

# Catheter-related Infection: Diagnosis, Prevention and Treatment

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## Abstract

**Introduction:** Catheter infection continues to be a serious problem in critically ill patients. This review will examine the incidence, epidemiology, microbiology, diagnosis, risk factors for and treatment of catheter-related bloodstream infections. **Methods:** Relevant articles were culled from a Medline search and other review articles on catheter-related infection. Important abstracts presented within the past year were included in the review if the data had not been published in a peer-reviewed journal. **Results:** Catheter-related bloodstream infections (CRBSI) increase morbidity and the cost of care of patients. The predominant organisms associated with CRBSI are coagulase negative staphylococci, enterococci and *Staphylococcus aureus*. Diagnosis usually requires catheter removal and culture but newer techniques such as “differential time to positivity” may permit diagnosis of CRBSI in situ. Reducing risk factors for infection are important: education of house staff, use of the subclavian insertion site, skin preparation with chlorhexidine solutions, use of maximum barrier precautions during catheter insertion and catheter maintenance with chlorhexidine sponges. If infection rates are still high after institution of these measures, use of antiseptic or antibiotic-impregnated catheters should be considered. Treatment of CRBSI in critically ill patients mandates catheter removal and treatment with systemic antibiotics. **Conclusions:** The best treatment for CRBSI is prevention. Ongoing studies are evaluating the effectiveness of newer antiseptic catheters, the risk of developing antibiotic resistance when using antibiotic-impregnated catheters and the contribution of multiple interventions on the development of CRBSI.

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**Key words:** Antibiotic-coated, Antiseptic, Bloodstream infection, Central venous catheters, Intensive care unit

## Introduction

Intravascular catheters are indispensable for patient care. Despite advances in catheter technology and patient care, catheter infection remains a significant clinical problem. The annual incidence of catheter-related bloodstream infections (CRBSI) in the United States caused by central venous catheters in the intensive care unit is approximately 80,000.<sup>1</sup> Previous studies suggest that CRBSI results in increased mortality. However, more recent data indicate that when patients are stratified according to severity of illness, the mortality due to CRBSI is not increased (Fig. 1). However, morbidity, hospital length of stay and costs associated with treating the bacteraemia are substantially increased.<sup>1,2</sup> This review will examine the pathogenesis, diagnosis, prevention and treatment of catheter-related infections.

## Definition

Consensus definitions<sup>6</sup> for catheter-related infection and CRBSI are presented in Table I.

## Pathogenesis

Catheter-related infection occurs by several mechanisms (Fig. 2).<sup>1</sup> First, skin microbes can proliferate along the subcutaneous tract and colonise the external surface of the catheter. In the case of short-term catheters, this is the commonest mechanism of infection. Second, contamination of hubs and stopcocks can lead to luminal colonisation. In the case of longer-term catheters, this mechanism assumes more importance. Third, bacteraemia originating from a distant site can cause secondary seeding of the catheter. Lastly, contamination of intravenous fluids can result in nosocomial bacteraemias.

The degree of catheter colonisation is influenced by certain characteristics of the microbe. After insertion, catheters become encased in a biofilm<sup>7</sup> comprising host proteins such as fibrin, fibronectin and laminin. These proteins can bind a number of bacteria and fungi such as *Staphylococcus aureus*, coagulase-negative staphylococci and *Candida albicans*. Adhesion to catheters is also augmented by the production of an extracellular

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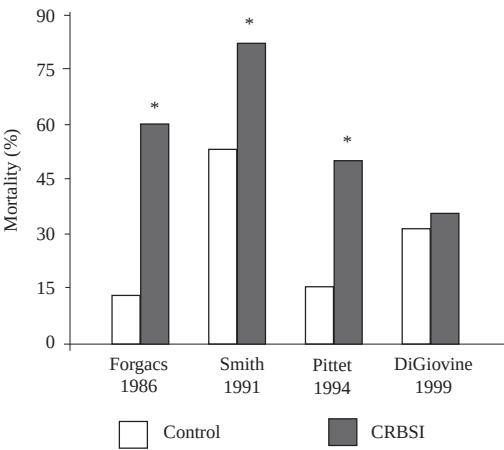


Fig. 1. Data from several studies<sup>2,3-5</sup> examining the death rates attributable to CRBSI. Control = matched patients who did not have a bloodstream infection. Recent studies<sup>2</sup> which have adjusted for severity of illness have failed to demonstrate an increased mortality due to CRBSI. \*P <0.05 between groups.

