

REVIEW

for SB

Prevention of Intravascular Catheter-Related Infections

Leonard A. Mermel, DO, ScM, AM(Hon)

Purpose: To review the literature on prevention of intravascular catheter-related infections.

Data Sources: The MEDLINE database, conference proceedings, and bibliographies of review articles and book chapters were searched for relevant articles. Primary authors were contacted directly if data were incomplete.

Study Selection: Studies met the following criteria unless otherwise stated: Trials were prospective and randomized; catheters were inserted into new sites, not into old sites over guidewires; catheter cultures were done by using semi-quantitative or quantitative methods; and, for prospective studies, catheter-related bloodstream infection was confirmed by microbial growth from percutaneously drawn blood cultures that matched catheter cultures.

Data Extraction: Data on population, methods, preventive strategy, and outcome (measured as catheter-related bloodstream infections) were gathered. The quality of the data was graded by using preestablished criteria

Data Synthesis: The recommended preventive strategies with the strongest supportive evidence are full barrier precautions during central venous catheter insertion, subcutaneous tunneling short-term catheters inserted in the internal jugular or femoral veins when catheters are not used for drawing blood; contamination shields for pulmonary artery catheters; povidone-iodine ointment applied to insertion sites of hemodialysis catheters; specialized nursing teams caring for patients with short-term peripheral venous catheters, especially at institutions with a high incidence of catheter-related infection; no routine replacement of central venous catheters; antiseptic chamber-filled hub or hub-protective antiseptic sponge for central venous catheters, and use of chlorhexidine-silver sulfadiazine-impregnated or minocycline-rifampin-impregnated short-term central venous catheters if the rate of infection is high despite adherence to other strategies that do not incorporate antimicrobial agents (for example, maximal barrier precautions).

Conclusions: Simple interventions can reduce the risk for serious catheter-related infection. Adequately powered randomized trials are needed.

Several million intravascular catheters are purchased each year by U.S. hospitals and clinics. Use of these devices place large numbers of patients at risk for catheter-related bloodstream infection. Most serious infections are associated with central venous catheters rather than small peripheral catheters (1); this is particularly evident in intensive care units (ICUs). According to a computer model of utilization of ICU beds based on American Hospital Association data (Halpern N. Personal communication), there were approximately 31 million patient-days annually in ICUs in the United States over the past 6 years. On the basis of data from the Centers for Disease Control and Prevention (2), the risk for exposure to these devices per ICU day was 48%, leading to approximately 15 million central line-days per year in ICUs. With an average of 5.3 central line-associated bloodstream infections per 1000 catheter-days in ICUs (2), approximately 16 000 central line-associated bloodstream infections occurred in ICUs in the United States each year. The attributable mortality has ranged from 12% to 25% in prospective studies (1, 3) but was an average of 3% in a meta-analysis (4). The attributable cost per infection is \$3700 to \$29 000 (3, 5). Therefore, in U.S. ICUs, approximately 500 to 4000 patients die annually of central venous catheter-related bloodstream infections. The annual cost of caring for patients with central line-associated bloodstream infections is \$60 million to \$460 million. A significant proportion of non-ICU patients have central venous catheters (for example, patients on hematology-oncology wards), and many patients are discharged with central venous catheters in place. These patients are also at risk for serious catheter-related infections.

The microbes that colonize catheter hubs and the skin surrounding the insertion site are the source of most catheter-related bloodstream infections (6-8). Therefore, successful preventive strategies must reduce colonization of the insertion site and hubs or minimize microbial spread extraluminally from the skin or intraluminally from the hubs toward the catheter tip lying in the bloodstream (Figure). Inhibiting the adherence and growth of pathogens that reach the intravascular segment of the catheter would also be ideal.

Attention to simple and practical interventions

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For the author affiliation and current address, see end of text

reduces the risk for intravascular catheter-related bloodstream infections (9-11). This review updates the expanding body of literature on the prevention of these infections.

Methods

Clinical studies of intravascular catheters were identified by searching the MEDLINE database for articles published from January 1966 to February 1999. The proceedings of the Infectious Diseases Society of America from 1994 through 1999, the Interscience Conference on Antimicrobial Agents and Chemotherapy from 1984 through 1999, and the proceedings of the Society for Healthcare Epidemiology of America Annual Meetings from 1989 through 1998 were reviewed, as were bibliographies of review articles and book chapters. Unless otherwise stated, the randomized studies included in this article meet the following criteria: Catheters were inserted into new sites, not old sites over a guidewire; catheter cultures were done by using semi-quantitative or quantitative methods; and catheter-related bloodstream infections were confirmed by microbial growth from percutaneously drawn blood

cultures that matched microbial growth from the involved catheter. Authors were contacted directly if these criteria were not stated in published studies. Randomized studies that met these criteria but involved catheter exchange over guidewires into old insertion sites were included only if overwhelming evidence refuted the findings of a single randomized trial involving catheter insertion into new sites only. Any reference to these studies is specifically noted as such in this review. Case-control and cohort studies were included if they investigated issues not addressed in randomized trials regardless of whether they disclosed the site from which blood was drawn for culture or whether catheters were inserted into old sites over guidewires. Case-control or cohort studies are specifically noted as such in this review.

