300 Infections Caused by Percutaneous Intravascular Devices

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SHORT VIEW SUMMARY

Definition
- Infections caused by peripheral and central intravenous catheters, including nontunneled central catheters and tunneled catheters, peripherally inserted central venous catheters (PICCs), totally implanted intravascular access devices (ports), pulmonary artery catheters, and arterial lines

Epidemiology
- Rates of central line–associated bloodstream infections (CLABSIs) in 2009 ranged from 1.05 (pooled mean hemodialysis rate) to 1.14 (pooled mean inpatient ward rate) to 1.65 (pooled mean intensive care unit rate) bacteremias per 1000 central venous catheter (CVC) days.
- These rates reflect a 58% reduction in total estimated CLABSIs from 2001 to 2009; the reduction in incidence of *Staphylococcus aureus* CLABSIs was greater than for any other pathogen.
- The majority of CLABSIs now occur in inpatient wards and outpatient hemodialysis centers.

Microbiology
- Staphylococci predominate as the most frequently encountered pathogens in device-related infections; coagulase-negative staphylococci are the single most common cause of these infections, whereas *S. aureus* bacteremias have decreased.
- CLABSIs increasingly are caused by multidrug-resistant gram-negative rods.

Diagnosis
- Clinical markers show a poor correlation with intravenous device–related bacteremia.
- Blood culture results positive for coagulase-negative staphylococci, *S. aureus,* or *Candida* spp., in the absence of any other identifiable source of infection, increase the possibility of intravenous device–related bacteremia.
- Quantitative or semiquantitative culture of the catheter combined with two blood cultures (one peripheral and one through the catheter) is the most accurate diagnostic method for short-term central catheters.
- Paired quantitative blood culture was determined to be the most accurate diagnostic method for long-term devices, including tunneled and totally implanted catheters.
- Differential time to positivity (between cultures drawn through the catheter and peripherally) compares favorably with quantitative blood cultures for the diagnosis of CLABSIs.

Prevention
- Many CLABSIs can be prevented using simultaneous implementation of an array of practice improvements (i.e., "bundle").
- All health care personnel involved in catheter insertion and maintenance should complete an educational program regarding catheter-associated infections.
- Chlorhexidine solutions should be used for skin preparation before catheter insertion.
- Maximal sterile barriers should be used during insertion of CVCs.
- Do not routinely replace CVCs, PICCs, hemodialysis catheters, peripheral arterial catheters, or pulmonary artery catheters to prevent infection.
- Antimicrobial-impregnated catheters, if used, should only be used as part of a comprehensive nosocomial bacteremia prevention strategy.

The relentless progress of medical science and technology has been accompanied by the development of a host of new diagnostic and therapeutic medical devices, each of which is associated with its own complications. Included in the list of devices and the complications of their use to be discussed in this chapter are peripheral and central intravenous catheters, including nontunneled central catheters and tunneled catheters, peripherally inserted central venous catheters (PICCs), totally implanted intravascular access devices (ports), pulmonary artery catheters, and arterial lines.

As early as 1977, Maki[1] suggested that more than 25,000 patients develop device-related bacteremia in the United States each year. The burgeoning use of an ever-expanding array of vascular access devices in medicine has resulted in even more complications associated with their use. Rates of bacteremia associated with the use of intravascular devices increased significantly into the early 2000s. More recently, data indicate that the rates of central line–associated bloodstream infections (CLABSIs) are decreasing, at least partly as a result of prevention programs implemented in many hospitals in 2001. In 2016, the Centers for Disease Control and Prevention (CDC) estimated that CLABSIs decreased by 50% between 2008 and 2014.[2] An intense focus on prevention of health care–associated infections, including CLABSIs, and requirements for the incorporation of performance measures into regulatory and financial reimbursement systems is believed to have had a significant impact on these infections,[3] although some have suggested that linking infection rates directly to financial reimbursement may result in underreporting.[4–6] CLABSIs have been estimated to be the most costly health care–associated infection, increasing costs by $45,814 per case and thereby providing a clear incentive to invest in additional prevention measures.[7]

Such device-associated infections occur as sporadic cases, as well as in case clusters caused by the same organism. Vascular catheters have become an increasingly important source of bacteremias, increasing from 3% in the mid-1970s to 19% in the early 1990s.[8] Primary bacteremias (i.e., no apparent local infection elsewhere caused by the same organism) account for approximately one-half of all intensive care unit (ICU)–related bacteremias.[9–11] In cancer patients, 56% of all bloodstream infections from 1999 to 2000 were CLABSIs.[10] The problem of iatrogenic, device-associated bacteremia is not unique to the United States; in one prospective study of bacteremia from Australia, nosocomial bacteremias accounted for 40% of all cases of bacteremia, and half of the nosocomial cases were device associated.[12]

Both local and systemic infection may result from contamination of intravascular devices. Local cellulitis, abscess formation, septic thrombophlebitis, device-associated bacteremia, and endocarditis all occur as complications of intravascular therapy and monitoring.

PATHOGENESIS

For intravascular device–related bacteremia to occur, microorganisms must gain access to the extraluminal or intraluminal surface of the

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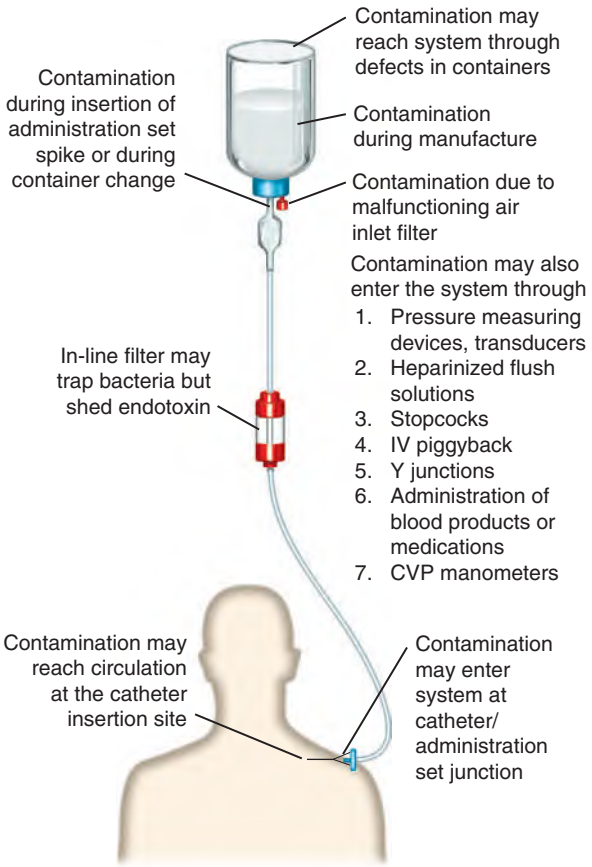

FIG. 300.1 Points of access for microbial contamination in infusion therapy. *CVP,* Central venous pressure; *IV,* intravenous.

device. Microbial adherence and incorporation into biofilms then occurs, resulting first in infection and then, in some instances, in hematogenous dissemination.[13] Fig. 300.1 illustrates the potential points of access to an intravascular device, each of which has been associated with both sporadic cases and case clusters of nosocomial bacteremia. Whereas the skin entry site has long been thought to be the most important portal of entry for invading microorganisms, the catheter hub–lumen has also been shown to be a major contributor to catheter-related bacteremia.[14,15] The most common point of access appears to vary, depending on the duration of time the catheter has been in place. Each of the three major sources of intravenous device–related bacteremia is discussed in the following sections.

Contamination of the Infusate

Contamination of the fluid administered through the device is a major cause of epidemic intravenous device–related bacteremias. Nonetheless, infusate contamination is a rare cause of bacteremia. Infusion-related sepsis has been reviewed in detail,[16] and both manufacture-related[17] and in-use[18] contamination of infusate have been documented as causes of device-associated sepsis.

Another factor influencing the pathogenesis of infusate-associated infection is the composition of the fluid. Different infusion fluids support the growth of differing pathogens. The microbiology of outbreaks of infusate-related sepsis is somewhat monotonous; pathogens such as *Enterobacter, Citrobacter,* and *Serratia* predominate. No infusate is entirely free of risk; even sterile water for injection can support the growth of *Burkholderia cepacia.*[19] Parenteral nutrition solutions are superb substrates for the growth of certain microorganisms.[20] Lipid emulsions support bacterial growth extremely well,[21] and their use has also been associated with a risk for fungemia caused by the lipid-dependent yeast *Malassezia furfur,* although not with contaminated infusates.[22] This risk has been primarily identified in the neonatal intensive care setting and has been less commonly seen in adults.[22] Several additional outbreaks of bacteremias have been linked to compounding pharmacies, some of which adhere to suboptimal quality control standards.[23,24] One national outbreak of *Serratia marcescens* bacteremias occurred as a result of contaminated magnesium sulfate solution,[24] and two more recently reported outbreaks were associated with contaminated heparin solutions.[23,25]

Parenteral nutrition solutions may also become contaminated during compounding in the hospital pharmacy.[26,27] Two similar outbreaks of *Candida parapsilosis* infections were linked to the backflow of yeasts into parenteral nutrition solution because vacuum pumps were used improperly.[26,27]

The composition of the infusate also influences the degree of irritation of the vascular intima at the site of infusion. Fluids that are not isotonic, those at nonphysiologic pH, and those containing particulates all may irritate the vascular wall, thus provoking thrombus formation. Such thrombi may be seeded with microbes—either hematogenously or by direct extension.

Contamination of the Catheter Hub and Lumen (Intraluminal Source)

Currently, bacteremias associated with long-term catheters appear to arise most frequently from an intraluminal source, perhaps after intraluminal colonization with biofilm-producing microbes.[28] Contamination of the catheter hub–infusion tubing junction is a significant contributor to device-associated infection.[15,29,30] Endemic coagulase-negative staphylococcal bacteremias often arise as a result of contamination of the catheter hub with these organisms. A randomized study examining the effects of a redesigned protective hub found these hubs to be associated with a significantly lower rate of catheter sepsis and culture-positive catheter hubs,[31] suggesting that the hub is a common portal of entry for bacteria. Other investigators have incriminated the hub-tubing junction (particularly when it does not allow a good fit) in the pathogenesis of epidemics of coagulase-negative staphylococcal infection.[32,33] Maki and Ringer[34] found hub contamination to be the second most heavily weighted risk factor for catheter-associated infection in a large, prospective study. Salzman and colleagues[35] noted that greater than 50% of episodes of central venous catheter (CVC)–related sepsis occurring in a neonatal ICU were preceded by colonization of the catheter hub with the infecting organism. In a subsequent experimental study, these investigators found that swabbing the catheter hub with disinfectant substantially reduced the hub's microbial burden and that preparations containing 70% ethanol were both more effective and more likely to be safer for the patient than preparations containing chlorhexidine. Sherertz[36] estimated that the hub, lumen, or both contributed two-thirds of the microorganisms that infected long-term catheters and that one-fourth of the microorganisms were from the skin.

Conversely, some newer technologies may be associated with increased risks for catheter-associated infection. Needleless intravenous systems were developed to provide a safer workplace environment for health care providers, and needle-free devices now constitute more than 80% of access devices and are recommended for all tubing/catheter access.[37] However, use of these devices has been associated with increased risk for device-associated infection.[38,39] Multiple investigations of bacteremia outbreaks associated with needleless devices have suggested that the mechanism for bacteremia may involve contamination from the end cap.[40–43] Disinfection is required before needleless connector access, with a minimum of 5 seconds of scrubbing,[44] but compliance has been poor in multiple studies.[45] Products to reduce contamination of needleless connectors have been developed, including silver-coated needleless connectors and disinfection caps.[46,47] A recent meta-analysis reported that needleless connectors with improved engineering design were associated with a lower central line–associated bloodstream infection risk.[48] Different studies have paradoxically found either increased or decreased risk with the same needleless system (e.g., the Interlink IV Access System [Baxter, Deerfield, IL]),[41,42] supporting the conclusion that the primary risk associated with these devices is related to how the systems are used (e.g., frequency of changing end caps and adherence to recommended infection control procedures) rather than factors intrinsic to the system.[42] Appropriate staff education regarding use of these devices, ensuring compliance with the manufacturer's recommendations, and consideration of needleless connectors with improved

engineering design when CLABSI rates remain stubbornly high is recommended to prevent device-related bacteremia.

