REVIEW ARTICLE

Overview of catheter-related infections with special emphasis on prevention based on educational programs

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Intra-vascular access is an unavoidable tool in sophisticated modern medical practice, and catheter-related infection remains a leading cause of nosocomial infections, particularly in intensive care units where it is associated with significant patient morbidity, mortality, and additional hospital costs. The incidence of catheter-related bloodstream infection ranges from 2 to 14 episodes per 1000 catheter-days. On average, microbiologically documented, device-related bloodstream infections complicate the use of a central venous line in three to five per 100 cases. But this represents only the visible part of the iceberg and most episodes of clinical sepsis are nowadays considered to be catheter-related. We briefly review the pathophysiology of these infections, highlighting the importance of the skin insertion site and the intravenous line hub as principal sources of colonization and infection. Principles of therapy are briefly addressed. A large proportion of these infections are preventable and this has been the objective of creating precise guidelines. It was recently suggested that the situation may evolve with the introduction of antibiotic/antiseptic-coated devices, whose impact on the epidemiology of antibiotic resistance remains to be determined. Recently, educational programs and/or a global preventive strategy based on the strict application of specific preventive measures and careful control of all factors associated with infection proved to be even more effective than coated devices in reducing rates of infection. Practical aspects regarding educational approaches will help clinicians to adapt and incorporate educational programs into clinical practice.

Keywords central venous catheter, catheter-related infections, nosocomial infection, bloodstream infection, prevention of infection, educational programmes

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INTRODUCTION

The Institute of Medicine in Washington recently estimated that preventable adverse events in the United States, including nosocomial infections, were responsible for 44 000–98 000 deaths annually and represent a cost of $17 to $29 billion [1]. Mostly based on extrapolation from two studies only, this report has generated considerable debate in the medical literature [2–9]. Nosocomial infections (NI) now concern 5–15% of hospitalized patients and can lead to complications in 25–50% of those admitted to intensive care units (ICUs) [10]. Pneumonia related to mechanical ventilation, intra-abdominal infections following trauma or surgery, and bacteremias or sepsis related to intravascular devices account for more than 80% of these types of infections [11,12]. Accordingly, their prevention should become a priority target of health-care systems.

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Definitions

Catheter-related infections (CRIs) include colonization of the device, skin exit-site infection and device-related bloodstream infection [13–19] (Table 1).

Table 1 Definitions of catheter-related infections and diagnostic cultures[a]

Type of infection	Definitions with sensitivity and specificity of the type of culture performed for the diagnosis of infection			
Catheter colonization	In the absence of any clinical signs of infection at the insertion site of the vascular access:			
	Type of microbiological technique applied in the laboratory	Cut-off values[b]	Sensitivity	Specificity
	quantitative culture (Brun–Buisson technique) [14]:	≥100 CFUs	94%	92%
	quantitative culture (sonication, vortexing technique) [16]:	≥1000 CFUs	94%	92%
	semiquantitative culture (roll-plate technique) [15]:	≥15 CFUs	85%	85%
Exit-site infection	Microbiologically documented:	a positive (semi)quantitative catheter culture in the presence of clinical signs of infection (erythema, tenderness, induration or purulence) at the insertion site of any vascular access		
	Clinically documented:	a clinical infection (erythema, tenderness, induration or purulence) at the insertion site		
Bloodstream infection	Primary bloodstream infection:	bacteremia (or fungemia) without documented distal source of infection. This includes those resulting from an intravenous or arterial line infection.		
	Clinical sepsis:	requires one of the following signs or symptoms with no other recognized cause: (i) fever (>38 °C); (ii) hypotension (systolic blood pressure ≤90 mmHg); (iii) oliguria (<20 mL/h) and the presence of all of the following conditions: (i) blood culture not performed or no organism detected in blood, (ii) no apparent infection at another site, (iii) clinical response to empiric antimicrobial therapy after catheter removal and/or change		
Catheter-related bloodstream infection	Isolation of the same organism (i.e. identical species, antibiogram) from a quantitative culture of the distal catheter segment and from the blood of a patient with clinical symptoms of sepsis and no other apparent source of infection			
	Type of microbiological technique applied to perform blood cultures		Sensitivity	Specificity
	Standard blood cultures (two sets with at least one drawn percutaneously) [17]		91%	86%
	Quantitative blood culture (differential quantitative cultures of two sets with at least one drawn percutaneously) [18]		79%	94%
	Differential time blood culture (differential time of two sets of blood cultures drawn simultaneously, percutaneously and from the suspected vascular access) [19]		91%	94%
	In the absence of catheter culture, defervescence after removal of an implicated catheter from a patient with primary bloodstream infection is considered as indirect evidence of catheter-related bloodstream infection			

[a]Adapted from references [13,17].
[b]CFUs: colony-forming units.