The significance of differences in prevention strategies was determined by using the Mantel-Haenszel test or the Fisher exact test if the value of a test variable was less than 5. Relative risks, odds ratios, and 95% CIs were calculated by using Epi-Info, version 6 (Centers for Disease Control and Prevention, Atlanta, Georgia). Recommendations for preventive strategies are modified from previously published criteria (12), and the strength of the

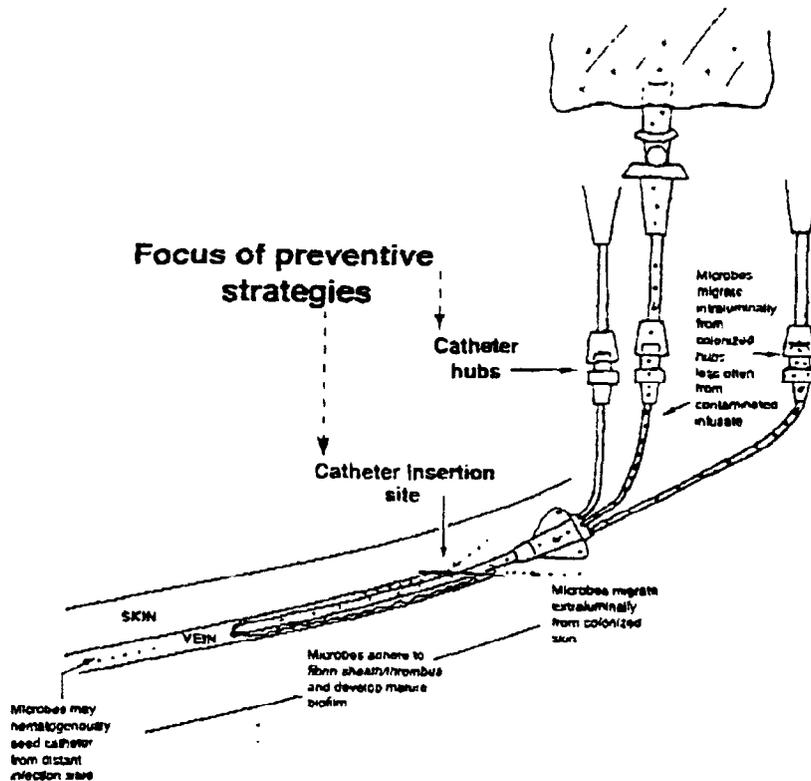


Figure. Source of intravascular catheter-related infections.

evidence is graded as follows: I, evidence from a well-designed meta-analysis of randomized, controlled trials; IIa, evidence from at least one randomized, controlled trial meeting the preceding criteria; IIb, evidence from at least one randomized, controlled trial that allowed catheter exchange over guidewires into old sites; III, evidence from at least one well-designed clinical trial without randomization; and IV, evidence from opinions of authorities in the field based on clinical experience, descriptive studies, or expert committee reports. If more than one type of evidence was available to support a specific recommendation (such as a meta-analysis [I] and an expert committee report [IV]), only the highest applicable evidence for the recommendation is listed. Recommendations for which results are conflicting reflect the prevailing view, and the highest rated trial based on the preceding criteria is cited.

Preventive strategies are reviewed in the order in which one would approach a patient undergoing intravascular catheterization. Prophylaxis is discussed, followed by procedures surrounding catheter insertion, such as the site of insertion, tunneling of catheters, and antisepsis. Recommendations for maintenance of catheters follows, such as nursing care of catheters and types of available catheter hubs. Antimicrobial-coated or antimicrobial-impregnated catheters are then reviewed.

Preventive Strategies

Intravenous Antimicrobial Prophylaxis

Prophylaxis with vancomycin or teicoplanin during central venous catheter insertion has not been demonstrated to reduce the incidence of catheter-related bloodstream infection (13–15 [Table 1]). Two studies (13, 14) failed to show a difference in early catheter-related bloodstream infection in the antibiotic prophylaxis groups, and in another study (15), the incidence of bloodstream infection was higher in the prophylaxis group (Table 1). Because these studies had small samples, they cannot rule out the possibility of a beneficial effect. Prophylaxis with vancomycin or teicoplanin at insertion of a central venous catheter is not recommended on the basis of the available data [IIa].

Addition of vancomycin to flush solutions or total parenteral nutrition solutions reduced the risk for catheter-related bloodstream infection with coagulase-negative staphylococci in one study of neonates (odds ratio, 0 [95% CI, 0.0 to 0.7]) (16). However, Centers for Disease Control and Prevention guidelines recommend against prophylactic use of vancomycin because it is an independent risk factor for acquisition of vancomycin-resistant enterococci (17).

Prolonged administration of vancomycin-containing dialysate through peritoneal dialysis catheters is associated with peritonitis due to *Staphylococcus epidermidis*, with markedly reduced susceptibility to vancomycin and exit-site colonization with vancomycin-resistant enterococci (18). Prolonged use of systemic vancomycin to treat *S. aureus* infection is associated with development of intermediate resistance to vancomycin (19–22) and subpopulations of *S. aureus* with reduced vancomycin susceptibility (22, 23). Therefore, prevention of intravascular catheter-related infections should not involve vancomycin or other therapeutic agents [IV]. Efforts should be focused on interventions that are not likely to encourage the emergence of antimicrobial resistance, such as maximal barrier precautions.