Contamination of Skin at the Device Insertion Site (Extraluminal Source)

Many authorities believe that the catheter insertion tract provides the major avenue for the ingress of microbial invaders.[a] Several studies have focused on microbial colonization around the catheter insertion site as a significant risk factor for catheter-associated infection.[52] Supporting this contention are the studies of Cooper and Hopkins that demonstrated organisms on the exterior surface of catheters rather than within the catheter lumen.[53] In the prospective study of Maki and colleagues,[54] colonization around the catheter insertion site was the most strongly associated risk factor for local catheter infection. Similarly, Safdar and Maki[55] determined that most catheter-related bacteremias occurring with short-term noncuffed central catheters were extraluminally acquired and derived from the cutaneous microflora. Skin appears to be the primary source of intravenous device–related bacteremia for short-term catheters placed for an average duration of less than 8 days.[56,57]

Skin colonization is a dynamic process, and the dynamics of the cutaneous microbiota are only now being explored aggressively using genomic technology. Atela and coworkers[49] conducted a prospective study to assess the turnover of superficial skin colonization by performing serial quantitative cultures of skin and the catheter hub. Strains recovered from the targeted superficial skin sites demonstrated a poor correlation both with strains from previous skin cultures and with catheter tip isolates. Herwaldt and colleagues examined the source of coagulase-negative staphylococcal bacteremias in hematology-oncology patients and found that the same strain was identified in both skin and blood cultures in only 6 of 20 episodes.[58] The matching strain was isolated only from other sites (primarily nares) in the remaining 70% of episodes, leading these investigators to the conclusion that mucous membranes might be a reservoir for strains of coagulase-negative staphylococci causing bacteremia in immunocompromised patients. Of importance, these investigators were unable to identify colonization with the same strain for the majority of bacteremias; only 4 of the 21 nosocomial bloodstream infections were preceded by colonization with the same strain. Most nosocomial coagulase-negative staphylococcal bacteremias in this study appeared to result from extrinsic introduction of the organism.

EPIDEMIOLOGY

CLABSI Rates

Rates of CLABSIs in the United States have decreased substantially over the last two decades.[59–62] The introduction of widely adopted guidelines for the prevention of CLABSI in 2002,[37] followed by additional guidelines and central line care maintenance "bundles" (see later in this chapter), have altered patient care practices and contributed significantly to the overall decrease in these infections.[59,63–68] Other factors that have impacted CLABSI rates include the requirement for mandatory reporting of CLABSI rates in some states,[69] Medicare reimbursement penalties for health care–associated conditions imposed beginning in October 2008 and other pay-for-performance programs,[70–72] changes in surveillance definitions,[73,74] universal decolonization,[75] attention to decreasing blood culture contamination rates,[76,77] and new technology-based interventions (discussed later in this chapter). Some data suggest that institutions may also attempt to "game" the system to artificially decrease CLABSIs, either by decreasing the number of blood cultures drawn or by attributing bacteremias to sources other than central lines.[4–6]

Patient-Related Issues

Intravenous device–related bacteremia rates are influenced by patient-related parameters, catheter-related parameters, and hospital-related parameters (Table 300.1). Because of methodologic difficulties in performing appropriate scientific studies to characterize relative risk, many of these risk factors have been identified either retrospectively or in the epidemic setting. Still, each of the patient-related factors identified in Table 300.1 has been associated with an increased risk of device-associated infection.[78] Alteration of the patient's skin microbiota, either as a result of antimicrobial therapy or by colonization with an epidemic strain carried on the hands of hospital personnel, is a common event preceding catheter site infection. Failure of hospital personnel to perform appropriate hand hygiene procedures, particularly in the ICU setting, has been well documented.[79–81] Numerous epidemics of device-associated bacteremia have been linked to hospital personnel carrying an epidemic strain on their hands. Manipulating the system for repositioning, for obtaining a sample, or for any other reason increases the likelihood that the catheter may become contaminated.[82] The increasing prevalence of multiple drug resistance among health care–associated isolates causing these infections (e.g., vancomycin-resistant enterococci, multidrug-resistant *Acinetobacter baumannii,* carbapenem-resistant Enterobacteriaceae) has magnified this problem in the past decade.

The risk of developing catheter-associated bacteremia is related to the patient and his or her intrinsic host defense mechanisms, as well as to factors related to the patient's hospital environment and therapy (see Table 300.1). The physician cannot alter most such patient-related factors; however, these data can be used when evaluating the risks associated with, the necessity for, and the duration of intravenous therapy.

Catheter-Related Issues

Several catheter characteristics or properties have been suggested to be associated with an increased risk for catheter-associated infection. Catheters that irritate the vascular intima and provoke thrombogenesis and catheters that are made of intrinsically thrombogenic materials are likely to be associated with an increased risk for device-associated infection.[83] Older studies suggest that stiff catheters were associated with higher infection rates.[84] Such catheters are likely to be more mobile in the insertion tract and are thought to be more thrombogenic. A clear association has been established between the thrombogenicity of a catheter and the risk for device-associated infection.[85,86] Despite differences in thrombogenicity, some authorities believe that all catheters become coated with a fibrin sheath soon after placement.[87] Currently, the majority of catheters are manufactured with antithrombogenic polymers, such as polyurethane, Teflon, or others.

Catheter composition may influence the risk for infection in another way. Sheth and coworkers[88] have shown that certain microorganisms,

TABLE 300.1 Risk Factors for Device-Associated Bacteremia

Granulocytopenia
Immunosuppressive chemotherapy
Hematologic malignancy (versus solid tumor)[440]
Loss of skin integrity (e.g., burns, psoriasis)
Severity of underlying illness
Active infection at other site
Alteration in patient's cutaneous microflora
Failure of health care provider to wash hands
Contaminated ointment or cream
Catheter composition/construction:
Flexibility/stiffness
Thrombogenicity[83]
Microbial adherence properties and biofilm production[87]
Size of catheter
Number of catheter lumens[91]
Catheter function/use
Catheter management strategies—number of entries into the system
Type of catheter: plastic > steel
Location of catheter:
Central > peripheral
Jugular > femoral > subclavian[57,112,441]
Lower extremity sites > upper extremity sites
Type of placement: cutdown > percutaneous
Duration of placement[a] (at least 72 hours > less than 72 hours)[16,34]
Emergent placement > elective placement
Skill of venipuncturist (others > intravenous team)[16,106]
Type/use of catheter[262]:
Balloon-tipped, flow-directed > percutaneously placed
Central venous > implanted central venous
Nursing staffing variables[114,435,437]:
Nurse-to-patient ratio[434]
Lower regular registered nurse-to-patient ratio
Higher float pool registered nurse-to-patient ratio

[a]Although several studies support this precept, another has questioned it.

[a]References 1, 12, 15, 16, 34, 49–51.

most notably staphylococci, are able to adhere better to a catheter made from polyvinyl chloride than to a Teflon catheter. Rotrosen and colleagues[89] demonstrated increased adherence of *Candida* spp. to polyvinyl chloride catheters compared with Teflon catheters. In a rabbit model, silicon catheters are easier to infect with *Staphylococcus aureus* than are those made of polyurethane, Teflon, or polyvinyl chloride.[90] One might hypothesize that materials that facilitate microbial adherence may be associated with an increased risk for device-associated infection. Newer therapeutic interventions have focused on diminishing adherence to the catheter through use of chelating agents, such as ethylenediaminetetraacetic acid (EDTA) or sodium citrate, or ethanol locks.

The physical size of the catheter (and therefore the size of the defect in the skin's intrinsic host defenses) is also likely to be correlated with increased risk. Similarly, increasing the number of lumens in a catheter has been suggested to increase the risk for catheter-associated infections. Several studies have suggested that the use of multiple-lumen catheters is associated with an increased risk for catheter-associated infection compared with the use of single-lumen catheters,[42,91,92] although not all studies have found this difference.[93,94]

The presence of distant infection resulting in hematogenous seeding of the intravascular device has been incriminated in the pathogenesis of device-associated infection in some series.[52,95] Several factors may influence the risk for catheter seeding, including catheter composition, local thrombus formation at the catheter insertion site, intensity of bacteremia, the infecting pathogen, duration of catheterization, duration of bacteremia, and the patient's ability to mount an immunologic response to the infection.

Formation of a bacterial biofilm is now thought to be a virtually universal phenomenon that begins within 3 days after insertion of intravascular devices.[87] Biofilm formation is more predominant on the external surface of catheters in place fewer than 10 days, and then predominates intraluminally in catheters in place for at least 30 days.[96] Microorganisms embed themselves in and under the biofilm layer and become the source of intraluminal colonization and, eventually, the sources of CLABSIs.[96] Certain chelators, including EDTA and sodium citrate, inhibit bacterial growth and fibrin formation.[97] Ethanol lock therapy, in which a high concentration of ethanol is instilled within a catheter and left to dwell, also results in biofilm reduction or eradication.[96] The presence of fibrin deposits may, at least in part, explain the difficulty in treating totally implanted venous access port bacteremias without removal of the device.[98,99] Antibiotic concentrations should be 100 to 1000 times greater to kill sessile bacteria within a biofilm than for planktonic bacteria.[100–102]

Finally, the manner in which the catheter is used may influence risk. For example, risks for infection with pulmonary artery catheters may be higher because of the manner in which they are used.[103] In critically ill patients, these catheters are used intensively (although now somewhat less frequently than in the recent past). They are frequently repositioned to obtain accurate readings, they are used to obtain samples for the measurement of cardiac output, and they can be used to obtain mixed venous blood to measure oxygen and carbon dioxide tensions.

Catheter management, including both insertion and maintenance, also may influence risk for infection. Several studies have shown that catheters placed by less experienced personnel are at increased risk for infection.[104,105] Another study analyzed the efficacy of using a skilled team for the placement of peripheral intravenous catheters.[106] In this study, an intravenous therapy team significantly reduced both local and bacteremic complications associated with the placement of peripheral intravenous catheters, in part related to the timely replacement of the catheters. Two studies suggest that insertion of CVCs with less than maximal sterile barriers increases the risk of catheter-related infection.[57,107] Several studies have suggested that the number of times the system is entered also influences the risk for infection.[82,108,109] More than a single attempt to insert the catheter has also been found to be a risk factor for bacteremia,[94] as has the number of venous catheters in place and the intensity of their use.[110] Insertion at a subclavian rather than a femoral site is clearly associated with a lesser risk of both infectious and thrombotic complications.[91,111,112] Ultrasound-guided insertion of nontunneled CVCs has been found to reduce mechanical complications and decrease time to insert these catheters, but was found to have no effect on incidence of CLABSI or on mortality.[113]

Hospital-Related Issues

In addition to patient-related risk factors, several hospital-related risk factors for CLABSIs have been either identified or proposed (see Table 300.1). In contradistinction to the patient-related factors, such hospital-related factors can often be altered for patient benefit. Nurse staffing variables, including nurse-to-patient ratio, level of training, and permanent assignment to the unit ("float" nurse vs. regular unit staff nurse), have been shown to affect bacteremia rates.[114,115] As noted previously, the level of experience of the individual inserting the catheter (i.e., the number of previous catheter insertions) was also found to affect catheter-related bacteremia rates.[116] In addition, a number of studies have found that an education program focusing on risk factors and practice modifications is associated with decreased rates of CLABSIs.[117,118]

MICROBIOLOGY

Staphylococci continue to predominate as the most frequently encountered pathogens in device-related infections. Although *S. aureus* is a frequent cause of device-associated infection, the coagulase-negative staphylococci are the most common causes of these infections, especially in immunocompromised patients and those in whom long-term central venous access is required.[119] Multiple reports indicate that CLABSIs caused by *S. aureus* have decreased more than other pathogens over the last decade.[120]

Although there are some minor microbiologic differences among the devices or therapies under discussion, as a genus, *Staphylococcus* accounts for the majority of the episodes of bacteremia associated with these devices.[8,121] Studies suggest that coagulase-negative staphylococci may be able to adhere to plastic catheters more aggressively than can other organisms.[122] This property would result in a selective advantage for coagulase-negative staphylococci in causing device-associated infections.

