

Prevention of intravascular catheter infection

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Purpose of review

To review recent evidence supporting the guidelines for preventing catheter-related and catheter-associated infections.

Recent findings

A series of studies has confirmed, over the past few years, that education-based preventive programmes can reduce these infections by one half to two thirds. The evidence supporting some specific measures has increased for the optimal timing for set replacement, for catheter-site dressing with chlorhexidine-impregnated devices, and for the use of some coated or impregnated intravascular devices.

Summary

Catheter-related and associated infections are largely preventable and should not be viewed as an unaffordable tribute to technical medicine. Improvements in existing techniques and new technologies should all be integrated into a structured process of continuous improvement in the quality of care.

Keywords

catheter, catheter-related infection, infection control, nosocomial infection, prevention

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Abbreviations

CDC Centers for Disease Control and Prevention
CHSS chlorhexidine–silver sulfadiazine
CVC central venous catheter
ICU intensive care unit

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Introduction

Infections associated with the use of intravascular catheters or devices represent 10–20% of all nosocomial infections. They may complicate the stays of up to 10% of intensive care unit (ICU) patients. Almost all patients staying in an ICU require at least one intravascular device for fluid/drug administration and approximately half are central venous catheters (CVCs) [1]. According to data from the National Nosocomial Infections Surveillance system, it is estimated that at least 48 600 ICU patients develop a CVC-related bloodstream infection every year in US ICUs (approximately five episodes per 1000 catheter-days). These infections, mostly caused by coagulase-negative staphylococci, *Staphylococcus aureus*, *Enterococcus* species and *Candida* species, are associated with considerable morbidity (prolonged length of stay and increased costs) and mortality [2•]. Although debated by experts with regard to magnitude, the attributable mortality of these infections may correspond to 5000–15 000 deaths directly caused by catheter-related infections; the benchmarking of rates is currently included in the assessment of quality of care in many institutions [3•].

As for other nosocomial infections, the cornerstone of prevention of intravascular device-associated or related infections relies first on a strict observation of the basic rules of hygiene, of which hand hygiene remains the first and most important procedure [4]. More specific measures, including the use of maximal sterile barriers for insertion, the optimal insertion site, skin preparation, detailed guidelines for catheter care and replacement, and defining particular situations in which the use of antiseptic/antibiotic-coated devices may be used, have been addressed in many clinical studies, and are extensively discussed in regularly updated evidence-based guidelines and recommendations [5–7]. A series of studies has confirmed, over the past few years, that education-based preventive programmes can reduce the incidence of these infections by more than two thirds.

Accordingly, infections associated with or related to intravascular devices are now considered among the most preventable nosocomial infections, and have become a focus for the 100 000 Live Campaign of the Institute for Healthcare Improvement [8•].

Prevention of vascular access-associated and related infections

Recommendations and guidelines for the prevention of catheter-associated and related infections consisted for

decades of exhaustive catalogues of many specific measures previously demonstrated to be efficient [5]. Specific measures include the use of maximal sterile barriers during insertion, optimal insertion site preparation, detailed guidelines for catheter insertion and replacement, and defining particular situations in which the use of antiseptic/antibiotic-coated devices may be useful. Data from surveillance programmes repetitively showed that they are generally not used or are insufficiently applied.

As with any nosocomial infections, however, their prevention should rely first on general measures, including on a strict observation of the basic rules of hygiene, of which hand hygiene represent the first and most important procedure [4]. They should be continuously emphasized and reinforced before considering any specific measures [9].

Early in the 2000s four cohort studies showed that multimodal educational programmes were able to reduce dramatically the rate of catheter-associated and related infections by more than two thirds [10–13]. These programmes all consisted of the systematic education of the personnel in charge of the insertion and care of intravascular access in ICUs. Emphasizing general measures first, including a strict observation of the basic rules of hygiene, these interventions produced a standardization of care at the bedside. Elaborated by personnel on the ward in close collaboration with infection control specialists, and implemented using communication and education tools, active participation and positive feedback, they all resulted in important behavioural changes.

The concept of preventing catheter-related infections has evolved accordingly, and education-based programmes were recommended as a first-line target in the 2002 renewed guidelines for the prevention of intravascular device-related infections [7].

