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Management of Catheter-Related Infection in Patients Receiving Home Parenteral Nutrition

by Phyllis A. Schiavone, Nancy E. Stoner, Charlene W. Compher, Bruce P. Kinosian, Joseph I. Boullata

Catheter-related infection is one of the most common clinical problems associated with the administration of parenteral nutrition at home. Morbidity, mortality, and costs associated with catheter-related infection are significant. In addition to bloodstream infection, infection can occur at the exit site, and in the subcutaneous tissue through which the catheter is placed. Methods for prevention are paramount. When a catheter-related infection is identified, treatment may require catheter removal in addition to an appropriate systemic antimicrobial regimen. The use of antimicrobial lock solutions may reduce the risk of infection in high-risk patients. If catheter salvage is considered, systemic antimicrobials may be supplemented with antimicrobial lock solutions.

INTRODUCTION

Parenteral nutrition (PN) is a supportive, life-sustaining modality for patients with either temporary or permanent intestinal failure. The administration of home PN requires the placement of a central vascular access device. The presence of this foreign body sets the stage for one of the most frequently encountered complications associated with home PN—catheter-related (CR) infection. This has the potential for significant morbidity and mortality as well as cost. In addition to catheter colonization, there are three types of CR infection: an exit site or cuff infection, a tunnel infection, and a bloodstream infection (BSI). The most common and complex type is CR-BSI. Systemic complications can include septic thrombophlebitis, infective endocarditis, and other metastatic infections. Clinicians caring for the home PN-patient faced with managing these infectious complications should have a working knowledge of the risk factors for, and presentation of the different types of CR infections, as well as understanding their prevention and treatment.

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Selection of Appropriate Central Intravenous Access

The morbidity, mortality, and cost of CR-BSIs are a responsibility that should be shared across the healthcare continuum. In choosing a catheter for each patient several factors need to be taken into account. Most important will be the expected duration of PN treatment. If the line will be required for <3 months, a peripherally inserted central catheter (PICC) would be most appro-

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priate. With this access, an alternative to subclavian catheterization, the catheter is inserted via a peripheral vein (e.g., cephalic, basilar) with the distal end in the superior vena cava. It is easier to maintain with fewer mechanical complications (1). However, if the patient will require PN therapy for a longer period of time, a tunneled central venous catheter is preferred. The surgically implanted catheter (e.g., Hickman, Broviac, Groshong) is tunneled in the subcutaneous space for about 10 cm and held in place with a Dacron cuff just before exiting the skin. This cuff stimulates growth of surrounding tissue to impede the migration of microorganisms from the skin across the external surface of the indwelling catheter (1). An alternative access for long-term placement is the totally implantable device (i.e., port) in the subcutaneous space that have a self-sealing septum beneath the skin, which can be accessed by a needle through the intact skin (1). For the patient requiring PN daily, this latter catheter is accessed with a needle for a week at a time, and changed by the visiting home nurse. If infusing fewer days per week, the patient may de-access them self.

Based on the expected duration of use, the catheter can be placed by a hospital-based PICC team (PICC), the interventional radiology service (PICC or tunneled catheter), or the surgical service (tunneled catheter or implantable device). Preference is for the subclavian site over others when available and at a distance from any open wounds. Patient preference should also be taken into consideration, as some prefer a tunneled catheter rather than an implanted device so that they can access/de-access themselves. A patient can have their access changed in time if necessary.

INCIDENCE, RISK FACTORS, AND CLINICAL PRESENTATION

The most common clinical problem associated with home PN is CR-BSI, representing 61% of all PN-related complications (2). Up to 63% of patients have at least one CR-BSI in a year (3). If viewed as CR-BSI per catheter year the incidence ranges from as low as 0.3 and up to 2.5 episodes per catheter year (3,4). Most large series report ~0.5 episodes per catheter year in patients receiving PN at home (5). These infections may progress to complicated septic events and ultimately to half of all PN-related deaths (3). To keep this in perspective, PN-related deaths represent only 9% of total mortality in contrast to the underlying disease process, which accounts for 58% (3).