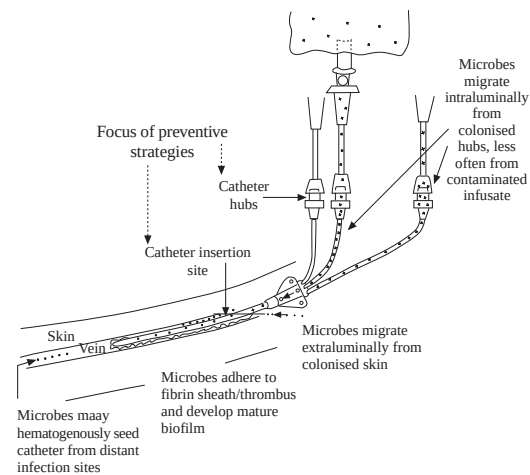


Fig. 2. Mechanisms for catheter-related infections (published with permission from Mermel<sup>1</sup>).

| TABLE I: DEFINITIONS FOR CATHETER-RELATED INFECTION |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Colonised catheter                                  | Growth of ≥15 colony-forming units (semiquantitative culture) or >10 <sup>3</sup> (quantitative culture) from a proximal or distal catheter segment in the absence of accompanying clinical symptoms.                                                                                                                                                                                                                                                                              |
| Exit-site infection                                 | Erythema, tenderness, induration or purulence within 2 cm of the skin at the exit site of the catheter.                                                                                                                                                                                                                                                                                                                                                                            |
| Pocket infection                                    | Erythema and necrosis of the skin over the reservoir of a totally implantable device or purulent exudate in the subcutaneous pocket containing the reservoir.                                                                                                                                                                                                                                                                                                                      |
| Tunnel infection                                    | Erythema, tenderness and induration in the tissues overlying the catheter and >2 cm from the exit site.                                                                                                                                                                                                                                                                                                                                                                            |
| Catheter-related bloodstream infection (CRBSI)      | Isolation of the same organism (i.e., identical species, antibiogram) from a semiquantitative or quantitative culture of a catheter segment and from the blood (preferably drawn from a peripheral vein) of a patient with accompanying clinical symptoms of BSI and no other apparent source of infection. In the absence of laboratory confirmation, defervescence after removal of an implicated catheter from a patient with BSI may be considered indirect evidence of CRBSI. |
| Infusate-related bloodstream infection              | Isolation of the same organism from the infusate and from separate percutaneous blood cultures, with no other identifiable source of infection.                                                                                                                                                                                                                                                                                                                                    |

Fig. 3. Scanning electron micrograph of the external surface of a catheter. Coccoid and bacillus-shaped bacteria are seen in the biofilm (published with permission from Passerini et al<sup>7</sup>).

polysaccharide (“slime”) by some microbes. Once embedded in the biofilm, some microbes differentiate into complex multicellular structures by means of cell-to-cell chemical messengers<sup>8</sup> composed of acyl homoserine-lactones.<sup>9</sup> The biofilm is a protective environment that reduces the ability of host defense mechanisms to eradicate the microbes (Fig. 3).

Catheter composition also plays a role in infection. The risk of infection increases with the development of thrombosis.<sup>10,11</sup> Polymers such as polyurethane (without hydromer) and polyvinylchloride are more thrombogenic than others.

Microbiology

Over the past two and half decades, Gram-positive organisms rather than Gram-negative species have been

largely responsible for CRBSI.<sup>3,12</sup> The four predominant pathogens include coagulase-negative staphylococci, *Staphylococcus aureus*, enterococcus and candida species. Vancomycin-resistant enterococci (VRE) have also emerged as an important source of infection. Risk factors

for VRE infection include administration of oral vancomycin, cephalosporins or antianaerobic drugs such as metronidazole, prolonged hospitalisation and close proximity to patients already colonised with VRE.<sup>13</sup> Gram-negative organisms are most commonly implicated when pressure monitoring systems and contaminated intravenous fluids are the sources of infection.

### Diagnosis

Two major culture techniques are used to establish catheter-related infection.

#### *Semiquantitative Technique*

When the catheter is removed, the tip or 5 cm of the intradermal segment is aseptically cut and rolled back and forth on a blood agar plate 4 times. The plate is incubated for 24 to 48 hours and growth of  $\geq 15$  colony forming units (CFUs) is considered significant.<sup>14</sup> Since this method samples only the external surface of the catheter, infections due to organisms within the lumen of the catheter may be missed. Nonetheless, this technique continues to be most popular because it is fast and easy to perform.

#### *Quantitative Technique*

Alternative methods sample both the external surface and lumen. In one technique,<sup>15</sup> the tip or subcutaneous catheter segment is immersed in tryptic soy broth and the lumen is flushed three times. The broth is serially diluted onto blood agar plates and cultured for 24 to 48 hours. CFUs of  $\geq 1000$  correlate with CRBSI. In the second method,<sup>16</sup> the catheter is inserted in tryptic soy broth and sonicated for one minute. The broth is serially diluted onto blood agar plates and cultured for 24 to 48 hours. A CFU count of  $\geq 1000$  is considered significant. When both the tip and subcutaneous segment are cultured, the sensitivity and specificity of the sonication method are greater than the roll plate method.<sup>17</sup>

#### *Stains*

Direct gram<sup>18</sup> or acridine orange<sup>19</sup> staining of catheters on removal correlates well with the roll plate method of culturing. However, these techniques have not gained wide spread popularity.