Microbiological criteria are a matter of debate for experts and in the absence of a standard reference technique a choice has to be made between sensitivity and specificity according to scientific considerations and technical or economic restraints. According to the data regularly reported by the National Nosocomial Infection Surveillance (NNIS) system more than 85% of primary bacteraemias are catheter-related [20–23]. The concept of bloodstream infection includes

Table 2 Colonization and catheter-related bloodstream infection rates in selected ICU series with antiseptic/antibiotic impregnated and nonimpregnated central venous lines

Author	Number in study	Catheter colonization		Catheter-related bloodstream infections	
Non-impregnated catheters					
Bach [33][a]	117	36	(30.8%)	3	(2.5%)
Hannan [35][b]	177	71	(40.2%)	8	(4.7%)
Heard [31][c]	157	82	(52.2%)	6	(3.8%)
Loo [34][d]	81	25	(30.9%)	3	(3.9%)
Maki [25][e]	195	47	(24.1%)	9	(4.6%)
Marik [36][f]	39	11	(28.2%)	2	(5.1%)
Raad [26][g]	136	32	(23.6%)	7	(5.0%)
Tennenberg [30][h]	145	32	(22.4%)	9	(6.4%)
van Heerden [32][i]	26	10	(38.5%)	0	–
Silver-sulphadiazine/chlorhexidine-impregnated catheters					
Bach [33][a]	116	21	(18.1%)	0	–
Hannan [35][b]	174	47	(27.0%)	3	(1.7%)
Heard [31][c]	151	60	(39.7%)	5	(3.3%)
Loo [34][d]	77	12	(15.6%)	3	(3.3%)
Maki [25][e]	208	28	(13.5%)	2	(1.0%)
Marik [36][f]	36	7	(19.4%)	1	(2.8%)
Tennenberg [30][h]	137	8	(5.8%)	5	(3.8%)
van Heerden [32][i]	28	4	(14.3%)	0	–
Darouiche [27][j]	382	87	(22.8%)	13	(3.4%)
Minocyclin/rifampin-impregnated catheters					
Marik [36][f]	38	4	(10.5%)	0	–
Raad [26][g]	130	11	(8.0%)	0	–
Darouiche [27][j]	356	28	(7.5%)	1	(0.3%)

[a]Quantitative level of bacterial colonization 52 ± 17 vs. 256 ± 86 CFUs for silver-sulphadiazine/chlorhexidine-impregnated as compared to non-impregnated catheters, respectively, $P < 0.05$. No significant differences for catheter-related bloodstream infections.

[b]Semiquantitative analysis of bacterial counts for colonization for silver-sulphadiazine/chlorhexidine-impregnated as compared to non-impregnated catheters $P < 0.01$. No significant differences for catheter-related bloodstream infections.

[c]Odds ratio for colonization only: 0.59 [CI 0.34–0.97] for silver-sulphadiazine/chlorhexidine-impregnated as compared to non-impregnated catheters, respectively, $P = 0.04$.

[d]Catheter-tip-positive cultures: for silver-sulphadiazine/chlorhexidine-impregnated as compared to non-impregnated catheters $P < 0.05$. No significant differences for catheter-related bloodstream infections.

[e]Odds ratio for colonization: 0.56 [CI 0.36–0.89] for silver-sulphadiazine/chlorhexidine-impregnated as compared to non-impregnated catheters, respectively, $P < 0.005$. Odds ratio for catheter-related bloodstream infection: 0.21 [CI 0.03–0.95] for silver-sulphadiazine/chlorhexidine-impregnated catheter as compared to non-impregnated catheters, respectively, $P = 0.03$.

[f]Semiquantitative cultures of distal segment: for minocyclin/rifampin-coated as compared to non-impregnated catheters $P = 0.5$. No significant differences for catheter-related bloodstream infections.

[g]Odds ratio for colonization: 0.25 [CI 0.12–0.53] for minocyclin/rifampin-coated as compared to non-impregnated catheters, respectively, $P < 0.001$. The rates of catheter-related bloodstream infection per 1000 catheter-days were 7.34 for non-impregnated and 0 for impregnated catheters ($P < 0.01$, binomial exact test).

[h]Risk reduction for colonization only: 43% for silver-sulphadiazine/chlorhexidine-impregnated as compared to non-impregnated catheters, respectively, $P < 0.001$.

[i]Semiquantitative cultures of distal segment: for silver-sulphadiazine/chlorhexidine-impregnated as compared to non-impregnated catheters $P < 0.05$. No significant differences for catheter-related bloodstream infections.

[j]Odds ratio for colonization: 0.35 [CI 0.23–0.52] for minocyclin/rifampin-coated as compared to silver-sulphadiazine/chlorhexidine-impregnated catheters, respectively, $P < 0.001$. Odds ratio for catheter-related bloodstream infection: 0.08 [CI 0.01–0.63] for micocyclin/rifampin-coated as compared to silver-sulphadiazine/chlorhexidine-impregnated catheters, respectively, $P < 0.0001$.