Other commonly encountered isolates are listed in Table 300.2. One study of patients with hematologic malignancies and having Hickman catheters inserted identified a predominance of gram-negative organisms (68%) causing catheter-related bacteremias in this nonneutropenic population.[123] Raad and colleagues[10] reported that gram-negative bloodstream infections in cancer patients with solid tumors were most likely catheter related. National Healthcare Safety Network (NHSN) data from 2009 to 2012 from adult oncology units still revealed a dominance of coagulase-negative staphylococci, but increased rates of CLABSI in this population with fluoroquinolone-resistant *Escherichia*

TABLE 300.2 Microbiology of Device-Associated Bacteremia

Coagulase-negative staphylococci, including *Staphylococcus epidermidis*[a]
Staphylococcus aureus
Enterococcus spp.
Serratia marcescens[b]
Candida albicans[c]
Candida tropicalis[c]
Pseudomonas aeruginosa[d]
Klebsiella spp.[b]
Enterobacter spp.[b]
Citrobacter freundii[b]
Corynebacterium (especially *C. jeikeium*)[e]
Acinetobacter (especially *A. baumannii*)[f]
Burkholderia cepacia complex[d]

[a]Most common pathogen for long-term lines; also associated with lipid infusions in neonates.
[b]Frequently associated with contaminated infusate.
[c]Most often associated with total parenteral nutrition; usually along the catheter path but occasionally as a result of contaminated infusate.
[d]May arise from a water source (e.g., infusate) or may reflect cutaneous colonization.
[e]*C. jeikeium* bacteremia occurs almost exclusively in severely immunosuppressed patients who are or have been receiving broad-spectrum antibiotics and who have indwelling intravascular devices.
[f]*A. baumannii* (often multiply drug-resistant) is becoming increasingly prevalent as a pathogen in intensive care units, especially among critically ill patients who require life support interventions (e.g., ventilator support) and those who have received multiple courses of antimicrobials.

coli and vancomycin-resistant *Enterococcus faecium* were also noted.[124] Our own experience would suggest that gram-negative bacilli may predominate among stem cell transplant recipients, particularly those who have gastrointestinal involvement with graft-versus-host disease. The past decade has witnessed an increasing occurrence of CLABSIs caused by multidrug-resistant gram-negative rods, most notably *A. baumannii.*[125] CLABSIs caused by *A. baumannii* often occur in critically ill, immunosuppressed, highly antimicrobial agent–experienced patients who can ill afford any bacteremia, let alone one caused by multidrug-resistant bacteria.[126]

Patients with femoral catheters in one study had higher rates of gram-negative bacteremias and yeast-related fungemias.[127] The occurrence of some of the more unusual isolates (e.g., *Enterobacter* spp., *B. cepacia,* and *Citrobacter freundii*) as a clear cause of the device-associated infection should at least suggest the possibility of a contaminated infusion product or an aqueous environmental reservoir for these pathogens.[128–130]

Other organisms may cause such infections (e.g., *Flavobacterium* and *Acinetobacter* spp.); however, such organisms have been infrequently associated with either infusion-related or cannula-related infections.[18] Concomitant with the increasing empirical use of broad-spectrum antimicrobials in severely immunosuppressed patients, cases of device-associated bloodstream infection caused by a variety of unusual bacterial, mycobacterial, and fungal pathogens have been reported with increasing frequency[12,131–138]

DIAGNOSIS

Clinical distinction between catheter-associated septicemia and sepsis from another site is sometimes difficult. Clinical markers show a poor correlation with intravenous device–related bacteremia.[139] Serum procalcitonin has been studied extensively as a marker of sepsis, and one analysis concluded that it was the best predictor of CLABSI of any available test.[140] Nonetheless, currently available assays often do not provide definitive results; many patients with bacteremia have indeterminate levels of procalcitonin.[141] The presence of fever has a high sensitivity for bacteremia but poor specificity, and local inflammation has better specificity but poor sensitivity. In addition to the presence of an indwelling intravascular device, several clinical features should alert the physician to the possibility of device-associated bacteremia. Salient features of device-associated sepsis that help distinguish it from other bacteremic syndromes are listed in Table 300.3. In general, blood culture results positive for coagulase-negative staphylococci, *S. aureus,* or *Candida* spp., in the absence of any other identifiable source of infection, increase the possibility of intravenous device–related bacteremia.[139] The 2009 Infectious Diseases Society of America (IDSA) guidelines add to this definition one of the following: (1) the same organism growing from a percutaneous blood culture and a catheter tip culture; (2) a catheter draw-back culture and a peripheral culture that have the same organism, with the catheter blood culture becoming positive 2 hours earlier or having a quantitative blood culture that is threefold higher; or (3) blood cultures drawn through different catheter lumens that differ threefold in quantitative cultures.[139] These definitions were intended to apply to treatment of catheter-acquired infections, not for surveillance purposes.

TABLE 300.3 Factors Differentiating Device-Associated Bacteremia From Other Septic Syndromes

Local phlebitis, inflammation, or both at catheter insertion site
Lack of other source for bacteremia
Sepsis occurring in a patient not otherwise at high risk for bacteremia
Localized embolic disease distal to cannulated artery[146]
Hematogenous *Candida* endophthalmitis in patients receiving total parenteral nutrition[230,231]
Presence of ≥15 colonies of bacteria on semiquantitative culture of the catheter tip[144,145]
Sepsis apparently refractory to "appropriate" antimicrobial therapy
Resolution of febrile syndrome after device removal
Typical (*Staphylococcus aureus, Staphylococcus epidermidis,* or other coagulase-negative staphylococci) or unusual (*Burkholderia cepacia* complex, *Pantoea [Enterobacter] agglomerans, Enterobacter cloacae*) microbiology
Clustered infections caused by infusion-related organisms

Although none of these criteria specifically identifies the intravascular device as the source of sepsis, the presence of these clinical findings should at least raise the possibility of device-associated bacteremia.

Cultures of the catheter tip have been reported to be of variable and limited value. Catheter tip cultures should not be performed for diagnosis of bacteremia related to subcutaneous venous ports; instead, culture of the material inside the port reservoir is more sensitive.[99,142,143]

Using the semiquantitative culture technique, which defines a positive catheter tip culture as yielding 15 or more colonies,[144,145] in combination with a relatively strict definition of catheter-associated sepsis, Maki and colleagues reported a specificity in short peripheral catheters ranging between 76% and 96% and a positive predictive value of a positive catheter tip culture ranging between 16%[145] and 31%[144] in four studies.[144–147] Data regarding the sensitivity of the semiquantitative culture technique are not available because the authors incorporated having a positive catheter tip culture as part of their definition of both local catheter infection and catheter-acquired bacteremia.[144–147] The cutoff point of 15 colonies per catheter as a definition for "infection" appears to have been somewhat arbitrary in these studies. The authors noted that most infected catheters yield confluent growth when using the semiquantitative technique. These original studies from the late 1970s found that *S. aureus,* rather than coagulase-negative staphylococci, *Candida* spp., and *Enterococcus* spp., were the predominant microorganisms causing bacteremia, and short peripheral catheters (5.7 cm) or steel needles comprised most of the catheters studied. Given the current differences in microbiology and in intravascular devices now in use, these studies are less relevant in the 21st century than they were 40 years ago.[148]

Several investigators have tried to modify Maki's technique to improve the predictability of the procedure. Cleri and coworkers[149] reported a technique for quantitatively culturing catheters in broth. This system, which is slightly more cumbersome for the laboratory, was considered by these authors to have three advantages over the system described by Maki and colleagues: (1) the ability to detect organisms within the lumen, (2) the ability to evaluate relative numbers of organisms from different catheter segments, and (3) the ability to compare relative numbers of organisms present in mixed infections.[149] Brun-Buisson and colleagues[150] used a simplified quantitative broth dilution tip culture to evaluate catheters as potential sources for infection and found this technique to be 97.5% sensitive and 88% specific for the diagnosis of device-associated bacteremia, using a strict clinical definition.[150] Use of this technique was not found to be predictive of subsequent bacteremia when all catheter tips were cultured upon removal.[151] Subsequently, Gutierrez and associates[152] found a modified broth dilution technique to be only slightly more sensitive, but substantially more labor intensive, than the semiquantitative technique. The latter authors advocated the use of semiquantitative cultures because of the ease with which this test is performed. Hnatiuk and coauthors[153] demonstrated a substantial increase in sensitivity for the semiquantitative technique when the catheter tip cultures are plated at the patient's bedside rather than cutting the tip into a sterile tube and sending the tip to the laboratory for culture.

Siegman-Igra and colleagues[154] conducted a meta-analysis of catheter culturing techniques and suggested that the accuracy increases for catheter segment cultures with increasing quantitation (i.e., qualitative < semiquantitative < quantitative). The increase in accuracy is primarily due to the increased specificity of the more quantitative tests. They found that quantitative catheter segment culture was the only method associated with sensitivity and specificity greater than 90%.[154] Similarly, Sherertz and associates[155] suggested that the common practice of culturing a single segment of a central vascular catheter is inadequate. Safdar and colleagues[156] also found that qualitative culture of the catheter segment was the least accurate of the tests they studied, primarily because of poor specificity.

Although the relative merits of these various procedures remain to be definitively delineated, the ease of performing the semiquantitative technique described by Maki and coworkers[144,145] has kept this procedure in widespread clinical use. Attempts to culture newer catheters with antimicrobial coating used for prevention of CLABSIs may lead to false-negative results.[157] Specific inhibitors are available to inhibit the effect for chlorhexidine–silver sulfadiazine–coated catheters,[157] but no inhibitors have been identified for minocycline-rifampin–coated catheters.

Other investigators have suggested alternative techniques for diagnosing catheter-associated infections[154,158–160] Acridine orange leukocyte cytospin testing of blood drawn through the catheter has been studied as a method of diagnosing infection while maintaining the catheter.[161,162] A meta-analysis concluded that this test offers rapid diagnosis of catheter-related bacteremia, with good accuracy but lower sensitivity.[156] Although some experience is being gained with the direct Gram stain, none of these newer techniques appears to be effective enough to supplant the semiquantitative method. Kite and colleagues[159] have published a description of an endoluminal brush method, suggesting that this procedure can be used without sacrificing the intravascular line. Although these authors suggest that the procedure is substantially more sensitive and more specific than the semiquantitative technique, only 1% of 692 infectious disease physician survey respondents recently reported using this method.[4] Others have reported that endoluminal catheter colonization is invariably present in cases of catheter-related bacteremia.[32] Some authors have recommended a combination of direct and microbiologic techniques.[154,158]

Mosca and associates[163] emphasized the benefits of obtaining blood cultures by using the Isolator system (Wampole Laboratories, Cranbury, NJ), which allows a quantitative estimate of microbial burden in the specimen. Whereas several additional studies have underscored the usefulness of the Isolator system, one study has suggested that results obtained with traditional blood cultures may be complementary to those obtained with the Isolator system and that, whenever feasible, both approaches should be used.[164] A survey of infectious diseases physicians published in 2012 found that quantitative blood cultures were unavailable in 75% of their institutions.[4] Paired quantitative blood cultures also have been studied.[142] This technique involves drawing one set of cultures through the device and another set percutaneously; catheter-related infection is diagnosed when cultures are positive from both sites and the concentration of microorganisms in the culture from the device is three- to fivefold higher than in the peripheral culture.

Safdar and colleagues[156] performed a meta-analysis to determine the most accurate diagnostic methods for intravenous device–related bacteremia. They determined that quantitative or semiquantitative culture of the catheter, combined with two blood cultures (one peripheral and one through the catheter), is most accurate for short-term central catheters.[156] Paired quantitative blood culture was determined to be the most accurate diagnostic method for long-term devices, including tunneled and totally implanted catheters. These authors specifically recommend, as does the IDSA,[68,139] that vascular catheters not be cultured if no signs of infection are present. As noted previously, several studies have recommended a differential comparison of quantitative cultures obtained peripherally and quantitative cultures obtained by drawing blood back through the suspected catheter to document the occurrence of catheter-acquired sepsis.[10,165,166] Some authors have suggested that paired quantitative blood cultures (as described previously) obviate the need to remove the catheter and include culture of the tip in the diagnostic algorithm.[167] Because of the complexity of the epidemiology of device-associated bacteremia and the increased technical complexity of the differential blood culturing procedure, the broad applicability of these and the earlier findings nonetheless remains unclear. In addition, despite the evidence that quantitative blood cultures are useful in diagnosing intravascular catheter bacteremias, many clinical microbiology laboratories do not offer this service because of the cost and complexity.[4]

Recently, interest has focused on a method that is based on differential time to positivity of qualitative blood cultures drawn simultaneously both from a catheter and peripherally.[168–172] Blot and coworkers[169] suggested that the speed with which bacterial isolates can be detected in the microbiology laboratory may distinguish catheter-associated from non–catheter-associated infection. Presumably because of a higher bacterial concentration, the blood cultures drawn through an infected CVC often demonstrate growth much more rapidly than those drawn peripherally.[171] Other groups have determined that this differential time to positivity (between cultures drawn through the catheter and peripherally) compares favorably with quantitative blood cultures for the diagnosis of CLABSIs.[168,172,173] This same differential time to positivity was examined in a group of cancer patients[173–175] and in critically ill patients[176] and was found not to be useful for many clinical presentations, leaving the validity of this factor undetermined for clinical use. Safdar and coauthors[156] examined this methodology in a meta-analysis and concluded that although paired quantitative blood cultures were the most accurate diagnostic method, using the differential time to positivity provides comparable sensitivity and acceptable specificity. This technique is available in most, but not all, clinical laboratories.[4] The recorded time is when the bottle is logged into the laboratory, not when the blood was placed in the bottle, assuming that growth was minimal before incubation.

The usefulness of "through-the-line" cultures has been questioned repeatedly because these cultures may become contaminated easily while being drawn from the catheter hub.[177,178] Other data suggested that rates of contamination for venipuncture versus cultures drawn through the catheter were not significantly different.[179] The incidence of false-positive draw-back cultures may greatly depend on the type of intravenous device used to draw the cultures and the care taken in obtaining the specimen. If the details of the method used to obtain the culture are unknown, relying entirely on cultures obtained by drawing blood through an indwelling catheter may be imprudent.[180] In well-defined circumstances in which device-associated bacteremia is an important consideration in the patient's differential diagnosis, these cultures may provide valuable information.[149–152,163–166,181] As reported by DesJardin and colleagues,[182] culture of blood drawn through either a central catheter or a peripheral vein shows excellent negative predictive value. Blood cultures drawn through a central catheter have a lower positive predictive value than do blood cultures drawn percutaneously, but drawing blood through a catheter may be an acceptable method for ruling out bacteremia. We recommend drawing at least two sets of blood cultures when device-related bacteremia is suspected, with at least one set drawn percutaneously.

