EXPERT REVIEWS

Management of catheter-related infection

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Jean-Luc Pagani and Philippe Eggimann†

†*Author for correspondence*
Department of Adult Intensive Care Medicine & Burn Centre, Centre Hospitalier Universitaire Vaudois (CHUV), BH 08-609, Bugnon 46, CH-1011 Lausanne, Switzerland

Nosocomial infections related to the development of catheter-related infections are a leading cause of morbidity and mortality among critically ill hospitalized patients. Despite important preventive efforts, these infections remain a daily concern for most clinicians. Significant improvements in the knowledge of their pathophysiology and diagnosis allow us to treat them more efficiently. Current practices, such as guidewire exchange of catheters suspected to be the source of clinical sepsis, are supported by indirect evidence only. Infected catheters should systematically be removed, but some of them may be salved by combining systemic and antibiotic-lock treatment. After reviewing some specific therapeutic aspects, we suggest a practical approach to manage catheter-related infections.

KEYWORDS: antibiotic-lock therapy • bloodstream infection • catheter-related infection • critical care • guidewire exchange • nosocomial infection

Central venous catheters (CVCs) are used for a wide range of indications, extending far beyond fluid and transfusion therapy, including parenteral nutrition, hemodynamic monitoring, continuous chemotherapy, home antibiotic therapy and chronic outpatient hemodialysis. Side effects are complications related to the insertion, occlusion of the catheter, venous thrombosis and catheter-related infections (CRIs). Among them, bloodstream infections (BSIs) are considered to be the most severe complication of healthcare that can occur, with a significant increase in morbidity and mortality [1–5].

Infections associated with the use of intravascular devices represent 10–20% of all nosocomial infections and 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/drugs administration and approximately half of them are CVCs [6–8]. According to the data from the National Nosocomial Infections Surveillance system, it is extrapolated that nearly 50,000 ICU patients develop a CVC-related BSI every year in US ICUs (five episodes per 1000 catheter-days) [3]. Among these, up to 24,000 die, including 8000 (35%) as a direct consequence of the infection [9]. In a large systematic review of 200 prospective studies evaluating the risk of BSI in adults, Maki *et al.* conclude that all types of intravenous devices should be viewed at risk of related BSI [4]. Arterial catheters used for hemodynamic monitoring and peripherally inserted central catheters used in hospitalized patients posed risks lower than those associated with CVC. Most of these infections are, however, preventable through education-based multimodal interventions [5,10]. Nevertheless, despite all these efforts, CRIs remain a daily concern for most clinicians and will potentially increase with the growing number of patients requiring sophisticated care.

We will not review all strategies targeted at their prevention [5,9,10]. After a brief review of some important work regarding pathophysiological and diagnosis aspects, we will address some practical aspects of the treatment of CRIs and, more specifically, about currently debated options, such as catheter salvage and catheter antibiotic-lock therapy.

Definitions of CRIs

Infections linked to the use of intravascular devices include exit-site infections and both catheter-associated infections and CRIs. Precise definitions are detailed in TABLE 1 [7,11,12].

Catheter-associated infections include primary BSI and clinical sepsis, which are epidemiologically associated with the use of intravascular devices. CRIs include colonization of the device, skin exit-site infection and microbiologically proven device-related BSI.

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Table 1. Definitions of infections linked to vascular access.