#### *In situ Catheter Cultures*

Because the aforementioned techniques require catheter removal, other methods have been developed in an attempt to diagnose catheter infection *in situ* including 1) quantitative skin cultures;<sup>20</sup> 2) lumen sampling with a brush;<sup>21</sup> 3) gram stain and acridine orange leukocyte cytopsin (AOLC) test;<sup>22</sup> 4) differential quantitative blood cultures;<sup>23,24</sup> and 5) differentially timed blood cultures.<sup>25</sup> Of these methods, the differentially timed blood cultures hold the most promise.

This technique examines the time required for blood cultures drawn from a catheter and peripheral vein to become positive. A time differential of  $>120$  minutes between the catheter and peripheral blood cultures becoming positive for growth has a 91% sensitivity and 94% specificity for catheter-related infection.<sup>25</sup> It is uncertain what the significance of a positive catheter blood culture and a negative peripheral percutaneous blood culture is. Validation of these results by other studies will be required before these methods can be recommended. Targeted quantitative skin cultures may be useful for long-term catheters.<sup>20</sup>

### Prevention

#### *Antimicrobial Prophylaxis*

Intravenous administration of antibiotics before catheter insertion does not reduce the incidence of catheter-related infection and is not recommended.<sup>26</sup> The use of a vancomycin/ciprofloxacin/heparin flush solution reduces the incidence of catheter-related infection in immunocompromised paediatric patients with long-term tunneled catheters;<sup>27</sup> however, vancomycin "lock" (or flush) solutions for short-term catheterisation should not be utilised because of the risk of acquiring vancomycin-resistant enterococci.<sup>1</sup>

#### *Insertion Site*

No randomised prospective study has demonstrated that a particular insertion site is associated with a lower risk of infection. Nonetheless, a number of prospective studies using multivariate logistic regression analyses have shown that the subclavian site of insertion is associated with a lower risk of infection than either the internal jugular or femoral locations.<sup>28</sup> This beneficial effect must be tempered with the small but finite increased risk of pneumothorax when the subclavian site is used.

#### *Skin Preparation*

Skin preparation with aqueous 2% chlorhexidine gluconate or a 0.25% chlorhexidine gluconate/0.025% benzalkonium chloride/4% benzyl alcohol solution is superior to 10% povidone-iodone in reducing significant catheter colonisation<sup>29</sup> and CRBSI.<sup>30</sup> Furthermore, preliminary data suggest that using a chlorhexidine alcohol solution followed by 10% povidone-iodine is better than either regimen alone.<sup>31</sup> Chlorhexidine preparations are now available in the United States. Some clinicians are using 4% chlorhexidine soap followed by a 10% povidone-iodine prep but there are no data supporting this practice.

Since preparation of skin with tincture of iodine compared to povidone-iodine reduces the risk of contaminating blood cultures when obtained via peripheral venipuncture,<sup>32</sup> some experts have recommended its use.

### Method of Insertion

**Maximum barrier precautions:** Using full barrier precautions (sterile gloves, sterile gown, cap, mask and a large fenestrated sterile drape that covers the entire patient) can reduce CRBSI during insertion of silastic central venous catheters or peripheral inserted central catheters (PICC).<sup>33</sup> In addition, another prospective, observational study found that the use of less than maximum barrier precautions in the operating room was associated with a higher risk of infection.<sup>34</sup> Thus, this simple precaution should be followed when inserting central venous or pulmonary artery catheters.

**Skill of the clinician:** Previous data showed that the skill of the person inserting the catheter correlates inversely with the risk of subsequent infection.<sup>35</sup> Providing a formal education programme to less experienced and skilled health care providers about infection control and the fundamental principles of catheter insertion can have a significant favourable impact on the incidence of CRBSI<sup>36</sup> (Fig. 4).

**Tunnelled catheters:** Data from recent studies indicated that the use of tunnelled short-term catheters in the internal jugular<sup>37</sup> or femoral<sup>38</sup> position reduce the risk of CRBSI when compared to untunnelled catheters inserted in the same site.

**“Hands off” catheters:** Use of pulmonary artery catheters encased in a contamination shield will significantly reduce the incidence of CRBSI.<sup>39</sup>

### Single versus Multilumen Catheters

The notion that multilumen catheters predispose to a higher rate of infection compared to single lumen catheters is controversial, as some investigations<sup>40,41</sup> have reported that triple lumen catheters increase the risk of infection whereas others<sup>42,43</sup> have not. A prudent policy to follow is to use catheters with the least number of lumens that enables adequate care of the patient.