CDC surveillance definitions for CLABSIs have become increasingly important over the last several years because the Centers for Medicare and Medicaid Services (CMS) now requires hospitals that receive reimbursement from Medicare to report CLABSIs acquired in their ICUs to the NHSN, and also now is using CLABSI rates to qualify hospitals for their annual payment update. In the CDC's 2013 update to the NHSN definitions and surveillance protocols, hospitals were then allowed to differentiate bloodstream infections associated with mucosal barrier injuries–laboratory-confirmed bloodstream infections (MBI-LCBIs) in their reports to the NHSN, although these infections are still considered to be CLABSIs for reporting purposes if central line requirements are met.[183] MBI-LCBIs are identified based on either a patient's white blood cell count or history of allogeneic stem cell transplant or both, combined with gastrointestinal graft-versus-host disease or a minimum amount of diarrhea in a 24-hour period. Inclusion of an NHSN definition for bloodstream infections associated with mucosal barrier injuries should assist with informing preventive efforts because this specific subset of infections is not amenable to bundled strategies to prevent CLABSIs (see later) and may otherwise prevent hospitals from "getting to zero."[184] Differences between the NHSN and IDSA definitions of CLABSI and MBI-LCBI may account for important differences in attributing infection to a catheter source. This difference in attribution has been assessed retrospectively at the MD Anderson Cancer Center. The distinction in attribution of source is largely based on the IDSA inclusion of quantitative blood cultures drawn simultaneously from the catheter and peripheral blood. In this cancer population, NHSN definitions overestimate the catheter as the source of bloodstream infection. However, the authors emphasized that patients with MBI should not just be excluded from assessments of CLABSI, which would lead to underestimation in cancer patients.[185] The CDC reported that CLABSI rates decreased significantly in location types after moving MBI-LCBI events.[74]

During the past 15 years, non–culture-based diagnostic methods have begun to play an increasingly prominent role in the diagnostic microbiology laboratory.[186,187] Examples of the usefulness of these techniques include the use of a variety of polymerase chain reaction–based diagnostics to more rapidly detect pathogens, compared with conventional blood culture,[188] and the molecular identification of antimicrobial resistance even before speciation can be completed.

These molecular techniques are particularly valuable in epidemiologic investigations.

Finally, avoiding contaminating blood cultures is vitally important to accurate diagnosis of bloodstream infection.[188] Blood culture contamination can result in unnecessary antibiotic treatment, laboratory expense, and longer hospitalization.[177,189,190] A number of approaches can decrease contamination rates, including drawing blood through peripheral venipuncture rather than via an intravascular catheter, use of sterile gloves, cleaning tops of blood culture bottles with antiseptics, inoculating blood culture bottles before other blood tubes, and using a phlebotomy team to draw blood cultures.[190] Several technologic approaches to reducing blood culture contamination have been suggested. For cultures drawn through existing lines, one study recommended changing the needleless cap before drawing blood cultures as a way to obtain more specific and reliable results.[191] A needleless device is used to inject blood into the blood culture bottles. More recently, Rupp and colleagues studied a specimen diversion device that diverts and sequesters the initial 1.5- to 2-mL portion of blood, which presumably carries contaminating skin cells, microbes, and infusate.[192]

DEVICE-SPECIFIC ISSUES

Peripheral Intravenous Cannulization

In general, peripheral catheters are associated with much lower infection risks than are central catheters. The incidence of bacteremia associated with peripheral catheters was recently estimated to be 0.18% (range 0%–2.2%), with a mean of 22% (range 7%–60%) of nosocomial catheter-related bloodstream infections due to peripheral catheters.[193] The CDC recommends that peripheral catheters be replaced every 72 to 96 hours in adults to prevent phlebitis, whereas catheters should not routinely be replaced in children.[68] A large, multisite, randomized trial of peripheral catheter replacement found no difference in the primary outcome of phlebitis (7%) when catheters were replaced every 3 days versus when clinically indicated.[194] A recent meta-analysis found that a dwell time beyond 3 days independently increases risk of colonization and independently increases risk of bloodstream infection in adult patients.[193]

The location of catheter placement also may influence subsequent infection rates. Catheters placed in the lower extremities, particularly those placed in the femoral veins, are associated with increased risk for many complications, including infection.[195–197] One in three health care–associated *S. aureus* catheter-related bloodstream infections is due to peripheral catheters, and these infections remain a cause of significant morbidity and mortality.[193,198,199]

Catheters placed percutaneously are associated with lower infection rates than are those placed by cutdown.[200] Catheters placed emergently are also at higher risk for infection, presumably as a result of breaks in technique at the time of placement.[201] Several authors have suggested that catheters placed by members of an intravenous therapy team are associated with lower complication rates than are those placed by other health care professionals.[106,202]

Finally, two studies have demonstrated that routinely changing intravenous administration sets at 48 rather than 24 hours was not associated with a significant increase in the infusion-related bacteremia rate.[203,204] Snydman and associates[205] and Maki and colleagues[206] compared the relative safety of changing administration sets at 72-hour intervals with changing them at 48 hours. Neither study identified an increased risk with the 72-hour interval.

Thus inserting a peripheral catheter, dressing it, hooking up the administration set, and changing all three at 72- to 96-hour intervals seems safe, practical, and reasonable.

Central Venous Catheters

Short-Term Issues

Because CVCs frequently remain in place longer than peripheral catheters, certain problems either occur with more frequency or are unique to these catheters. In addition, because of the placement of these catheters in the great veins, complications of placement, such as infective endocarditis and suppurative thrombophlebitis of the great veins, represent life-threatening events.

Safdar and colleagues,[78] in a review of risk factors for CVC-related bloodstream infections, found that heavy colonization of the insertion site or contamination of a catheter hub, as well as duration of catheter placement for more than 7 days, significantly increased the risk of catheter-related bloodstream infection. Insertion technique and follow-up care were also reported as significant risks.[78] A multicenter trial with 3027 adult ICU patients randomly assigned subclavian, jugular, or femoral vein nontunneled central vein catheters. Subclavian lines were associated with less infection and symptomatic thrombosis but held an increased risk of pneumothorax.[207]

The presence of either intraluminal or extraluminal fibrin has been proposed as predisposing to the development of catheter-associated infection.[85,86,208,209] Contaminated fibrin sheaths have also been implicated in infection of right heart structures, producing an endocarditis-like infection associated with vegetations near the location where the tip of a central catheter had previously been placed.[210] Stillman and colleagues[86] studied 94 central catheters and found that all 11 catheters categorized as infected in their study and 30 of 83 not found to be either infected or colonized had gross visible evidence of either intraluminal or surface thrombin at the time of removal. Lloyd and coworkers[211] failed to find a deleterious effect associated with the so-called fibrin sheath when evaluating a rat model of device-associated bacteremia. Another rat model found that catheter colonization decreases with the decrease in fibrin within the pericatheter sheath.[212]

Routine replacement of CVCs is not necessary and exposes the patient to the increased risks of catheter manipulation and mechanical complications with new sites.[213] The CDC has recommended against routine replacement of CVCs, PICCs, hemodialysis catheters, or pulmonary artery catheters to prevent catheter-related infections.[68] The issue of whether central catheters should be changed over a guidewire remains controversial. Use of a guidewire obviates the need for a second percutaneous puncture of the great veins and may be preferable for catheter exchanges judged routine or mandated by some reason other than suspected infection. Little scientific evidence supports guidewire use if catheter-associated infection is suspected. Maher and colleagues[214] used this technique successfully for catheter exchange in situations assessed as "low risk for infection." Two additional studies suggest that guidewire exchange may not be particularly useful if device-associated infection is suspected.[215,216] In one of these two studies, guidewire catheter exchange was associated with an increased risk of bloodstream infection but a lower risk of mechanical complications.[216] In one experimental study, replacement of a biofilm-colonized CVC over a guidewire was associated with an increased risk for colonization of the new catheter, as well as an increased risk for production of detached, slime-enclosed, antibiotic-resistant aggregates that may disseminate the infection to other sites.[166]

Whereas guidewire exchange of CVCs may be associated with a greater risk for catheter-related infection, this technique may result in many fewer mechanical complications than would be the case for repuncture.[217] Specifically, exchange over a guidewire is associated with lower risks for some complications (e.g., bleeding and pneumothorax).[215,216] If a guidewire is to be used for catheter exchange, culture of the removed or "old" catheter tip should be performed. In addition, blood cultures should be drawn through the old line before removal. If either of these cultures becomes positive, the most conservative approach would be to remove the "replacement" catheter and perform appropriate cultures. If central access is still desired, a third catheter should be placed at a new puncture site. In situations in which the catheter is being removed for suspected sepsis, in our opinion, exchange over a guidewire should not be attempted. Conversely, one study suggested a possible benefit of guidewire exchange for patients who have catheter-associated candidemia.[218]

Thrombosis of the great veins, with the attendant risk for suppurative thrombophlebitis, is a major complication of central catheter placement.[197] Thrombosis occurs with increased frequency in patients with malignancies[219] (particularly those who have mediastinal lymphadenopathy) and in patients with sickle cell disease.[220] In instances in which central catheters are placed in patients with these underlying illnesses, thrombotic and infectious complications should be anticipated, prevented (when possible), diagnosed early, and treated aggressively.

Additional issues relating to catheter composition and effectiveness of subcutaneous tunneling of catheters, and risks associated with electronic monitoring devices, are discussed elsewhere in this chapter.

Parenteral Nutrition Issues

Several aspects of the delivery of parenteral nutrition separate this mode of intravascular therapy from others. First, the composition of the infusate supports the growth of different microorganisms, most notably certain of the *Candida* spp.[20,221] Patients receiving parenteral nutrition in one study had an increased incidence of polymicrobial and multidrug-resistant bacteremias.[222] Second, catheters used to deliver parenteral nutrition are often required to remain in place much longer than either peripheral or other central venous cannulas. For this reason, problems with catheter contamination become much more of a concern. Third, the hypertonicity of the solution causes irritation of the vascular intima, which in turn may cause thrombosis. Thrombosis provides a nidus for, and an increased risk for, infection. Fourth, because patients who require parenteral nutrition are frequently severely ill as a result of neoplasms, trauma, or inflammatory bowel disease, the risk for bacteremia is higher. Therefore the potential for hematogenous seeding of the catheter is high. Several studies have found an association between use of parenteral nutrition and an increased risk of death.[223,224] One study found that use of total parenteral nutrition declined significantly from 2000 to 2005 in critical care trauma patients, and this decrease was associated with fewer complications, including bacteremia and sepsis.[224]

For these and other reasons, the placement, management, and care of catheters used for parenteral nutrition have received a great deal of attention. Ryan and colleagues,[108] in a prospective study of 200 catheters, documented that the risk of catheter-associated infection increased significantly when the integrity of the delivery system was interrupted. Snydman and coworkers[109] subsequently found that the occurrence of so-called line violations was highly associated with the development of catheter-associated sepsis. For these reasons, administration of parenteral nutrition should be supervised and conducted by members of a team (Table 300.4).[225] In their study, Snydman and coworkers also attempted to correlate the results of twice-weekly 1-mL pour-plate blood cultures with the subsequent development of catheter colonization and sepsis. Although concordance was high among blood cultures, catheter tip cultures, and peripheral blood cultures, cultures obtained through the catheter demonstrated a reasonably high incidence of false positivity, primarily as a result of *Staphylococcus epidermidis* contamination.[109] One study found that increased parenteral caloric intake is an independent risk factor for bacteremia and that this association is unrelated to hyperglycemia.[226] A recent study attempted to ameliorate the infectious complications of parenteral nutrition by prospectively maintaining tight glucose control.[227] Tight glucose control in these patients was still associated with a greater than fourfold increase in the odds of having a catheter-related bloodstream infection.