Warfarin and Heparin Prophylaxis

Several of the different protein components of a thrombus increase adherence of *S. aureus*, *S. epidermidis*, and *Candida* species to catheters (24–27). Thrombus formation on indwelling intravascular catheters is associated with catheter-related bloodstream infection (28, 29). Very-low-dose warfarin reduces venographically documented thrombosis with long-term use of central venous catheters (relative risk, 0.25 [CI, 0.09 to 0.7]) (30) and reduced thrombosis in an observational study (31). Prophylaxis with very-low-dose warfarin should be strongly considered for patients with long-term, indwelling intravascular catheters [IIa].

In a meta-analysis, prophylactic heparin reduced the risk for catheter-related central venous thrombosis (relative risk, 0.4 [CI, 0.2 to 0.8]) (32); however, the analysis failed to show a significant difference in the risk for central venous catheter-related bloodstream infection when it was given in a bolus infusion or added to intravenous solutions (relative risk, 0.26 [CI, 0.07 to 1.03]) (32). Most heparin solutions contain preservatives with antimicrobial

Table 1. Efficacy of Systemic Antimicrobial Prophylaxis during Central Venous Catheter Insertion in the Prevention of Catheter-Related Infection*

Single-Dose Prophylactic Regimen (Reference)	Catheter-Related Bloodstream Infection/Catheters n/n (%)	Relative Risk (95% CI)	Catheter-Related Bloodstream Infection per 1000 Catheter-Days n
Vancomycin	6/24 (25)		0.15
No vancomycin (13)	7/29 (24)	1.0 (0.4–2.7)	0.14
Teicoplanin	50/194 (26)		1.5
No teicoplanin (14)	46/221 (21)	1.2 (0.9–1.8)	1.2
Teicoplanin	7/33 (21)		–
No teicoplanin (15)	2/32 (6.3)	3.4 (0.8–15.1)	–

* Data from randomized studies that used quantitative or semi-quantitative microbiological methods to define catheter colonization and percutaneously drawn blood cultures to define bloodstream infection in catheters inserted into a new site (without antimicrobial ointment applied to the site) rather than over a guidewire into an old site.

activity (33). Thus, the fewer catheter-related infections associated with heparin use may be due to the preservative, reduced thrombus formation, or both. Prophylactic heparin should be administered to patients with short-term central venous catheters [I]. Three U of heparin per mL in total parenteral nutrition solution, 5000 U every 6 or 12 hours in a flush solution, or 2500 U of subcutaneous low-molecular-weight heparin daily all reduce the risk for catheter-related central venous thrombosis (32). Heparin treatment should be discontinued if an unexplained decrease in the platelet count is observed, particularly if it is less than 100 000 cells/mL, or a new thrombotic event occurs (34).

Site of Insertion

No randomized trials have assessed the risk for infection associated with catheter insertion into the subclavian, internal jugular, or femoral vein. However, four prospective, observational studies using multivariate analysis found that risk for infection was significantly increased with insertion into the internal jugular vein compared with insertion into the subclavian vein (6, 35-37). Therefore, insertion of a catheter into the subclavian vein is preferred to reduce the risk for infection [III]. However, this risk must be weighed against noninfectious complications associated with subclavian vein insertion (38, 39). In one prospective, observational study, Cox proportional hazards analysis showed that catheter insertion into the femoral vein was associated with catheter colonization (hazard, 4.2 [CI, 2.0 to 8.8]) (40). The risk for deep venous thrombosis is higher with femoral vein insertion than with subclavian or internal jugular vein insertion (41). Therefore, femoral venous catheterization should be limited to circumstances that prevent the use of alternative access sites [III].

Subcutaneously Tunneled Catheters

Subcutaneous tunneling of short-term catheters inserted into the internal jugular vein independently reduces the risk for catheter-related bloodstream infection (relative risk, 0.2 [CI, 0.1 to 0.7]) (42). A study of subcutaneously tunneled femoral vein catheters failed to show a statistically significant difference in risk for catheter-related bloodstream infection (relative risk, 0.3 [CI, 0.0 to 1.9]) (43). In a meta-analysis, subcutaneous tunneling of subclavian vein catheters did not significantly reduce the risk for catheter-related bloodstream infection (relative risk, 0.71 [CI, 0.36 to 1.43]) (44). In the studies that showed the greatest benefit from tunneling (42, 43), potential colonization of catheter hubs was minimized because the catheters were not used for drawing blood. This may have magnified the impact of the intervention by increasing the probability that catheter infections emanate from the insertion site rather than the hub (45). The restricted manipulation of the catheter hub in these studies contrasts sharply with clinical practice in U.S. hospitals, where central venous catheter hubs are frequently manipulated during blood drawing. Therefore, subcutaneous tunneling of short-term internal jugular or femoral vein catheters is recommended if the catheters are not accessed for drawing blood [IIa].