As with all infections host factors and virulence of the organism determine patient presentation. There are three sources from which organisms gain access (Figure 1) to the catheter (6). As expected, skin colonization is a major factor associated with the development of CR infections with heavy colonization highly predictive of CR infection (6). Although a variety of organisms can cause CR infection, there are a few that predominate (5,7). CR-BSIs are most commonly caused by Gram-positive organisms, which include the

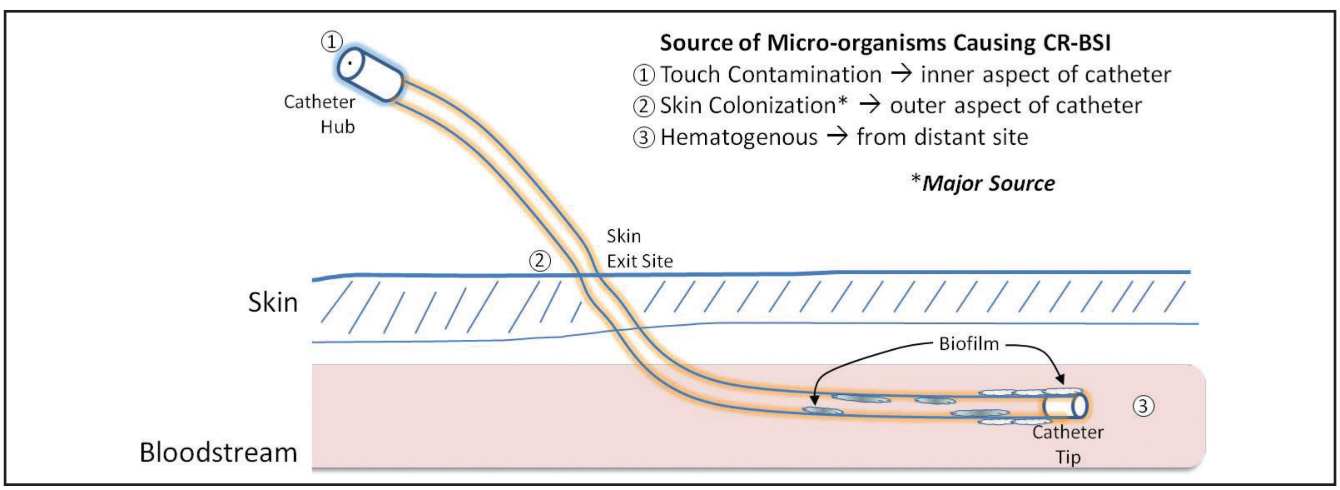

Figure 1

Table 1.
Catheter-Related Infections (1)

Infection	*Microbiologic Findings*	*Clinical Findings*
Exit site	Purulent drainage at the exit site is culture positive for micro-organisms Blood culture may be positive or not	Redness, induration, tenderness within 2 cm of catheter exit site on skin May have fever and purulent drainage
Tunnel	Blood culture may be positive or not	Pain, redness, induration outside immediate exit site extending along the subcutaneous tunnel tract
Pocket	Infected fluid in the subcutaneous pocket of the implantable device Blood culture may be positive or not	Pain, tenderness, redness, induration over the pocket Rupture and drainage Necrosis of skin over the pocket site
Bloodstream		
• Infusate-related	Growth of same micro-organism from PN and peripheral blood culture No other source of infection	Fever, with symptoms temporally related to administration of PN Obvious disruption of PN integrity/sterility Documented contamination of infusate related to poor aseptic technique
• Catheter-related	Presence of micro-organism from >1 peripheral blood culture	Fever, chills, hypotension No other source of infection Subtle signs may include hyperglycemia, night sweats, flu-like symptoms (fatigue, body aches)
Colonization	Presence of micro-organism from >1 blood cultures drawn via the catheter	Intermittent fevers Fever spikes at onset of infusion

coagulase-negative staphylococci and *Staphylococcus aureus* (*S. aureus*) some of which may be resistant to methicillin (i.e., MRSA) and rarely to vancomycin (i.e., VRSA). Coagulase-negative staphylococci (CNS) include *S. epidermidis*. Enterococci may also be involved. A number of Gram-negative organisms have also been implicated. These include *Escherichia coli* (*E. coli*), as well as *Klebsiella*, *Serratia*, *Acinetobacter*, and *Enterobacter* species. Fungi can also cause CR-BSI with *Candida* species being most common.