Candida infection has been a particular problem in patients receiving parenteral nutrition.[228–231] Curry and Quie[229] reported a 16% incidence of candidemia among patients receiving parenteral nutrition in a prospective study in a hospital that did not have a dedicated team. In another prospective study of 131 postoperative patients who were receiving parenteral nutrition, 13 patients were detected as developing chorioretinal lesions consistent with hematogenous *Candida* endophthalmitis; 7 of the patients had positive blood cultures for *Candida*.[230] Although most of these infections are presumed to arise as a result of yeast contamination at the catheter entry site, occasional outbreaks of *Candida* infection resulting from parenteral nutrition solution that was intrinsically contaminated have been reported.[26,27]

Because the catheter frequently must be left in place for an extended period of time and because of the increased thrombogenicity of parenteral nutrition fluid, several modifications of the delivery system of the catheter have been advocated. Among the suggested mechanisms for decreasing infections in this situation are (1) either bonding heparin or a heparin-like substance to the catheter or infusing heparin with the infusate in an attempt to minimize fibrin sheath formation[232,233]; (2) constructing the catheter of a more flexible substance, thereby producing less trauma to the vascular endothelium[234]; and (3) tunneling the catheter under the skin in an attempt to decrease access of pathogens to the circulation.[234]

A final and often difficult issue is deciding when to remove a parenteral nutrition catheter for suspected sepsis. In the past, most authorities recommended the removal of a catheter whenever infection was suspected. In separate studies, Ryan and coworkers[108] and Maher and associates[214] suggested that nearly 70% of catheters removed for suspected sepsis are apparently removed unnecessarily. Thus the parenteral nutrition team is often faced with the dilemma of whether or not to remove the catheter from a patient in whom the evidence for infection is equivocal. Such a patient may have many reasons for fever; therefore the diagnosis of infection may be difficult. Often patients are severely immunosuppressed, thrombocytopenic, or both, and the risks associated with catheter replacement may be quite high. Several clinical features may help the physician decide how to manage the catheter.[208,235] The presence of positive blood cultures (particularly for *Candida* or coagulase-negative staphylococci) in the absence of another source for the infection or in the presence of hemodynamic instability, embolic phenomena, leukocytosis, or profound leukopenia may herald the onset of catheter-associated sepsis. In addition, the development of new glucose intolerance in a parenteral nutrition patient whose carbohydrate metabolism had been previously well regulated may be an early subtle sign of bacteremia.[208,230]

TABLE 300.4 Prevention of Infusion-Related Infection in Total Parenteral Nutrition (TPN)

- Administration of TPN should be under the supervision of a team of health care professionals (usually a nurse, pharmacist, and physician). Both the decision regarding appropriateness of TPN therapy and protocols for insertions, maintenance, and delivery of TPN should be under the responsibility of this team.
- TPN solution should be prepared using sterile or aseptic technique, when possible in a laminar flow hood. Once prepared, the solution should be infused immediately or stored at 4°C.
- Placement of the catheter should be performed by using maximal sterile barrier precautions, including mask, sterile gown and gloves, large sterile drape, and appropriate skin preparation preferably with chlorhexidine.[349–351]
- Once placed, the catheter should be anchored to avoid movement, which may result in local irritation of the insertion site or transport of organisms along the insertion path.
- If possible, the system should be kept closed, avoiding unnecessary entry for blood drawing and administration of other fluids or blood products via the TPN line.
- If multiple lumens/ports are present, one lumen/port should be designated as the parenteral nutrition site.
- Other aspects of TPN administration are either of empirical or theoretical value, have shown equivocal or borderline results in studies, have shown conflicting results in studies, or have been demonstrated to be of value in small studies. Definitive studies to document the merit of these techniques are needed before they are routinely implemented; these include the following:
  - Routine application of antiseptic cream at the site of catheter insertion (either at the time of venipuncture or at routine dressing change)
  - Routine dressing changes and skin defatting with acetone
  - Routine use of semipermeable dressing materials. A meta-analysis of data from several studies suggests that these dressings may actually play a detrimental role in catheter infections.[368]
  - Routine use of in-line membrane filters (no benefit demonstrated)
  - Use of silicone or other less traumatic, nonthrombogenic catheters; use of heparin-bonded catheters; use of low-dose heparin infusions
  - Tunneling the catheter subcutaneously to increase the anatomic distance between catheter insertion site and the point at which the catheter enters the vessel (appears to be useful in several small studies)
  - Routine use of antibiotic lock prophylaxis with heparin plus vancomycin

Modified from Goldmann D, Maki D. Infection control in total parenteral nutrition. JAMA. *1973;223:1360–1364.*

Long-Term Issues

In 1973, Broviac and colleagues[236] reported their initial experience with the use of a chronic indwelling right atrial catheter for the delivery of long-term parenteral nutrition. Venous access also has long been a problem for patients receiving chemotherapy for malignancy. Hickman and coworkers[237] modified the Broviac catheter, which has a smaller lumen, for use in patients undergoing bone marrow transplantation. This modified catheter can be used for the administration of intensive chemotherapy, the administration of other medicines and fluids, transfusion, and phlebotomy. These catheters spare the patient both physical and psychological trauma. In the ensuing years, a number of additional modifications of these catheters have been devised, including the Groshong valve.[238] These modified catheters and implanted infusion

TABLE 300.5 Infectious Complications Associated With Implanted, Long-Term Catheters

AUTHORS AND YEAR PUBLISHED	PATIENT NUMBER, TYPE	TYPE OF CATHETER	CLABSIs (%)	CATHETERIZATION DURATION (RANGE) OR TOTAL CATHETER DAYS	CLABSIs PER 100 CATHETER DAYS
Blacklock et al. (1980)[239]	25, oncology	T	2 (8)	70 (5–256)	0.11
Larson et al. (1981)[250]	34, oncology	T	4 (11.8)	110.3 (3–355)	0.12
Wade et al. (1982)[442]	51, oncology	T	3 (5.9)	91 (4–457)	0.06
Lokich et al. (1985)[251]	92, oncology	T	2 (2.2)	127 (7–450)	0.02
Cairo et al. (1986)[242]	46, pediatric oncology	T	23 (50)	163 (9–365)	0.30
Johnson et al. (1986)[248]	64, pediatric oncology	T	33 (51.6)	251 (NG)	0.19
Shulman et al. (1987)[254]	31, pediatric oncology	P	4 (12.9)	232 (14–607)	0.05
Ross et al. (1988)[253]	39, pediatric oncology 49, pediatric oncology	T P	4 (10) 0 (0)	365 (30–426) 350 (7–395)	0.03 0.00
Viscoli et al. (1988)[256]	145, pediatric oncology	T	57 (39)	171 (2–647)	0.19
Hockenberry et al. (1989)[245]	82, pediatric oncology	P	4 (4.9)	168 (7–1030)	0.02
Kappers-Klunne et al. (1989)[249]	23, oncology 20, oncology	T P	19 (83) 9 (45)	166 (1–605) 164 (1–971)	0.50 0.27
van Hoff et al. (1990)[443]	59, pediatric oncology	T	30 (51)	220 (NG)	0.23
Ulz et al. (1990)[255]	111, oncology	T	63 (57)	81 (1–167)	0.66
Rizzari et al. (1992)[252]	125, pediatric oncology	T	106 (85)	134 (6–488)	0.51
Hogan and Pulito (1992)[246]	84, NICU	T	9 (10.7)	33.4 (2–119)	0.29
Alurkar et al. (1992)[241]	91, oncology	T	31 (34)	74.6 (NG)	0.41
Wacker et al. (1992)[257]	44, pediatric oncology 33, pediatric oncology	T P	15 (34) 6 (18)	236 (15–806) 316 (12–1294)	0.06 0.10
Biffi et al. (1997)[444]	175, oncology	P	4 (2.2)	180 (4–559)	0.003
Schwarz et al. (1997)[445]	680, oncology	P	31	310 (2–1960)	0.01
Elishoov et al. (1998)[243]	242, oncology	T	46 (19)	40 (7–187)	0.52
Jean et al. (2002)[446]	89, hemodialysis	T	56 (63)	52,030 total days	0.11
Chang et al. (2003)[228]	572, oncology	P	21 (3.7)	358 (1–1742)	0.01
Hung et al. (2009)[447]	209, pediatric oncology	P	18 (8.6)	597 (15–1962); 137,924 total days	0.013
Martin-Pena et al. (2012)[448]	123, hemodialysis	T	11 (8.9)	284 (NG)	0.034
Toure et al. (2012)[449]	315, oncology	P	41 (13)	170.5±117	0.076
Moore et al. (2014)[450]	555, hemodialysis[a]	T	174 (31)	155,518 total days	0.112
Nurse et al. (2014)[451]	191, LTAC[b]	P	15 (7.9)	183,183 total days	0.008
Hord et al. (2016)[452]	99, pediatric oncology 190, pediatric oncology	P T	144 (100) 193 (100)	97,212 total days 55,048 total days	0.148 0.351
Wildgruber et al. (2016)[453]	681, oncology[c]	P	41 (6)	299 (4–1228); 208,740 total days	0.02
Viana Taveira et al. (2017)[454]	188, pediatric oncology	P	94 (50)	NG (4–778)	0.121
Subtotal (by catheter type)	**2232** **3325**	**T (20 studies)** **P (14 studies)**	**881 (39.5)** **432 (13.0)**	— —	**0.240 (range 0.02–0.52)** **0.061 (range 0.0–0.27)**
Total	**5557**	—	**1313 (23.6)**	—	**0.15**

[a]Trial of gentamicin/citrate versus heparin catheter locking solutions.
[b]Medically complex patients at long-term acute care hospital.
[c]Trial of polyurethane versus silicone catheters.
CLABSIs, Central line–associated bloodstream infections; *LTAC,* long-term acute care hospital; *NG,* not given; *NICU,* neonatal intensive care unit; *P,* totally implantable port; *T,* tunneled central venous catheter.

ports, which were introduced in 1982, represent a major step forward in the management of all patients who require long-term central venous access but have been especially useful in the management of immunosuppressed patients (and particularly in immunosuppressed children) in whom venous access is frequently problematic. Use of these devices in a variety of clinical settings is currently the standard of care.

Several centers have reported their experiences using these catheters, and many series report remarkably low rates of infection. Initial reports suggested that the rate of catheter infection in nonneutropenic patients was approximately one infection per 5.5 patient-years.[239] Press and colleagues[240] summarized 1088 catheter placements from 18 studies in their literature review. In their summary data, these authors reported approximately 0.14 infections per 100 catheter days. Table 300.5 presents a similar summary, including several published studies evaluating infection and bacteremia risks associated with the use of tunneled catheters and infusion ports.[241–257] The elevated risk for bacteremia (0.15 infections for each 100 catheter days), may be more of a reflection of the severity of the patients' illnesses, the increasing immunosuppression associated with their therapies, and the invasive care provided to critically ill patients.

Several centers have reported remarkable success—few infections and few other complications as well—with totally implantable access

ports.[258–261] In one of the earliest of these studies, the rate of infections for each 100 catheter days was 0.43—comparable to rates of other implantable catheters.[258] Subsequent studies have demonstrated even lower infection risks.[b] One epidemiologic study concluded that infections are the primary reason for late-term complications and port removal.[263] This group determined that patients with recurrent device implantation and with ongoing chemotherapy are significantly more likely to need device removal.[263]

Pocket infections, defined as the spread of infection into the subcutaneous pocket of a totally implanted intravascular device,[139] are considered an absolute reason for device removal because of the poor response to antimicrobial therapy by bacteria inside the biofilms on the port inner surface.[139,264] Pocket infections remain among the most difficult infectious complications associated with implanted ports. Evidence from studies of intravascular cardiac device infections suggests that risk of local device infections, including pocket infections, in these devices is increasing at a faster rate than the corresponding increase in device implantations.[265,266]

Peripherally Inserted Central Venous Catheters

The use of PICC lines for intermediate and long-term access has increased dramatically in both home care and hospital settings.[267–270] These catheters have several advantages over some of the other long-term access devices: PICCs may be inserted at the bedside[267] by nonphysician providers[271,272]; they are placed into children and neonates under fluoroscopy or ultrasound guidance with relative ease[94,268]; and they are useful for administration of chemotherapy, antimicrobial agents, and parenteral nutrition,[268,270,273] particularly in pediatric patients requiring long-term nutritional support.[270,273] Skilled interventional radiology is needed for difficult insertions, for catheter salvage, and to ensure that the catheter is not misplaced or misdirected.[267]

A major problem is device failure, with as many as 10%[273] to 27%[274] of these catheters developing mechanical malfunction. Another group determined that PICC lines are more likely to develop mechanical complications and have a shorter survival time than CVCs.[274] Many institutions have elected to develop a skilled team approach to the insertion and management of these catheters. Nurse PICC teams inserted these devices in at least 60% of US hospitals in 2013 in one survey, and were more likely to use a variety of best-practice prevention approaches.[275] Placement of PICCs in our hospital requires scheduling in a procedure room with a trained team, ultrasound guidance, and follow-up chest x-ray to assure tip placement in the superior vena cava. PICC lines may be less cost-effective than currently believed because of the more difficult insertion into some patients and higher thrombophlebitis rates.[271,276] The extra expense and procedural requirements may be warranted when more than a week of intravenous therapy is anticipated. Placement complications are still less than with implanted CVCs, and removal is easy.

Improved insertion and maintenance practices have resulted in longer durations of PICC catheterization, as reviewed by Milstone and Sengupta.[277] Studies that evaluated routine catheter replacement as a strategy to prevent CLABSIs compared catheter replacements at up to 7 days; no studies have addressed whether catheter replacement beyond 7 days might reduce CLABSI. Milstone and Sengupta[277] therefore suggested that, in some instances, PICC replacement may reduce the incidence of CLABSI. One risk factor for CLABSI found in two recent studies is the number of lumens in the PICC catheter, with a higher odds ratio for infection with more lumens.[278,279]

Care and Maintenance of Implanted Central Venous Catheters

Intraluminal contamination may represent the most important route of infection for implanted catheters and ports, further suggesting that strategies aimed at decreasing the risks for intraluminal contamination could substantially lower infection rates with these types of intravascular devices. Several issues regarding the care and maintenance of these catheters remain unsettled. Among these issues are the following:

1. Should a dressing be placed over the exit site, and if so, what dressing materials should be used and how frequently should the dressing be changed?
2. Should the system be routinely flushed, and if so, how frequently and with what?
3. Are blood cultures obtained through the catheter reliable indicators of catheter contamination?
4. What are the indications for catheter removal, and can either or both local infection and bacteremia be treated with the catheter in place?