The objective of this paper is to review further important evidence on a series of topics that has appeared in the literature since the publication of these guidelines.

Education-based programmes

Increasing amounts of evidence come from at least 17 additional cohort studies, confirming that when included in education-based programmes, combined specific measures can reduce intravascular device-associated and related infections by one half to two thirds (Table 1) [14–25,26••–30••].

In Table 1 the impact of multimodal educational programmes that target the prevention of intravascular device-related infections in adult intensive care units,

between 2000–2006 is discussed. The interventions are categorized as follows:

Sherertz *et al.* [10]: Education consisted of one day course including 1-h stations in which participants received training in: (1) blood draws through vascular lines; (2) arterial puncture for obtaining an arterial blood gas; (3) insertion of arterial catheters and central venous catheters (CVCs); (4) urinary catheter insertion; (5) lumbar puncture; (6) peripheral venous catheter insertion; (7) phlebotomy.

Eggimann *et al.* [11]: Multiple-approach intervention targeted at the reduction of vascular-access infections including a 30-min slide show and practical demonstrations completed by individual in-service training. The programme included detailed written information on clinical pathways on hand hygiene procedures, for vascular access insertion, and device maintenance and use.

Yoo *et al.* [12]: The intervention included: (1) distribution of new guidelines for the care of catheters (skin and hand disinfection, occlusive gauze dressing) with insertion sets that included a sterile gown and gloves, a mask, and a large sterile drape; (2) daily surveillance in the ICU to monitor all catheters by a checklist; (3) recommendation for systematic blood cultures and removal of the catheter if the patient develops fever of unknown origin or any symptoms or signs of CR-BSI.

Coopersmith *et al.* [13]: Based on audits to determined differences between the Centers for Disease Control and Prevention (CDC) guidelines and current practice, a task force built an education intervention to improve practices related to CVC insertion and care: (1) 10-Page self-study module with pre and post-question exam including the following topics: (a) epidemiology and scope of the problem; (b) risk factors; (c) aetiology; (d) definition; and (e) methods to decrease risk. Specific risk-reduction strategies addressed included: (i) handwashing and aseptic techniques; (ii) methods for detecting potential clinical signs and symptoms of local infection; (iii) techniques for sending catheter-tip culture; (iv) routine catheter site care; (v) replacing administration sets and fluids; (vi) cleaning and changing injection ports and luer-lock caps; (vii) how to handle parenteral fluids and multidose vials; and (viii) procedure for drawing blood cultures. (2) Guidelines for catheter maintenance included changing injection caps and intravenous tubing for fluids and medications every 72 h (or immediately if blood accumulated in or around the cap or its integrity was compromised). In addition, transparent line dressings were replaced every 7 days, whereas gauze dressings (which were used solely when there was bleeding or oozing at the insertion site) were changed every 48 h. The guidelines also recommended that dressings that

Table 1 Impact of multimodal educational programmes targeted at the prevention of intravascular device-related infections in adult intensive care units, 2000–2006

