibiotic therapy, yet many experts believe that such infections should be treated with antibiotics (table 4). Specific strategies for the management of coagulase-negative staphylococcal infections associated with different catheters and devices are summarized in tables 5 and 6 and in figures 1–4.

S. aureus. There are no data from randomized trials with adequate sample size and statistical power to show an optimal

Table 6. Recommendations for the management of iv catheter-related bloodstream infection caused by specific microorganisms.**Coagulase-negative staphylococci**

- Treat empirically with vancomycin and change to semisynthetic penicillin if the isolate is susceptible (A-II) [69, 70]
- Combination therapy with vancomycin plus gentamicin or rifampin is not recommended for routine therapy (D-III) [71–74]
- If the CVC is removed, appropriate systemic antibiotic therapy is recommended for 5–7 days (B-III) [75]
- If nontunneled CVC is retained and intraluminal infection is suspected, systemic antibiotic therapy for 10–14 days and antibiotic lock therapy are recommended (B-III) [38–43, 76]
- A tunneled CVC or an ID can be retained, if necessary, in patients with uncomplicated, catheter-related, bloodstream infection (C-III) [26]; if the CVC or the ID is retained, patients should be treated with systemic antibiotic therapy for 7 days and with antibiotic lock therapy for 14 days (B-II; figure 4) [37–44, 76]
- Treatment failure that manifests as persistent fever, persistent positive blood culture results, or relapse of infection after antibiotics have been discontinued is a clear indication for removal of the catheter (A-II) [77–79]

Staphylococcus aureus

- β -Lactam antibiotics should be first choice for parenteral treatment of *S. aureus* bacteremia when the isolate is susceptible; for patients with penicillin allergy without anaphylaxis or angioedema, first-generation cephalosporins, such as cefazolin, can be used without allergic response in 90%; for patients with serious allergy to β -lactams and for those with methicillin-resistant *S. aureus*, vancomycin is the drug of choice (A-II) [69, 80–82]
- Vancomycin should not be used when infection with β -lactam-susceptible *S. aureus* is diagnosed; excessive vancomycin use selects vancomycin-resistant organisms; vancomycin has higher failure rates than do either oxacillin or nafcillin, and it results in slower clearance of bacteremia among patients with *S. aureus* endocarditis (D-III) [28, 80–82]
- Nontunneled CVCs suspected to be the source of *S. aureus* bacteremia should be removed, and a new catheter should be reinserted at a different site (B-II) [30, 77, 78, 83]
- Tunneled CVCs or IDs should be removed if there is evidence of tunnel, pocket, or exit-site infection (B-II) [36, 84]
- TEE should be done for patients without contraindications, to identify those who have complicating endocarditis that requires therapy for 4–6 weeks (B-II) [29, 30]
- Sensitivity of transthoracic echocardiography is low and thus is not recommended for excluding a diagnosis of catheter-related endocarditis if TEE can be done (B-II) [29, 30]
- Patients who have negative TEE results and from whom the catheter is removed should be treated for 14 days with systemic antibiotic therapy (B-II) [29, 30]
- Tunneled CVCs or IDs with uncomplicated intraluminal infection and *S. aureus* bacteremia should be removed or, in selected cases, retained and treated with appropriate systemic and antibiotic lock therapy for 14 days (B-II) [40, 85, 86]