Cutaneous Antisepsis

In the United States, povidone-iodine is the most widely used antiseptic for cleansing catheter insertion sites (46). However, in three of four studies, chlorhexidine significantly reduced the incidence of microbial colonization of catheters compared with povidone-iodine (47-50) (Table 2). Three studies failed to show a statistically significant difference in catheter-related bloodstream infection when catheters inserted into new sites were cleansed with chlor-

Table 2. Efficacy of Chlorhexidine-Containing Cutaneous Antiseptics in the Prevention of Central Venous, Pulmonary Artery, and Peripheral Arterial Catheter-Related Infection*

Reference	Disinfectant Type	Catheter Colonization	Relative Risk (95% CI)	Catheter-Related Bloodstream Infection	Relative Risk (95% CI)
		n/n (%)		n/n (%)	
47	Chlorhexidine†	5/214 (2.3)	0.3 (0.1-0.8)	1/214 (0.5)	0.2 (0.0-1.9)
	Control‡	33/454 (7.3)		9/454 (2.9)	
48	Chlorhexidine†	3/169 (1.8)	0.3 (0.1-0.9)	-	-
	Control‡	12/177 (6.8)		-	
49	Chlorhexidine§	12/170 (7.1)	0.4 (0.2-0.8)	3/170 (1.8)	0.9 (0.2-4.2)
	Control‡	24/145 (17)		3/145 (2.1)	
50	Chlorhexidine¶	31/92 (34)	1.2 (0.6-1.9)	3.5/1000 catheter-days	-
	Control‡	24/88 (27)		4.1/1000 catheter-days	

* Data from randomized studies that used quantitative or semi-quantitative microbiological methods to define catheter colonization and percutaneously drawn blood cultures to define bloodstream infection in catheters inserted into a new site (without antimicrobial ointment applied to the site) rather than over a guidewire into an old site.

† Aqueous chlorhexidine

‡ Povidone-iodine or alcohol

§ Povidone-iodine

¶ Alcoholic chlorhexidine mixed with benzalkonium chloride

‡ Alcoholic chlorhexidine

hexidine compared with sites cleansed by using povidone-iodine or alcohol (47, 49, 50) (Table 2). Limited power in these studies was due to the low incidence of catheter-related bloodstream infection. Alcoholic and aqueous chlorhexidine products are not approved in the United States for use at intravascular catheter insertion sites but are permitted for such use in Canada and Europe. Chlorhexidine-containing antiseptics should be used, where approved, for skin preparation before catheter insertion [IIa]. Tincture of iodine is superior to povidone-iodine as a cutaneous antiseptic (51, 52) and should be considered for preparation of intravascular sites [IV].

Sterile Barrier Precautions

Full barrier precautions during insertion of the central venous catheter (sterile gloves, long-sleeved sterile gown, mask, cap, and large sterile sheet drape) reduce the incidence of catheter-related bloodstream infection compared with standard (sterile gloves and small drape) precautions (0.08/1000 and 0.5/1000 catheter-days, respectively; $P = 0.02$) (53). These findings are supported by the results of a prospective, observational study (6). Full barrier precautions should be the standard of care during central venous catheter insertion [IIa] and should be considered during insertion of midline and peripheral artery catheters [IV].

Catheter Dressing

In two meta-analyses, the risk for central venous catheter-related bloodstream infection did not differ for groups using transparent dressings compared with gauze dressings to cover catheter insertion sites (54, 55), but both analyses included studies with methodologic problems. One study (56) reported a reduced risk for catheter-related bloodstream infection associated with gauze dressings (odds ratio, 0 [CI, 0.0 to 0.8]). No bloodstream infections were reported in another study (57). No significant difference in catheter-related bloodstream infection was observed between patients with gauze dressings and those with transparent dressings in three large randomized studies that included catheters exchanged over guidewires into old sites (7, 58, 59). On the basis of all available evidence, the choice of central venous catheter dressing may be a matter of preference and cost [IIb]; however, gauze dressings are preferred if blood is oozing from the catheter insertion site (58) [IIb].

Ointments

Results of randomized studies of the efficacy of triple antibiotic ointment (polymyxin, bacitracin, and neomycin) applied to catheter insertion sites are indeterminate because of the low number of catheter-related bloodstream infections observed

(odds ratio 0 [CI, 0.0 to 1.5] [60]; relative risk, 1.0 [CI, 0.2 to 7.3] [61]). These studies cannot rule out the possibility of a prophylactic effect. Increased catheter colonization by *Candida* species associated with use of triple antibiotic ointment has been reviewed elsewhere (62). Thus, applying triple antibiotic ointment to catheter insertion sites is not recommended [IIa].

Results of randomized studies of prophylactic use of povidone-iodine ointment applied to insertion sites of short-term catheters for the prevention of catheter-related bloodstream infections are also indeterminate (relative risk, 0.5 [CI, 0.1 to 2.7] [60], relative risk, 1.0 [CI, 0.1 to 7.1] [61]). Catheter-related bloodstream infections were reduced in a study of long-term hemodialysis catheters (relative risk, 0.1 [CI, 0.0 to 0.7]) (63). No nasal carriers of *S. aureus* in the povidone-iodine group developed catheter-related bloodstream infection, compared with 29% of the control group ($P = 0.03$). Thus, most of the treatment effect was due to reduced infections in nasal carriers of *S. aureus*.