Study/year of publication	Study period	Setting	Type of intervention [10–25,26**–30**]	Infection rate (/1000 device-days) pre-intervention	Effect (% reduction)	Comments
Sherertz <i>et al.</i> [10], 2000	1995–1997	6 ICUs 1 Step-down unit	Education, multimodal	3.3 CR-BSI	27	Intervention targeted at third-year medical students and physicians completing their first postgraduate year Cost savings estimates of US\$815 309 BSI including both primary bacteraemia (6.3 ≥ 2.9/1000 device-days) and clinical sepsis (18.3 ≥ 5.0/1000 device-days). Overall nosocomial infections decreased by 65% (52.4 ≥ 34.0/1000 patient-days) Presented as an active surveillance and control programme Primarily directed towards nurses
Eggimann <i>et al.</i> [11], 2000	1995–1997	1 Medical ICU	Education, multimodal	24.6 BSI	75	
Yoo <i>et al.</i> [12], 2001	1997–1998	1 Mixed ICU	Education, multimodal	4.2 CR-BSI	69	
Coopersmith <i>et al.</i> [13], 2002	1998–2000	1 Surgical ICU	Education, multimodal, self-study module	10.8 CR-BSI	66	
Warren <i>et al.</i> [14], 2003	1998–2000	2 Mixed ICUs	Education, multimodal, self-study module	4.2 CR-BSI	50	Non-teaching hospitals All catheters inserted during the entire study period were chlorhexidine and silver sulfadiazine-bonded
Zuschneid <i>et al.</i> [15], 2003	1997–2001	84 ICUs	Voluntary adherence to the German hospital infection surveillance system (KISS) Education, multimodal, sequential interventions	2.1 Primary BSI	24	Methodology for surveillance comparable to that used by the NNIS system
Rosenthal <i>et al.</i> [16], 2003	1999–2001	2 Mixed ICUs 2 Coronary ICUs	Education, multimodal, sequential interventions	45.9 CR-BSI	78	Significant increase in compliance with intravascular device site care: Gauze on device site 53 ≥ 96% Date on IV administration set 0.6 ≥ 74% Good gauze condition 48.7 ≥ 89.6% No impact on ventilator-associated pneumonia
Misset <i>et al.</i> [17], 2004	1995–2000	1 Mixed ICU	Infection control programme	3.5 CR-BSI	100	Significant decrease in urinary tract infection (21.1 ≥ 12.9/1000 catheter-days)
Coopersmith <i>et al.</i> [18], 2004	2001–2002	1 Surgical ICU	Education, multimodal, self-study module, behavioural intervention	3.4 CR-BSI	18	Non-significant reduction, but improvements in documenting the dressing date (11–21%; $P < 0.001$) and stopcock use (70–24%; $P < 0.001$)
Berenholtz <i>et al.</i> [19], 2004	1998–2002	1 Surgical ICU	Education, multimodal (5 components introduced sequentially over 2 years)	11.3 CR-BSI	100	Prevention of eight deaths Estimated cost saving per year: US\$1 900 000 per year
Warren <i>et al.</i> [20], 2004	2000–2003	1 Medical ICU	Education, multimodal, self-study module	9.4 CR-BSI	49	Estimated cost savings over 34 months: US\$1 036 000–1 573 000
Lobo <i>et al.</i> [21], 2005	2001–2002	1 Medical ICU	Education, multimodal	20.0 CR-BSI	45	Primarily directed towards nurses
Wall <i>et al.</i> [22], 2005	2002–2004	1 Medical ICU	Education, multimodal	7.0 CR-BSI	46	Increase in compliance with hand hygiene, use of maximal sterile barrier precaution and skin preparation
CDC [23], 2005	2001–2005	69 ICUs	Education, multimodal	4.3 BSI	55	Medical/surgical ICUs: 3.64 ≥ 1.18
Eggimann <i>et al.</i> [24]	1995–2002	1 Medical ICU	Education, multimodal	24.6 BSI	75	Other type of ICUs: 4.72 ≥ 1.47 BSI including both primary bacteraemia (6.3 ≥ 3.4/1000 device-days) and clinical sepsis (18.3 ≥ 2.8/1000 device-days)

Table 1 (continued)

Study/year of publication	Study period	Setting	Type of intervention [10–25,26••–30••]	Infection rate (/1 000 device-days) pre-intervention	Effect (% reduction)	Comments
Higuera <i>et al.</i> [25], 2005	2003–2004	1 Mixed ICU 1 Neurosurgical ICU	Education, multimodal	46.3 BSI	68	Reduction of crude unadjusted mortality: 32.8 ≥ 48.5% per 100 discharges (RR 0.68; 95% CI 0.31–0.5) Cost-saving estimate per year: US\$350 000
Young <i>et al.</i> [26••], 2006	2001–2003	1 Mixed ICU	Education, multimodal	11.3 CR-BSI	77	Nurse-initiated intervention Improvement in compliance: Femoral site insertion: 12.9 ≥ 9.4% (RR 0.71; 95% CI 0.61–0.88) Dated dressings 26.6 ≥ 34.4% (RR 1.29; 95% CI 1.17–1.42) Reduction in ventilator-associated pneumonia: 54% Reduction in length of stay: 18% Cost savings estimate per year US\$220 150–1 309 000
Tsuchida <i>et al.</i> [27••]	2000–2002	1 Mixed ICU	Education, multimodal	4.0 BSI	75	
Warren <i>et al.</i> [28••], 2006	2002–2003	12 ICUs 1 BMT unit	Education, multimodal, self-study module	11.2 CR-BSI	21	
Hatler <i>et al.</i> [29••], 2006	2003–2004	1 Medical ICU	Education, multimodal	12.8 CR-BSI	77	
Prnovost <i>et al.</i> [30••], 2006	2003–2005	103 ICUs	Education, multimodal	2.7 CR-BSI	100	See text for comments