Gram-negative bacilli and miscellaneous pathogens

- Patients with catheter-related, gram-negative bacteremia with nontunneled CVCs and no evidence of septic thrombosis or endocarditis should have the catheter removed and should receive appropriate antimicrobial therapy for 10–14 days (B-III) [87, 88]
- Patients with tunneled CVCs or IDs that cannot be removed, who have suspected catheter-related, gram-negative bacteremia without associated organ dysfunction, hypoperfusion, or hypotension, can be treated for 14 days with systemic and antibiotic lock therapy (B-III) [41]; quinolones, such as ciprofloxacin with or without rifampin, may be preferred because they can be given orally and because they have been shown to eradicate gram-negative bacilli from foreign bodies in animal models (C-III) [89–91]
- For episodes of bacteremia due to *Pseudomonas* species other than *Pseudomonas aeruginosa*, *Burkholderia cepacia*, *Stenotrophomonas* species, *Agrobacterium* species, and *Acinetobacter baumannii*, serious consideration should be given to catheter removal, especially if bacteremia continues despite appropriate antimicrobial therapy or if the patient becomes unstable (A-III) [87, 88, 92]
- Empirical antimicrobial therapy for suspected gram-negative, catheter-related bloodstream infection should include drugs that are active against *P. aeruginosa*, especially in patients with neutropenia (C-III) [93]
- For patients with prolonged bacteremia after appropriate antimicrobial therapy and catheter removal, especially in the presence of underlying valvular heart disease, 4–6 weeks of antibiotic therapy should be undertaken (C-III) [93]
- Because the vast majority of catheter-related bloodstream infections caused by *Bacillus* and *Corynebacterium* species require catheter removal, catheters should be removed in these instances (A-II) [92, 94]
- Intravenous catheter-related infections due to mycobacteria, such as *Mycobacterium fortuitum* and *Mycobacterium chelonae*, require catheter removal (A-II) [92, 94]

Candida albicans and other fungi

- All patients with candidemia should be treated; amphotericin B is recommended for suspected catheter-related candidemia in patients who are hemodynamically unstable or who have received prolonged fluconazole therapy (A-I); patients who are hemodynamically stable and who have not had recent therapy with fluconazole, or those who have a fluconazole-susceptible organism, can be treated with fluconazole instead of amphotericin B (A-II) [95, 96]
- Duration of antifungal treatment for candidemia should be for 14 days after the last positive blood culture result and when signs and symptoms of infection have resolved (A-III) [95, 97]
- Catheter-related *Candida krusei* infections should be treated with amphotericin B (A-II) [92, 94, 98]
- Tunneled CVCs or IDs should be removed in the presence of documented catheter-related fungemia (A-II) [11, 97, 99]
- Salvage therapy for infected tunneled CVCs or IDs is not recommended for routine use, because salvage rates with systemic fungal therapy and antibiotic lock therapy for *Candida* species have been in the 30% range (D-II) [43, 76, 100, 101]
- Treatment of catheter-related bloodstream infection due to *Malassezia furfur* includes discontinuation of intralipids and removal of intravascular catheter, especially with nontunneled catheter infections (B-III) [102, 103]
- Patients with catheter-related *M. furfur* fungemia should be treated with amphotericin B (B-III) [102]

NOTE. CVC, central venous catheter; ID, implantable device; TEE, transesophageal echocardiography. The letter and Roman numeral in parentheses after each recommendation represent Infectious Diseases Society of America evidence-based criteria to reflect the strength and quality of evidence (table 1) [1].

duration for the treatment of catheter-related *S. aureus* bloodstream infection. In the past, *S. aureus* bacteremia was treated for 1 month because of greater concern about the risk of endocarditis than would be expected as a result of bacteremia due to other microbes [29, 168–170]. However, several recent studies have suggested that the risk of endocarditis or other deep tissue infection related to *S. aureus* bacteremia may be sufficiently low to recommend a shorter course of therapy (e.g., 10–14 days) for patients with apparently uncomplicated catheter-related bloodstream infection [31, 77, 171–175]. Most of these studies were quite small, and some had design flaws, which resulted in imprecise estimates of the risk involved. In a meta-analysis, 8 (6.1%) of 132 subjects in 11 studies had a relapse after receiving short-course therapy, developing either endocarditis or deep tissue infection at another site [176].

A subsequent study that used the Duke diagnostic criteria for endocarditis found that 16 (23%) of 69 patients with catheter-related *S. aureus* bloodstream infections had endocarditis documented by use of TEE [30]. Among patients considered to have endocarditis on the basis of these criteria, the sensitivity of transthoracic echocardiography was only 27%. The authors of this study have suggested that the use of TEE to determine the duration of therapy for patients with apparently uncomplicated bacteremia would be a cost-effective alternative to administration of therapy for 1 month to all patients with *S. aureus* bacteremia [29]. Only 1 (5%) of 21 patients who completed a course of therapy for *S. aureus* endocarditis had a relapse after therapy, compared with 12 (18%) of 67 patients who had *S. aureus* bacteremia and a negative result on TEE and who presumably had received a shorter course of therapy, although duration of therapy was not specified [30]. Of note, none of these patients who had a negative result on TEE had a relapse of endocarditis, but they had deep tissue infections at other body sites [30].