Table 3 Catheter-related nosocomial infections rates in selected ICUs

Author [ref]	Type of ICU	Period	Number of units	Bloodstream infections per 1000 CVC-days	
NNIS[a] [22]	medical	1997–99	135	5.3	(3.6–7.1)[b]
NNIS[a] [20]	coronary	1997–99	112	4.0	(1.7–6.3)[b]
NNIS[a] [12]	surgical	1997–99	157	5.1	(2.6–7.0)[b]
NNIS[a] [23]	mixed[c]	1992–98	135	5.9	(4.0–7.8)[b]
NNIS[a] [23]	mixed[d]	1992–98	69	5.1	(2.6–7.0)[b]
NNIS[a] [21]	paediatric	1997–99	73	6.9	(4.1–9.3)[b]
Brasic [37]	mixed	1990–97	1	11.3	
Gastmeier [38]	mixed	1994	89	4.9	
Legras [39]	mixed	1995	5	4.8	
Sherertz [40]	mixed	1997	6	3.3[e]	
Sherertz [40]	mixed	1997	6	2.4[f]	
Finkelstein [41]	mixed	1997–99	1	12.0	
Eggimann [42]	medical	1995–96	1	6.6[g]	
Eggimann [42]	medical	1997	1	2.3[h]	
Wallace [43]	surgical	1997–99	1	8.0	
Wallace [43]	trauma	1995–97	1	9.1	
Weber [44]	burn	1990–91	1	4.9	
Sing-Naz [45]	pediatric	1993	1	8.9	
Sing-Naz [45]	pediatric	1995	1	16.8	
Gastmeier [46]	pediatric	1994–95	73	12.5	(5.7–24.7)[b]
Simon [47]	pediatric	1998	1	10.7	

[a]National Nosocomial Infection Surveillance (NNIS) system.
[b]50th percentile (25th to 75th).
[c]Non-major teaching hospitals.
[d]Major teaching hospitals.
[e]Before implementation of an educational programme targeted at the reduction of catheter-related infections.
[f]After implementation of an educational programme targeted at the reduction of catheter-related infections.
[g]Before implementation of a global strategy targeted at the reduction of catheter-related infections.
[h]After implementation of a global strategy targeted at the reduction of catheter-related infections.

not only primary bacteremia, but also clinical sepsis. Secondary bacteremia, included in some reports, should not be considered as catheter-related as it is related to another documented focus of infection.

Epidemiology and impact

Bloodstream infections represented 12% of all NI reported in 10 038 patients from 1417 ICUs in the European Prevalence of Infection in Intensive Care (EPIC) study [24]. As previously mentioned, the NNIS system reported that most nosocomial bloodstream infections are related to intravascular access, with rates substantially higher among patients with central venous catheters (CVCs) than among those with peripheral lines [11,12]. More than 50% of ICU patients are already equipped with at least one central line and it is generally reported that micro-organisms eventually colonize 20–30% of these. The prevalence of catheter-related bloodstream infection (CR-BSI) in the studies published in the 1990s ranged from 2.5% to 6.5% [25–36] (Table 2). However, comparisons between different types of ICUs are more accurate when these infections are reported as incidence-densities related to CVC, and they range between 2.3 and 16.8 episodes per 1000 catheter-days [12,20–23,37–47] (Table 3).

Studies have determined the impact of CRI on patient morbidity and hospital costs in ICUs. Recent case–control studies reported no attributable mortality, but overmatching may have played a role and resulted in a possible underestimation [32,48–54] (Table 4).

Pathophysiology and risk factors

Four distinct pathways may be identified in the infection process of CRIs (Figure 1). The two major pathways are the external and internal bacterial colonization of the catheter surface, both eventually leading to catheter-tip colonization, with the potential for subsequent bacteraemia [11].

Table 4 Impact of nosocomial bloodstream infection (BSI) in selected groups of patients in ICUs

Author	Type of BSI	Year of publication	Study period	Number of cases	Mortality		Attributable	
					Crude	Attributable	LOS[a] (days)	Costs ($)
Smith [48]	nosocomial[b]	1991	1986–89	34	82%	30%		
Relo [49]	nosocomial[b]	1994	1990–92	111	65%	35%[d]	8.0	40 000
Pittet [50]	nosocomial[b]	1994	1988–90	86	50%	35%	6.5	29 000
Pittet [51]	catheter-related	1994	1988–90	20	45%	25%	20.0	
Wisplinghoff [32]	nosocomial[e]	1998	1990–92	29	31%	16%		
Soufir [52]	catheter-related	1999	1990–95	38	50%	29%	10.0	35 000
DiGiovine [53]	nosocomial[f]	1999	1994–96	68	35%	4%[g]	20.0	4000
Rello [54]	catheter-related	2000	1992–99	49	22%	13%[g]		

[a]LOS, Length of stay.
[b]Includes both primary and secondary bloodstream infections.
[c]Primary coagulase-negative staphylococci (CNS) bacteremia only.
[d]Attributable mortality was determined by simple comparison with the crude mortality of all patients who did not develop a bloodstream infection.
[e]*Acinetobacter baumannii* nosocomial bloodstream infections only.
[f]Includes primary bloodstream infections only.
[g]Differences are non-significant.