Application of mupirocin ointment to insertion sites for temporary hemodialysis catheters reduces the risk for catheter-related bloodstream infection with *S. aureus* (relative risk, 0.1 [CI, 0.0 to 0.7]) (64). Prolonged use of mupirocin ointment at catheter insertion sites has been associated with the development of mupirocin resistance (65), which may reduce the utility of mupirocin for other purposes (66). Mupirocin ointment may adversely affect the integrity of polyurethane catheters (67, 68). Therefore, mupirocin ointment should not be applied to catheter insertion sites [IV].

Povidone-iodine ointment should be applied to the insertion site of hemodialysis catheters [IIa]. Applying povidone-iodine ointment to insertion sites of nontunneled, long-term central venous catheters in immunocompromised patients with heavy *S. aureus* carriage (such as patients with AIDS [69] or cirrhosis [70]) should be considered [IV].

Contamination-Shielded Pulmonary Artery Catheters

Patients who were randomly assigned to have their pulmonary artery catheters self-contained within a thin plastic sleeve that prevented touch contamination had a reduced risk for catheter-related bloodstream infection (odds ratio, 0 [CI, 0.0 to 0.5]) (71). Therefore, a contamination shield should be used for all pulmonary artery catheters [IIa].

Catheter Maintenance

Two prospective, observational studies demonstrated that excessive manipulation of central venous catheters independently increases the risk for catheter-related bloodstream infection (57, 72).

probably because of the greater risk for a breach in aseptic technique with multiple manipulations. Inappropriate care of intravascular catheters independently increased the risk for catheter-related bloodstream infection in another observational study (73). Continuing quality improvement programs to assure compliance with catheter care guidelines significantly reduced primary bloodstream infection or catheter-related bloodstream infection in four prospective cohort studies (74–78). Continuing quality improvement programs aimed at improving compliance with catheter care guidelines are recommended [III].

Case-control and cohort studies of patients with central venous catheters in ICUs have demonstrated that a reduction in the nurse-to-patient ratio from 1:1 to 1:2 independently increased the risk for catheter-related bloodstream infection (odds ratio, 61.5 [CI, 1.2 to 3074]) (79). An adequate nurse-to-patient ratio in ICUs is strongly recommended to prevent life-threatening central venous catheter-related infections [III].

Two trials assessed specialized care provided by trained nursing teams that assured stringent adherence to aseptic technique during insertion of peripheral catheters and catheter dressing changes (80, 81). No bloodstream infections occurred in one study (80). In the other study (81), catheter-related bloodstream infection was reduced in the specialized care group (odds ratio, 0 [CI, 0.0 to 0.6]). Specialized nursing care significantly reduced phlebitis in both studies. Specialized nursing teams caring for patients with short-term peripheral venous catheters should be used to reduce the risk for phlebitis and catheter-related bloodstream infection, particularly at institutions with an increased incidence of these events [IIa]. Specialized nursing teams should also be used to reduce catheter-related infections in patients receiving total parenteral nutrition [IV].

The results of a meta-analysis (82) are inconclusive with regard to any benefit toward reduction of catheter-related bloodstream infection by routine replacement of central venous catheters by using guidewire exchange (relative risk, 1.7 [CI, 0.9 to 3.3]). Routine replacement of central venous catheters is not indicated [I] as long as the integrity of the catheter polymer is stable for the expected use of the catheter and the duration of catheterization (83).

Intravascular catheters may remain in place long after their intended use (84), increasing the risk for catheter-related bloodstream infection. Physicians and nurses should assess patients' need for intravascular catheters, and all other temporary foreign bodies, on a daily basis. These devices should be

removed as soon as possible after their intended use [IV] (85).

Injection Hub and Connection Port

Catheter hubs and sampling ports should be disinfected before they are accessed [IV] (8–10). Alcohol, povidone-iodine, and chlorhexidine are effective (86, 87) but are only slightly more effective than saline because premoistened cotton swabs physically remove most pathogens from catheter hubs (86).

In one trial (88), a hub containing an antiseptic chamber filled with iodinated alcohol reduced the risk for central venous catheter-related bloodstream (relative risk, 0.2 [CI, 0.1 to 0.7]). This hub is available in Europe but not the United States. Another trial assessed the efficacy of a sponge saturated with povidone-iodine housed within a plastic casing and fitted around the catheter hubs (89). It reduced the incidence of catheter-related bloodstream infection from 24% to 0% ($P = 0.02$). This device is available in the United States but not in Europe. In both trials, catheters were in place for approximately 2 weeks. Greater catheter hub manipulation increases the risk for contamination (90). During prolonged catheterization, catheter hubs are accessed multiple times, increasing the likelihood that catheter-related bloodstream infection emanates from colonized hubs rather than the insertion site (91). Either of these two specialized hubs should be considered for patients without iodine allergies who require central venous catheterization for approximately 2 weeks [IIa] or possibly longer. These devices may benefit ICU patients whose central venous catheters are heavily manipulated but will be in place for a shorter duration [IV].