Type of infection	Criteria
Catheter colonization	A significant growth of a microorganism (>15 cfu) from the catheter tip, subcutaneous segment, or catheter hub in the absence of clinical signs of infection
Exit-site infection	Microbiologically documented: exudates at catheter exit site yields a microorganism with or without concomitant bloodstream infection. Clinically documented: erythema or induration within 2 cm of the catheter exit site in the absence of associated bloodstream infection and without concomitant purulence
Positive blood culture	Microorganism, potentially pathogenic, cultured from one or more blood culture
Bloodstream infection	Positive blood culture with a clinical sepsis (see below)
Primary bloodstream infection	Laboratory-confirmed bloodstream infection or clinical sepsis occurring without documented infection
Secondary bloodstream infection	Laboratory-confirmed bloodstream infection secondary to another documented infection
Clinical sepsis	Requires one of the following with no other recognized cause: fever (>38°C), hypotension (SBP ≤ 90 mmHg), oliguria (<20 ml/h); and all of the following: blood culture not performed or no organism detected in blood, no apparent infection at another body site and clinical response to therapy following catheter removal or change
Catheter-associated bloodstream infection	Primary bloodstream infection or clinical sepsis in the presence of an intravascular device
Catheter-related bloodstream infection	Laboratory-confirmed bloodstream infection in the presence of an intravascular access: at least one positive blood culture obtained from a peripheral vein, clinical manifestation of infection and no apparent source of the bloodstream infection except the vascular access, and with one of the microbiological methods: a positive result of semi-quantitative (≥15 colony forming units per catheter segment) or quantitative culture (>10^3 cfu/catheter segment) with the same organism, paired quantitative blood cultures with a ≥ 5:1 ratio device versus peripheral, differential time to positivity (blood culture obtained from a CVC is positive at least 2 h earlier than a peripheral blood culture)

cfu: Colony-forming unit; CVC: Central venous catheter; SBP: Systolic blood pressure.
Adapted with permission from [7,11,12].

Microbiological criteria remain a matter of debate among experts [5]. However, the absence of a gold standard reference technique may provide an explanation for the large difference in the published rates of infections. Accordingly, CRIs may underestimate the true rate of infections linked to intravascular devices [7].

Pathophysiology of CRIs

The microorganisms responsible for a CRI may gain access to the device through four main routes [5]. They include the extraluminal surface, mostly colonized through the contamination at the skin insertion site; the intraluminal surface, which is contaminated through catheters hubs and lines contamination by manipulations of the device by patients and/or healthcare workers, by contaminated drugs or infusates, and by hematogenous colonization from a distant site of infection. This variety of sources should be taken into account in the methods used to diagnose an infection [7].

Foreign materials inserted into the body are rapidly covered by extracellular polysaccharides resulting in the formation of a biofilm. This emphasizes the natural capacity of microorganisms to attach to nonliving surfaces. From this colonization, microorganisms may produce symptomatic infections [13]. Structurally, an important proportion of biofilms are microorganisms themselves, where they are able to modify their physiology and escape antimicrobials and host defenses [14]. There is currently no possibility to eradicate *in vivo* the biofilm produced on intravascular devices, and this supports removal of an infected device as the first principle of management of any CRI.

Diagnosis of CRIs

The morbidity associated with the insertion of new catheters emphasizes the necessity to get strong arguments to support the relationship between a bacteremia of unknown origin, also characterized as primary bacteremia, and a suspect intravascular device that should be removed. Hence, if appropriate cultures are not obtained, false-negative results may be associated with increased morbidity. By contrast, false-positive culture may be associated with unnecessary catheter removal and/or inappropriate prescription of antibiotics with further promotion of the emergence of resistant strains [7].

Two techniques susceptible to document a catheter as the source of a primary bacteremia have been extensively studied over the last 10 years. They are paired quantitative blood cultures and paired qualitative blood cultures with observation of a differential time to positivity (DTP) [15,16].

Both require the simultaneous drawing of blood from the peripheral vein and catheter. The use of quantitative culture, which is the most accurate technique, is, however, of limited practical use because of its complexity, cost and lack of availability in most laboratories. The paired qualitative method, including recording of the DTP is an elegant alternative. The DTP method monitors the bacterial growth and compares the time to positivity for the samples obtained by both peripheral veins and through the suspected catheter. A diagnosis of catheter-related bacteremia is highly probable when the culture samples obtained from the catheter become positive at least 2 h earlier than those obtained from peripheral blood cultures [15,17]. These methods are particularly useful when retention of the catheter is desirable. To avoid false-negative cultures, it is obvious that cultures should be drawn before the start of systemic antibiotic use.

Treatment of CRIs

Treatment should begin promptly following the diagnosis or suspicion of CRI. Any delay in catheter removal and/or in the start of appropriate antimicrobial therapy is associated with increased morbidity and mortality [18].