More recently collected data from the same investigators have shown that 17 patients who had catheter-related *S. aureus* bacteremia with negative results for vegetations and valvular abnormality on TEE, negative results of follow-up blood cultures done at 2–4 days after initiation of therapy, defervescence within 3 days of initiation of therapy, absence of any new local complaint, and absence of any indwelling prosthetic device had no relapse of infection during 3 months of follow-up after having received standard parenteral therapy for only 7 days (V. Fowler, personal communication). An additional 18 patients who had catheter-related *S. aureus* bacteremia and negative results for vegetations on TEE were treated for 14 days and did not have relapse of infection during a 3-month follow-up period, despite the presence of each of the following clinical characteristics in some of the patients: TEE that showed preexisting valvular abnormality, positive results of follow-up blood cultures done 2–4 days after initiation of therapy, a superficial

nonremovable focus of infection, and fever that had persisted for >3 days (V. Fowler, personal communication) The preliminary findings should be confirmed by larger studies.

Removal of vascular catheters that are infected with *S. aureus* has been associated with a more rapid response to therapy and/or a higher cure rate in 3 observational studies [36, 77, 78]. None of these studies was a randomized, controlled trial, however, so definitive data are unavailable. It appears reasonable that removable nontunneled catheters that can be easily replaced should be removed immediately when they are found to be the source of *S. aureus* bacteremia, even for mild to moderate cases. By contrast, with long-term tunneled or hemodialysis catheters, which are more expensive and more difficult to replace, this recommendation is more controversial (except in the setting of tunnel infection), despite the fact that 2 of the 3 studies suggested a higher rate of failure when catheters were not immediately removed [36, 78].

In a recent study, which used the antibiotic lock technique in addition to standard parenteral therapy for patients with hemodialysis catheter-related infection, all 40 catheter-related bloodstream infections (including all 12 cases reported to involve *S. aureus*) were cured and the catheter salvaged [40]. The mean duration of follow-up of the study subjects was 20.5 months. These results differ from the results of the observational studies cited above, and they suggest that, in some cases, uncomplicated *S. aureus* infection of tunneled catheters may be managed without catheter removal in the absence of tunnel or exit-site infection (i.e., when infection is confined to the lumen of the catheter) by means of standard parenteral therapy combined with antibiotic lock therapy (figure 4).

For patients who remain febrile and/or have bacteremia for >3 days after catheter removal and/or initiation of antibiotic therapy, a longer course of therapy has been recommended because of the perception of an increased risk for underlying endocarditis [31, 83, 110]. The aforementioned preliminary data, however, suggest that the results of TEE may be more important than these variables for determination of the optimal duration of therapy (V. Fowler, personal communication). AIDS has been reported to be an adverse prognostic factor in patients with catheter-related *S. aureus* bacteremia [177]. In 1 study, 6 (35%) of 17 patients developed metastatic complications after having received antibiotic treatment for a mean of 18 days. For this reason, a longer course of therapy has also been recommended for patients with HIV infection who develop catheter-related *S. aureus* bloodstream infection [178].

Management recommendations for *S. aureus* are summarized in figures 1–4 and in tables 4–7. Of note are the preliminary results of a recently published, randomized trial that suggested that treatment of severe *S. aureus* infections with the use of rifampin and a fluoroquinolone (treatment initially involved iv administration and was rapidly switched to oral ad-

Table 7. Evidence-based recommendations for the management of iv device–related complications.

Septic thrombosis

In all cases, the involved catheter should be removed (A-II) [2, 104–107]

Incision and drainage and excision of the infected peripheral vein and any involved tributaries should be done, especially when there is suppuration, persistent bacteremia or fungemia, or metastatic infection, in conjunction with appropriate antibiotic therapy (B-III) [108, 109]

Surgical exploration is needed when infection extends beyond the vein into surrounding tissue (B-II) [104]

Surgical excision and repair is needed in cases of peripheral arterial involvement with pseudoaneurysm formation (A-III) [110, 111]

Heparin should be used in the treatment of septic thrombosis of the great central veins and arteries (A-II) [104–106], but it is not indicated for the routine management of septic thrombosis of the peripheral veins (D-III) [112–114]