Regular surveillance screening for infection has a much lower yield than maintaining a low threshold for appearance of clinical signs of infections (1). Microbiologic and clinical findings help to differentiate the types of CR infections (Table 1). Diagnosis of a possible CR-BSI begins with the report of a patient having new onset fever or chills/rigor when flushing the catheter or infusion of PN. The symptoms associated with CR-BSI include fever (84%), often with chills (62%) (4). Erythema (14%) and purulence at the catheter insertion site (7%) can also occur (4). In 56%, clinical signs were discrete and resulted in a delay of 6 days between first symptom and diagnosis. When patients complain of any change in temperature ≥2ºF from baseline, temperature up to 101.5ºF with chills, or general malaise, or if there is tenderness, erythema or purulence at the catheter insertion site, blood cultures should be drawn. If the patient is hemodynamically unstable or is acutely febrile (>101.5ºF), presentation to the nearest hospital emergency department for evaluation and support, probable admission and possible catheter removal is required.

Central Lines and Lumen Number

The three general types of catheters used most commonly for PN infusion have been described. Not mentioned was the impact on CR infection of the number of catheter lumens. The use of a multi-lumen catheter increases the risk of CR-BSI almost 3-fold (4). CR-BSI incidence is significantly greater with 2 vs. 1 lumen catheters (8). Catheters with 3 lumens, however, do not increase the odds of CR-BSI beyond the rate with 2 lumens (9). When only single-lumen catheters were used, no difference in CR-BSI was observed between tunneled catheters and implanted ports (4). Thus, the use of single-lumen catheters may be more important than type of catheter in reducing risk of CR-BSI. Although it should be noted that silastic catheters are more prone to infection than those made of polyurethane (10). A history of BSI also increases the risk of recurrent CR-BSI (4). CR-BSI increased from 0.16 per 1000 catheter days in patients with none of the risk factors discussed to 0.46 with a single risk factor, to 2.22 with two risk factors and 6.77 episodes per 1000 catheter days for those with 3 or more risk factors (4).

When CR-BSI occurs, the infection is related to the number of organisms on the catheter tip. Understanding the catheter micro-environment may help explain why catheters are so likely to be involved with infection. Essentially all venous catheters develop biofilm (Figure 1) on the surface, and longer-use catheters also develop biofilm on the inner lumen (11). The biofilm seems to account for much of the CR-BSI. This biofilm is made up of the bacteria entrenched in an extracellular polysaccharide matrix which they secrete on the inner and outer aspects of the catheter. Biofilm is thought to begin to develop within 24 hours after catheter insertion and certainly within 3 days (1,6). While the external surface is the initial colonization site in the first several days, the intraluminal surface becomes involved after 10 days from placement (1). In this environment the micro-organisms have slower growth rates, which contribute to increased tolerance to antimicrobial agents. Although less virulent than *S. aureus* in causing bacteremia, *S. epidermidis* is adept at biofilm formation making the organism difficult to eradicate from the surface of catheters (12).

PREVENTION

Infection prevention is essential to avoid patient morbidity and interruption of nutrition care.

Catheter Care

The two most common routes for transmission of micro-organisms in CR infection are contamination from the skin at the catheter exit site, and contamination of the hub connections on the catheter or catheter tubing (Figure 1). Principles of aseptic technique are the cornerstone to successfully reducing the incidence of CR infections. Protocols outlining procedures related to catheter insertion and catheter maintenance are essential. Prevention involves optimal patient preparation and insertion technique as well as use of catheters that may prevent biofilm colonization (13). Given the difficulty of treating bacteria embedded in biofilm on catheters, both the prevention of initial contamination of the device and minimization of microbial attachment are critical.