BMT, Bone marrow transplant; BSI, bloodstream infection; CI, confidence interval; CR-BSI, catheter-related bloodstream infection; ICU, intensive care unit; NNIS, National Nosocomial Infections Surveillance; RR, relative risk. ^aThe type of intervention referred to is discussed in the text [10–25,26••–30••].

were either soiled or no longer occlusive be replaced immediately.

Warren *et al.* [14]: Identical to the interventions in Coopersmith *et al.* [13].

Zuschneid *et al.* [15]: The Hospital Infection Surveillance System (Krankenhaus Infektions Surveillance System; KISS) uses CDC definitions for reporting in ICUs and focuses on primary bloodstream infections, urinary tract infections, pneumonia, and bronchitis. The participating hospitals receive their rates of infection and device use twice yearly so as to provide feedback and encourage infection control activities in the participating ICUs.

Rosenthal *et al.* [16]: The intervention included three steps: (1) active surveillance for intravascular device-associated infections and compliance with intravascular device site care; (2) education and training of all health-care workers for catheter care on the basis of the CDC guidelines; (3) monthly performance feedback documenting rates of compliance with handwashing, gauze on CVC insertion sites, dates on intravenous administration sets, and maintaining the condition of catheter gauze dressings.

Misset *et al.* [17]: Implementation of infection control practices produced by the ICU staff together with the infection control unit according to the CDC recommendations including general measures such as hand hygiene and antibiotic control, and specific guidelines targeted at the prevention of ventilator-associated pneumonia and of intravascular device-related infections.

Coopersmith *et al.* [18]: Identical to Coopersmith 2002 [13] with an additional multifactorial behavioural intervention targeted at improving compliance deficiencies noted in audits in intravascular device insertion and maintenance.

Berenholtz *et al.* [19]: Five components sequentially introduced from February 1999 to November 2001: (1) educational intervention to increase provider awareness of evidence-based infection control practices; (2) creation of a central catheter insertion cart; (3) asking providers daily whether catheters can be removed; (4) implementation of a checklist to be completed by the bedside nurse; (5) empowerment of nurses to stop procedures if guidelines are not followed.

Warren *et al.* [20]: The intervention included: (1) review and update of hospital or unit policies and procedures concerning the insertion and the use of devices by infection control team and ICU staff and members; (2) staff education by three methods: (a) didactic lectures and presentations; (b) self-study module with pre and post-test; (c) fact sheets and posters; (3) the primary messages

were: (i) hand hygiene procedures; (ii) avoidance of femoral site; (iii) maximal sterile barrier precautions for insertion; (iv) precise guidelines for catheter handling and dressing.

Lobo *et al.* [21]: The intervention consisted of: (1) observation and 10 pretest questions about hand hygiene and catheter insertion and handling; (2) education classes and poster for hand hygiene and catheter insertion (skin preparation) and handling (dressing replacement).

Wall *et al.* [22]: The intervention consisted of: (1) education: provider, trainee supervision, insertion site, hand hygiene procedures, skin antisepsis, and use of maximal sterile barriers; (2) standardized checklist for nurse including: hand hygiene, trainee supervision, maximal sterile barriers, skin preparation with chlorhexidine (2% solution), circumstance of catheter insertion; (3) audits and monthly feedback.

CDC [23]: The intervention consisted of: (1) education for catheter insertion practices (maximum sterile barrier precautions; chlorhexidine solution for skin disinfection; avoidance of the femoral insertion site; guidelines for dressing; removal of catheters no longer indicated); (2) promotion of educational module on device-associated bloodstream infections and strategies for their prevention; (3) promotion of standardized tools for recording adherence to recommendations; (4) promotion of a standardized list of contents for catheter insertion kits; (5) measurement of CVC-associated bloodstream infection rates, with quarterly reports allowing anonymous benchmarking between participating ICUs.

