**REVIEW ARTICLE** 

# Prevention of Central Line–Associated Bloodstream Infections in Hemodialysis Patients

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An increasing proportion of central line-associated bloodstream infections (CLABSIs) are seen in outpatient settings. Many of such infections are due to hemodialysis catheters (HD-CLABSIs). Such infections are associated with substantial morbidity, mortality, and excess healthcare costs. Patients who receive dialysis through a catheter are 2–3 times more likely to be hospitalized for infection and to die of septic complications than dialysis patients with grafts or fistulas. Prevention measures include minimizing the use of hemodialysis catheters, use of CLABSI prevention bundles for line insertion and maintenance, and application of antimicrobial ointment to the catheter exit site. Instillation into dialysis catheters of antimicrobial solutions that remain in the catheter lumen between dialyses (antimicrobial lock solutions) has been studied, but it is not yet standard practice in some dialysis units. At least 34 studies have evaluated the impact of antimicrobial lock solutions on HD-CLABSI rates. Thirty-two (94%) of the 34 studies demonstrated reductions in HD-CLABSI rates among patients treated with antimicrobial lock solutions. Recent multicenter randomized controlled trials demonstrated that the use of such solutions resulted in significantly lower HD-CLABSI rates, even though such rates were low in control groups. The available evidence supports more routine use of antimicrobial lock solutions as an HD-CLABSI prevention measure in hemodialysis units.

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Central line-associated bloodstream infections (CLABSIs) continue to be an important healthcare problem in the United States. A substantial proportion of CLABSIs now occur in outpatient settings, and many of these infections are due to temporary nontunneled catheters or long-term tunneled hemodialysis catheters.<sup>1</sup> Such hemodialysis-related CLABSIs are referred to here as HD-CLABSIs. In 2008, an estimated 37,000 HD-CLABSIs occurred among patients receiving outpatient hemodialysis.1 Bloodstream infections continue to be an important cause of hospitalization among hemodialysis patients.<sup>2</sup> Hospitalizations for bacteremia and/or sepsis in patients with chronic kidney disease have increased recently, with the rate in 2007 being the highest since 1991.<sup>3</sup> Rates of hospitalization among patients using a catheter are considerably higher than those among patients with an arteriovenous (AV) fistula or graft, regardless of age or race.<sup>3</sup> Patients dialyzed through catheters are 2-3 times more likely to be hospitalized for infection and to die of septic complications than dialysis patients with grafts or fistulas.<sup>4-6</sup> The substantial number of HD-CLABSIs illustrates the need for continued and intensified prevention efforts to minimize the frequency of these serious infections.<sup>3</sup>

HD-CLABSIs are one of the most common causes of fatal healthcare-associated infections among hemodialysis patients, with a mortality rate of 12%–25%.<sup>7</sup> Infection is the second

most common cause of death in patients with end-stage renal disease (ESRD), with bacteremic sepsis causing 75% of infection-related deaths.<sup>8</sup> In a study of *Staphylococcus aureus* bloodstream infections in hemodialysis patients seen at Duke University, the mortality rate among patients with *S. aureus* bacteremia related to a catheter was 22.7%, compared with a mortality rate of 10% among patients whose bacteremia was related to an AV graft.<sup>9</sup>

While rates of HD-CLABSIs are not as high as they have been in the past, the rate of such infections in the National Healthcare Safety Network (NHSN) 2006 database was 1.4 cases per 1,000 catheter-days (CDs).<sup>10</sup> More recent data from the NHSN found that the pooled mean estimated HD-CLABSI rate was 1.05 cases per 1,000 CDs.<sup>1</sup>

## COST OF CLABSIS

In addition to the substantial morbidity and mortality suffered by affected patients, CLABSIs add significant cost to the healthcare system. The Centers for Disease Control and Prevention (CDC) has estimated that the excess healthcare costs associated with each CLABSI is approximately \$16,550.<sup>1</sup> The cost of an HD-CLABSI may be even higher. For example, Engemann et al<sup>11</sup> reported that mean excess costs (including readmissions and outpatient costs) associated with an episode of *S. aureus* bacteremia in hemodialysis patients was \$22,430

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(2001 dollars), with costs even higher in patients with complicated bacteremia. Patients with bacteremia attributed to dialysis catheters, AV grafts, and other devices were included. More than 10% of patients required rehospitalization, and approximately 30% of patients with an *S. aureus* bloodstream infection developed complications related to the bacteremia. Mean costs for the initial hospitalization for a complicated bloodstream infection was \$32,462, compared with \$17,011 for an uncomplicated bloodstream infection. Similarly, Ramanathan et al<sup>12</sup> found that the mean cost of hospitalization for an HD-CLABSI was \$23,451, with a median length of stay of 11 days.