Although definitive answers to these questions remain elusive, at the National Institutes of Health Clinical Center, a semipermeable membrane is kept in place over the exit site. These dressings are changed at least weekly. For the few remaining catheters that require it, we also use an every-other-day heparin flush (5 mL of 100 units/mL) to attempt to keep the catheters patent. Higher heparin concentrations are associated with an increased risk for anticoagulating the patient. Newer, valved catheters do not require heparin and are locked with saline after use. One recent study suggested that disruption of catheter dressings was common and was an important risk factor for catheter-related infections.[280] The CDC guidelines suggest that well-healed exit sites might not require dressings.[68]

Repeated isolation of the same organism from cultures drawn through the catheter indicates a need for therapy. Individual positive cultures and sporadic positive cultures are difficult to interpret in the absence of clinical or laboratory correlates. As noted previously, some groups believe that quantitative cultures may prove particularly helpful in establishing a diagnosis in this setting.

Pulmonary Artery Catheters

The use of indwelling, balloon-tipped pulmonary artery catheters[281] revolutionized the management of hemodynamically unstable, critically ill patients. Despite an ongoing controversy about the safety of and benefit associated with the use of these catheters,[282,283] approximately 1.5 million are used each year in the United States alone.[284] The placement of such a catheter in one of the great veins, across the tricuspid and pulmonic valves, and into the pulmonary vasculature is not without complications, however. Michel and coworkers[285] demonstrated that 29 of 153 pulmonary artery catheter tips produced microbial growth in thioglycolate broth. Although no patient in this study was considered to develop sepsis secondary to the contaminated catheter, other studies have suggested a reasonably high rate of contamination, with occasional episodes of catheter-related sepsis and nosocomial endocarditis.[286] The majority of these catheters are heparin bonded, which reduces catheter thrombosis and microbial adherence to the catheter.

Katz and colleagues[286] retrospectively studied complications associated with the placement of 392 balloon-tipped catheters; of these, 17 (4.2%) were assessed to be associated with bacteremia. Maki[235] estimated that 3% to 5% of these catheters kept in place for more than 72 hours will result in CLABSIs, and concluded that efforts should be made to limit the duration of pulmonary artery catheters to no more than 4 days.[287] A study of 1000 patients randomized to receive either pulmonary artery catheters or CVCs found similar rates of infection in both groups (five CLABSIs in the pulmonary artery catheter group vs. three CLABSIs in the CVC group).[283] Another group found that 4 of 215 (1.9%) patients undergoing pulmonary artery catheterization developed infection, compared with no infections in the control group.[288] One study evaluated complications associated with the use of a "hands-off" pulmonary artery catheter that is completely shielded during balloon testing, preparation, and insertion[289]; use of this catheter was associated with a substantial reduction in systemic infections related to the catheter.[289]

Another problem relatively unique to the flow-directed, balloon-tipped pulmonary artery catheter is that such catheters may traumatize the right-sided heart valves and the right-sided endocardium. In a study of 102 consecutive autopsies of patients who died in the hospital, 26 (25.5%) had had an indwelling intracardiac catheter inserted before death.[290] Six of these patients were excluded from analysis (4 patients died 48 hours or less after catheter placement; 2 patients had permanent transvenous pacemakers in place for many years, with the anticipated endocardial fibrosis). Of the remaining 20 patients, 6 had vegetations

[b]References 246, 249, 251, 253, 254, 257, and 260–262.

present, and 88% of the patients had some evidence of intracardiac damage.[290] One patient had infective endocarditis on the tricuspid valve. Other studies have reported slightly lower but significant incidences of right-sided heart vegetations among monitored patients coming to autopsy.[291] Greene and coworkers[291] noted a 10-fold increase in the incidence of valvular vegetations when they compared a period of time before the introduction of balloon-tipped pulmonary artery catheters with a time in which the catheters were in wide use. Nosocomial endocarditis is increasing in frequency. In one study, 9.3% of cases of endocarditis diagnosed in a referral hospital were both nosocomial in origin and unrelated to prior cardiac surgery.[292] Two studies found that 28%[293] to 33%[294] of cases of endocarditis were nosocomial in origin, with the majority from line-related sepsis. Hemodialysis patients, in particular, are at increased risk of nosocomial or health care–associated endocarditis.[295,296]

No prospective study has addressed risk factors associated with infection of these catheters, nor have studies assessed the efficacy of devices designed to decrease the risk of catheter-associated infection (e.g., leaving the introducer sheath in the vein to protect the catheter).[285] Changing these catheters over a guidewire may present a major risk factor for infection. A study in cardiac surgery patients found that more than 4 days of catheterization was the single variable associated with increased risk of pulmonary artery catheter colonization.[297] CDC guidelines currently recommend that pulmonary artery catheters need not be changed more frequently than every 7 days.[68] Infection risks associated with other aspects of monitoring equipment (e.g., transducer domes and heparin flush solution) are discussed next.

Arterial Lines, Transducers, and Transducer Domes

The widespread use of arterial lines for blood pressure monitoring or for obtaining arterial samples for blood gas determinations yields yet another source of device-associated infection. In addition, the technical electronic equipment used for hemodynamic monitoring—transducers and their associated paraphernalia—has also been cited as a source of device-associated infection.

Stamm and colleagues[18] reported an outbreak of *Flavobacterium* bacteremia among monitored patients in an ICU. Ultimately, these organisms were cultured from in-use radial artery catheters, from stopcocks, and from ice used to cool syringes for blood gas determinations.[18] Band and Maki[146] used the semiquantitative catheter tip culture technique to study 130 arterial catheters in 95 patients. In their series, 23 catheters were classified as showing "local infection" (e.g., >15 colonies per semiquantitative culture), and there were five episodes of sepsis.[146] Factors associated with increased risk for infection were (1) duration of catheterization (especially longer than 96 hours); (2) placement by cutdown rather than percutaneously; and (3) clinical signs of local inflammation. Femoral placement of arterial catheters also has been associated with higher rates of colonization and catheter infection than other placement sites.[298,299] Two studies published in 2011 reported differing results with regard to length of arterial catheterization.[300,301] The French study found a lower rate of catheter-related bloodstream infections with nonscheduled replacement (0.6% with an average duration of 5 days vs. 1.4% with an average duration of 4 days).[301] In contrast, a Spanish group reported that both days of insertion and length of ICU stay increased the risk of catheter-associated bloodstream infection.[300] Recent CDC guidelines recommend against routine replacement of arterial catheters and for replacement only with clinical indication.[68]

Maki and colleagues[262] reviewed 14 studies of arterial catheters used for hemodynamic monitoring, and they determined that the pooled mean rate of arterial catheter–related bacteremia per 100 catheters was 0.8 (95% confidence interval [CI], 0.6–1.1) and the pooled mean rate of arterial catheter–related bacteremia per 1000 catheter-days was 1.7 (95% CI, 1.2–2.3), a rate approaching that of short-term CVCs. Koh and associates[298] found similar incidence densities of arterial and CVC colonization but more than twofold increased rates of bacteremic infection with CVCs compared with arterial catheters. Mermel (as cited in Maki and colleagues[262]) noted in an editorial that if 6 million arterial catheters are used each year in the United States and the risk of bacteremia is 0.8, then there are approximately 48,000 arterial catheter–related bloodstream infections each year.[302] Others have noted similar infectious risks with arterial catheters and short-term CVCs.[303]

Several epidemics of infection resulting from improper sterilization of reusable transducer domes have been reported.[304,305] However, with the introduction of disposable transducer domes, one might assume that these problems would be overcome. Buxton and colleagues[304] reported an epidemic of *Enterobacter* infections that was associated with the contamination of disposable transducer domes during their initial setup. The chambers and domes were apparently contaminated by the hands of hospital personnel who had handled heavily contaminated transducer heads.[304] West and coworkers[306] also reported *Serratia* sepsis resulting from transducer dome cracks. In this study, supposedly disposable transducer domes were being resterilized, with resultant cracks or breaks in the dome membrane.

Another potential reservoir for nosocomial bacteremia is the heparin flush solution used to irrigate certain intravascular devices continually. This fluid has been implicated as a reservoir for outbreaks of device-associated bacteremia in several instances.

Several authors have made recommendations regarding the prevention of infection associated with intravascular monitoring devices.[68,146,305] A summary of these recommendations is presented in Table 300.6.

Treatment of CLABSIs

In this section we discuss the therapeutic interventions associated only with the management of CLABSIs. Treatment strategies for other device-associated intravascular infections is beyond the scope of this chapter. A summary of these recommendations is presented in Table 300.7.

The antibiotic choice for empirical therapy for suspected CLABSI depends on an individual patient's risk factors for infection, underlying

TABLE 300.6 Prevention of Infection Associated With Hemodynamic Monitoring

- Place arterial lines, central venous lines, and flow-directed, balloon-tipped catheters using sterile technique. Maximal sterile barrier precautions should be used. The skin should be prepared with an effective antiseptic solution (e.g., chlorhexidine).[68,349,352,354]
- Place the catheters percutaneously and anchor well to avoid catheter movement. Dress the insertion site appropriately.
- Use heparinized saline (not dextrose-containing solutions or parenteral nutrition) for continuous-flush solutions.
- Do not reuse transducer domes; sterilize reusable part of transducer setup according to manufacturer's instructions between patients.
- Replace transducers, tubing, and continuous-flow devices every 96 hours[68,455]; do not routinely replace peripheral arterial catheters to prevent infection.
- Use sterile fluid to fill the chamber dome; use aseptic technique in the assembly.
- Avoid placing unnecessary junctions or stopcocks into the apparatus; minimize manipulation of the system.
- Whenever possible, avoid exchanging arterial catheters over guidewires; use of guidewire exchange technique for arterial catheters is associated with increased infection risk.

TABLE 300.7 Management of CLABSI in Hospitalized Patients

Catheter removal advised at diagnosis:
- Patients in septic shock or unstable vital signs
- Tunnel infection of tunneled catheter
- Pocket infection of subcutaneous port
- Yeast, *S. aureus,* gram-negative bacilli, or mycobacteria
- Endocarditis or suppurative thrombophlebitis

Trial of antibiotic infusion through suspected catheter ports:
- Coagulase-negative staphylococcal CLABSI treated with vancomycin is most likely to succeed.
- All ports should be infused with antibiotic daily by splitting or rotating doses.
- Repeat blood cultures through catheter every day until negative.

Antibiotic lock therapy plus catheter infusion:
- Lock solution is prepared separately by pharmacy.
- Dwell time often interferes with catheter use.
- Advantages for treatment remain controversial.

Bacteremia/fungemia persisting after 72 hours of appropriate antibiotic therapy requires catheter removal.

diseases, known allergies, documented past colonization or infection with resistant organisms, and likely pathogens associated with the specific CVC type. Coagulase-negative staphylococci remain the single most common cause of CLABSI, making vancomycin the drug of choice for empirical therapy with daptomycin the preferred alternative. Empirical coverage for gram-negative bacilli should be based on local antimicrobial susceptibility data and the severity of disease (e.g., a fourth-generation cephalosporin, carbapenem, or β-lactam–β-lactamase inhibitor combination, with or without an aminoglycoside).[139] Empirical coverage for multidrug-resistant gram-negative bacilli, including *Pseudomonas aeruginosa,* should be added for patients who are neutropenic, septic, or known to be colonized with such pathogens. Empirical coverage for suspected catheter-related candidemia should be used for septic patients who receive parenteral nutrition or have had prolonged broad-spectrum antibiotics, a hematologic malignancy, any transplant, or colonization due to *Candida* species at multiple sites.

While catheter salvage is an appealing concept because of risks and costs associated with replacement, patients in whom retention is considered should be carefully selected. Catheter salvage should not be attempted for patients with *S. aureus* CLABSI because early removal of the line has been associated with improved outcome.[307] Catheter salvage also should not be attempted for catheter-related candidemia or mycobacteremia. The gram-negative bacilli most associated with CLABSI are those that form biofilms, including *Klebsiella, Pseudomonas,* and *Acinetobacter* species; catheters should be removed for infections with these organisms.[308] Catheter salvage also should not be attempted for long-term catheters when there are signs or symptoms of exit site or tunnel infections, or a pocket infection. If salvage is attempted, the patient should be closely observed for the development of acute complications, persistent infection, or sepsis. The catheter should be removed if complications develop or if bacteremia or fungemia persists after 72 hours of appropriate antibiotic therapy.[139] Although evidence is limited, intravenous antibiotics should be divided through all lumens of the CVC by splitting or rotating doses. Antibiotic lock treatment should be used for catheter salvage where possible, and is discussed below.