### Catheter Maintenance

**Catheter dressing:** Multiple clinical studies and one meta-analysis showed that the use of transparent occlusive dressings increases the risk of significant catheter colonisation.<sup>44</sup> Newer, more highly permeable transparent dressings do not predispose to CRBSI.<sup>1</sup>

**Ointments:** Antibiotic ointments reduce the density of bacterial colonisation on catheters but do not appear to reduce the risk of CRBSI.<sup>45</sup> Moreover, their use is associated with increased catheter colonisation with fungi.<sup>46</sup>

**Chlorhexidine sponges:** Preliminary findings from randomised, controlled trials<sup>47,48</sup> showed that a chlorhexidine-impregnated sponge, used as a dressing for central venous, pulmonary artery and arterial catheters,

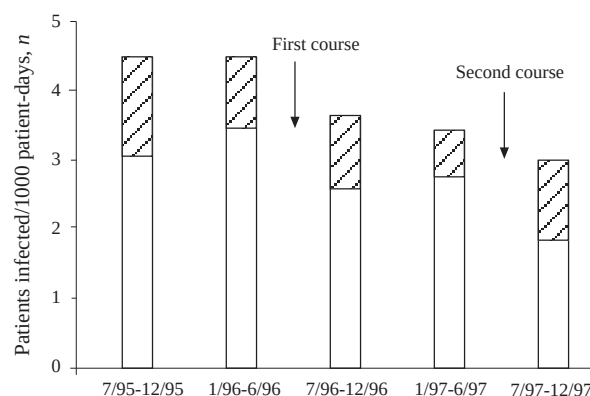


Fig. 4. The effect of an educational programme on the incidence of bacteraemias and significant catheter colonisation. House staff were instructed on infection control procedures and correct methods for catheter insertion during one 8-hour session. Each intervention (arrow) translated into reductions of primary bloodstream infections (white bars) and catheter infections (striped bars) (published with permission from Sherertz et al<sup>36</sup>).

which was changed every 7 days, significantly reduced catheter colonisation from 29% to 16% and CRBSI from 3.3% to 1.2%. The dressing for the control group consisted of a transparent occlusive dressing that was changed every 2 days.

**Intravenous therapy team:** Dedicated intravenous therapy<sup>49</sup> or nutritional support<sup>50</sup> teams will reduce the incidence of catheter-related infection but their value is primarily for peripheral or dedicated total parenteral nutrition (TPN) catheters. The role of such teams in the ICU is uncertain.

**Scheduled catheter changes:** Because the cumulative risk of catheter-related infection increases the longer the catheter remains in place, many clinicians will routinely change catheters after a predetermined number of days (ranging from 3 to 7 days). Several studies have called this practice into question, as scheduled changes (either via guide wire or insertion at a new site) did not translate into reduced rates of infection<sup>51-53</sup> (Fig. 5). Routine change of catheters cannot be recommended.

### Catheter Hubs and Injection Ports

Increased hub manipulation will increase catheter colonisation and the risk of subsequent CRBSI.<sup>1,54</sup> Some<sup>55,56</sup> but not all studies<sup>57</sup> have shown that hub protection devices can reduce the risk of CRBSI when duration of catheterisation is in excess of 7 days.

The effect of needleless systems on catheter infection is unclear as some studies have shown that the use of such systems results in an increased risk for CRBSI whereas others have shown no increased risk or a decrease in infusate contamination.<sup>1</sup> Proper training, adequate disinfection of the diaphragm before accessing the system and regular changes of the system are recommended.<sup>1</sup>

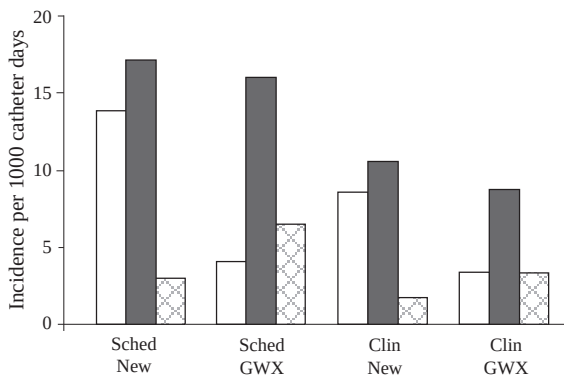


Fig. 5. Effect of the frequency and method of catheter change on mechanical complications (white bars), catheter colonisation (black bars) and catheter-related bloodstream infections (hatched bars). Sched new = catheter change every 3 days to a new site; Sched GWX = catheter change every 3 days using a guidewire at the same site; Clin New = catheter change to a new site when clinically indicated; Clin GWX = catheter change when clinically indicated at the same site using a guidewire. There were no significant differences among the groups (data published with permission from Cobb et al<sup>63</sup>).

### Antiseptic or Antibiotic Impregnated Catheters

**Silver impregnated collagen cuff:** Most of the infections associated with short-term catheterisation are a result of colonisation of the external surface of the catheter. A silver impregnated collagen cuff is available that fits around the catheter and resides in a subcutaneous pocket.<sup>58</sup> Although initial studies showed that the cuff reduced the density of bacterial growth on the catheter, there was no effect on CRBSI.<sup>46,58</sup> Other investigators have failed to demonstrate a reduction in either colonisation or CRBSI.<sup>59</sup> In addition to questions about its efficacy, seating the cuff in the subcutaneous pocket can be difficult for inexperienced operators and the cuff tends to be extruded over time.