In a subsequent Duke University study of the relationship between outcomes and type of vascular access, the mean cost of the initial hospitalization for an *S. aureus* HD-CLABSI was \$16,679, and the cost of these infections over a 12-week period was \$22,944 per patient.<sup>9</sup> At 12 weeks, mean costs for patients who had a catheter but no alternative access was \$25,738, compared with \$15,831 for patients who had a catheter and a maturing AV graft or fistula. Costs of *S. aureus* HD-CLABSIs treated in the outpatient setting have been estimated to range from \$7,000 to \$15,000 per episode.<sup>13</sup>

## **PREVENTION OF HD-CLABSIS**

The CDC has issued a list of core interventions for the prevention of dialysis-related bloodstream infections.<sup>14</sup> They include the following:

- Surveillance and feedback of CLABSIs using the NHSN.
- Monthly hand hygiene compliance audits with feedback to clinical staff.
- Quarterly audits of vascular access care to ensure it adheres to recommended procedures. This includes use of aseptic technique while connecting and disconnecting catheters and during dressing changes.
- Providing standardized education to all patients on infection prevention issues, such as vascular access care and hygiene, risks related to catheter use, recognizing signs of infection, and instructions for access management when away from the dialysis unit.
- Providing regular training of staff on infection control topics, including access care and aseptic technique. Perform competency evaluation for skills such as catheter care and accessing at least every 6–12 months and upon hire.
- Efforts to reduce use of catheters by identifying barriers to permanent vascular access placement and catheter removal.
- Use of chlorhexidine for skin antisepsis for both line insertion and during dressing changes. Povidone-iodine, preferably with alcohol, or 70% alcohol are acceptable alternatives.
- Cleansing of catheter hubs with an appropriate antiseptic after the cap is removed and before accessing.
- Application of bacitracin-gramicidin-polymixin B ointment or povidone iodine ointment to catheter exit sites during dressing change or use of chlorhexidine-impregnated sponged dressing.

#### Avoiding Dialysis Catheters

A major prevention strategy is to avoid use of central lines in hemodialysis patients in favor of AV fistulas or, in some patients, AV grafts. A recent US Renal Data System report recommends promoting early removal of catheters and replacement with an internal access device.<sup>3</sup> In March 2010, a clinical technical expert panel of the Center for Medicare and Medicaid Services concluded that one of the most important measures for reducing CLABSIs was avoidance of catheter use.<sup>15</sup> In addition, the CDC has stated that to prevent CLABSIs in hemodialysis patients efforts to reduce central line use for hemodialysis and improve the maintenance of central lines should be expanded.<sup>1</sup> Although there has been considerable effort in recent years to reduce the use of catheters for maintenance of hemodialysis, the proportion of patients dialyzed through catheters has declined only moderately in recent years; as of 2008, 18% of hemodialysis patients in the United States continued to receive dialysis through a catheter.<sup>3</sup> Moreover, approximately 80% of ESRD patients in the United States begin hemodialysis via a catheter,<sup>1</sup> suggesting that efforts to minimize HD-CLABSIs among this population will continue to be required for the foreseeable future. When temporary vascular access is needed for dialysis, a tunneled cuffed catheter is preferable to a noncuffed catheter if the catheter is expected to be in place for more than 3 weeks.<sup>16</sup>

When catheters must be used, recommended interventions to improve central line maintenance can be predicted to reduce CLABSIs in hemodialysis patients and should be consistently implemented. The CDC has noted that the current patterns of CLABSIs in outpatient settings suggest a need for improved implementation of postinsertion line maintenance practices as well as strategies to ensure prompt removal of unneeded central lines.<sup>1</sup> The CDC has also recommended that prevention strategies, such as measures to reduce central line colonization in hemodialysis patients, have also shown promise and should be explored.<sup>1</sup>