Despite numerous preliminary results reported in the literature, only a minority of catheters associated with an infection can be maintained and prompt device removal is strongly recommended in all cases complicated by metastatic infection. This is also the case for infections caused by microorganisms particularly difficult to eradicate from the biofilm, such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Corynebacterium* spp., *Bacillus* spp., mycobacteria and yeasts.

Empiric antimicrobial treatment should be initiated immediately after appropriate sampling and the choice of agents(s) should take into account the severity of the patient's illness, the site of insertion and the local data of the hospital ecology [19]. More specifically, targeted treatment with potential de-escalation should be archived after identification and susceptibility testing of the causative microorganism.

In a large majority of clinical cases, at least in critically ill patients, the development of a clinical sepsis without a primary source of infection leads to the suspicion of a CRI [5]. However, in such situations, a CRI will be microbiologically documented in only 20–30% of cases. Accordingly, in cases without local signs of infection at the insertion site and in the absence of positive blood cultures, or before their results, guidewire exchange of the device has become a standard practice in many institutions [7,20]. Removed catheters are cultivated and exchanged. Catheters should be further removed with insertion of new devices at new sites only if the removed ones become positive. Despite the absence of strong evidence supporting this pragmatic practice, it is recommended, or agreed, by some experts and guidelines [5,21].

Management of CRIs due to specific pathogens

Coagulase-negative staphylococci

Coagulase-negative staphylocci are the most common cause of CRI. Severe forms of sepsis with a poor outcome are rare. Isolated fever or fever with inflammation at the catheter exit-site are common clinical manifestations [11].These infections may resolve with removal of the catheter only without further antibiotic therapy, although many experts suggest that antibiotics should be administered for a limited period of time. Except for endovascular infections, such as septic thrombosis, endocarditis and metastatic infections, antibiotics can be stopped after 5–7 days if the catheter has been removed and 10–14 days if it was maintained or exchanged over a guidewire.

Staphylococcus aureus

Catheter-related infections due to *S. aureus* may manifest as devastating metastatic infections and the risk of infective endocarditis is higher than for other microorganisms. In this context, the exact duration of the treatment is difficult to determine. In patients with uncomplicated CRI, a short course of 2 weeks of antibiotics is sufficient, provided the source has been removed. A transesophageal echocardiography could help to determine the duration of the treatment for patients with apparently no complicated infection [22,23]. Endocarditis may be clinically occult and the demonstration of echocardiographic abnormalities imply prolonging the treatment for 4–6 weeks [24]. Preliminary results from a Phase II study conducted by Weems *et al.*, including 63 patients, suggested that passive immunization with human monoclonal antibodies targeted at *S. aureus* may be potentially useful as adjunctive therapy [25]. Tefibazumab was well tolerated but further studies are required to determine the dosing range and the clinical efficacy of this antibody.

Gram-negative bacilli

Gram-negative bacilli are commonly associated with contaminated infusates and catheter-related BSIs in immunocompromised patients with tunneled devices. Their incidence is increasing. There are no specific data to guide the duration of therapy, which should be at least up to 2 weeks and determination of blood levels of antibiotics are recommended [11].

Candida

Intravenous catheters are among the leading source of candidemia and a large proportion of candidemic patients are still treated without vascular access removal. To date, no randomized, controlled study has been specifically designed to assess the benefit of systematic access removal which remains a controversial issue [26,27]. However, in 14 studies that evaluated the outcome of candidemia in relation to vascular access

management, removal was associated with an improved outcome or more rapid cure in nine of them [28]. In addition, the investigators of these studies and most experts recommend to systematically consider the prompt removal of all vascular accesses [26]. In any case, treatment with appropriate antifungal should be maintained at least 2 weeks after the last positive microbiological culture.

Antibiotic-lock therapy

Systemic antibiotic prophylaxis at the time of insertion of intravascular devices has not proven to be effective in reducing the incidence of CRI. Accordingly, the 2002 guidelines strongly discourage this practice [5]. In a more recent Cochrane review, van de Wetering *et al*. conclude that there is no evidence to administer antibiotics prophylaxis to prevent CVC Gram-positive infections in oncology patients [29].