Duration of antimicrobial therapy for septic thrombosis of great central veins should be same as that for endocarditis (4–6 weeks); in most cases, vein excision is not required (D-III) [105, 107]

For septic thrombosis of the great central vein due to *Candida* species, a prolonged course of amphotericin B therapy has been shown to be effective and is recommended; fluconazole can be used if the strain is susceptible (A-II) [105]

Use of thrombolytic agents in addition to antimicrobial agents in patients with catheter-related bloodstream infection and thrombus formation is not recommended (E-I) [64]

Persistent bloodstream infection and infective endocarditis

For nontunneled catheters and in most instances involving long-term catheters, persistent bacteremia or fungemia warrants removal of the device (A-II) [77–79]

Patients with repeatedly positive blood culture results and/or unchanged clinical status for 3 days after catheter removal should be treated presumptively for endovascular infection for ≥ 4 weeks of antimicrobial therapy in most cases and with surgical intervention when indicated (B-II) [31, 115]

Empirical therapy in this situation must include coverage for staphylococci (A-II) [116–119]

For uncomplicated right-side (tricuspid valve) endocarditis due to staphylococci in injection drug users, a 2-week duration of antimicrobial therapy with use of penicillinase-resistant penicillin for susceptible isolates, with or without gentamicin, appears to be effective (B-I) [54, 115, 120, 121]

With rare exception, *Candida* endocarditis will require surgical intervention in addition to antimicrobial therapy (A-III) [122]

NOTE. The letter and Roman numeral in parentheses after each recommendation represent Infectious Diseases Society of America evidence-based criteria to reflect the strength and quality of evidence (table 1) [1].

ministration) was as effective as the use of standard parenteral therapy with a β -lactam antibiotic or vancomycin in patients who are allergic to β -lactam antibiotics [179]. These results are credible because of the excellent results achieved with the use of oral rifampin and quinolone for the treatment of right-side endocarditis due to *S. aureus* [180, 181]. If rifampin is used to treat such infections, a single daily dose results in higher area-under-the-curve values for rifampin than do divided doses that total to the same amount [182, 183].

Gram-negative bacilli. Although staphylococci are the quintessential microbial pathogens involved in device-related infections, a number of other bacteria, mycobacteria, fungi, and algae have caused intravascular device–related bloodstream infection and may be gaining prominence in this regard [11, 92, 94]. The incidence of intravascular catheter–related bloodstream infection due to gram-negative bacilli may also be increasing. These microorganisms are commonly associated with contaminated infusate and are a common cause of bloodstream infection in immunocompromised patients with tunneled catheters or devices [2, 93].

No controlled studies have addressed whether intravascular catheters must be removed for treatment of bloodstream infections caused by the myriad of gram-negative bacilli, nor have

there been any controlled trials to evaluate the optimal antimicrobial agents for this condition or the optimal duration of therapy. Successful treatment of tunneled catheter–related, gram-negative bacteremia has been reported by means of antimicrobial therapy without catheter removal, especially in studies of pediatric patients [40, 94]. A limitation in some of the pediatric studies was a failure to require that cultures of percutaneously drawn blood be done to document bloodstream infection. Other studies have demonstrated that catheter removal in cases of catheter-related bacteremia with *Pseudomonas* species other than *P. aeruginosa*, *Burkholderia cepacia*, *Acinetobacter baumannii*, and *Stenotrophomonas* species reduced the rate of treatment failure and improved survival.

Management of gram-negative bacillary catheter-related bacteremia is summarized in figures 1–4 and in tables 4–7. There are no data to guide the duration of therapy with iv antibiotics versus oral antibiotics for gram-negative bloodstream infections. For some antibiotics, such as the quinolones (e.g., ciprofloxacin) or trimethoprim-sulfamethoxazole, blood levels after oral administration differ minimally from levels after iv administration as long as medications that reduce absorption are not coadministered (e.g., antacids or iron, which reduce quinolone absorption).