### **CLABSI Bundles**

Using a combination (bundle) of infection control measures that have been shown to reduce CLABSI rates is strongly recommended by a variety of healthcare organizations. The routine use of CLABSI bundles has been shown to dramatically reduce the incidence of CLABSIs in intensive care units (ICUs).<sup>17</sup> The CLABSI bundle includes hand hygiene prior to inserting the line, use of maximal barrier precautions when inserting central lines, cleansing of the skin at the catheter entry site with a chlorhexidine-containing antiseptic solution, avoiding femoral line insertion whenever possible, and removing catheters when no longer indicated. Additional elements that may be considered part of a CLABSI bundle include applying a chlorhexidine-containing dressing to the catheter site after insertion and using a checklist to make sure that each element of the bundle is adhered to by the individuals inserting the catheter. Given the dramatic reductions

· · · · · · · · · · · · · · · · · · ·	Meta-analysis or systematic review						
Trial, year	Jaffer et al <sup>23</sup>	James et al <sup>24</sup>	Labriola et al <sup>22</sup>	Yahav et al <sup>21</sup>	Snaterse et al <sup>25</sup>		
Cooper and Saad, <sup>37</sup> 1999 (abstract)		X		X			
Dogra et al, <sup>39</sup> 2002	х	Х	Х	Х	Х		
Pervez et al, <sup>40</sup> 2002		Х		Х	Х		
Betjes and van Agteren, <sup>42</sup> 2004	Х	Х	X				
McIntyre et al, <sup>43</sup> 2004	Х	Х	Х	Х	Х		
Bleyer et al,45 2005		Х	Х	Х	Х		
Weijmer et al, <sup>46</sup> 2005	Х		Х				
Kim et al,49 2006	Х	Х	Х	Х	Х		
Saxena et al, <sup>51</sup> 2006	Х	Х			Х		
Saxena et al, <sup>69</sup> 2006			Х	Х	Х		
Nori et al, <sup>50</sup> 2006	Х	Х	Х	Х	Х		
Zhang et al, <sup>52</sup> 2006 (abstract)		Х		Х			
Al-Hwiesh and Abdul-Rahman, <sup>56</sup> 2007		Х		Х	Х		

TABLE 1. Studies Included in Meta-analyses and Systematic Reviews

in CLABSIs noted in multiple institutions that have implemented a CLABSI bundle in ICUs,<sup>17</sup> it is reasonable to assume that full implementation of these bundles when caring for hemodialysis patients will reduce the incidence of these serious infections.

## Application of Antimicrobial Ointment to Exit Site

Although chlorhexidine-containing dressings are normally used at catheter entry sites in ICUs, national guidelines recommend that bacitracin-gramicidin-polymixin B ointment or povidone iodine antiseptic ointment be used at the hemodialysis catheter exit site after catheter insertion and at the end of each dialysis session if this ointment does not interact with the material of the dialysis catheter.<sup>18</sup> The recommendation to use a triple-antibiotic ointment was based on a single study in hemodialysis patients that compared the use of triple-antibiotic ointment with a placebo at the catheterinsertion site. The rate of CLABSIs in the triple-antibiotic group (0.63 cases per 1,000 CDs) was significantly lower than that in the placebo group (2.48 cases per 1,000 CDs), and there were significantly fewer deaths in the triple-antibiotic group (P = .004).<sup>19</sup> A subsequent observational study of triple-antibiotic ointment applied to the exit site also found a substantial reduction in the incidence of CLABSIs among hemodialysis patients, compared with preintervention CLABSI rates.20