The key factors for pathogenesis include bacterial adherence and host defence mechanisms. Host glycoproteins, such as fibrinogen, fibronectin, collagen and laminin, adsorbed on the surface of intravenous devices, form a layer that enhances bacterial adherence to foreign material, in particular, *Staphylococcus aureus* and coagulase-negative staphylococci. In addition, some strains produce a mucoid exopolymeric substance (slime), conferring some protection against antimicrobial agents and interfering with neutrophil function [55].

Skin colonization is a strong predictor of CRIs, and several studies have demonstrated a high association between significant distal catheter-tip colonization and CR-BSI [15,56]. Accordingly, external surface pathway infection may start with the colonization of the skin insertion site by micro-organisms of the skin flora that may move by capillary action through the transcutaneous part of the dermal tunnel surrounding the catheter. This phenomenon was already considered as the major source of CRIs. Internal surface pathway infection may occur by colonization of the hub and intraluminal surface of the catheter [57]. The exact role of the manipulations necessary for the replacement of administration sets, infusion of fluids or drugs, and hemodynamic monitoring or blood sampling is not yet precisely established. However, frequent opening of the hub is now viewed as a potential cause of CRIs [15,25,27,56,57], the incidence of which increases in any case with the duration of placement [58]. Additional risk factors, such as the catheter material, its localization, or the type of care, are currently viewed as specific targets for preventive measures and will be discussed further.

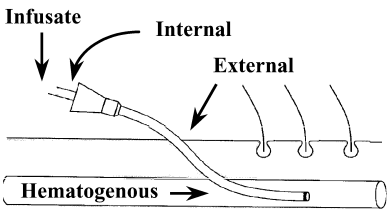

Figure 1 Colonization pathways involved in intravenous catheter-related infection. External and internal catheter surface colonization pathways involve colonization of the skin insertion site, and hub, respectively. Additional pathways include microbial contamination of the infusate (so-called 'intrinsic contamination'), and hematogenous seeding.

Hematogenous seeding of the catheter during bloodstream infection of any origin represents a third pathway of CRIs [59].

Finally, contamination of the fluids or drugs intravenously administered constitutes another process responsible for CRIs, sometimes resulting in outbreaks. Uncommon micro-organisms such as *Enterobacter* spp., *Serratia marcescens*, *Malasezia furfur*, or *Candida parapsilosis* are identified in some circumstances [60].

Table 5 Micro-organisms associated with catheter-related bloodstream infection

Type of micro-organism	Proportion[a]
Coagulase-negative staphylococci	60–70%
Staphylococcus aureus	5–15%
Candida spp.	5–10%
Enterobacteriacae	5–10%
Enterococci	2–4%
Methicillin-resistant *Staphylococcus aureus*	<5%
Burkholderia spp.[b]	<2%
Malassezia spp.[b]	<2%

[a]Large variations according to local epidemiology of micro-organisms' resistance to antimicrobials.
[b]Occasionally responsible for outbreaks.

Microbiology

Most of the micro-organisms implicated in CRIs arise from the skin flora [11,15,27,30,31,61] (Table 5). Gram-positive cocci are responsible for at least two-thirds of the infections. Coagulase-negative staphylococci (60% *Staphylococcus epidermidis*) are the leading bacteria cultured from catheters, but enterococci are not uncommon [16,27,30,31]. The recent emergence of vancomycin-resistant enterococci (VRE), accounting for 3.8% of bloodstream infections reported in NNIS hospitals between 1989 and 1993, is particularly alarming [62]. The importance of this pathogen in terms of CRI remains to be studied [62]. *Staphylococcus aureus* is responsible for 5–15% of the infections and is associated with a higher rate of complications [61,63].

Gram-negative bacilli are responsible for a higher proportion of CRIs in ICU than in non-ICU patients. They are due to colonization of invasive monitoring pressure systems, complicated remote infections, or a high degree of orotracheal colonization [56].

Candida spp. have emerged as important pathogens of CRIs and account for a high proportion of the dramatic increase in the rate of candidemia over the last decades [64]. They represented more than 30% of pathogens reported from 1992 to 1998 in 204 mixed ICUs participating in the NNIS system [23], confirming that intravascular devices constitute the leading source of nosocomial candidemia.