Candida species. Antifungal therapy is necessary in all cases of vascular catheter–related candidemia. In one study, 4 of 26 patients with catheter-associated candidemia who were treated with catheter removal but without systemic antifungal therapy developed endophthalmitis, resulting in loss of vision in 3 patients [184]. A prospective, randomized study of 206 patients with candidemia (72% of whom were considered to have vascular catheter–associated candidemia) but without neutropenia showed that fluconazole (400 mg/day given for ≥ 14 days) was as effective as, but was less toxic than, amphotericin B (0.5 mg/kg/day) given for the same length of time [95]. Fluconazole may be used if the organism is susceptible [185].

The impact of CVC removal on the outcome of candidemia has been evaluated in several studies [97, 186–189]. Many of these studies did not use strict definitions of catheter-related candidemia. In 1 study, removal of the catheter on or before the first day that the study drug was administered (i.e., within 4 days of at least 1 positive blood culture result) was associated with a significant reduction in the duration of candidemia [97]. None of the patients had neutropenia, and patients who did not undergo catheter removal had greater severity of illness. In a multicenter, prospective, observational study that assessed the efficacy of amphotericin B and fluconazole in the treatment of candidemia, vascular catheter retention was a significant, independent prognostic factor for persistence of candidemia after 72 h of antifungal therapy and for mortality [79]. In a large retrospective study of 416 patients with cancer who had a CVC and candidemia, CVC retention was associated with poor outcome (death or persistence of infection at 3 months after initiation of therapy) compared with outcomes among patients who underwent either a guidewire exchange or removal of the catheter (OR, 2.2; 95% CI, 1.6–3.2; $P = .02$) [190].

For a patient who has candidemia and a nontunneled CVC, initial management should include an attempt to exchange the catheter and perform semiquantitative or quantitative catheter cultures. If the catheter is colonized with the same species of *Candida* as is the blood, the CVC should be removed, as shown in table 6 and figure 2. If culture of blood samples from a patient with a tunneled catheter or implantable port yields a *Candida* species, the decision about catheter removal should be based on the likelihood of catheter-related candidemia rather than on candidemia from another source, such as the gastrointestinal tract. Predictors of tunneled CVC–related candidemia are summarized in figure 3 and include the following: isolation of *Candida parapsilosis* from blood samples; quantitative blood cultures that suggest catheter-related candidemia (5-fold the number of colonies isolated from blood drawn through the CVC, compared with blood drawn from a peripheral vein); differential time to positivity (>2 h) for blood samples drawn from a percutaneous site, compared with those drawn through

the CVC [20, 21]; candidemia in a patient without neutropenia who has a CVC and no other apparent source for the bloodstream infection, with the exception of the vascular catheter; candidemia in a patient who is receiving hyperalimentation through the catheter; and persistent candidemia in a patient who is not responding to systemic antifungal therapy [34, 190]. Any of these situations should cause the clinician to consider the possibility of catheter-related bloodstream infection and the need to remove the CVC. Management of infections caused by *C. albicans* and other fungi is summarized in tables 4–7, figures 2–4, and the recent IDSA guidelines for the management of candidiasis [96].

PEDIATRIC INFECTIONS

The pediatric population is diverse, and the risk of infection varies with age, birth weight, underlying disease (e.g., cystic fibrosis, cancer, AIDS, prematurity, or short bowel syndrome), host factors (e.g., neutropenia), medications, type of device, and nature of the infusate (e.g., lipid emulsions) [191]. The importance of iv catheters with regard to bloodstream infection is difficult to assess, particularly when the iv catheter is not removed. Furthermore, controlled trials have provided few available data regarding appropriate management of intravascular catheter–related infection in children, because the currently available data are often derived from patients in pediatric or neonatal intensive care units or from those in oncology wards.

Most nosocomial bloodstream infections in pediatric patients are related to the use of an intravascular device [4]. The incidence of CVC-related infection ranges from 3% to 60%, with a rate of 1.7–2.4 infections per 1000 catheter-days, depending on the type of device and the age and underlying disease of the patient [142, 192–196]. Rates of bloodstream infection associated with CVCs in patients in pediatric intensive care units and with central and umbilical catheters in infants in neonatal intensive care units are higher than those in patients in adult intensive care units [197].

As in adults, most catheter-related infections in children are caused by coagulase-negative staphylococci (34%), followed by *S. aureus* (25%) [192]. In the neonate, coagulase-negative staphylococci account for 51% of catheter-related bloodstream infections, followed by *Candida* species, enterococci, and gram-negative bacilli [191, 198].