## Antimicrobial Lock Solutions

Instilling antimicrobial solutions into hemodialysis catheters and allowing the solution to remain in the catheter lumen between dialyses has been widely studied as a strategy for reducing CLABSIs in hemodialysis patients.<sup>21-25</sup> Such solutions are referred to as antimicrobial lock solutions. Antibiotics that have been used alone or in combination for lock solutions include vancomycin, gentamicin, ciprofloxacin, minocycline, amikacin, cefazolin, cefotaxime, and ceftazidime.<sup>18</sup> Antiseptics that have been used in lock solutions include alcohol, taurolidine, and trisodium citrate; recently, a combination of sodium citrate-methylene bluemethylparaben-propylparaben was used. Such antiseptic agents have often been used in combination with an anticoagulant, such as heparin or ethylenediaminetetraacetic acid (EDTA). Four meta-analyses published in 2008 and a systematic review published in 2010 all concluded that antimicrobial catheter lock solutions reduce the risk of CLABSIs in hemodialysis patients (Tables 1 and 2).<sup>21-25</sup>

Since publication of the meta-analyses, 5 observational studies and 6 randomized controlled trials (RCTs) have been conducted.<sup>26-36</sup> Three observational studies that evaluated gentamicin-heparin lock solutions, 1 that used 46.7% triso-dium citrate, and 1 that evaluated both a gentamicin-heparin solution and taurolidine-citrate solution all found that the antimicrobial lock solutions were associated with reduced CLABSI rates among hemodialysis patients.<sup>26-30</sup>

In an RCT by Power et al<sup>31</sup> that compared 46.7% sodium citrate with 5% heparin lock solutions, the investigators found no difference in the rate of CLABSIs (0.7 cases per 1,000 CDs in each group). Catheter thrombosis was significantly more common in the citrate group. A double-blind RCT by Solomon et al<sup>32</sup> compared a taurolidine-citrate lock solution with heparin and found that the CLABSI rate was lower in the taurolidine-citrate group (1.4 cases per 1,000 CDs) than in the heparin group (2.4 cases per 1,000 CDs), but the difference was not statistically significant.

Campos et al<sup>33</sup> performed an RCT of minocycline and EDTA versus heparin lock and found that the CLABSI rate in the minocycline-EDTA group (1.1 cases per 1,000 CDs) was significantly lower than that in the heparin group (3 cases per 1,000 CDs). Hemmelgarn et al<sup>34</sup> performed an RCT of a standard heparin solution 3 times a week with recombinant tissue plasminogen activator (rtPA) substituted for heparin at the midweek session. The CLABSI rate in the standard heparin lock group was 1.37 cases per 1,000 CDs, compared with 0.4 cases per 1,000 CDs in the rtPA group (P = .02).

Meta-analysis or review, year	No. of studies	Findings	Limitations	Conclusions	
Jaffer et al, <sup>23</sup> 2008	c et al, <sup>23</sup> 2008 7 CLABSI was 7.72 times less frequent with ALS. No increase in catheter thromobosis.		Relatively short follow-up periods to exclude emer- gence of Abx-R.	ALS decreases catheter-related infections without significant side effects. Not possible to identify most effective ALS.	
James et al, <sup>24</sup> 2008	11	ALS reduced CLABSI rate from 3.2 to 1.2 cases per 1,000 CDs.	Most studies had follow-up period of <6 months.	ALS decreases CLABSI rate and need for catheter removal. Longer studies needed to ex- clude emergence of Abx-R.	
Labriola et al, <sup>22</sup> 2008	8	ALS significantly reduced risk of CLABSI (RR, 0.32). Subgroup analy- sis did not show significantly differ- ent results, except that gentamicin ALS appeared to be more effective.	Some heterogeneity of stud- ies. Limited follow-up does not exclude onset of adverse effects or emer- gence of Abx-R.	ALS reduces CLABSIs by a fac- tor of 3.	
Yahav et al, <sup>21</sup> 2008 11		ALS significantly reduced CLABSIs (RR, 0.44). Catheter removal rates were significantly lower (RR, 0.35). Abx-R was documented in 1 patient.	Study heterogeneity was noted.	ALS reduces CLABSI and cathe- ter removal rates. The use of ALS should be considered in routine clinical practice in conjunction with other pre- vention modalities.	
	5	High-quality non-ALS studies showed significant reduction in CLABSIs (RR, 0.25).	Study heterogeneity was noted. Small number of studies.	NNT to prevent 1 CLABSI is 4.	
Snaterse et al, <sup>25</sup> 2010	9	All 9 studies found that CLABSIs were more common in the heparin group; differences reached statistical significance in 7 studies. The CLABSI rate in control groups was 3 cases per 1,000 CDs.	None were clearly defined as double blind. Only 1 trial performed analysis by in- tention to treat.	ALS appears to be more effec- tive than heparin in reducing CLABSIs. NNT to prevent 1 CLABSI is 3.	