Antimicrobial Lock Therapy

A number of studies have shown that instilling antimicrobials into a catheter and leaving the solution to dwell (i.e., antimicrobial catheter lock) is effective in treating some catheter-related bacteremias.[309–312] Benoit and colleagues[309] suggested in the 1990s that intraluminal antibiotic treatment was effective in treatment of bacteremia in a small uncontrolled study. These investigators also found that intraluminal therapy with amphotericin B also may suppress, but not eradicate, *Candida* infections in tunneled catheters.[309] Three more recent studies suggested that antibiotic lock therapy in combination with appropriate systemic antimicrobials was effective in clearing the bacteremia and allowing retention of the catheter in 84%,[310] 67%,[311] and 93%[312] of patients. A retrospective study reported successful salvage in 74% of catheters, with an average duration of treatment of 13.4 days.[313] Despite data indicating that coagulase-negative staphylococci are better at adhering to foreign material with biofilm production than is *S. aureus,* coagulase-negative staphylococci apparently are more responsive to antibiotic lock therapy,[139,310,313] and routine vancomycin antibiotic lock therapy may not be appropriate for patients with *S. aureus* catheter-related bacteremia.[313,314] Success rates in one study did not differ by type of catheter[313] but, rather, were dependent on the infecting organism, with higher rates of successful catheter retention for gram-negative bacilli[313,315] and lower rates for coagulase-negative staphylococci,[316] and lowest rates for *S. aureus* and yeasts. A review found that a combination of systemic antibiotics and culture-guided lock therapy was superior to systemic antibiotics alone, with 10% of the locked catheters requiring replacement compared with 33% of catheters not locked.[317]

A large variety of antibiotic lock solutions and dosing regimens have been proposed, more recently including agents that are not usually used to treat serious infections because of concern about development of antibacterial resistance. Daptomycin, minocycline, and tigecycline have been used,[318] as well as minocycline-EDTA (with or without) 25% ethanol.[319,320] Use of an ethanol catheter lock in combination with systemic antimicrobials may be relatively effective in treatment of CLABSIs caused by a variety of organisms.[321–323] Ethanol is an antiseptic that demonstrates bactericidal and fungicidal activity against a broad range of gram-positive and gram-negative bacteria and fungi.[324] A study of pediatric patients found that the combination of a 70% ethanol solution with standard antibiotic therapy resulted in a 77% catheter salvage rate.[325] Nonetheless, a systematic review concluded that use of ethanol locks has been associated with structural changes in catheters, as well as the elution of molecules from the catheter polymers.[326] These authors recommended that if ethanol locks are used, the shortest dwell time and lowest concentration needed to eradicate microbes in biofilm might reduce these risks.

Thus additional experience has suggested that, perhaps with the exception of true tunnel and pocket infections, many infections of indwelling central catheters may be amenable to lock therapy if the device must be left in place. Of interest, despite support for use of lock therapy in some circumstances by current guidelines,[139] a 2007 survey of infectious diseases physicians found that fewer than half used antimicrobial lock therapy for any organism causing CLABSI.[327] One limitation of antibiotic locks is that dwell time is limited when the catheter is needed for frequent infusion. Patients should be carefully evaluated for evidence of complicated device-related infections, including tunnel infection, pocket infections of ports, bloodstream infection that continues despite 72 hours or more of antimicrobial therapy to which the infecting organisms are susceptible, septic emboli, septic thrombosis, endocarditis, and osteomyelitis. The device/catheter should be removed for any of these conditions.

PREVENTION OF DEVICE-ASSOCIATED BACTEREMIA

Avoiding the unnecessary use of CVCs should be a high priority. Criteria for the use of PICCs include proposed duration of use of more than 5 days and irritant or vesicant infusions.[328] A number of reports have suggested that CLABSIs can be prevented by using simultaneous implementation of an array of practice improvements (i.e., "bundle").[59,64,329–331] A summary of practice improvement recommendations is presented in Table 300.8. Evidence of improved outcomes after multifaceted interventions, along with the emergence of prevention of health care–associated infections as a national priority,[3,332] resulted in the publication of a compendium

TABLE 300.8 Summary of Practice Improvement Recommendations ("Bundle" Components) for CLABSI Prevention

Before and At Insertion
• Educational programs for all personnel involved in catheter insertion and maintenance
• Hand hygiene
• Catheter insertion checklists
• Standardized catheter insertion kits/carts
• Maximal sterile barrier precautions
• Site disinfection with chlorhexidine gluconate–alcohol solution
• Avoid femoral sites when possible
Maintenance
• Daily assessment of need for catheter; remove all nonessential catheters promptly
• Disinfect catheter hubs/injection ports with mechanical friction for ≥5 seconds
• Use chlorhexidine-impregnated dressing for short-term nontunneled CVCs
• Attempt to decrease dressing disruptions; replace dressing if it becomes damp, loose, or visibly soiled
• Do not routinely replace CVCs, PICCs, hemodialysis catheters, arterial catheters, or pulmonary artery catheters
• Chlorhexidine bathing daily for intensive care unit patients
Special Approaches
• Antibiotic lock prophylaxis in select patient populations
• Central catheters impregnated with chlorhexidine–silver sulfadiazine or minocycline-rifampin
• Use of needleless connectors with improved engineering design, including silver-coated needleless connectors and disinfection caps
• Adequate nurse staffing

of strategies to prevent CLABSIs by the Society for Healthcare Epidemiology of America and the IDSA Standards and Practice Guidelines Committee[67,333] that supplement existing, more detailed guidelines.[68] The limitation of additional reimbursement by the CMS for a diagnosis of vascular catheter–associated infection will provide additional financial incentives for health care facilities to prevent these infections.

Before Insertion of Vascular Catheters

Education of health care personnel regarding standardized catheter insertion, catheter care, and prevention of infection has been shown to reduce the incidence of catheter-associated infections.[105,118,334–336] All health care personnel involved in catheter insertion and maintenance should complete an educational program regarding catheter-associated infections before performing these duties.[67] Engaging hospital leadership and allowing for flexibility in implementation have been suggested as key components to maximize the benefits of these programs.[337] In a meta-analysis, Safdar and Abad[338] concurred that educational interventions can reduce rates of health care–associated infections. They also concluded that additional studies with clearly described, easily reproducible, and widely generalizable educational tools that had been validated were needed, particularly in general hospital settings rather than ICUs.[338]

Catheter insertion checklists to ensure adherence to infection control practices have been used as part of the practice improvement bundle in a number of studies.[59,330] These recommendations have recently been summarized.[339] Use of these checklists should be accompanied by standardized catheter insertion kits/carts containing all necessary items for insertion.[59,67]

Whereas the implementation of bundles of interventions has had a clear and measurable impact on rates of device-associated bacteremias in many centers,[340] the relative importance (or unimportance) of each of the various components of the bundles in varied clinical settings (e.g., oncology units, trauma units, burn units) remains unclear.[341] Nonetheless, while a recent study found that compliance with all bundle elements was associated with the lowest CLABSI rates, excellent compliance with even one bundle element was associated with lower CLABSI rates in adult ICUs.[64] Conversely, for many of the individual components of such bundles, we do not have scientific evidence for independent efficacy—most available data are for implementation of the entire bundle. Therefore it remains possible that some of the interventions may be superfluous—or perhaps actually even harmful.

At Insertion

Hand hygiene before catheter insertion or manipulation is an absolute requirement[342] and has been shown to be successful in reducing health care–associated infections.[336,343–345] Maximal sterile barrier precautions, including a mask, a cap, sterile gown and gloves, and a large sterile drape to cover the patient, have also been shown to reduce CVC-associated infections.[107,346,347] This tenet was confirmed by a prospective study that demonstrated that use of maximal sterile barrier precautions had an independent and significant association with a decrease in the risk of catheter infection of more than fivefold.[348] This same group performed a multivariate logistic regression analysis to determine that wearing a mask alone had a statistically significant association with a reduced infection rate.[348]

Techniques used for skin preparation before catheter insertion also have been shown to influence the risk for infection. In one study, skin preparation and decontamination with 0.5% chlorhexidine gluconate in 70% isopropyl alcohol was more effective than 10% povidone-iodine in preventing colonization of peripheral catheters in neonates.[349] Chlorhexidine-containing antiseptics have been shown to be effective in diminishing rates of catheter colonization, and they have shown varying efficacy in reducing intravenous device–related bacteremias.[350] A 2002 meta-analysis determined that chlorhexidine gluconate significantly reduces the incidence of bacteremia in patients with CVCs compared with povidone-iodine for insertion-site skin disinfection.[351] A comparison of 10% aqueous povidone-iodine, 2% aqueous chlorhexidine gluconate, and 0.5% alcoholic chlorhexidine gluconate determined that both chlorhexidine solutions were similarly effective in preventing colonization of central venous and arterial catheters.[352] Small and colleagues[353] found that 2% chlorhexidine gluconate in 70% isopropyl alcohol was more effective in reducing the number of peripheral venous catheters that were colonized or contaminated than 70% isopropyl alcohol alone. Likewise, Mimoz and coworkers[354] recommended use of chlorhexidine-based solutions rather than povidone-iodine. An open-label randomized trial enrolling 2546 patients assessed catheter insertion with 2% chlorhexidine–70% isopropyl alcohol or 5% povidone iodine–69% ethanol, each with or without scrubbing. Scrubbing provided no benefit, but chlorhexidine-alcohol provided significantly greater protection for the primary outcome of catheter-related infections per 1000 catheter-days.[355] However, hypersensitivity reactions to chlorhexidine have been reported.[356,357] The CDC guidelines recommend disinfecting skin before CVC and peripheral arterial catheter insertion by using greater than 0.5% chlorhexidine preparation with alcohol.[68] The antiseptic solution must be allowed to dry before making the skin puncture. Finally, chlorhexidine tolerance has increased, according to data from Texas Children's Hospital. *Staphylococcus aureus* isolates with the *qacA/B* and *smr* genes were associated with elevated minimal inhibitory concentrations to chlorhexidine and were often associated with CVC use, elevated vancomycin minimal inhibitory concentrations, and increased rates of bloodstream infection.[358] We agree that skin should be disinfected with an alcoholic chlorhexidine solution containing more than 0.5% chlorhexidine for patients without chlorhexidine allergy and allowed to dry before catheter insertion.

After Insertion

Even with the most stringent application of strategies to decrease catheter-associated infections, the presence of a vascular catheter remains a clear risk factor for infection. Thus the need for continued vascular access should be assessed at least daily,[359] and all nonessential catheters should be removed immediately.[360]

Contamination of catheter hubs, needleless connectors, and injection ports is a major risk factor for catheter-associated infection, and disinfection has been determined to reduce microbial burden.[35,40,361,362] Recent guidelines recommend cleaning all catheter hubs and injection ports with an alcoholic chlorhexidine preparation or 70% alcohol to reduce contamination[67]; access ports for needleless intravascular devices should be scrubbed with an appropriate antiseptic for a minimum of 5 seconds.[68] Because monitoring compliance with this vital step is difficult, passive port protectors have been developed. Caps with passive port protection have alcohol in the cap that scrubs and remains in contact with the port. While passive port disinfection may decrease the risk of CLABSI, randomized controlled trials in hospitalized adults are needed because these devices potentially represent an additional component of a comprehensive CLABSI reduction strategy.[363–367] We agree that, at a minimum, all catheter hubs and injection ports should be disinfected thoroughly, with mechanical friction applied for a minimum of 5 seconds, and allowed to dry before access.

Authorities have recommended placing a sterile dressing over the catheter entry site, using either sterile gauze or sterile, transparent, semipermeable dressings.[68] Maki and colleagues[54] studied standard tape and gauze dressings in comparison with two transparent polyurethane dressings. They concluded that polyurethane dressings appear to be safe and may be left on for up to 5 days.[54] Hoffmann and associates[368] performed a meta-analysis of studies in an attempt to assess the use of semipermeable membrane dressing materials at catheter insertion sites. These investigators found a significantly increased risk of catheter-tip colonization when transparent compared with gauze dressings were used to dress either central or peripheral catheter insertion sites. In addition, they found a trend (although not statistically significant in their meta-analysis) toward an increased risk for bacteremia and catheter sepsis associated with the use of semipermeable dressings as insertion-site dressings for CVCs.[368] The CDC guidelines suggest that because the risk for catheter-related bacteremias did not differ between the groups,[368] choice of dressings can be a matter of preference.[68]

Chlorhexidine gluconate–impregnated dressings have been studied extensively, and there are substantial supporting data for the use of both chlorhexidine sponge dressings and gel dressings.[369–374] The CDC recommended in 2017 that chlorhexidine-impregnated dressings with a US Food and Drug Administration–cleared label that specifies a clinical

indication for reducing catheter-related bloodstream infection are recommended to protect the insertion site of short-term, nontunneled CVCs.[375] We agree that chlorhexidine-impregnated dressings are appropriate in adult patients with short-term nontunneled CVCs, although the relative contribution of these dressings in addition to chlorhexidine bathing is unknown. In addition to the type of dressing, the frequency of dressing disruption may also affect catheter-related infections.[280] Efforts to decrease dressing disruptions should be included in postinsertion bundles of care.