**Heparin:** Ionic bonding of heparin to catheters via quaternary ammonium surfactants provides activity against a number of Gram-positive organisms but has little effect on Gram-negative bacteria. In addition, the clinical utility is questionable. After 24 hours of catheter exposure to serum, greater than 50% of the antimicrobial effect have dissipated.<sup>60</sup> Heparin can be attached to catheters by covalent end-point bonding. This method provides a longer duration of activity and appears to reduce the density of bacterial colonisation compared to uncoated catheters.<sup>61</sup>

**Antiseptic catheters:** A plethora of studies have evaluated the utility of catheters coated with chlorhexidine and silver sulfadiazine (CSS) on the external surface. Most concluded that this antiseptic surface reduces the incidence of significant bacterial growth on catheters<sup>28</sup> without an effect on CRBSI. Only one<sup>62</sup> study demonstrated a reduction in the incidence of CRBSI. However, a meta-analysis<sup>63</sup>

confirmed that the incidence of both significant bacterial growth on the catheter and CRBSI is reduced. Moreover, these catheters are cost-effective as a decision analytic model demonstrated a cost savings ranging from USD \$68 to USD \$391 per catheter.<sup>64</sup> CSS catheters are now available with the lumen surface coated with chlorhexidine and the external surface coated with both antiseptics. A clinical study is currently underway to evaluate the effectiveness of these new catheters.

Case reports of anaphylaxis associated with the use of these catheters have been published in Japan;<sup>65</sup> consequently, the patient must be questioned about allergies to chlorhexidine or silver sulfadiazine. One preliminary study has suggested there is an increased risk for the development of resistance by Gram-positive bacteria.<sup>66</sup>

**Catheters impregnated with antibiotics:** Anionic antibiotics can be bound to catheters by the use of a cationic surfactant, tridodecylmethylammonium chloride (TDMAC). Clinical studies have demonstrated that catheters coated with cefazolin, vancomycin or the antibiotic combination of minocycline/rifampin (MR) on both the external surface and lumen will reduce the incidence of significant catheter colonisation.<sup>67-69</sup> MR catheters will also reduce the risk of CRBSI compared to uncoated catheters.<sup>69</sup> The MR catheters are now manufactured in such a way that the antibiotics are integral to the polymer. A cationic surfactant does not have to be used. MR catheters when compared to the older generation of chlorhexidine/silver sulfadiazine catheters significantly reduce the rate of bacterial colonisation and CRBSI<sup>70</sup> (Fig. 6). When assessed *in vitro*, the duration of antimicrobial activity of the MR catheters is longer compared to the CSS catheters<sup>71</sup> (Fig. 7). Preliminary results from a study using a Markov decision analytic model in a hypothetical cohort of hospitalised patients at high risk for infection demonstrate that MR catheters compared to CSS catheters are cost-effective, if the duration of catheterisation exceeds 10 days.<sup>72</sup>

Concerns have been expressed about the development of resistance to minocycline and rifampin but neither aforementioned clinical study demonstrated the emergence of such resistance. However, a recent *in vitro* study suggested that this antibiotic combination might lead to resistance.<sup>73</sup>

Similar to the chlorhexidine/silver sulfadiazine catheters, the patient must be queried about allergies to either antibiotic.

**Silver:** Recently, a new catheter was introduced to the market that is composed of polyurethane, silver, carbon and platinum. The silver is integral to the catheter; therefore, antibacterial activity is present on both the surface and the lumen of the catheter. *In vitro* studies indicate that this catheter has activity against a broad range of Gram-positive and negative organisms and yeast. There are currently no

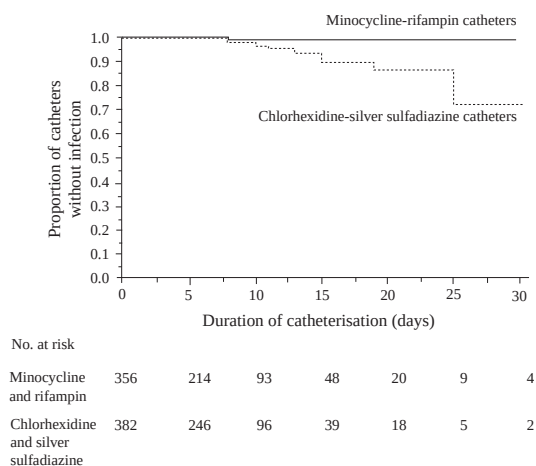


Fig. 6. Kaplan-Meier curve depicting the proportion of antiseptic or antibiotic impregnated catheters without infection (published with permission from Darouiche et al<sup>70</sup>). The two curves are significantly different.

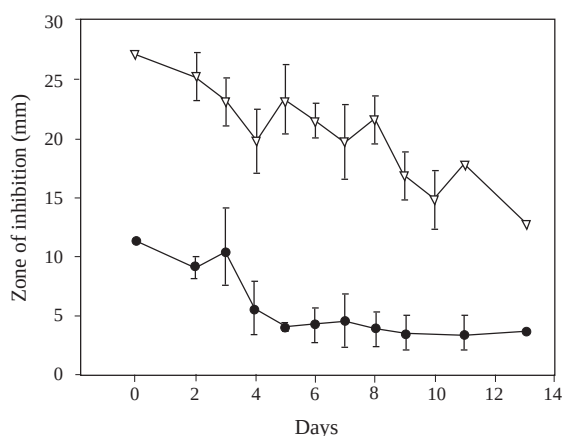


Fig. 7. Zone of inhibition (mm) against *Staphylococcus aureus* by catheters impregnated with minocycline/rifampin (open triangles) or chlorhexidine/silver sulfadiazine (solid circles) as a function of duration of catheterisation (published with permission from Marik et al<sup>71</sup>).

clinical studies that have demonstrated the usefulness of this catheter in preventing CRBSI.