Many needleless systems are available for use with intravascular catheters. Several case-control and cohort studies have demonstrated an increased risk for catheter-related bloodstream infection with these devices (92–102). This may reflect suboptimal design of the device (93, 96), infrequent replacement of the needleless device or the end caps covering the device (94, 97, 99), contamination of the device with water-borne gram-negative bacilli during bathing or other activities (96, 98, 100), or self-administered intravenous infusions (98). In vitro experiments have shown that proper disinfection of needleless system injection sites prevents microbial transfer from the hub to the intraluminal fluid path of catheters (100–102). In a crossover clinical trial (103), use of a needleless system after adequate training did not increase the risk for catheter-related bloodstream infection. In a larger trial, a needleless system was independently associated with reduced contamination of infusate (104). To prevent intravascular catheter-related bloodstream infection associated with needleless systems, the device and the

Table 3. Efficacy of a Silver-Impregnated Subcutaneous Cuff for the Prevention of Central Venous Catheter-Related Infection*

Reference	Catheter Type	Catheter Colonization	Relative Risk (95% CI)	Catheter-Related Bloodstream Infection	Relative Risk (95% CI)	Mean Duration of Catheterization <i>d</i>
		<i>n/n</i> (%)		<i>n/n</i> (%)		
107	Silver-impregnated subcutaneous cuff	- (15)		- (5/3)		5
	Control	- (18)		- (0)		
108	Silver-impregnated subcutaneous cuff	7/99 (7.1)	0.3 (0.1-0.6)	1/99 (1.0)	0.3 (0.0-2.3)	9
	Control	33/135 (24)		5/135 (3.7)		7
109	Silver-impregnated subcutaneous cuff	2/42 (4.8)	1.0 (0.2-6.9)	5/42 (12)	0.9 (0.3-2.6)	20
	Control	2/43 (4.7)		6/43 (14)		23
110	Silver-impregnated subcutaneous cuff	7/47 (15)	0.7 (0.3-1.7)	2/47 (4.3)	1.2 (0.2-7.8)	35
	Control	11/54 (20)		2/54 (3.7)		42
111	Silver-impregnated subcutaneous cuff	-		33/92 (36)	1.1 (0.8-1.6)	147
	Control	-		35/108 (32)		143

* Data from randomized studies that used quantitative or semi-quantitative catheter culture methods and percutaneously drawn blood cultures of $>10^3$ colony-forming units of microbial growth/mL of blood collected through the catheter to define bloodstream infection in catheters inserted into a new site (without antimicrobial ointment applied to the site) rather than over a guidewire into an old site.

end cap (if present) should be changed regularly in accordance with manufacturers' guidelines, the surface of the device should be adequately disinfected before it is accessed (for example, by using an isopropyl alcohol-saturated pad), and special care should be taken to reduce direct contact with non-sterile water [III].

Inline Filters

Inline 0.22- μ m filters in intravenous tubing reduce the risk for phlebitis (105). There are no adequate studies showing that filters reduce the risk for catheter-related bloodstream infection. Inline filters are not recommended for prevention of these infections [IV].

Antimicrobial-Coated or Impregnated Catheters and Cuffs

Antimicrobial-impregnated or antimicrobial-coated devices and cuffs are important additions to the group of preventive strategies. Most pulmonary artery and umbilical artery catheters are heparin-bonded with benzalkonium chloride. The benzalkonium chloride provides the catheters with short-lived antimicrobial activity (106). Benzalkonium chloride-coated pulmonary artery catheters should be used because they may prevent catheter-related infections [IV].

A silver-impregnated subcutaneous collagen cuff attached to a central venous catheter acts as a tissue-interface barrier. The findings of two studies of short-term catheter-related bloodstream infections associated with use of this commercially available cuff are inconclusive because of the small number of catheter-related bloodstream infections observed (107, 108) (Table 3). In the combined trials, with dwell times of 20 days or longer, use of this cuff did

not reduce the incidence of catheter-related bloodstream infection (109-111) (Table 3). Extrusion of the silver cuff from the catheter tunnel tract to the skin and minimal subcutaneous anchorage of tunneled, silver-cuffed central venous catheters have been observed, possibly because of a cytotoxic effect of the silver (112). On the basis of all available evidence, use of this device is not recommended with short-term [IIa] or long-term [IIa] catheters.

The efficacy of catheters impregnated with chlorhexidine and silver sulfadiazine on the outer surface was the subject of a meta-analysis (113). The Mantel-Haenszel method was used in the present review to estimate a summary measure of the effect of this device on catheter-related bloodstream infections by combining the results from six of eight prospective studies of short-term (less than 2 weeks) central venous catheterization (8, 114-120) (Table 4). This analysis demonstrates that short-term use of a catheter impregnated with chlorhexidine and silver sulfadiazine reduced the risk for central venous catheter-related bloodstream infection (Mantel-Haenszel weighted relative risk, 0.4 [Greenland-Robins CI, 0.2 to 0.8]). One study (121) failed to show a difference in central venous catheter-related bloodstream infection with use of this catheter for a more prolonged dwell time (Table 4). Use of this catheter should reduce cost in settings in which the incidence of bloodstream infection caused by use of short-term central venous catheters is greater than 3.3 per 1000 catheter-days (8). On the basis of a multivariate sensitivity analysis, use of this catheter should lead to a cost saving of \$68 to \$391 per catheter (122). The currently marketed chlorhexidine-silver sulfadiazine-impregnated catheter is not effective for catheters in place for an average of 3 weeks (121) (Table 4). This finding