The data on frequency of dressing changes are not conclusive. Randomized clinical trials have most often concluded that increasing time to dressing changes with transparent dressings does not affect site colonization.[376–378] Anecdotal institutional data suggest that increased time intervals between dressing changes and perhaps transparent dressings themselves are associated with increased bacteremia rates.[379] The increased ease of visual inspection and savings on nursing personnel time related to less frequent dressing changes likely does affect dressing choices in at least some institutions. One study of 55 hospitals' practices found that two-thirds used transparent, semipermeable dressings.[380] Nonetheless, no definitive data exist to determine the best dressing methodology. Failure of dressing integrity is a risk factor for catheter-related infection,[280] so dressings should be changed if they become soiled, damp, or loosened. The CDC has recommended changing the site dressing at least every 7 days for transparent dressings for adults. When gauze dressings are used for short-term CVCs, those dressings should be replaced every 2 days.[68]

Use of topical antibiotic or antiseptic ointments at the insertion site of catheters is currently not recommended by US authorities[68] except in the case of hemodialysis catheter insertion sites in patients with a history of recurrent *S. aureus* CLABSIs.[67] Several studies examining the use of povidone-iodine ointment have produced conflicting results. Results of topical mupirocin ointment application have been more promising,[381] but mupirocin resistance has been documented.[382] In addition, ointments without fungicidal activity have been associated with increased rates of catheter colonization with *Candida* spp.[383] The clinical utility of these ointments is questionable, and we do not recommend their routine use except as an adjunct for extremely high-risk hemodialysis patients with recurrent CLABSIs. Maki and Band[384] prospectively studied the following three regimens of catheter care: (1) application of polymyxin-neomycin-bacitracin ointment at insertion and every 48 hours, (2) application of iodophor ointment at insertion and every 48 hours, or (3) no ointment. In their study of 827 random catheter insertions, there were no differences in either catheter-acquired sepsis (two cases in each group) or local inflammation among the regimens (38.9% vs. 41.9% vs. 41.7%, respectively). The only difference noted was in semiquantitative cultures of catheter tips.[384] In the polymyxin-neomycin-bacitracin ointment group, there were 6 positive cultures, in the iodophor group there were 10, and in the control group there were 18. This difference was greatest in catheters that were left in place for more than 4 days. Thus information regarding the efficacy of these antimicrobial ointments or creams for intravascular cannulas is contradictory and confusing, and the clinical utility of these compounds remains questionable.

CVCs, PICCs, hemodialysis catheters, peripheral arterial catheters, and pulmonary artery catheters should not be routinely replaced to prevent catheter-related infections.[68] Guidewire exchanges should not routinely be used to prevent infection.

Another tool in the armamentarium of preventive measures is chlorhexidine gluconate bathing. Three cluster-randomized trials examining the efficacy of this measure were recently published: one evaluating patients in a crossover trial in adult ICUs[385]; one evaluating universal decolonization for methicillin-resistant *Staphylococcus aureus*, including chlorhexidine bathing in ICU patients[386]; and a crossover trial in adult ICU patients.[387] A reduction in blood cultures with skin-colonizing organisms was observed in two of these studies, although the overall benefit of chlorhexidine bathing was less clear.[388] Reduced chlorhexidine susceptibility has been reported,[389] though the clinical significance of this resistance is unclear. Intuitively, such resistance would seem foreboding.[390] Although these and some other studies have shown a reduction in hospital-acquired bloodstream infections with daily chlorhexidine bathing, the largest benefit appears to be in settings where the baseline prevalence of multidrug-resistant organisms is high. Improved adherence to hand hygiene may have a similar effect, with less risk of allergy, higher costs, and resistance to antiseptics and disinfectants.[391] Nevertheless, the 2011 CDC guidelines for prevention of intravascular catheter–related infections recommend using a 2% chlorhexidine wash for daily skin cleansing to reduce catheter-related bloodstream infections in ICU patients.[68]

Special Approaches for the Prevention of CLABSIs

Antimicrobial Prophylaxis

Some investigators have advocated using prophylactic antimicrobials in specific, defined circumstances to prevent catheter-associated infection. For example, Baier and colleagues[392] found that prophylactic treatment of neonates with central catheters with vancomycin effectively prevented coagulase-negative staphylococcal bacteremia associated with the use of these catheters. The use of continuous-infusion vancomycin for low-birth-weight infants has been shown to decrease rates of coagulase-negative staphylococcal bacteremia.[393] Unfortunately, prolonged low levels of vancomycin, such as result from this form of prophylaxis, could predispose to vancomycin resistance. Rates of early infection after implantation of totally implantable venous access devices were recently reported as 0.6%.[394] These authors concluded that the rate of early infection without antibiotic prophylaxis was so low that use of prophylactic antibiotics for totally implantable venous access devices is not recommended. Systemic antimicrobial prophylaxis is strongly discouraged.[67,68]

Antimicrobial Lock Prophylaxis

The use of antimicrobial lock solutions, in which an antibiotic or other antimicrobial is injected into the catheter lumen and the solution is left to dwell within the lumen for periods of some hours or days, has been examined as a method of preventing catheter infection during the past several years.[395–399] Currently, antimicrobial locks for prevention of CLABSIs or other catheter-related infections are not recommended for use in all patients with CVCs.[67,68] This technique has been shown in four meta-analyses to help prevent CLABSIs among hemodialysis patients.[396,397,400] Similar results have been found in patients with malignancy,[399] although the American Society of Clinical Oncology, in recent clinical practice guidelines, indicated that data are not sufficient to recommend for or against this prophylaxis modality.[401] Four of five studies in hematology-oncology patient populations demonstrated efficacy of vancomycin plus heparin as antibiotic lock prophylaxis[398,402–404]; the fifth study found no significant difference in bacteremia rates or time to the first episode of bacteremia when heparin flush was compared with a heparin plus vancomycin flush solution.[405] Although neither vancomycin[404] nor ciprofloxacin[403] could be detected in the blood after flushing with either antibiotic, concern about development of vancomycin-resistant organisms after widespread use of small amounts of vancomycin has limited use of this prophylactic technique. Safdar and Maki[406] performed a meta-analysis examining the use of vancomycin-containing locks in preventing bloodstream infection in patients with long-term central venous access devices. They concluded that use of vancomycin lock solution in high-risk patient populations, including patients with malignancy, with long-term central catheters reduces the risk of bloodstream infection. These authors also acknowledged the concern regarding promotion of antimicrobial resistance with use of antibiotic lock solutions, and they suggested that antiinfective solutions should be studied that have broad-spectrum antiinfective activity but that do not select for resistance.[406] Another group used a gentamicin and heparin lock, and within 6 months gentamicin-resistant catheter-related bloodstream infections had emerged.[407] Alternative agents include taurolidine,[408–410] minocycline-EDTA,[319,411] and ethanol.[412,413] Antimicrobial locks are currently recommended for use in preventing CLABSIs for two groups of patients: (1) those with limited venous access and a history of recurrent CLABSIs[68] and (2) those with heightened risk for severe sequelae from CLABSIs.[67] We believe that, in general, vancomycin use in antimicrobial locks should be avoided.

Antimicrobial Catheters

Another approach that has been advocated to reduce the risk for CVC-associated infection is bonding of an antimicrobial agent or antiseptic to the device or the addition of a subcutaneous catheter cuff impregnated with an antiseptic or antimicrobial, most commonly including chlorhexidine–silver sulfadiazine and minocycline-rifampin. A 2005 review of these catheters concluded that 40% of intravascular device–related bloodstream infections are preventable with the use of antimicrobial-impregnated CVCs.[414] These authors also emphasized that, based on the results of 19 randomized controlled trials, three meta-analyses, and two cost-benefit analyses, the overwhelming preponderance of evidence concerning the use of antimicrobial catheters suggests efficacy.[414] Another systematic review examined 32 trials of various types of antimicrobial CVCs and concluded that the pooled results for all catheters suggest a statistically significant advantage in reducing CLABSIs, with an odds ratio of 0.45.[415] This review also found that the pooled results of nine studies examining catheters treated only externally showed a nonsignificant effect on decreasing CLABSIs.[415]

Minocycline-rifampin coating appears to have superior and more prolonged activity against staphylococci.[416] Several subsequent studies have shown that these minocycline-rifampin catheters significantly decrease the risk of CLABSIs.[417–421] In vitro and in vivo data suggest that the efficacy of the minocycline-rifampin catheters may be prolonged beyond that of chlorhexidine–silver sulfadiazine catheters.[419,422] The efficacy of the minocycline-rifampin catheters, when kept in situ for longer periods of time, has been assessed in one study.[420] In this study, the minocycline-rifampin silicone catheters had a mean dwell time of 68.2 days and were associated with a significant decrease in CLABSIs.[420] These antibiotic-impregnated catheters are associated with a theoretical risk of increased antimicrobial resistance,[423] and one in vitro study found that second-generation chlorhexidine–silver sulfadiazine catheters appear to be more resistant to colonization with rifampin-resistant *S. epidermidis* than minocycline-rifampin catheters.[424] Another study of minocycline-rifampin catheters over 7 years reported no increased resistance of staphylococcal isolates to tetracycline or rifampin.[421]

Chlorhexidine–silver sulfadiazine catheters have been shown to be cost-effective in patients at high risk of intravenous device–related bacteremia. Another cost-effectiveness analysis suggested that the clinical and economic benefits of minocycline-rifampin catheters increase with days of catheterization.[425] For patients with CVCs in situ for 8 days, minocycline-rifampin catheters were more beneficial than chlorhexidine–silver sulfadiazine catheters, and cost savings accrued in patients catheterized for at least 13 days. Another review examined 11 randomized studies comparing patients with CVCs impregnated with antimicrobial agents with control patients receiving nonimpregnated CVCs.[426] These authors concluded that the efficacy of antimicrobial-impregnated CVCs in preventing catheter-related bacteremias is questionable, and that routine use of these catheters must be reevaluated. Halton and Graves[427] reviewed a series of cost-effectiveness studies in 2007 and concluded that use of antibiotic-coated catheters, compared with use of either antiseptic-coated or standard catheters, was both clinically effective and cost-saving. Another study suggested that only patients receiving parenteral nutrition may benefit from antiseptic-impregnated CVCs.[114] The most recent meta-analysis suggested that minocycline-rifampin catheters appear to be the most effective in preventing catheter-related bacteremia, although overall benefits in reducing clinical sepsis and mortality remain uncertain.[428] These authors also suggested that surveillance for antibiotic resistance attributed to use of these catheters should be emphasized in future trials.[428]

Recent guidelines suggest that use of antimicrobial-impregnated catheters should be reserved for locations or patient populations, or both, that have unacceptably high CLABSI rates despite implementation of the basic prevention strategies, including education, use of maximal sterile barriers, and use of chlorhexidine antisepsis of skin before catheter insertion.[67,68] None of these antimicrobial catheters were, alone, capable of reducing CLABSI rates to zero. We believe that antiinfective catheters should be implemented only as part of a comprehensive nosocomial bacteremia prevention strategy, which also includes education of staff and adequate skin antisepsis. Institutions may choose to implement one of these catheters after reviewing both their current and their goal intravenous device–associated bacteremia rates. Further research is needed to define the actual effect of these catheters on bacteremia rates, as well as the most efficacious catheters for different durations of catheterization and different subpopulations of patients.

Use of heparin or other anticoagulants has also been advocated as a method for reducing both thrombotic and infectious complications of central venous catheterization. Randolph and coworkers[429] concluded that heparin administration effectively reduces thrombus formation and may reduce catheter-related infections in patients who have CVCs and pulmonary artery catheters in place. Several anticoagulants have been suggested for use in this setting, and Randolph and coworkers[429] noted that cost-effectiveness comparisons of these several preparations (e.g., unfractionated heparin, low-molecular-weight heparin, and warfarin) are needed. Recombinant tissue plasminogen activator used once weekly instead of heparin three times per week significantly reduced the incidence of both catheter malfunction and bacteremia in another study.[430] Several reviews of various anticoagulants used in the prevention of CLABSIs all concluded that these agents, including urokinase,[431] tissue plasminogen activator,[432] and heparin-bonded catheters,[433] may be effective, but they underscored the fact that more adequately powered clinical trials are needed. Currently, we do not recommend routine use of urokinase or other thrombolytic agents as adjunctive therapy in patients with catheter-related bacteremia.

Other Prevention Issues

The role of appropriate nurse staffing in preventing catheter-associated infection deserves attention. In one study, nursing staff reductions during a period of increased use of parenteral nutrition were directly associated with an increase in catheter-associated bacteremias in a surgical ICU.[434] Robert and colleagues[435] reported in 2000 that bacteremias in surgical ICU patients increased when nurse staffing changed to include fewer "regular" registered nurses and more pool/agency nurses. "Float" nurses (usually assigned elsewhere in the hospital or from an agency) were associated with an increased risk of CLABSIs in ICU patients in another study,[114] suggesting that an increased proportion of nurses with less than 1 year of experience in the ICU can lead to increased risk of CLABSIs.[436] Adequate nurse staffing has been identified as one factor integral to preventing bacteremia.[437] In this era of increased focus on preventing these infections, the impact of staffing reductions on untoward outcomes is deserving of careful scrutiny.[434]

New scientific approaches are needed to help establish optimal techniques for catheter management, and further technologic advances, such as bonding antimicrobial and antiseptic agents to the intravascular device, may also reduce risks for device-associated infection. A 2005 survey of use of CLABSI prevention practices in 516 US hospitals found that fewer than half of non–Veterans Affairs hospitals reported concurrent use of maximal sterile barrier precautions, chlorhexidine gluconate, and avoidance of routine central line changes.[438] Although recommended prevention practices, including the bundling of complementary strategies, is increasing both in hospitals subject to the CMS no-payment rule as well as in Department of Veterans Affairs hospitals,[439] additional effort is needed to reach the desired outcome of zero CLABSIs. Increased attention to such details can significantly lower the endemic rate of device-associated infection as well as decrease the number of epidemics of such infections.

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The complete reference list is available online at Expert Consult.

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