TABLE 2. Meta-analysis and Systematic Review of Antimicrobial Lock Solutions (ALSs) for Hemodialysis

NOTE. Abx-R, antimicrobial resistance; CD, catheter-day; CLABSI, central line-associated bloodstream infection; NNT, number needed to treat; RR, relative risk.

Catheter malfunction was more common in the heparin-only group. The authors concluded that use of rtPA instead of heparin once weekly as a locking solution significantly reduced the incidence of CLABSI and catheter malfunction.

In the largest study of its kind, Maki et al<sup>35</sup> conducted a multicenter RCT involving 407 patients undergoing hemodialysis via a catheter. The investigators compared a saline lock containing 5,000 U of heparin to a new lock solution containing 7% sodium citrate, 0.15% methylene blue, and 0.15% methylparaben in 0.015% polypropylparaben (C-MB-P; Zuragen; Ash Access Technology). The investigators found that catheters locked with C-MB-P were significantly less likely than catheters in the control arm to cause CLABSI (0.2 vs 0.82 cases per 1,000 CDs; P = .005) and were less likely to be lost because of patency failure (0 vs 4; P = .04).

In a recently published multicenter RCT, Moran et al<sup>36</sup> studied 303 maintenance hemodialysis patients who were using tunneled cuffed catheters for vascular access. An antibiotic lock solution containing 320  $\mu$ g/mL gentamicin in 4% sodium citrate was compared with a standard catheter lock containing 1,000 U/mL heparin. They found that the CLABSI rate in the gentamicin-citrate group (0.28 cases per 1,000 CDs) was sig-

nificantly lower than that in the control group (0.91 cases per 1,000 CDs; P = .003). The rate of tPA usage was similar in the treatment and control groups. The investigators concluded that the gentamicin-citrate lock solution markedly reduced the incidence of CLABSI and was as effective as 1,000 U/mL heparin in preventing catheter clotting.

Overall, at least 34 trials have evaluated the impact of antimicrobial lock solutions on CLABSI rates among hemodialysis patients (Table 3).<sup>26-59</sup> Twelve were observational trials, 1 was a nonrandomized controlled trial, and 21 were RCTs. Thirty-two (94%) of the 34 studies demonstrated a reduction in the CLABSI rate among patients treated with antimicrobial lock solutions. Nineteen (90.5%) of the 21 RCTs reported a reduction in HD-CLABSI rates among patients treated with antimicrobial lock solutions. 31-37,39,40,42,43,45,46,48-52,54-56 Of note, 2 RCTs and 1 arm of an observational study that used 47% sodium citrate as lock solutions were the only trials that did not demonstrate reductions in HD-CLABSIs.<sup>31,55,59</sup> Of the 16 RCTs for which statistical analysis was available, 14 (87.5%) demonstrated statistically significant reductions in HD-CLABSI rates in patients treated with antimicrobial lock solutions. 31-36,39,42,43,45,46,48-51,56

TABLE 3. Trials of Antimicrobial Lock Solutions (ALSs) for the Prevention of Central Line-Associated Bloodstream Infections (CLABSIs) in Hemodialysis Patients