Diagnosis

As local signs may be completely absent, clinical diagnosis of CVC-related infections may be difficult. In addition, thrombophlebitis may be of non-infectious origin and may render eventual clinical criteria neither sensitive nor specific. Microbiological criteria are then essential to establish the presence of CRI. Various methods for culturing the insertion site, the catheter, and the blood have been described and a choice must be made according to preferred sensitivity or specificity [13,17,19] (Table 1).

Culture of the skin insertion site appears to be very sensitive in detecting colonization, but since all colonized patients will not develop CRI, it may not be systematically indicated in the absence of local signs of thrombophlebitis. Nevertheless, the absence of micro-organisms at the skin insertion site might have a high negative predictive value for the detection of CVC colonization and thus permit the avoidance of unnecessary catheter replacement [65,66].

Several methods are used to culture catheters. The choice of the optimal segment to be cultured is controversial. Cultures from proximal intradermal portions are more predictive for colonization, but positive distal cultures are more sensitive and specific for CRIs. Quantitative cultures using the flush, sonication, vortex and centrifugation techniques allow the identification of micro-organisms from both the internal and the external surfaces of the catheters [16]. They are highly sensitive in detecting CR-BSIs; but some are difficult to generalize in current routine practice [14]. Semiquantitative culture techniques have been widely used since their introduction by Maki in 1977 [15]. A 2-inch (5-cm) distal portion of catheter should be transmitted immediately to the laboratory in a dry sterile container. The catheter is rolled four times over the surface of a sheep-blood agar plate and the number of micro-organisms is determined after 48 h of incubation. The presence of >15 colony-forming units (CFUs) of a single organism per catheter is considered to indicate infection rather than colonization [15]. The limitations of the technique include that only micro-organisms from the external surface of the catheter are cultured and that the cut-off may underscore CVC-related infections; internal lumen colonization may predominate with increased catheterization time. Rapid diagnosis of CRI might be obtained by direct microscopic examination of the catheter tip stained with Gram or acridine orange techniques. In a cohort of 400 ICU patients, Gowardman et al. recently reported that this

technique was negative in the 12 catheters subsequently shown to be responsible for a BSI [67]. Although useful, these methods are time-consuming; they depend on the skill of the observer and may not be routinely used [68].

Importantly, cut-off for the diagnosis of CRI varies according to the technique used: in particular, quantitative culture techniques using sonication ($\geq$1000 CFUs) [16], vortex ($\geq$100 CFUs) [14]; and roll-plate semiquantitative technique ($>$15 CFUs) [15].

Quantitative blood culture technique, in which there is a differential count of micro-organisms in blood taken simultaneously from the catheter and from a peripheral vein, has proven useful in predicting CRIs. A single bacterial count of $>$100 CFUs/mL in the catheter blood specimen can be suggestive of CR-BSI in the presence of a positive peripheral blood culture. Not routinely used in clinical practice, this complex technique may also help facilitate monitoring the efficacy of antibacterial treatment to be monitored if the catheter is left in place [69]. The measurement of the differential time to positivity between blood drawn from the catheter port (hub-blood) and peripheral blood cultures was recently suggested as a potentially reliable tool for diagnosis of CR-BSI [70]. In a group of 93 patients, in whom a CVC was consecutively removed for suspicion of CRI over a 14-month period, the same group included a diagnosis of definite CR-BSI in 16 of 17 ICU patients in whom a positive hub-blood culture was detected at least 2 h earlier than peripheral blood culture. A CRI was excluded in 10 of the 11 patients in whom the differential time to positivity was lower than 2 h, conferring a 91% sensitivity and 94% specificity to this cut-off [19]. If further studies did confirm these data, this simple technique may be imposed in hospital clinical practice, using automatic devices for detection of positive blood cultures.

Treatment strategies

In general, removal of a catheter suspected to be infected is strongly recommended. Catheter retention may result in a several-fold higher risk for recurrence of BSI. Removal is mandatory in severe or complicated infections such as shock, persistent fever, or bacteremia, or with certain micro-organisms (*S. aureus*, Gram-negative bacilli, *Candida* spp.) [11,71].

However, removal of a CVC was proven to be unnecessary in 75–90% of cases, even when CR-BSI was suspected. This may explain, in part, why catheter exchange over a guidewire, which allows the avoidance of new venous punctures, has become common practice in most ICUs. This will be discussed in more detail in the section on prevention.

Several studies have reported successful treatment of CRIs, particularly bacteremia due to coagulase-negative staphylococci, with intravenous antibiotics (vancomycin with or without aminoglycoside) and without removal of the catheter. The technique of antibiotic lock may be particularly helpful in avoiding difficult vascular access replacement in patients with implanted or permanent devices [72]. However, catheter retention may result in a several-fold higher risk for the recurrence of bloodstream infections with resistant micro-organisms or yeasts [73].