**Experimental devices: Low-voltage electrical current:** Carbon impregnated polyurethane polymers have been developed which allow the application of small electrical currents (10  $\mu$ amps).<sup>74</sup> The negative charge from this current repels bacteria near the device. The current also produces hydrogen peroxide and chlorine by electrolysis, both of which are bactericidal. The antimicrobial spectrum of the low current includes Gram-negative and positive bacteria as well as *Candida* species. It appears that bacteria within a biofilm are also susceptible. Further work is ongoing to evaluate the efficacy of this technology.

**Silver iontophoretic device:** Silver iontophoresis is an application in which silver wires are attached to the intradermal portion of the catheter and silver ions are released from the wire by means of an electrical current

from a small power source.<sup>75,76</sup> The silver ions are bactericidal. Preliminary data suggested that this device is effective both *in vitro* and *in vivo*. More data are needed to establish clinical safety and efficacy.<sup>77</sup>

## Treatment

Recent guidelines<sup>78</sup> promulgated by the Infectious Diseases Society of America (ISDA), American College of Critical Care Medicine and the Society of Healthcare Epidemiology of America for the management of intravascular catheter-related infections have been published. The reader is referred to that document for more detail.

If there are any signs of local infection such as erythema, induration, tenderness or purulence, the catheter should be removed. The tip and/or subcutaneous catheter segment and any exudate at the insertion site should be cultured to help guide antibiotic therapy if it is planned. Blood cultures via venipuncture are also recommended if there are signs of an associated bacteraemia such as fever or leukocytosis. If blood cultures are negative but the catheter culture is positive for microbial growth, most clinicians will not treat with antibiotics. Some practitioners treat if catheters grow with  $\geq 15$  CFUs of *Staphylococcus aureus*.

The febrile patient with a central venous catheter is a frequent dilemma in the intensive care unit. Without local signs of infection, the chances of the catheter being the cause of the fever are only about 10% to 15%.<sup>79</sup> One option is to leave the catheter in place and obtain peripheral blood cultures. If the blood cultures become positive, consideration should be made for catheter removal. The second option is to obtain catheter and peripheral blood cultures (*vide supra*). If both cultures are positive and the time differential to positivity (catheter to peripheral blood) is greater than 2 hours, the catheter should be removed. The last alternative is to remove the catheter over a guide wire and culture the tip and/or subcutaneous segment of the catheter suspected of infection. If significant microbial growth occurs, the replacement catheter should be removed and another catheter inserted at a different site.

Should the patient develop CRBSI, the catheter should be removed and appropriate systemic antibiotic therapy started. There is a lack of consensus regarding the appropriate duration of antibiotic therapy. For an uncomplicated *Staphylococcus aureus* CRBSI, some investigators have reported that a relative short course of therapy (10 to 14 days) for an uncomplicated *Staphylococcus aureus* CRBSI is adequate.<sup>80</sup> However, if fever and/or bacteraemia persist beyond 3 days, a longer duration of antibiotic therapy is needed. Other clinicians recommend the use of a transoesophageal echocardiogram to help guide the duration of therapy.<sup>81</sup> If fever or bacteraemia

TABLE II INTRAVENOUS ANTIMICROBIAL TREATMENT OF INTRAVENOUS CATHETER-RELATED BLOODSTREAM INFECTION IN ADULTS, ACCORDING TO SPECIFIC PATHOGEN ISOLATED