Table 4. Efficacy of Chlorhexidine-Silver Sulfadiazine-Impregnated Central Venous Catheters in the Prevention of Catheter-Related Infection*

Reference	Catheter Type	Catheter Colonization	Relative Risk (95% CI)	Catheter-Related Bloodstream Infection	Relative Risk (95% CI)	Mean Duration of Catheterization ^o
		n/n (%)		n/n (%)		
8	CHSS	-		1/98 (1.0)		-6
	Control	-		5/113 (4.4)	0.2 (0.0-1.9)	-6
114	CHSS	4/23 (14)		-		7
	Control	10/25 (38)	0.4 (0.1-1.0)	-		7
115	CHSS	22/68 (32)		5/68 (7.4)		7
	Control	22/60 (37)	0.9 (0.6-1.4)	7/60 (12)	0.6 (0.2-1.9)	6
116	CHSS	21/116 (18)		0/116 (0)		8
	Control	36/117 (31)	0.6 (0.4-0.9)	3/117 (2.6)	0.5 (0.4-0.7)	8
117	CHSS	1/67 (1.5)		1/67 (1.5)		9
	Control	13/87 (15)	0.1 (0.0-0.7)	4/87 (4.6)	0.5 (0.4-0.7)	7
118	CHSS	10/44 (23)		-		-
	Control	25/35 (71)	0.3 (0.2-0.6)	-		-
119	CHSS	-		2/32 (6.3)		10
	Control	-		3/40 (7.5)	0.8 (0.2-4.7)	11
120	CHSS	45/199 (23)		1/199 (0.5)		11
	Control	63/189 (33)	0.7 (0.5-0.9)	4/189 (2.0)	0.2 (0.0-2.1)	11
121	CHSS	-		17/338 (5.0)		20
	Control	-		15/342 (4.4)	1.2 (0.6-2.2)	20

* Data from randomized studies that used quantitative or semi-quantitative catheter culture methods and percutaneously drawn blood cultures to define bloodstream infection in catheters inserted into a new site (without antimicrobial ointment applied to the site) rather than over a guidewire into an old site. CHSS = chlorhexidine-silver sulfadiazine-impregnated catheters.

probably reflects reduced antimicrobial activity of the catheter over time (116, 121) and a lack of protection from microbes invading the luminal surface of the catheter from contaminated hubs. Resistance to the chlorhexidine-silver sulfadiazine catheter has not been demonstrated in clinical studies. In vitro studies designed to induce microbial resistance to chlorhexidine have been successful (123). These experiments were done in the absence of silver sulfadiazine, with bacteria not usually associated with catheter-related infections and under conditions that differ from the clinical conditions in which the chlorhexidine-silver sulfadiazine catheter is used. There are reports, predominantly in Japan, of anaphylactic reactions to the chlorhexidine component of this catheter (124). As of 30 December 1999, no such reactions were reported to the U.S. Food and Drug Administration (Freedom of Information Inquiry). Use of central venous catheters impregnated with chlorhexidine and silver sulfadiazine should be considered when catheterization is expected to last less than 2 weeks and when the rate of infection is high despite adherence to other strategies, such as maximal barrier precautions [1]. Adverse reaction associated with this or any other device should be reported to the U.S. Food and Drug Administration's MedWatch program (www.fda.gov/medwatch) and the Centers for Disease Control and Prevention (www.cdc.gov).

Use of commercially available central venous catheters impregnated intraluminally and extraluminally with minocycline and rifampin reduces the risk for catheter-related bloodstream infection compared with the currently available chlorhexidine-silver

sulfadiazine-impregnated catheter (relative risk, 0.1 [CI, 0.0 to 0.6]) (125). Resistance to minocycline and rifampin impregnated on catheter surfaces has not been demonstrated in clinical studies, but population analysis (22, 23) was not used to determine whether subpopulations of skin microbes develop resistance after prolonged exposure to this antibiotic-impregnated catheter. One in vitro study suggested that use of catheters impregnated with minocycline and rifampin may lead to development of resistance to these agents (126). However, use of these devices may reduce the use of systemic antibiotics, such as vancomycin. Use of central venous catheters impregnated with minocycline and rifampin should be considered when the rate of bloodstream infection related to use of short-term central venous catheters is high despite use of preventive strategies that do not incorporate agents otherwise used for systemic antimicrobial therapy [IIa].

Current recommendations for the prevention of catheter-related bloodstream infection are listed in Table 5.

The Future

Over the past 25 years, much has been learned about catheter-related infections and their prevention. However, additional adequately powered randomized studies with appropriate microbiological methods are needed.

A study of covalently linked heparin on the surface of central venous catheters to reduce the risk

for catheter-related bloodstream infection was indeterminate (odds ratio, 0 [CI, 0.0 to 1.5]) (127). This strategy is attractive because it does not incorporate antimicrobial agents; further studies of it are warranted. A study of a catheter externally coated with silver was also inconclusive (relative risk, 0.5 [CI, 0.2 to 1.0]) (128); again, further clinical trials with this catheter are needed. Electrically charged catheters prevent colonization by various microbes (129, 130), but there are no published clinical trials of these catheters.