Although some authors recommend no treatment once the catheter is removed, many authorities prefer to treat with an appropriate antibiotic course (5–7 days for uncomplicated coagulase-negative staphylococci). In patients with *S. aureus* CRIs, treatment duration should be 10–14 days. Furthermore, recent data suggested that a transesophageal echocardiogram may help to identify vegetation(s) which require specific management in a significant proportion of patients [74]. In any case, antimicrobial agents should then be adapted according to susceptibility testing. Knowledge of the ecology of CRIs in particular institutions is especially useful for empiric antibiotic treatment [11,56].

Relapse, continuous fever, or bacteremia, despite removal of the catheter is consistent with the suspicion of a persistent focus of infection. This implies prolonged or modified antimicrobial treatment and an active search for a CRI complicating another venous line, metastatic abscess, septic thrombophlebitis, or endocarditis. Following completion of treatment, careful follow-up is required due to the frequent occurrence of late complications [11,56].

PREVENTION

More than 50% of patients admitted to ICUs are already colonized at the time of admission with the organism responsible for subsequent infection [75]. Nevertheless, the prevention of CRIs relies

on careful control of all the factors associated with the colonization of vascular accesses by micro-organisms; evidence-based guidelines and preventive measures have been published by the Hospital Infections Control Practices Advisory Committee [59]. Recently, this topic was also extensively reviewed elsewhere [76,77]. However, most of these measures are supported by clinical studies with a limited strength of evidence. Some are discussed below.

Hand hygiene measures

Infection prevention is mostly based on the application of standard precautions [78]. A strict adherence to hand hygiene measures (hand washing and/or hand disinfection) and to aseptic techniques in caring for patients and devices is the key requirement of these precautions [79].

There have been persistent reports of low-level compliance with hand hygiene, particularly in ICUs [80,81]. Experience with alcohol-based handrubs showed that hand disinfection may reduce hand contamination more than handwashing. This may also save precious time in the ICU where theoretically almost two-thirds of the staff's working time could be required for optimal adherence to infection control guidelines [82–84].

However, following successful interventions, compliance with hand hygiene decreased again over the next few months [84]. We recently showed that the promotion of an elementary bedside hand disinfection technique, by a hospital-wide education campaign, resulted in a sustained improvement in compliance with hand hygiene guidelines from 48% to 66% over a 4-year period [85]. In addition, during the same period, the prevalence of overall NIs decreased significantly from 17% to 9%.

Technique of catheter insertion

Skin preparation should include hair-cutting rather than shaving [40,42]. Maximal sterile barrier precautions during insertion, including not only small fenestrated drapes and the use of sterile gloves, but also gown, cap, mask and a large drape, can minimize catheter colonization and further CRIs [86]. Rigorous cleansing and disinfection of the insertion site is regarded as a key point. Povidone iodine (10%) and alcohol (70%) are effective, but aqueous chlorhexidine (2%) has been shown to be superior in preventing CVC colonization [87]. An alcohol-based preparation of chlorhexidine gluconate (0.5%) may combine the advantages of a greater antimicrobial spectrum, very rapid killing of skin micro-organisms, and fast drying time at low cost.

Topical antimicrobial ointments have been proposed to prevent catheter colonization, but they favour colonization by resistant organisms and are no longer recommended [59].

Site of insertion

Central lines inserted in the jugular site are more likely to be colonized than those inserted by the subclavian route [27,31,54]. This is due to factors favoring skin colonization, such as proximity of oropharyngeal secretions, higher skin temperature, difficulties in immobilizing the catheter and maintaining an optimal dressing, particularly in men [27]. CVCs inserted through the femoral route have not been reported to be more frequently responsible for infectious complications, but may be associated with a higher rate of deep venous thrombosis. Accordingly, insufficient data are presently available to recommend their use [88].

A meta-analysis suggested that tunnelled short-term CVCs are associated with a decreasing rate of CRI, but this may be the case only for those inserted in the jugular site [89]. However, an accompanying editorial highlighted the fact that drawing of blood through the catheters was not allowed in the study which must be kept in mind when determining the positive result of this analysis [90,91]. This was also the case in a recent study from the same group which reported that catheter-related sepsis occurred in five out of 168 patients who received a femoral tunneled CVC, as compared with 15 out of 168 in non-tunnelled CVC (relative risk 0.25, CI 0.09–0.72) [92].

Careful fixation of the catheter at the skin exit-site might avoid complications such as leakage of the fixing device and movements in the intradermal portion. This technique allows the installation of small dressings that are easier to secure.

Dressing

Semi-permeable transparent dressings are now widely used. Easy to place, they allow continuous observation of the skin insertion site and may reduce the risk of extrinsic contamination. However, they promote moisture and bacterial

proliferation and have been repeatedly associated with higher CRIs rates in comparison with traditional gauze dressings [93]. Therefore, the use of transparent dressings cannot be recommended in critically ill patients. The precise duration that a dressing can be safely left on a central line is unknown, but it should be systematically renewed every 48–72 h, if an earlier change is not clinically indicated.