Nevertheless, antibiotic-lock therapy is a conceptually attractive technique of both local prophylaxis and treatment. It consists of flushing and then filling of the lumens of the catheter with an antibiotic solution that is left to dwell in the lumen of the catheter. This provides very high concentrations of antimicrobial agents at the site of infection with a low incidence of systemic toxicity of these antibiotics. It has been studied in the treatment of patients with a long-term cuffed or tunneled catheter or port with multiple catheter-related BSI despite optimal maximal adherence to aseptic technique [30]. However, this practice has been reported to an increase in antimicrobial-resistant microorganisms, and the 2002 guidelines did not find sufficient evidence to support this procedure except for patient with recurrent bacteremia in whom maximal adherence to aseptic techniques have failed [5].

Safdar *et al*. performed a meta-analysis of prospective, randomized trials of vancomycin-lock solution as prophylaxis in high-risk patient populations requiring long-term central intravascular access [31]. Only seven studies out of 63 yielded could be analyzed. The other studies used solutions other than vancomycin, used no control groups, were not randomized, were reviews, used vancomycin in forms other than a lock or flush solution and therefore cannot be combined for analyses. These seven studies included 463 patients (five studies with cancer patients, one with neonates and one with cancer and neonates with parenteral nutrition). The meta-analysis showed a reduction of 50% in the relative risk for BSI. It did not find any report of colonization or BSI with vancomycin-resistant microorganisms. The authors conclude that it is highly unlikely that microorganisms in a patient's microflora would develop resistance to vancomycin from the very low dosage of vancomycin used in intravascular devices lock or flush protocol. In a retrospective study, Feely *et al*. explored the efficacy of these solutions in high-risk hemodialyzed patients [32]. They identified a subgroup of patients with three or more documented BSIs over 2 years, in whom lock solutions (gentamicin–heparin, minocycline–ethylenediaminetetraacetic acid [EDTA] or vancomycin–heparin) dramatically decreased the rate of catheter infections from 9.1 to 1.04 episodes per 1000 patient-days. Doxycline–EDTA is a possible alternative to minocycline–EDTA, which is no longer available on the market. By analogy, this suggests that for situations in which removal of the catheter is particularly difficult, or where venous access is limited, the antibiotic-lock therapy might be attempted in conjunction with systemic therapy to save the catheter.

In this context, new anti-infective lock solution with broad-spectrum anti-infective activity against multiresistant Gram-positive and Gram-negative bacteria, as well as fungi, are progressively studied. Taurolidine (a derivative of aminosulfonamide–taurinamide with antimicrobial activity against a broad range of bacteria and fungi), minocycline–EDTA (EDTA is a potent calcium and iron chelateur and has antistaphylococccal and anticandidal activity), gentamycine–citrate solution, ethanol and hydrochloric acid are currently under evaluation [33]. Among them, ethanol appears promising and a double-blind randomized trial to evaluate the efficacy of a 50% ethanol-lock solution instilled for 1–3 h once daily is ongoing [34,35]. Tetrasodium–EDTA, has been tested *in vitro* and *ex vivo* with explanted infected hemodialysis catheters [36]. This solution could significantly reduce or potentially eradicate CVC-associated biofilms of clinically relevant microorganisms (*Staphylococcus epidermidis*, *P. aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, methicillin-resistant *S. aureus* and *Candida albicans)*. This agent is also a potent anticoagulant that could replace the use of heparin and eliminate the risk of heparin-induced thrombocytopenia.

Expert commentary & five-year view

In contrast to prevention for which guidelines and recommendations are regularly published by medical societies, those for the management of CRIs are rare [5,11]. In the absence of large clinical series, they are mostly based on expert opinions and some differences remain in the approach regarding the possibility of catheter salvage. The modification of microbiological techniques, such as DTP, allows to improve diagnostic yield and further catheter salvage. Recent preliminary, encouraging data with anti-infective-lock therapy should now be confirmed.

Practical approach

We put together many aspects discussed above and we propose a practical work-up to help clinicians in the management of suspected CRIs (FIGURE 1).