Eggimann *et al.* [24]: Identical to the interventions in Eggimann *et al.* [11].

Higuera *et al.* [25]: The intervention consisted of: (1) education: 1 h classes on epidemiology of nosocomial infections, on hand hygiene, disinfection, on prevention of intravascular device-associated bloodstream infections, on prevention of ventilator-associated pneumonia, and on prevention of catheter-associated urinary tract infections; (2) performance feedback: monthly chart (hand hygiene compliance, gauze on CVC insertion sites, dates on intravenous administration sets, maintenance of gauze dressings on catheter sites) posted on the walls of the ICUs; (3) the infection control guidelines included the introduction of the use alcohol hand-rubs or hand washing with povidone-iodine soap.

Young *et al.* [26^{••}]: The intervention consisted of: (1) educational sessions that emphasized the use of maximal sterile barrier precautions and the use of chlorhexidine for skin antisepsis during insertion of CVCs; (2) introduction of a special customized CVC kit including a large

sterile drape (41" by 55" with 4" fenestration) and 2% chlorhexidine gluconate in 70% isopropyl alcohol for skin antisepsis.

Tsuchida *et al.* [27^{••}]: The intervention consisted of: (1) enhanced skin preparation by scrubbing with regular bathing soap and tap water; (2) a new method for stabilization of the catheter inserted into the internal jugular vein, in which an additional dressing was placed over the sterilized dressing; (3) education of the staff for maximal sterile precautions by teaching staff members and displaying posters; (4) use of a check-list and observation of catheter insertion by link nurses to monitor compliance; (5) selection of a disinfectant that requires shorter contact time and has longer residual effect (from 10% povidone-iodine to 0.5% chlorhexidine-78% ethanol).

Warren *et al.* [28^{••}]: Identical to the interventions in Warren *et al.* [20].

Hatler *et al.* [29^{••}]: The intervention consisted of: (1) staff members received a one-page document detailing new strategies to address the prevention of ventilator-associated pneumonia and CR-BSI, thus increasing their abilities to control and perform the desired behaviours; (2) chart of expected activities was posted in each patient's room; (3) daily rounds, led by the unit's nursing supervisor, helped establish adherence to the targeted procedures as 'normal' behaviour for staff members; (4) daily goals were posted on white boards in patients' rooms; (5) regular feedback about the rates; (6) use of a rapid-cycle approach to increase the flexibility of implementing the change measured for 2-4 weeks.

Pronovost *et al.* [30^{••}]: the intervention included five of the highly ranked (CDC category IA) evidence-based recommendations identified as having the greatest effect on the rate of catheter-related bloodstream infection and the lowest barriers to implementation [7]. The recommended procedures were: (1) hand washing; (2) using full-barrier precautions during the insertion of CVCs; (3) cleaning the skin with chlorhexidine; (4) a subclavian site is preferred and the femoral site is avoided if possible; (5) removing unnecessary catheters. They were promoted by local physicians and nurses team leaders as follows: (a) staff were educated about practices to control infection and harm resulting from catheter-related bloodstream infections; (b) central-line cart with necessary supplies was promoted or created; (c) a checklist was used to ensure adherence to infection-control practices; (d) providers were stopped (in non-emergency situations) if these practices were not being followed; (e) the removal of catheters was discussed at daily rounds; (f) the teams received feedback regarding the number and rates of catheter-related bloodstream infections at monthly and quarterly meetings, respectively.

The successful prevention of infections has not only been demonstrated in cases of high initial rates, but also in institutions with considerable experience in the prevention of nosocomial infections and initially low rates of infections [10,15,17,18,30**]. A majority of these programmes has been shown to be largely cost-effective. Moreover, such programmes may also work when impregnated catheters were already in use before the intervention [14].

The most recent report concerned an interventional cohort study involving 103 ICUs in 67 hospitals in Michigan with more than 375 000 catheter-days of observation [30**]. The intervention, detailed in Table 1, was remarkable in several points. The programme was promoted by local physicians and nurses organized by team leaders. It was supported by the introduction of daily goal sheets to improve clinician-to-clinician communication within the ICUs. Furthermore, it was integrated in a comprehensive unit-based safety programme to improve the safety culture, which also included an intervention to reduce the incidence of ventilator-associated pneumonia. Over the 18 months after the implementation of the intervention, the median rate of catheter-related bloodstream infections was reduced by 66%, from 2.7 (mean 7.7) to 0 (mean 1.4) per 1000 catheter-days.