Catheter handling

Currently, except for blood products and lipid emulsions, administration sets can be safely replaced every 72 h only [59]. Infusion therapy teams have been reported to decrease CRI rates. However, this may not be possible in the ICU and a recent study suggested that appropriately trained personnel might be as efficacious [94].

A four-fold decrease of CRI rates was reported with the use of a new antiseptic hub model in a prospective survey of 151 subclavian CVCs inserted for a mean duration of 2 weeks. These results were associated with a significant reduction of the CR-BSI attributed to the hub (1% vs. 11%) and with the fact that catheters were removed for clinical suspicion of CRI (19% vs. 42%) [95]. Such preliminary results call for further randomized trials.

Catheter replacement and/or guidewire exchange

The duration of catheterization has been linked to the risk of CRIs, particularly after 7 days [27,31,96], but systematic routine replacement of central lines has failed to prove its efficacy in decreasing the risk [97].

Guidewire exchange may increase the likelihood of infection of the new catheter, but reduces the rate of complications associated with CVC placement in a new site which may be technically difficult, particularly in severely ill patients [97]. Randomized prospective studies failed to detect any preventive benefit associated with guidewire exchange compared to insertion at a new site [98]. For many experts, guidewire exchange with systematic (semi)quantitative culture of the catheter tip is mandatory in any case of sepsis without clinical evidence of another source of infection [42]. This allows removal of the exchanged catheter and mandates further insertion at a new site only if the culture of the removed material is positive.

Intraluminal antibiotic lock or flush

Intraluminal antibiotic lock as well as flush with antibiotics have been reported to reduce the rate of CRIs, but only a few studies have been conducted in ICU patients [99]. Moreover, the use of antimicrobial agents for this purpose could lead to the emergence of vancomycin-resistant Gram-positive organisms, which must be avoided as the glycopeptide antibiotics are the only drugs currently available for the treatment of infections due to methicillin-resistant staphylococci and penicillin-resistant enterococci [59].

Antibiotic- and antiseptic-coated catheters

Several randomized clinical studies suggested that the use of CVCs impregnated with either chlorhexidine and silver sulphadiazine or minocycline and rifampin was associated with significant reductions of microbiologically documented CRIs, from 30% to 45% and from 65% to 80%, respectively [25,26,31,100] [Table 2]. In a meta-analysis and a cost-effectiveness analysis, Veenstra et al. suggested that the use of chlorhexidine–sulphadiazine-impregnated catheters decreased the incidence of CR-BSI by between 1.2% and 3.4%, corresponding to a cost saving between $68 and $391 per catheter used [101].

As compared to the chlorhexidine–sulphadiazine-coated catheters the minocycline–rifampin-impregnated catheter was reported to be associated with significantly lower colonization (relative risk 0.35; CI 0.24–0.55) and CR-BSIs (relative risk 0.08; CI 0.01–0.63) [27]. The authors argue that this difference may be due, in part, to the absence of silver–sulphadiazine in the intraluminal surface. This is consistent with another study in which the silver/chlorhexidine catheters were not associated with a reduction of the CRI rates [28]. Recent data on the determination of colonization and residual antimicrobial ex vivo activity after removal of 113 CVCs that were no longer required strongly favors this hypothesis [102].

However, the duration of catheter placement may well have played a role. Impregnated catheters failed to prevent CRIs in neutropenic cancer patients with a mean catheterization time of

20 days as compared to 6, 7 and 8.3 days for others [25–28]. We confirmed in a meta-analysis that the potential benefit of these devices may be lost after 7–10 days [103].

Educational programs

Sherertz et al. recently reported that an educational program of physicians in training can decrease the risk of CRIs. A 1-day course on infection control practices and on procedures of vascular access insertion was shown to reduce the infection rate by 73%, from 3.3 to 2.4 per 1000 CVC-days [40] [Table 3]. The educational program included a 1-h introduction to basic infection control principles (handhygiene, isolation and barrier use, handling of patients with resistant organisms and varicella virus). Thereafter, these students and physicians rotated through a series of 1-h stations, during which they received 5–15 min of didactic instruction followed by hands-on instruction that was overseen by faculty members. Training was provided in (i) blood-draws through vascular lines, (ii) arterial puncture, (iii) insertion of arterial lines and CVCs, (iv) peripheral venous catheter insertion, (v) phlebotomy, and (vi) urinary catheter insertion. Participants were also instructed to change dressings and intravenous tubing every 3 days and not to adhere to fixed schedules for changing CVCs.