A clinical decision to remove a catheter suspected of infection should be based on the eventual presence of a local sign of infection at the insertion site. Such situations should justify prompt removal of the device in virtually all cases. Potential exceptions may be rare situations, such as the presence of an isolated erythema, without systemic sign of infection

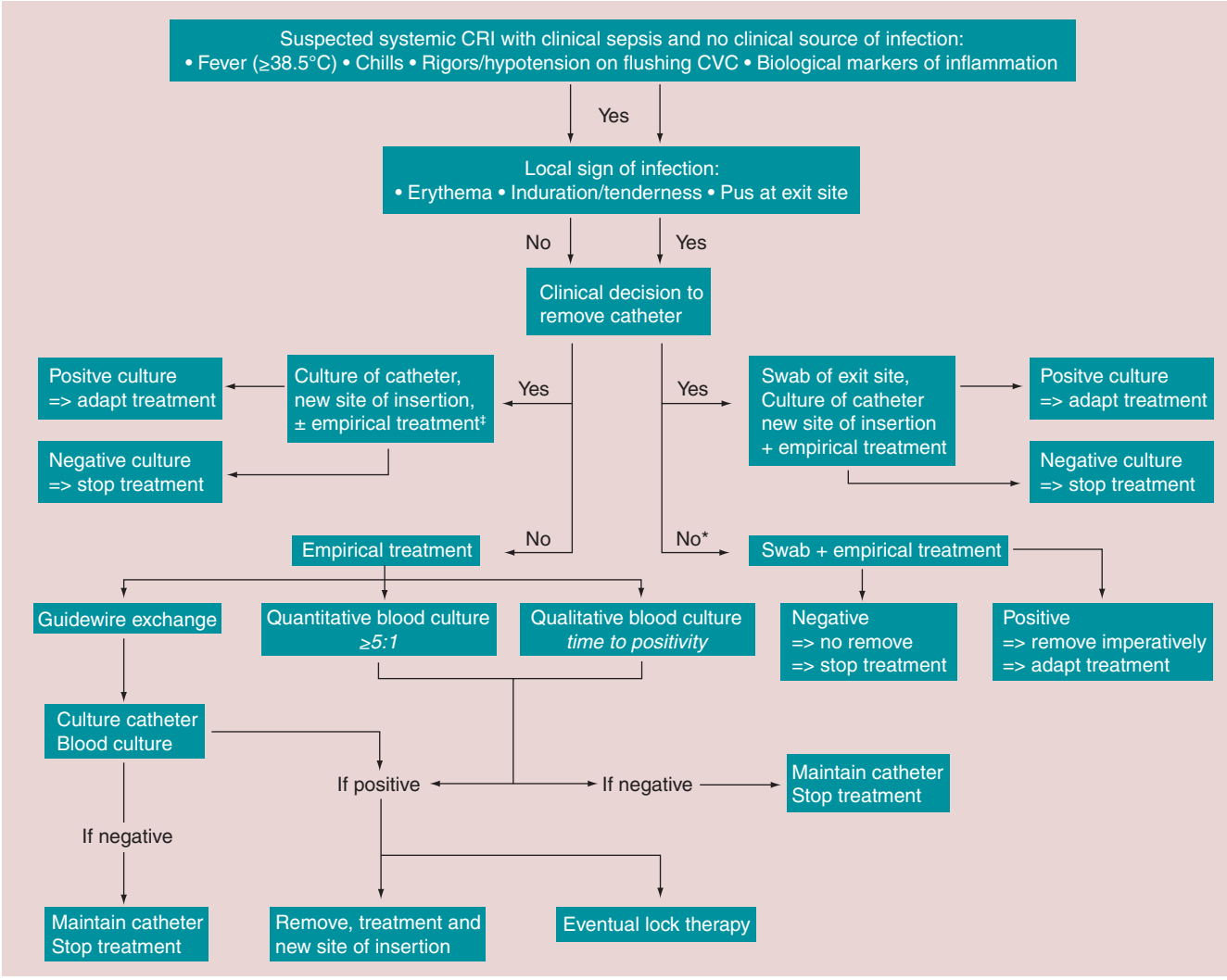

Figure 1. Proposed work-up for the management of suspected catheter-related infection in adult patients.
*Reconsider the impact of catheter bloodstream infection.
‡Empirical treatment strongly recommended except for a clincally stable patient, if all intravascular access can be removed.
CRI: Catheter-related infection; CVC: Central venous catheter.
Adapted with permission from [7,10–12,21,37].