| Pathogen                                                                  | Preferred antimicrobial agent                                                                                                                                 | Alternative antimicrobial agent                                                                                                                     |
|---------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Gram-positive cocci</b>                                                |                                                                                                                                                               |                                                                                                                                                     |
| <i>Staphylococcus aureus</i> :                                            |                                                                                                                                                               |                                                                                                                                                     |
| Methicillin susceptible                                                   | Penicillinase-resistant penicillin<br>Penicillin if strain is susceptible                                                                                     | Cefazolin or cefuroxime                                                                                                                             |
| Methicillin resistant                                                     | Vancomycin                                                                                                                                                    | Linezolid; or quinupristin/dalfopristin;<br>or vancomycin + (rifampin or gentamicin);<br>or trimethoprim-sulfamethoxazole alone<br>(if susceptible) |
| Vancomycin resistant                                                      | Linezolid or quinupristin/dalfopristin                                                                                                                        | Vancomycin                                                                                                                                          |
| Coagulase-negative staphylococci:                                         |                                                                                                                                                               |                                                                                                                                                     |
| Methicillin susceptible                                                   | Penicillinase-resistant penicillin                                                                                                                            | First-generation cephalosporin or vancomycin<br>or trimethoprim-sulfamethoxazole<br>(if susceptible)                                                |
| Methicillin resistant                                                     | Vancomycin                                                                                                                                                    | Linezolid or quinupristin/dalfopristin                                                                                                              |
| <i>E. faecalis</i> / <i>E. faecium</i> :                                  |                                                                                                                                                               |                                                                                                                                                     |
| Ampicillin susceptible                                                    | Ampicillin or [(ampicillin or penicillin)<br>+ aminoglycoside]                                                                                                | Vancomycin                                                                                                                                          |
| Ampicillin resistant,<br>vancomycin susceptible                           | Vancomycin or vancomycin + aminoglycoside                                                                                                                     | Linezolid                                                                                                                                           |
| Vancomycin resistant                                                      | Linezolid or quinupristin/dalfopristin                                                                                                                        |                                                                                                                                                     |
| <b>Gram-negative bacilli (pending susceptibility results for isolate)</b> |                                                                                                                                                               |                                                                                                                                                     |
| <i>E. coli</i> and <i>Klebsiella</i> species                              | Third-generation cephalosporin                                                                                                                                | Fluoroquinolone, such as ciprofloxacin or<br>levofloxacin, or aztreonam                                                                             |
| <i>Enterobacter</i> species and <i>S. marcescens</i>                      | Carbapenem                                                                                                                                                    | Cefepime or fluoroquinolone, such as<br>ciprofloxacin or levofloxacin                                                                               |
| <i>Acinetobacter</i> species                                              | Ampicillin/sulbactam or carbapenem                                                                                                                            |                                                                                                                                                     |
| <i>S. maltophilia</i>                                                     | trimethoprim-sulfamethoxazole                                                                                                                                 | Ticarcillin and clavulanate                                                                                                                         |
| <i>P. aeruginosa</i>                                                      | Third- or fourth-generation cephalosporin<br>or carbapenem or antipseudomonal $\beta$ -lactam<br>(ticarcillin, piperacillin, mezlocillin)<br>+ aminoglycoside |                                                                                                                                                     |
| <b>Fungi</b>                                                              |                                                                                                                                                               |                                                                                                                                                     |
| <i>C. albicans</i> or <i>Candida</i> species                              | Amphotericin B or fluconazole<br>(if organism is susceptible)                                                                                                 | Lipid amphotericin B preparations                                                                                                                   |

Modified with permission from Mermel et al<sup>78</sup>

persists, a work-up to search for deep-seated infection should be instituted. Guidelines for the management of these types of infections and for intravenous antimicrobial therapy of CRBSI based on the causative pathogen are delineated in Figure 8 and Table II, respectively.<sup>78</sup>

For long-term tunnelled catheters including totally implantable devices (e.g. Porta-Cath), various antibiotic regimens to treat CRBSI without catheter removal have been proposed. Such techniques include systemic antibiotics with an “antibiotic lock”,<sup>82</sup> a “thrombolytic lock”,<sup>83</sup> a minocycline and ethylenediaminetetraacetate flush<sup>84</sup> or hydrochloric acid instillation<sup>85</sup> into the catheter lumen.

Approximately 80% of *Staphylococcus epidermidis* CRBSI associated with long-term catheters may be treated successfully with systemic antibiotics but there is still a high risk of relapse compared to those cases where the catheter is removed.<sup>86</sup> For complicated infections such as tunnel infections or port abscesses or infections with more virulent organisms, removal of the catheter is recommended.<sup>78</sup> An algorithm<sup>78</sup> for the management of these types of catheter infections is presented in Figure 9. Because of the consequences of a second CRBSI for the patient in the intensive care unit, the most prudent course of action is to remove a short-term catheter regardless of