We recently completed a study to evaluate the impact of a global strategy targeted at the reduction of CRIs in 3154 critically ill patients consecutively admitted to a medical ICU. Specific guidelines included in the strategy and implemented through an educational program targeted at vascular access care are discussed in the preceding sections and summarized in Table 6. The program consisted of slide-show-based educational sessions and bedside training of the entire staff, including nurses. Following the introduction of the program, the incidence density of exit-site catheter infection decreased by 64%, and that of BSI by 67%. Although the overall exposure to CVC did not significantly differ between the control and the intervention periods (median duration, 4 days, $P = 0.94$), the incidence density of bloodstream infection markedly decreased from 22.9 to 6.2 episodes per 1000 CVC-days due to a reduced incidence of both microbiologically documented infection (from 6.6 to 2.3 episodes per 1000 CVC-days) and clinical sepsis (from 16.3 to 3.9 episodes per 1000 CVC-days). Overall, the incidence density of nosocomial infections was reduced by 35% (from 52.4 to 34.0 episodes per 1000 patient-days). This corresponded to the prevention of 50–104 nosocomial infections over an 8-month period, including at least 1–11 cases of primary BSIs, 15–29 cases of clinical sepsis and 15–32 cases of vascular-access related infections [42].

The impact in terms of reduction of NI in these two studies was largely superior to that expected with the use of antimicrobial- and/or antisepsis-coated catheters [100,101]. Sherertz et al. estimated that their program was associated with a cost saving of at least $63 000, perhaps exceeding $800 000. This may represent the salary of one full-time infection control nurse per unit involved in the programme for 1 month to 1 year. This may also correspond to the anticipated benefit gained with 161–926 catheters for the lower benefit hypothesis, and from 2035 to 11 767 catheters for the upper hypothesis [101,104]. Although the precise attributable costs of CRIs remain to be determined, using a conservative approach, we estimated that the implementation of our global strategy would correspond to the annual salary of three to six full-time infection control nurses [42]. According to the aforementioned cost-efficacy analysis, this may also correspond to the anticipated benefit gained with 540–3103 catheters for the lower benefit hypothesis, and from 3061 to 6102 catheters for the upper hypothesis as compared to an average of 400 catheters annually used in the unit [101,104].

These observations indicate that behavioral changes may have played a key role in the success of these educational programs, which were based on multimodal and multidisciplinary approaches, including communication and education tools, active participation and positive feedback, and systematic involvement of institution leaders [105,106].

CONCLUSION

Catheter-related infections should no longer be considered as an indirect tribute to sophisticated care or regarded as a fate, but must become one of the priority targets of a multidisciplinary approach emphasizing quality-of-care improvement. Although the true impact of the introduction of antibiotic- and/or antiseptic-coated catheters in a unit remains to be determined, the data extrapolated from the studies which explored the

Table 6 Detailed guidelines for insertion and handling of vascular accesses to prevent catheter-related infections, University of Geneva Hospitals[a]

Hygiene	Hand disinfection:	Strongly emphasized for any care (http://www.hopisafe.ch)
	Hand washing:	Restricted for dirty hands, followed by hand disinfection
Material	Preparation:	Material available and arranged systematically to avoid interruptions during insertion[b]
Patient	Installation:	Patient and devices placed to provide sufficient access to the insertion site for the operator
Insertion	Skin preparation:	Hair-cutting instead of shaving
	Antisepsis:	Alcohol-based (70%, v/v) solution with chlorhexidine gluconate (0.5%)
	Technique:	Maximal barrier precautions: sterile gown and gloves, cap, surgical mask, large sterile drapes
	Site:	Promotion of subclavian (CVC) and wrist vein (short lines) sites
	Fixation:	Promotion of simple node at the exit-site, without special fixing device
Dressing	Transparent dressing:	Occlusive devices without gauze not allowed
	Dry gauze:	Occlusion with porous adhesive band imposed
Handling	General measure:	New caps after any opening of the hubs
	Blood sampling:	On antiseptic-impregnated pads
	Drug infusions:	*Idem*, new temporary pipe for each administration
	Cardiac output:	Closed system only, without opening of the circuit
Replacement	72-h intervals:	For dressing, sets, pipes and devices
	24-h intervals:	For lipid or blood product lines
Removal	In general:	Peripheral lines after 72 h Central lines as clinically indicated Prompt removal if vascular access not absolutely necessary
	Special conditions:	Guidewire exchange systematically performed for any unexplained clinical sepsis[c]

[a]Adapted from references [42,59].
[b]Precise listing of the material needed as well as detailed description of the insertion process must be given to all the staff of the unit including physicians, nurses and nursing assistants.
[c]Clinical sepsis was defined as one of the following clinical signs or symptoms with no other recognized cause: fever (>38 °C), hypotension (systolic blood pressure ≤90 mmHg), or oliguria (<20 mL/h) and all of the following: blood culture not performed or no organism antigen detected in blood; no apparent infection at another site; physician institutes appropriate antimicrobial therapy for sepsis [13].

impact of educational programs suggest that educational strategies targeted at vascular-access reduction should be implemented in any unit before considering the use of coated catheters. Nevertheless, the use of such sophisticated devices should probably be considered if the infection rates remain higher than those reported in the NNIS despite the introduction of other preventive measures.

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