before the reception of the results of cultures. In general, the decision to maintain the device could be discussed in the absence of clinical signs of severity of infection, such as the absence of severe sepsis or septic shock in patients with potential technical difficulties in inserting a catheter at a new site. Identification or previous information regarding the presence of coagulase-negative staphylococci may also be taken in to account to maintain the catheter. However, any temptation to maintain a device suspected of infection should be balanced with the potential serious complications that may develop, such as endovascular and or metastatic infections.

Empirical treatment should cover all microorganisms potentially responsible for the infection. It could be targeted on previous microbiological results obtained from specimen taken from the patients, but it should include Gram-positive cocci of the skin flora in almost all cases. As a large majority of coagulase-negative staphylococci are resistant to β-lactams, a glycopeptide, such as vancomycin or teicoplanin, should be considered in virtually all cases. This would also integrate the potential presence of methicillin-resistant *S. aureus*, which has emerged as an important pathogen in many institutions. A good knowledge of the local epidemiology is of crucial importance, and the presence of high proportion of vancomycin-resistant enterococci may influence the initial choice. The empirical treatment of patients with identified significant colonization with *Candida* spp. or multiresistant Gram-negative microorganisms should be adapted accordingly.

Empirical treatment should be adapted for narrowing the spectrum of coverage to the results obtained from the cultures in any case. The duration of the antimicrobial treatment should be adapted to the type of catheter and microorganism, and to the eventual presence of endovascular infections, such as septic thrombosis, endocarditis and metastatic infections, which require prolonged treatment and specialized advice.

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Key issues

- Despite all preventive measures, catheter-related infections remain a serious healthcare associated infections.
- Clinical suspicion should be documented by appropriate microbiological sampling for cultures.
- Removal of any infected catheter is the rule, with only few exceptions that should be carefully discussed in some particular circumstances.
- Guidewire exchange can be used for suspicion of catheter-related infection without local signs of infection at the insertion site and provided adequate cultures are obtained for further evaluation.
- Antibiotic-lock therapy may only be considered for some subsets of catheter-related infections due to microorganism with low potential of virulence such as coagulase-negative staphylococci in the absence of disseminated or metastatic infection.

References

Papers of special note have been highlighted as:

• of interest

▶1 Pratt RJ, Pellowe CM, Wilson JA *et al*. EPIC2: national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. *J. Hosp. Infect.* 65(Suppl. 1), S1–S64 (2007).

▶2 Higuera F, Rangel-Frausto MS, Rosenthal VD *et al*. Attributable cost and length of stay for patients with central venous catheter-associated bloodstream infection in Mexico City intensive care units: a prospective, matched analysis. *Infect. Control Hosp. Epidemiol.* 28(1), 31–35 (2007).

▶3 Pronovost P, Needham D, Berenholtz S *et al*. An intervention to decrease catheter-related bloodstream infections in the ICU. *N. Engl. J. Med.* 355(26), 2725–2732 (2006).

• Educational multicenter intervention to prevent catheter-associated bloodstream infections and ventilator-associated pneumonia.

▶4 Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. *Mayo Clin. Proc.* 81(9), 1159–1171 (2006).

• Comprehensive determination of the absolute and relative risks of microbiologically documented bloodstream infections associated with the use various types of intravascular devices.

5 O'Grady NP, Alexander M, Dellinger EP *et al*. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. *Morb. Mortal. Wkly Rep.* 51(RR-10), 1–29 (2002).

6 National Nosocomial Infections Surveillance (NNIS) System Report. Data summary from January 1992 through June 2004, issued October 2004. *Am. J. Infect. Control* 32(8), 470–485 (2004).