When the clinical and laboratory definitions of infection that have been established for adults are applied to children, several problems arise [3, 197]. Physician interpretation of the contaminant versus the pathogen may be affected by the age and underlying condition of the patient. For example, the coagulase-negative staphylococci isolated from blood samples obtained from a very-low-birth-weight infant are more likely to

be interpreted by physicians as being clinically significant, in comparison with such staphylococci from blood from an older patient [199, 200]. Peripheral blood cultures are not often done when catheter samples are obtained, because venipuncture can be a daunting task in infants and young children; however, percutaneous blood cultures are preferred because of their greater positive predictive value. In addition, placement of a catheter or changing of a catheter over a guidewire is difficult in young children, and removal of a catheter for diagnostic purposes often is not done because of concern about losing access (figure 1).

Management of intravascular catheter-related infections in infants and children is challenging. In figures 1–4, most of the recommendations that are shown for adults are also applicable to children, but removal of a catheter may not be feasible for infants and young children, especially neonates. Several studies have reported successful management of catheter-related bacterial infections without catheter removal [142–144, 192]. Although there have been anecdotal reports of cure of fungemia without catheter removal, treatment of catheter-associated fungemia without removal of the catheter has a low success rate and may be associated with higher mortality [143, 187, 201–203]. Antibiotic lock therapy is an alternative treatment approach for patients with persistently positive blood culture results despite antimicrobial therapy or recrudescence of infection, which would otherwise require catheter removal. For example, Johnson et al. [100] reported that 10 of 12 episodes of infection caused by a variety of organisms, including 2 *Candida* species, were cured without removal of the catheter. Indications for catheter removal in children remain controversial and warrant further evaluation. Those children who are treated without catheter removal should be closely monitored, and the device should be removed if clinical deterioration occurs.

Initial antibiotic selection should be based on the expected identity and susceptibility of the isolate and should be modified when results are available from the clinical laboratory (table 4) [196]. Empirical therapy for suspected catheter-related infection should be based on local knowledge of the distribution of isolates by species and the susceptibility patterns of nosocomial pathogens. In general, empirical therapy should include an agent that is effective against gram-positive bacteria, such as vancomycin, especially when coagulase-negative staphylococci with significant methicillin resistance are present in the hospital, and, if appropriate, an agent that is effective against gram-negative bacteria, such as an aminoglycoside or third-generation cephalosporin (antifungal therapy should be initiated when yeast is isolated from a blood culture or, on occasion, when suspicion of fungemia is high) [192, 196, 199, 201]. Certain antimicrobial agents that are used in adults, such as the fluoroquinolones, have not yet been approved for use in children (see [7, 8] for antimicrobial agents that are appropriate for use

in infants and children, and for doses of specific agents, according to age and weight).

Treatment regimens should be altered appropriately once culture information is available. Conventional treatment for intravascular catheter-related infection has not been established to be different than that which has previously been described for adults (table 4; figures 1–4), but certain procedures may not apply to infants and young children. For example, TEE, as noted in figures 2 and 4, is not commonly used in small infants and children who have CVC-related bloodstream infection without other indicators of endocarditis. Finally, the optimal duration of therapy has not been established for the treatment of catheter-related infections in children with or without catheter removal [142–144, 192].

COMPLICATIONS

Septic thrombosis. Septic thrombosis is a serious complication of intravascular catheterization and may involve central veins or arteries after prolonged dwell times [104–114, 204–206]. Septic thrombosis is an intravascular infection in which patients often have high-grade and persistent bacteremia or fungemia. Continued positive blood culture results after catheter withdrawal suggest a diagnosis of septic thrombosis or endocarditis. Septic pulmonary emboli and other metastatic infections may complicate this condition [104, 207].

Because an infected intravascular thrombus and intraluminal abscess may remain intact until after catheter removal, this infection may not become manifest until after catheter removal [107, 208]. When peripheral veins are involved, many older children and adult patients have localized pain, erythema, and edema, and fewer demonstrate an abscess, palpable cord, or purulent drainage [113, 114, 204]. Septic thrombosis due to a peripheral arterial catheter may present with a pseudoaneurysm or embolic lesions of the involved hand [110, 111]. Patients with septic thrombosis of the great central veins may have ipsilateral neck, chest, or upper extremity swelling [105, 107]. In general, *S. aureus* is the most common infecting organism [108, 112, 206]; less common pathogens include *Candida* species [209] and gram-negative bacilli [114, 204].