Aseptic Technique—Strict adherence to aseptic technique begins with the placement of the vascular access device. Preparation of the skin site with antiseptics (e.g., povidone iodine, alcohol, chlorhexidine) has been identified in studies examining which solution is the most effective in reducing the risk of CR infections. Chlorhexidine (2% concentration) results in lower catheter colonization and infection rates than either 10% povidone-iodine or 70% alcohol, and can reduce CR infection by 49% (14).

Hand Washing—A recent study of over 375,000 catheter-days indicated that an intervention that included good hand washing as well as full barrier precautions significantly reduced incidence of CR-BSI (15). Additionally, use of maximal sterile barrier precautions is associated with a lower risk of CR-BSI (16). The fact that compliance with maximal barrier precautions is not complete remains problematic and provides ample opportunity for improvement in patient safety (16).

Catheter Dressing—Both the type of catheter dressing and the frequency of dressing change are important considerations in reducing skin colonization. The two most common types of catheter dressing are 1) gauze and tape, and 2) transparent semi-permeable polyurethane. The disadvantage of the gauze and tape dressing are that it requires more frequent changes (every 48 hours). Transparent dressing protocols generally require dressing changes every 7 days. A transparent dressing also allows the clinician to visually inspect the tunneled catheter exit site without removing the dressing.

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Chlorhexidine impregnated dressings or sponge (Biopatch™) can reduce colonization, local infection and CR-BSI (17). Numerous studies have tried to identify the most effective dressing type and/or frequency of changes to reduce the incidence of CR infections. There is limited evidence demonstrating superiority of one type of dressing change over another in preventing CR infections. Perhaps the most important factor in dressing care is that the dressings remain adherent, clean and dry. Any dressing that becomes wet, soiled, or presents with edges lifting up should be changed. This will prevent accumulation of moisture beneath the dressing which otherwise supports bacterial growth. The use of topical antibiotics is not recommended at insertion sites of catheters used for PN. Clean or sterile gloves should be worn when changing the dressing on the catheter or manipulating the catheter. Contamination of the hub connections can also result in the transmission of micro-organisms either on the intraluminal or extraluminal portion of the catheter. Common protocols use either 70% alcohol or 10% povidone iodine swabs to clean the catheter hub prior to connections and disconnections. The catheter cap should be changed every 5–7 days.

Antimicrobials

Systemic—Given the risk for toxicity (hypersensitivity, side effects, interactions) the use of systemic antimicrobials as prophylaxis against CR-BSI is not appropriate. More importantly, the data do not support systemic antibiotic prophylaxis prior to catheter insertion or during catheter use to prevent colonization or CR-BSI (6). As most CR-BSIs originate in the catheter lumen, systemic antibiotics would not be expected to eradicate these intraluminal colonies of sessile organisms. However, given that infections can occur subsequent to this intraluminal colonization and biofilm elaboration in long-term catheters, an approach to prophylaxis could be the use of antimicrobial-containing catheter lock solutions.

Preventative Lock Solutions—Most antimicrobials work through an effect on an organism's cell wall construction or protein synthesis, but both processes are at a lower activity in a biofilm. This is one of the factors associated with the difficulty in eradicating biofilm organisms. The use of antimicrobial solutions to fill the catheter lumen attempts to address this source of infection. The lumen of the catheter is filled with an antimicrobial solution and once the catheter is clamped, the solution is locked in place during the time off from PN infusion. There are several indications for the use of lock therapy (Table 2). Although a number of antimicrobials and antiseptic agents have been evaluated, the best drug for use in prophylaxis has not yet been determined (18,19). For antimicrobial lock solutions to be clinically effective they must remain active in the biofilm matrix, with a rapid bactericidal effect, and with a mechanism of action that does not depend solely on micro-organism growth rate (20). Prophylactic use of specific antibiotic lock solutions reduces the incidence of CR-BSIs (6). The agents selected, their concentrations and dwell time must be adequate for the likely organisms and their biofilm environment. Except for ciprofloxacin and vancomycin,