▶7 Eggimann P. Diagnosis of intravascular catheter infection. *Curr. Opin. Infect. Dis.* 20(4), 353–359 (2007).

▶8 Eggimann P, Pittet D. Infection control in the ICU. *Chest* 120(6), 2059–2093 (2001).

▶9 Wenzel RP, Edmond MB. Team-based prevention of catheter-related infections. *N. Engl. J. Med.* 355(26), 2781–2783 (2006).

• Recommends to the medical community to adhere to such concept-to-caring behavior that consistently leads to safety and comfort for patients.

▶10 Eggimann P. Prevention of intravascular catheter infection. *Curr. Opin. Infect. Dis.* 20(4), 360–369 (2007).

▶11 Mermel LA, Farr BM, Sherertz RJ *et al*. Guidelines for the management of intravascular catheter-related infections. *Clin. Infect. Dis.* 32(9), 1249–1272 (2001).

▶12 Worthington T, Elliott TS. Diagnosis of central venous catheter related infection in adult patients. *J. Infect.* 51(4), 267–280 (2005).

▶13 Donlan RM, Costerton JW. Biofilms: survival mechanisms of clinically relevant microorganisms. *Clin. Microbiol. Rev.* 15(2), 167–193 (2002).

▶14 Giacometti A, Cirioni O, Ghiselli R *et al*. Comparative efficacies of quinupristin–dalfopristin, linezolid, vancomycin, and ciprofloxacin in treatment, using the antibiotic-lock technique, of experimental catheter-related infection due to *Staphylococcus aureus*. *Antimicrob. Agents Chemother.* 49(10), 4042–4045 (2005).

▶15 Bouza E, Alvarado N, Alcala L, Perez MJ, Rincon C, Munoz P. A randomized and prospective study of 3 procedures for the diagnosis of catheter-related bloodstream infection without catheter withdrawal. *Clin. Infect. Dis.* 44(6), 820–826 (2007).

• Prospective comparison of three microbiological methods avoiding the remove of the intravascular device in 204 patients with suspicion of central venous catheter-related infection.

16 Linares J. Diagnosis of catheter-related bloodstream infection: conservative techniques. *Clin. Infect. Dis.*44(6), 827–829 (2007).

• Editorial regarding the difficulties in diagnosing catheter-related infections.

▶17 Calandra T, Cohen J. The international sepsis forum consensus conference on definitions of infection in the intensive care unit. *Crit. Care Med.* 33(7), 1538–1548 (2005).

▶18 Warren DK, Quadir WW, Hollenbeak CS, Elward AM, Cox MJ, Fraser VJ. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. *Crit. Care Med.* 34(8), 2084–2089 (2006).

- After adjusting for potential confounders in a cohort of 41 catheter-associated bloodstream infections, these infections resulted in an attributable cost of US$11,971, intensive care unit length of stay of 2.41 days, and hospital length of stay of 7.54 days.

19 Lorente L, Jimenez A, Iribarren JL, Jimenez JJ, Martin MM, Mora ML. The micro-organism responsible for central venous catheter related bloodstream infection depends on catheter site. *Intensive Care Med.* 32(9), 1449–1450 (2006).

20 Pottecher T, Gauzit R. [Should we use catheter replacement with the aid of wire introducer?]. *Ann. Fr. Anesth. Reanim.* 24(3), 294–297 (2005).

21 Timsit JF. [Updating of the 12th Consensus Conference of the Societe de Reanimation de Langue Francaise (SRLF): catheter related infections in the intensive care unit]. *Ann. Fr. Anesth. Reanim.* 24(3), 315–322 (2005).

22 Rosen AB, Fowler VG Jr, Corey GR *et al.* Cost–effectiveness of transesophageal echocardiography to determine the duration of therapy for intravascular catheter-associated *Staphylococcus aureus* bacteremia. *Ann. Intern. Med.* 130(10), 810–820 (1999).

23 Fowler VG Jr, Li J, Corey GR *et al.* Role of echocardiography in evaluation of patients with *Staphylococcus aureus* bacteremia: experience in 103 patients. *J. Am. Coll. Cardiol.* 30(4), 1072–1078 (1997).