The series of mono and multicentre studies, which includes a large variety of ICUs all around the world, strongly suggests that the process of training is progressively, and hopefully definitely, moving from the traditional widespread approach 'see one, do one, teach one' to an integrated and structured process of continuous improvement of the quality of care.

Optimal timing for intravenous administration set replacement

The current guidelines recommend, scored with the highest level of evidence, to replace administration sets, including secondary sets and add-on devices, no more frequently than at 72-h intervals, unless a catheter-related infection is suspected or documented. It is recommended, with a slightly less high level of evidence, to decrease this delay to 24-h intervals for the administration of blood products or lipid emulsions [7].

Gilles *et al.* [31] from the Cochrane Anesthesia Group performed a systematic review to identify the optimal interval for the routine replacement of intravenous administration sets. From their analysis of the data extracted from 13 out of 23 studies, the authors concluded that administration sets that do not contain lipids, blood or blood products may be left in place for intervals of up to 96 h without an increase in the risk of infection. There was no evidence to suggest that administration sets containing lipids should not be changed every 24 h as currently

recommended. In addition, subgroup analysis found no differences between CVCs and peripheral catheters, nor between participants who did and did not receive parenteral nutrition, or between children and adults.

Needleless catheter access systems

Designed to reduce the incidence of sharp injuries to healthcare workers, needleless infusion systems have been developed by several manufacturers. They have not been proved to be able to prevent catheter-related infections, and were scored as an unresolved issue in the 2002 guidelines [7].

Niel-Weisse *et al.* [32**] recently reviewed five randomized trials evaluating the effect of vascular access needleless closed systems on catheter-related infections among hospitalized patients. The quality of these trials and the way they were reported were generally unsatisfactory, and their heterogeneity did not allow a meta-analysis to be performed. Nevertheless, there was a trend towards the needleless closed devices decreasing catheter-related bloodstream infections. Catheter tip and hub colonization were significantly reduced in one out of three and two out of three studies, respectively. From their detailed review, the authors specified that in contrast to several previous reports, they did not find a trend in needleless closed devices towards an increased risk of infection [33,34]. They concluded that there is currently insufficient evidence to recommend needleless closed vascular devices, and that new studies are necessary to confirm that these systems reduce catheter-related infections.

Catheter site dressing with chlorhexidine-impregnated devices

Gluconate of chlorhexidine is a powerful antimicrobial agent widely used for surgical scrub and for hand hygiene, with a good safety profile. When used as a skin disinfectant, it is more effective than povidine-iodine solutions in reducing catheter-related bloodstream infections [35]. Devices impregnated with chlorhexidine gluconate (Biopatch; Ethicon Inc., Somerville, New Jersey, USA) are able to release it up to 10 days over the skin surface when placed over the epidural catheter insertion site [36]. Whether these devices could be routinely used in the care of short-term intravascular accesses, however, remained unresolved in the 2002 guidelines [7].

Ho and Litton [37**] found 10 prospective, randomized, controlled clinical trials comparing chlorhexidine-impregnated dressings with placebo or povidine-iodine dressing, and included eight of them in a meta-analysis. The chlorhexidine-impregnated dressing reduced the risk of intravascular catheter or exit-site colonization [14.8 versus 26.9%; odds ratio (OR) 0.47; 95% confidence interval (CI) 0.34–0.65; $P < 0.00001$]. After excluding the study that compared chlorhexidine-impregnated

dressings with povidine-iodine dressings, they were associated with a significant reduction in catheter-related bloodstream infections when compared with placebo (OR 0.40; 95% CI 0.21–0.75; $P=0.004$). Local cutaneous reactions to chlorhexidine-impregnated dressings were reported in 5.6% of patients in three studies (OR 8.17; 95% CI 1.19–56.14; $P=0.04$), and 96% of these reactions occurred in neonatal patients. The number needed to prevent one episode of bloodstream infection was 142 for an average period of catheterization of 10 days and a change of dressings every 5 days. The cost of preventing one catheter-related bloodstream infection was estimated to be US\$532.5. The authors concluded that the use of chlorhexidine-impregnated dressings is safe and may be cost-effective in adult patients with intravascular devices. This should now be confirmed in a large prospective, randomized controlled trial.