Table 2.
Lock Therapy (6,18,19)

Rationale	*Candidate*	*Duration*	*Examples of Antimicrobials and Antiseptics*
Prevention	Infection history (≥2/yr) Limited vascular access Prosthetic devices	Indefinite	Amikacin, ciprofloxacin, ciprofloxacin-rifampin, daptomycin, gentamicin, minocycline, minocycline-rifampin, tigecycline, vancomycin, vancomycin-rifampin Ethylene diamine tetra acetic acid (EDTA), ethanol, taurolidine
Treatment	Uncomplicated infection	Defined course	Ciprofloxacin, daptomycin, linezolid, minocycline, rifampin, tigecycline, vancomycin EDTA-minocycline-ethanol, ethanol

all antimicrobials are effective alone against *S. aureus* including MRSA (18,19). In fact vancomycin may be the least effective agent probably because of its poor activity in biofilm. Despite well documented compatibility and stability data when combined with heparin as a lock solution, cefazolin has poor activity (19).

Ethanol produced the largest effect on *S. aureus* compared to the other antiseptics. In a series of ten patients receiving PN at home, the use of a 70% ethanol lock solution (4–14 hours daily) was effective at preventing CR-BSI (21). Despite in vitro data, a systematic literature review suggests clinical evidence is not yet sufficient for taurolidine (a taurine derivative) as a lock to prevent CR-BSI (22). Development of resistance is less likely with ethylene diamine tetra acetic acid (EDTA) and ethanol based on mechanisms of action. EDTA disrupts the biofilm possibly through chelation of calcium required for biofilm formation. EDTA, ethanol and taurolidine appear to also possess anticoagulant activity, which is advantageous as thrombi may serve as a nidus for infection. Whether this would preclude heparin lock solutions is not clear. Anticoagulants should not be used routinely in lock therapy solely as a means of reducing CR-BSI risk (6).

If despite appropriate prevention technique a patient has recurrent CR-BSI, consideration can be given to placing a catheter coated with an antiseptic or antibacterial. Over a dozen single or combination agents have been studied in inpatient settings using short-term catheters (23). These more expensive catheters have not been explored systematically in the home PN population, and given that the antimicrobial coverage reportedly does not extend beyond 25 days this use is questionable (6).

DIAGNOSIS AND MANAGEMENT

The major challenge in the management of an existing CR-BSI in patients requiring PN at home is to cure the infection without having to remove the catheter. There is a balance between preserving the catheter and preventing venous occlusion (the result of repeated catheterization) and protecting the patient from the morbidity and mortality of infection. Much of the time the resistance of the organism is such that catheter removal—the definitive treatment for CR-BSI—will become necessary.

Diagnosis

The diagnosis of CR-BSI is definitive when 2 sets of paired blood cultures through the catheter and a peripheral vein meet criteria for quantitative blood culture or differential time to positivity (DTP) (1). Quantitative blood culture refers to colony counts via the catheter that are at least 3 times > the count from peripheral blood. The DTP compares the time to positive culture from peripheral blood to that from the catheter. This is significant if the detection of micro-organisms from the catheter blood sample occurs at least 2 hours before microbial growth in the peripheral blood sample. The peripheral skin site and the catheter hub should be cleaned with alcohol, tincture of iodine or alcoholic chlorhexidine (>0.5%). For quantitative cultures, a sufficient volume of blood permits inoculation into aerobic and anaerobic media for the peripheral sample and that obtained through the catheter. These samples should be obtained prior to initiating antibiotic therapy. Preliminary findings should be available within 24–48 hours. The symptomatic patient should then receive appropriate empiric antimicrobials until return of the culture and susceptibility data. Predictably, the presence of a Gram-positive organism is most likely. Exit site infections require a positive culture of exit site drainage.