There are no randomized studies to guide the optimal choice or duration of antibiotics; the use of anticoagulants, such as heparin, for this condition; or the excision of the involved vessel. Management, in terms of removal of the catheter, use of antibiotic therapy, need for surgical excision or drainage, and use of thrombolytic agents, is summarized in table 7.

Persistent bloodstream infection and infective endocarditis. Colonized intravascular catheters are the most common identified source of nosocomial endocarditis, accounting for one- to two-thirds of reported cases [115, 117–119, 210]. Staphylococci are the most common causative pathogen(s) in these

cases. For nontunneled catheters, and in most instances involving tunneled catheters, persistent bacteremia or fungemia warrants removal of the device, especially in patients with sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Repeatedly positive blood culture results and/or unchanged clinical status for 3 days after catheter removal usually reflect serious sequelae of intravascular catheter-related infections, such as septic thrombosis, endocarditis, or metastatic foci of infection [65], and these diagnoses should be aggressively pursued in this situation. Such patients should be treated presumptively for an endovascular infection by use of antimicrobial therapy for >4 weeks (in most cases) and surgical intervention, when indicated, unless septic thrombosis has been ruled out radiographically and endocarditis has been excluded by TEE. Management points are summarized in table 7.

AREAS FOR FUTURE RESEARCH

On the basis of the information in the preceding sections, it is clear that many studies are necessary before the optimal approach for management of vascular catheter infection is known. We have identified what we believe are some of the most important questions to stimulate readers to help fill in the gaps.

1. How long do patients with catheter-related bloodstream infection need to be treated? Anecdotal evidence suggests that the duration may vary from no therapy, for catheter-related coagulase-negative staphylococcal bloodstream infection, to therapy for as long as 4–6 weeks, for patients who respond slowly and whose catheters are left in place. Randomized trials are necessary to determine the optimal duration of treatment and how the duration is affected by the infecting organism, by leaving the catheter in place, and by use of the antibiotic lock technique.
2. Can catheter-related bloodstream infections caused by *S. aureus* and *Candida* species be appropriately treated with systemic antimicrobial therapy combined with antimicrobial lock therapy without removal of the catheter? To date, no prospective, randomized studies have addressed this issue for different catheter-related infections.
3. Do patients with positive results of quantitative or semi-quantitative catheter cultures (but with negative blood culture results) and no other obvious site of infection need to be treated with antibiotics? Randomized trials are needed to answer this question. If it turns out that patients with positive catheter culture results and negative blood culture results do not need to be treated, then there may be no need to obtain samples from catheters for culture at all. If patients respond better with treatment in this situation, a related secondary question is whether the differences in sensitivity between different catheter culture methods are clinically significant.

4. After a colonized catheter is removed from a patient with catheter-related bloodstream infection, when is it safe to place a new catheter? There currently are no adequate data to help clinicians with this question.
5. What is the diagnostic usefulness and accuracy of differential time to positivity for catheter and peripheral blood cultures? Larger, prospective studies, especially of nontunneled CVCs, are needed to determine the diagnostic significance of a culture of a blood sample obtained from a CVC that yields positive results at least 2 h earlier than does a simultaneous culture of a blood sample drawn through the peripheral vein. Given the increased availability of automated culture systems for cultures of blood samples, such data would be highly useful to clinicians.
6. Will cultures of both the tip and the subcutaneous segments of central catheters lead to a clinically significant improvement in the sensitivity of diagnosing catheter-related infection? Data from a recent clinical trial comparing the roll plate, sonication, and flush culture methods suggested that culturing both the tip and the subcutaneous segments might increase the sensitivity for catheter-related bloodstream infection up to nearly 90%. Further studies need to be done to verify this possibility.

PERFORMANCE INDICATORS

1. Assess whether the medical staff (physicians and nurses) are aware of these guidelines.
2. Distribute copies of these guidelines to all medical staff and have them acknowledge that they have read them.
3. Third, monitor compliance with the guidelines at your institution.

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