Coated or impregnated intravascular devices

The use of antibiotic or antiseptic-impregnated catheters reduces device-related infections but remains controversial. In the last guidelines, experts recommended considering the use of such devices if the rate of catheter-related bloodstream infections remains higher than 3.3 episodes per 1000 CVC-days, after having enhanced other preventive measures, including multimodal educative programmes [7].

Several meta-analyses that included studies published after the release of those guidelines appeared in the literature.

Walder *et al.* [38] reviewed the impact of coated devices in 23 trials, including chlorhexidine-silver sulfadiazine (CHSS) internal coating in 12, silver-based coating or cuffing in seven, and various antibiotic coatings in five. The major finding of that meta-analysis was that in five trials on CHSS coating (1269 CVCs), in which the average insertion time ranged from 5.2 to 7.5 days (median 6 days), the risk of bloodstream infections significantly decreased from 4.1% in controls to 1.9% with anti-infective catheters (OR 0.48; 95% CI 0.25–0.91). In five additional trials on CHSS coating (1544 CVCs), in which the average insertion time ranged from 7.8 to 20 days (median 12 days), the risk of bloodstream infections was 4.5% in controls and 4.2% with anti-infective catheters (OR 0.94; 95% CI 0.58–1.54). The authors concluded that antibiotic and CHSS coatings are anti-infective for short insertion times (less than one week). For longer insertion times (more than one week), there were no data on antibiotic coating, and some evidence of a lack of effect for CHSS coating.

Geffers *et al.* [39] assessed the methodological quality of 11 randomized controlled studies (3131 catheters) with

CHSS-impregnated catheters (on their internal surface only) and the effect on catheter-related infection. The pooled data did not show a significant reduction of catheter-related bloodstream infections (OR 0.69; 95% CI 0.46–1.03). Statistical significance was achieved only when both studies with a more appropriate type of definition were separated out (OR 0.58; 95% CI 0.46–0.96), or when only studies with a short average duration of catheterization (maximum 8 days) were considered (OR 0.34; 95% CI 0.15–0.75). The authors highlighted the fact that all methods of diagnosing catheter colonization used in the studies were evaluated with uncoated catheters. They suggested that failure to use neutralizers could lead to an underestimation of the rate of catheter-related bloodstream infections; conversely, the absence of inhibitory agents may lead to an overestimation of the antibacterial efficacy of coated catheters.

Falagas *et al.* [40**] performed a meta-analysis of eight prospective randomized clinical trials including a total of 1715 rifampicin-based impregnated CVCs, 956 uncoated catheters, 451 catheters coated on their internal surface by CHSS, and 237 silver-platinum-carbon-impregnated catheters. Overall, the rifampicin/minocycline-impregnated catheters significantly reduced bacterial colonization (OR 0.46; 95% CI 0.31–0.69) and catheter-related bloodstream infections (OR 0.23; 95% CI 0.14–0.40). On the basis of the available data, no clear conclusions could be drawn regarding the impact of the use of rifampicin/minocycline-impregnated CVCs on the development of antimicrobial resistance. The authors concluded that these catheters are safe and effective in reducing the rate of catheter colonization and related infections. Regarding the development of resistance, reviewing the effectiveness and safety of rifampicin-based regimens in eradicating *S. aureus* carriage, the same authors recently concluded that the available evidence suggested that oral rifampicin is effective in its eradication [41*]. They also specified that the development of resistance occurs in a considerable proportion of patients.

The potential greater efficacy of catheters coated with minocycline/rifampicin compared with those coated with CHSS in preventing infections has largely been attributed to the fact that CHSS coating concerned only the internal lumen of the device [42]. Since then, a second generation of CHSS catheters with coating of both the internal and the external surface was produced by the manufacturer. At least three studies [43–45], including two large multicentre ICU studies, have failed to demonstrate a significant reduction in catheter-related bloodstream infections. All showed a significant reduction in bacterial colonization. The overall low rate of infection in the placebo arms could, however, argue in favour of insufficient power. By pooling the data, Gastmeier and Geffers [46] demonstrated a significant reduction in the

rate of catheter-related bloodstream infections [relative risk (RR) 0.40; 95% CI 0.18–0.90].