If the catheter is removed, quantitative cultures should be performed on the distal tip and the tunneled or subcutaneous segment to confirm the diagnosis of CR-BSI. The diagnosis of CR-BSI is definitive when the same micro-organism grows from at least one percutaneous peripheral blood sample and the catheter tip (1). The most accurate diagnosis is made in retrospect after the catheter has been removed and cultured positive in association with peripheral blood cultures that are positive (CR-BSI) or negative (local infection) and with subsequent resolution of patient signs and symptoms.

Treatment

The primary decision is whether to salvage the catheter or remove it. Delay of catheter removal can increase infectious complications and subsequent treatment failure. Infection of the tunnel or port site requires catheter removal, incision and drainage as needed, with 7–10 days of appropriate systemic antibiotics.

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Table 3.
Management Approach for Most Common CR-BSI (1)

Organism	*Clinical Presentation*	*Recommendation**
Any	Tunnel infection or port abscess	Remove the catheter Treat with systemic antimicrobials 7–10 days
Any	Septic thrombosis, endocardidtis, osteomyelitis	Remove the catheter Treat with systemic antimicrobials 4–6 weeks Treat for 6-8 weeks for osteomyelitis
Staphylococcus aureus	No active malignancy or immunosuppression	Remove the catheter Treat with systemic antimicrobials 2 weeks at least
Staphylococcus aureus	Diabetic, immunosuppressed, prosthetic intravascular device, or metastatic infection	Remove the catheter Treat with systemic antimicrobials 4–6 weeks
Coagulase-negative staphylococcus	Uncomplicated	May retain catheter and treat with antimicrobials Systemic 10–14 days and lock therapy 10–14 days
Coagulase-negative staphylococcus	Clinical deterioration, or persisting/relapsing bacteremia	Remove the catheter Work up for complicated infection Treat with systemic antimicrobials accordingly
Enterococcus	Uncomplicated	May retain catheter and treat with antimicrobials Systemic 10–14 days and lock therapy 10–14 days
Enterococcus	Clinical deterioration, or persisting/relapsing bacteremia	Remove the catheter Work up for complicated infection Treat with systemic antimicrobials accordingly
Gram-negative rods	Uncomplicated	For salvage, retain catheter and treat with antimicrobials Systemic 10–14 days and lock therapy 10–14 days
Gram-negative rods	No response to salvage attempt	Remove catheter Treat with systemic antimicrobials 10–14 days
Gram-negative rods	Endocarditis, suppurative thrombophlebitis	Remove catheter Treat with systemic antimicrobials 4–6 weeks
Gram-negative rods	Uncomplicated	Otherwise, remove the catheter Treat with systemic antimicrobials 7–14 days
Candida spp	Uncomplicated	Remove catheter Treat with systemic antimicrobials for 14 days after first negative blood culture

*The therapeutic antimicrobial regimen should be appropriate for the organism identified and it's MIC (minimum inhibitory concentration)

Also remove the patient's catheter in the face of sepsis, supparative thrombophlebitis, or endocarditis. If uncomplicated, consideration can be given to treatment with the line in place depending on the organism involved and the patient's clinical presentation (Table 3). If this salvage technique is considered, then repeat sets of blood cultures should be obtained (e.g., at 72 hours after initiating systemic antimicrobials). Thrombolytic agents are not recommended as adjunct treatment in CR-BSI. If there are no remaining access sites or there is a risk of bleeding diathesis, then an antimicrobial-coated catheter could be considered. Exchanging a catheter over a guidewire for CR-BSI should only be reserved for rare circumstances.