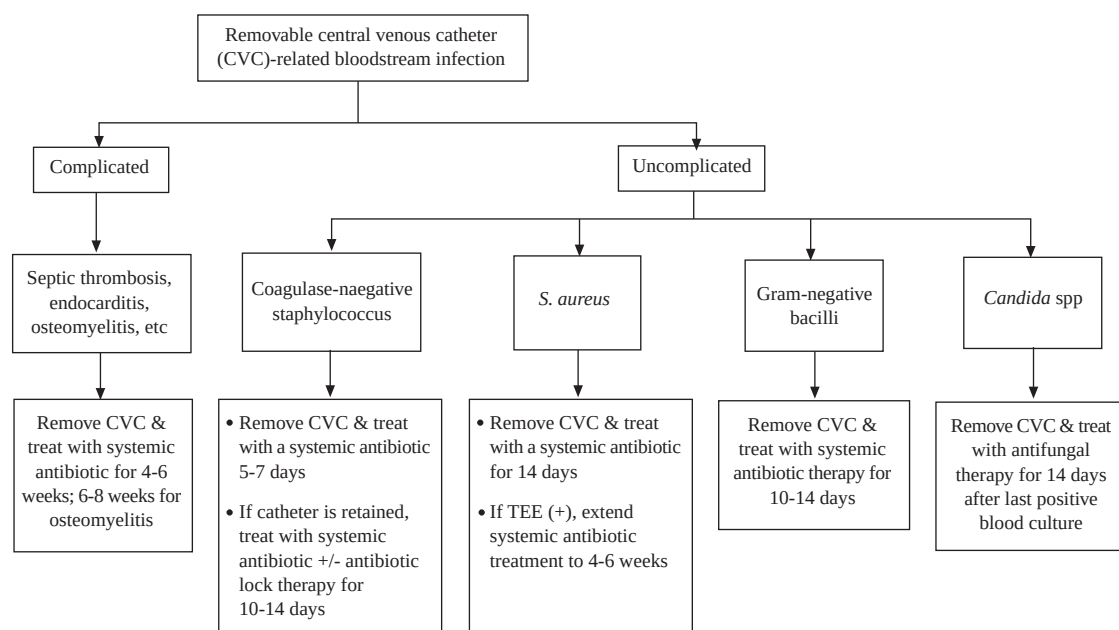


Fig. 8. Algorithm for the approach to the management of patients with a non-tunneled central venous catheter (CVC)-related bloodstream infection. Duration of the treatment will depend on whether the infection is complicated or uncomplicated (published with permission from Mermel et al<sup>78</sup>).

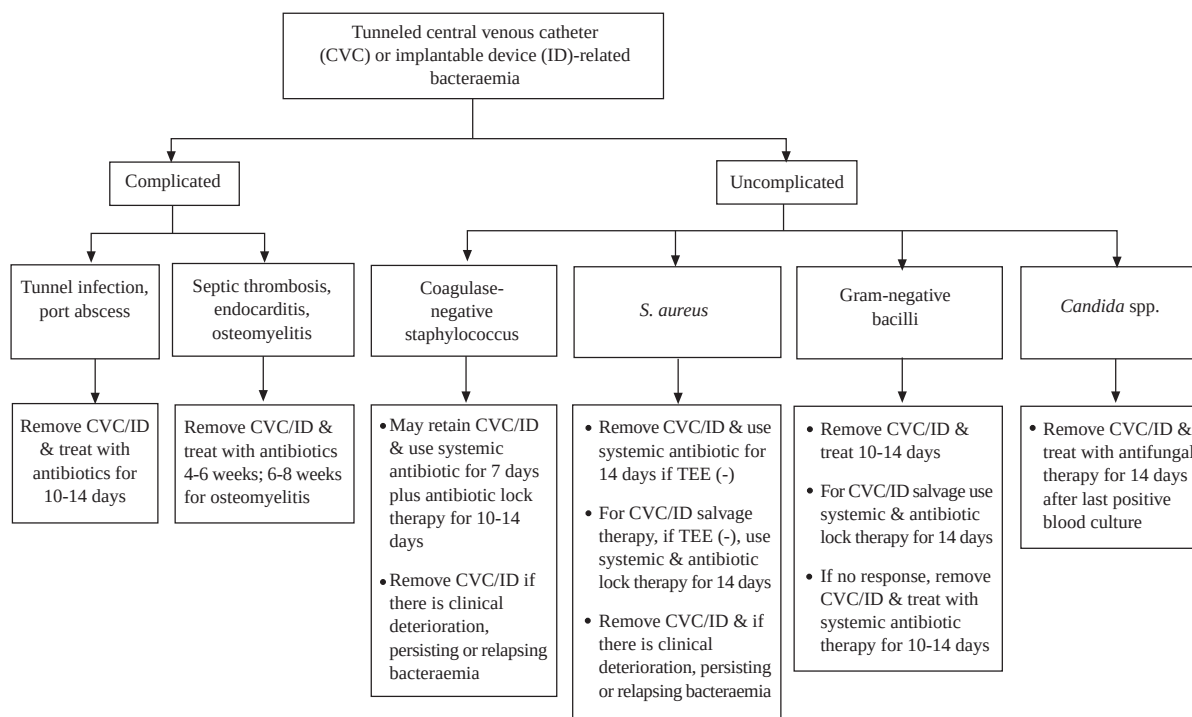


Fig. 9. Algorithm for the approach to the management of patients with a tunneled central venous catheter (CVC) or a surgically implanted device (ID)-related bloodstream infection (published with permission from Mermel et al<sup>78</sup>).

the pathogen unless there are serious problems with achieving venous access.

Patients who developed catheter-associated fungaemia are at high risk for developing complications and should receive systemic antifungal therapy.<sup>87,88</sup> The catheter should be removed as retention increases the risk for persistence of fungaemia.<sup>89</sup> If *Candida albicans* is found and is sensitive to fluconazole, a 14-day course (400 mg/day) is recommended. For fungi that are resistant to fluconazole, therapy with amphotericin B (0.5 mg/kg for 14 days) is indicated. Consideration should be made for the extension of therapy if signs of deep-seated infection become evident.

## Conclusion

The best method to treat catheter-related infection is prevention. Adherence to practices that have been proven to reduce the risk of infection should be actively encouraged in every ICU. For those ICUs where the rate of CRBSI is still high despite the use of preventive strategies, the use of antiseptic or antibiotic impregnated catheters is recommended.

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