Gene products of an identified operon mediate the *S. epidermidis* autoaggregation and biofilm formation so commonly encountered on the surface of colonized intravascular catheters (131). Blocking the expression of this operon may prevent adherence of

S. epidermidis to the catheter surface. Antibodies that block the fibronectin-binding protein adhesin of *S. aureus* have been developed (132). Coating future catheters with similar antiadhesin molecules may thwart *S. aureus* infection. Quorum sensing among microbes is necessary for the maturation of biofilm (133). A better understanding of this form of microbial communication may lead to the development of chemical messengers that block biofilm formation.

Future prospects for the prevention of foreign body infections are bright. Our expanding knowledge of the molecular pathogenesis of catheter infections will undoubtedly guide us in the continued struggle against microbial colonization of tomorrow's catheters.

Table 5. Recommendations for the Prevention of Intravascular Catheter-Related Infection

Preventive Strategy Recommended for Clinical Use	Grade*	Recommended in Current Review	Recommended by the Hospital Infection Control Practice Advisory Committee†
Catheter insertion			
Subcutaneous tunneling short-term catheters inserted in the internal jugular or femoral veins when catheters are not used for drawing blood	IIa	Yes	No official recommendation
Full barrier precautions during central venous catheter insertion	IIa	Yes	Yes
Contamination shield for pulmonary artery catheters	IIa	Yes	No official recommendation
Preparation of insertion site with chlorhexidine-containing antiseptics	IIa	Yes	No official recommendation
Prophylaxis with vancomycin and other therapeutic agents	IIa	No	No
Femoral vein catheter insertion	III	No	No official recommendation
Subclavian vein rather than internal jugular vein catheter insertion	III	Yes	Yes
Preparation of insertion site with tincture of iodine	IV	Yes	Yes
Full barrier precautions during insertion of midline, peripheral artery, and pulmonary artery catheters	IV	Yes	Yes
Catheter maintenance			
Routine replacement of central venous catheters‡	I	No	No
Chlorhexidine-silver sulfadiazine-impregnated short-term central venous catheters	I	Yes	Yes
Low-dose heparin for patients with short-term central venous catheters	I	Yes	Yes
Specialized nursing teams caring for patients with short-term peripheral venous catheters at institutions with a high incidence of infection	IIa	Yes	Yes
Povidone-iodine ointment applied to hemodialysis catheter insertion sites	IIa	Yes	Yes
Hub with chamber filled with iodinated alcohol for central venous catheters with an expected duration of approximately 2 weeks	IIa	Yes	No official recommendation
Povidone-iodine-saturated sponge enclosed in plastic casing fitted around the hubs of central venous catheters with an expected 2-week duration	IIa	Yes	No official recommendation
Minocycline-riampin-impregnated short-term central venous catheters	IIa	Yes	Yes
Triple antibiotic ointments applied to insertion sites	IIa	No	No
Silver-impregnated subcutaneous collagen-cuffed short-term central venous catheters	IIa	No	Yes
Silver-impregnated subcutaneous collagen-cuffed long-term central venous catheters	IIa	No	No official recommendation
Low-dose warfarin for patients with long-term central venous catheters	IIa	Yes	No official recommendation
Transparent or gauze dressing for central venous catheters	IIb	Yes	Yes
Gauze dressings when blood is oozing from the insertion site	IIb	Yes	No official recommendation
Adequate nurse-to-patient ratio in ICUs	III	Yes	No official recommendation
Change needleless system, device, and end cap (if present) on a regular basis in accordance with manufacturer's guidelines and reduce contact with nonsterile water	III	Yes	No official recommendation
Continuing quality improvement programs to improve compliance with catheter care guidelines	III	Yes	Yes
Remove catheters as soon as possible after intended use	IV	Yes	Yes
Disinfect catheter hubs and sampling ports before accessing	IV	Yes	Yes
Pulmonary artery catheters heparin-bonded with benzalkonium chloride	IV	Yes	No official recommendation
Povidone-iodine ointment applied to insertion sites nontunneled central venous catheters of immunocompromised patients with heavy <i>Staphylococcus aureus</i> carriage (for example, patients with AIDS or cirrhosis)	IV	Yes	No official recommendation
Specialized nursing teams caring for patients with catheters used for total parenteral nutrition	IV	Yes	Yes
Hub with chamber filled with iodinated alcohol or hub-protective povidone-iodine-saturated sponge for heavily manipulated central venous catheters in ICUs	IV	Yes	No official recommendation
Mupirocin ointment applied to the insertion site	IV	No	No
Inline filters	IV	No	No

* See Methods section for criteria used to grade recommendations. ICU = intensive care unit.

† Reference 9.

‡ Recommendations refer to prevention of catheter-related thrombosis.

From Rhode Island Hospital and Brown University School of Medicine, Providence, Rhode Island

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Requests for Single Reprints: Leonard Mermel, DO, ScM, Division of Infectious Diseases, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903; e-mail, lmermcl@lifespan.org

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