Table 4.
Empiric Intravenous Antimicrobial Therapy (1)

Suspected Organism	*Antimicrobial*	*Dosing*	*Comment*
MSSA, MS-CNS	Nafcillin or Cefazolin	2 g 2 g	Administer q4h, less frequently in renal impairment Administer q8h, less frequently in renal impairment
MRSA, MR-CNS	Vancomycin	15 mg/kg	Administer q12h, less frequently in renal impairment Infusion rate ≤ 10 mg/min; target serum trough >10 µg/mL
MRSA, VRSA	Daptomycin	6 mg/kg	Administer q24h, less frequently in renal impairment *S. aureus* vancomycin-resistant if MIC* >2 µg/mL
Enterococci	Ampicillin	2 g	Administer q4-6h, less frequently in renal impairment If resistant strain suspected, use vancomycin or daptomycin
Gram-negative bacilli	Cefepime	2 g	Administer q12h, less frequently in renal impairment If ESBL, *Serratia*, or *Acinetobacter* suspected, use a carbapenem
Candida	Fluconazole	400 mg	Administer once daily If hemodynamically unstable or any exposure to fluconazole in previous 90 days, use an echinocandin

*Minimum inhibitory concentration (MIC)

Antimicrobials

Systemic Therapy—The antimicrobial regimen should be active against the identified or suspected organism(s)—whether bacterial or fungal—based on available culture and susceptibility data. Empirically, a drug active against the most likely pathogens should be provided (Table 4). If the patient is naïve to the systemic antimicrobial being considered, it is best practice for the home care nurse to be present with an anaphylaxis kit for the first dose administered. If the infection is at the exit site only, initial management can be topical antimicrobial therapy based on the organism (e.g., mupirocin, clotrimazole), otherwise systemic therapy is required and is selected based on local susceptibility data. Patient-specific culture and susceptibility data will allow streamlining to more definitive treatment. The duration of antimicrobial therapy will depend on the micro-organism and the patient co-morbidities (Table 3). The duration of antimicrobial treatment should be longer for patients with persistent bacteremia >72 hours following catheter removal. The resistance of the organisms in the biofilm makes catheter removal the best option in most cases. Systemic antibiotics are valuable in treating the bacteremia that results from biofilm release, but are rarely effective in treating those organisms that remain in biofilm, yet still cause infection (24).

Therapeutic Lock Solutions—In the case requiring an attempt to salvage the catheter, it can be managed with simultaneous systemic antimicrobial therapy and lock therapy. Antibiotic lock therapy is complementary to systemic antimicrobial therapy, not in place of it. Lock therapy has been used successfully in combination with systemic antimicrobials to eradicate CR-BSI and prevent recurrence in long-term catheters (25). High concentrations of antimicrobials for a dwell time of at least 12 hours can treat bacterial CR-BSI within 14 days (20). The antimicrobial concentration used in the lock solution is critical, and should be 100-1000 times above the organism's minimum inhibitory concentration (MIC) to kill the bacteria within the biofilm (19). Compatibility and stability of select combined agents need to be taken into account. Although various dwell times have been reported, the lock solution should not sit for longer than 48 hours. The dwell time for antibiotic lock solutions is based more on the PN-free time interval available. In vitro and in vivo studies have shown that drug concentrations are maintained for at least 12 hours if not several days (20). The duration of 1–2 weeks may be adequate for treatment—the success of which is determined by resolution of signs and symptoms and negative catheter blood cultures. Maintain a low threshold for pulling the catheter if improvement is not seen in the first few days, but do not remove a catheter based only on fever. The risks of using antimicrobial lock therapy include potential toxicity if the solution reaches the systemic circulation by leak or inadvertent flush, as well the potential to develop resistance. Emergence of resistance has not yet been reported with this approach.

Use of antiseptic agents (e.g., ethanol) in lock solution has been considered (12,26). EDTA can be antibacterial and antifungal in its action. Taurolidine at a concentration of 5000 units/mL for 24 hours was able to eradicate *S. aureus*, *S. epidermidis*, and *Enterococcus faecalis* (27).

CONCLUSION

Catheter-related infections in the home PN patient are responsible for significant morbidity, mortality, and health care cost. These patients benefit from close monitoring and every effort should be made to prevent infection. Prophylactic therapy and early detection can reduce infectious morbidity and mortality. Prompt institution of therapy (traditional or lock) is key to avoid repeated or prolonged hospitalization, disseminated infection, and catheter loss. The most evidence-based and practical methods to prevent or treat CR infections should be used to improve patient outcomes. ■

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