New composite catheters, consisting of polyurethane combined with silver, carbon, and platinum, have been introduced onto the market. They were demonstrated to be able to release ions of silver with prolonged antimicrobial activity (oligon) [47–51]. Those studies showed a significant reduction in bacterial colonization. Even by pooling the data (822 impregnated versus 833 non-impregnated catheters), Gastmeier and Geffers [46] did not find a significant reduction in the rate of catheter-related bloodstream infections (RR 0.81; 0.46–1.45).

To summarize the information of the many randomized studies, the impact of these devices is in the same range as those of the educational programmes. Nevertheless, they should never replace them. It should be highlighted that in at least one of the studies demonstrating a significant reduction in infections after the introduction of a multimodule educational programme, coated catheters were used during the entire study period [14].

Borschel *et al.* [52**] recently reported the impact in a real-world setting after the introduction of CHSS CVCs (second generation with internal and external coating) in all consecutive patients requiring central venous access in six adult ICUs at a large, tertiary care teaching hospital. The intervention significantly increased the rate of reduction of the incidence of catheter-related bloodstream infections by approximately 4% per month, corresponding to an overall 35% relative risk reduction over a 16-month period (from approximately nine to less than four episodes per 1000 device-days). With 41 infections avoided for approximately 1647 coated catheters inserted, the authors estimated that the intervention saved US\$266 325 over one year. Assuming that not all of the observed effect was caused by the coated catheters, the intervention would remain cost-effective even if only 13% of the observed decrease in infection rate was attributable to it. Furthermore, the intervention was associated with a significant reduction in the rate of vancomycin use.

If such a positive and cost-effective impact of antiseptic-coated devices in a real-world setting could be confirmed in large multicentre studies, it may contribute to increase the level of evidence to include them in all strategies targeted at the reduction of catheter-related infections.

New areas of development

Antibiotic-lock or flush solutions are not routinely recommended for the prevention of device-related infections by the 2002 guidelines [7]. They were confirmed to be able to reduce significantly the rate of catheter-related infections and be useful in the treatment of persistent bacteraemia in long-term catheters by two recently pub-

lished meta-analyses [53**,54*]. These techniques should, however, be restricted to this setting when infection with coagulase-negative staphylococci is documented but without systemic signs of sepsis or secondary dissemination [55]. Accordingly, as a result of the risk of promoting the spread of resistance, and the lack of data in other types of settings, they should continue not to be used routinely.

The 2002 guidelines recommend the use of a 2% solution of chlorhexidine for skin antiseptics before intravascular device insertion and further maintenance care. The majority of the commercially available chlorhexidine-based solutions for use with intravascular devices consist of 2% chlorhexidine gluconate in 70% isopropyl alcohol. Medical-grade ethanol has already been in use for many years for the management or prevention of the occlusion of intravascular devices used for parenteral nutrition [56,57]. A series of reports has suggested that 25–70% of ethanol used as a lock solution may be of value both as an adjunct to the treatment of intravascular device-related bloodstream infections and for the prevention of infection with the use of long-term intravascular devices [58,59*,60*]. Crnich and colleagues [61] demonstrated that a 70% ethanol lock solution has a negligible impact on the mechanical properties of polyetherurethane and silicone catheters, despite continuous exposure times as long as 10 weeks. These findings should prompt further studies of ethanol as an anti-infective lock solution for the prevention and treatment of intravascular device-related bloodstream infections in other settings, including shorter catheterization times.

Conclusion

Catheter-related and associated infections are largely preventable and should not be viewed as an unaffordable tribute to technical medicine. Their prevention is a very active and stimulating field for clinical research. Improvements in many specific technical measures, such as new catheter securement or fixation devices, will probably continue to be studied. New technologies are stimulating the design of new types of impregnated devices. After being shown to be useful, all these improvements should then be integrated into structured multimodal educational programmes. Moreover, these interventions should all be integrated in a structured process of continuous improvement of the quality of care.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 436).

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