24 Abraham J, Mansour C, Veledar E, Khan B, Lerakis S. *Staphylococcus aureus* bacteremia and endocarditis: the Grady Memorial Hospital experience with methicillin-sensitive *S aureus* and methicillin-resistant *S aureus* bacteremia. *Am. Heart J.* 147(3), 536–539 (2004).

25 Weems JJ Jr, Steinberg JP, Filler S *et al.* Phase II, randomized, double-blind, multicenter study comparing the safety and pharmacokinetics of tefibazumab to placebo for treatment of *Staphylococcus aureus* bacteremia. *Antimicrob. Agents Chemother.* 50(8), 2751–2755 (2006).

26 Mermel LA. New technologies to prevent intravascular catheter-related bloodstream infections. *Emerg. Infect. Dis.* 7(2), 197–199 (2001).

27 Rex JH, Walsh TJ, Sobel JD *et al.* Practice guidelines for the treatment of candidiasis. Infectious Diseases Society of America. *Clin. Infect. Dis.* 30(4), 662–678 (2000).

28 Nucci M, Anaissie E. Should vascular catheters be removed from all patients with candidemia? An evidence-based review. *Clin. Infect. Dis.* 34(5), 591–599 (2002).

29 van de Wetering, van Woensel JB. Prophylactic antibiotics for preventing early central venous catheter Gram positive infections in oncology patients. *Cochrane Database Syst. Rev.* 1, CD003295 (2007).

30 Segarra-Newnham M, Martin-Cooper EM. Antibiotic lock technique: a review of the literature. *Ann. Pharmacother.* 39(2), 311–318 (2005).

31 Safdar N, Maki DG. Use of vancomycin-containing lock or flush solutions for prevention of bloodstream infection associated with central venous access devices: a meta-analysis of prospective, randomized trials. *Clin. Infect. Dis.* 43(4), 474–484 (2006).

32 Feely T, Copley A, Bleyer AJ. Catheter lock solutions to prevent bloodstream infections in high-risk hemodialysis patients. *Am. J. Nephrol.* 27(1), 24–29 (2007).

33 Chiou PF, Chang CC, Wen YK, Yang Y. Antibiotic lock technique reduces the incidence of temporary catheter-related infections. *Clin. Nephrol.* 65(6), 419–422 (2006).

34 Opilla MT, Kirby DF, Edmond MB. Use of ethanol lock therapy to reduce the incidence of catheter-related bloodstream infections in home parenteral nutrition patients. *J. Parenter. Enteral. Nutr.* 31(4), 302–305 (2007).

35 Onland W, Shin CE, Fustar S, Rushing T, Wong WY. Ethanol-lock technique for persistent bacteremia of long-term intravascular devices in pediatric patients. *Arch. Pediatr. Adolesc. Med.* 160(10), 1049–1053 (2006).

36 Percival SL, Kite P, Eastwood K *et al.* Tetrasodium EDTA as a novel central venous catheter lock solution against biofilm. *Infect. Control Hosp. Epidemiol.* 26(6), 515–519 (2005).

37 Raad I, Hanna H, Maki D. Intravascular catheter-realted infections: advances in diagnosis, prevention, and management. *Lancet Infect. Dis.* 7, 645–647 (2007).

Affiliations

- Jean-Luc Pagani, MD
Department of Adult Intensive Care Medicine & Burn Centre, Centre Hospitalier Universitaire Vaudois (CHUV), BH 08-609, Bugnon 46, CH-1011 Lausanne, Switzerland
Tel.: +41 213 140 584
Fax: +41 213 143 045
jean-luc.pagani@chuv.ch
- Philippe Eggimann, MD
Department of Adult Intensive Care Medicine & Burn Centre, Centre Hospitalier Universitaire Vaudois (CHUV), BH 08-609, Bugnon 46, CH-1011 Lausanne, Switzerland
Tel.: +41 213 142 923
Fax: +41 213 143 045
philippe.eggimann@chuv.ch