			CLABS cases/1,0	I rate, 00 CDs		
	Type of	No. of	Control	ALS		
Trial, year	study	patients	group	group	Р	ALS constituents
Cooper and Saad, <sup>37</sup> 1999	R, C	36	3.1	0	NA	Gentamicin
Ash et al, <sup>38</sup> 2000	Obs	NS	1.44	0	NA	47% trisodium citrate
				0.59	NA	23% trisodium citrate
				0.56	NA	Gentamicin–trisodium citrate
Dogra et al, <sup>39</sup> 2002	R, C	83	4.2	0.3	.003	Gentamicin-trisodium citrate
Pervez et al, <sup>40</sup> 2002	R, C	36	2.1	0.62	NA	Gentamicin–trisodium citrate
Allon, <sup>41</sup> 2003	С	50	5.6	0.6	<.001	Taurolidine-trisodium citrate
Betjes and van Agteren, <sup>42</sup> 2004	R, C	58	2.1	0	.047	Taurolidine-trisodium citrate
McIntyre et al, <sup>43</sup> 2004	R, C	50	4	0.3	.02	Gentamicin-heparin
Dogra et al, <sup>44</sup> 2004	Obs	130	4.2	1.3	NA	Gentamicin-trisodium citrate
Bleyer et al,45 2005	R, C	60	0.47	0	.35	Minocycline-EDTA
			4	0.4	.02	Minocycline-EDTA
Weijmer et al, <sup>46</sup> 2005	R, C	291	4.2	0.8	<.001	30% trisodium citrate
Lambie et al,47 2005	Obs	48	3.12	0.76	<.05	Gentamicin-heparin
Duncan et al, <sup>55</sup> 2005	R, C	232	0.7	0.6	NA	47% trisodium citrate
Geron et al, <sup>48</sup> 2006	R, C	13	9.5	1.15	<.05	Taurolidine-trisodium citrate
Kim et al,49 2006	R, C	120	3.12	0.44	.03	Gentamicin-cefazolin-heparin
Nori et al, <sup>50</sup> 2006	R, C	61	4	0	.008	Gentamicin-trisodium citrate
Saxena et al, <sup>51</sup> 2006	R, C	96	3.68	1.56	<.0001	Cefotaxime-heparin
Zhang et al, <sup>52</sup> 2006	R, C	101	0.89	0	NA	Gentamicin-heparin
Fluck et al, <sup>53</sup> 2006	Obs	NS	3.7	0.12	NA	Gentamicin-heparin
D'Avella et al, <sup>54</sup> 2007	R, C	NA	1.7	1.1	NA	18% saline-heparin
Al-Hwiesh and Abdul-Rahman, <sup>56</sup> 2007	R, C	63	13.1	4.54	.05	Vancomycin-gentamicin-heparin
Feely et al, <sup>57</sup> 2007	Obs	33	9.13	1.04	.001	Gentamicin-heparin, minocycline- EDTA, or vancomycin-heparin
Winnett et al, <sup>26</sup> 2008	Obs	1,097	2.13	0.81	<.001	47% trisodium citrate
Abbas et al, <sup>27</sup> 2009	Obs	320	0.9	0.62	.01	Gentamicin-heparin
Onder et al, <sup>58</sup> 2009	Obs	45	16.8	6.2	.2	Tobramycin-tPA
Power et al, <sup>31</sup> 2009	R, C	232	0.7	0.7	>.05	46.7% citrate
Solomon et al, <sup>32</sup> 2010	R, C	110	2.4	1.4	.1	Taurolidine-citrate
Venditto et al, <sup>59</sup> 2010	Obs	NS	2.9	3.4	>.05	46% citrate
			2.9	0.4	.06	Gentamicin-heparin
Chow et al, <sup>28</sup> 2010	Obs	149	4.6	1.5	.002	Gentamicin-heparin
Landry et al, <sup>29</sup> 2010	Obs	1,410	17	0.83	NA	Gentamicin-heparin
Filiopoulas et al, <sup>30</sup> 2011	Obs	118	9.9	2.74	.01	Gentamicin-heparin
•		59		3.67	.03	Taurolidine-citrate
Campos et al, <sup>33</sup> 2011	R, C	150	4.3	1.1	.005	Minocycline-EDTA
Hemmelgarn et al, <sup>34</sup> 2011	R, C	225	1.37	0.4	.02	rtPA-heparin
Maki et al, <sup>35</sup> 2011	R, C	407	0.82	0.24	.005	Citrate-methylene blue-
•						methylparaben-propylparaben
Moran et al, <sup>36</sup> 2012	R, C	303	0.91	0.28	.003	Gentamicin-citrate

NOTE. C, controlled; CD, catheter-day; EDTA, ethylenediaminetetraacetic acid; NA, not available; NS, not stated; Obs, observational; R, randomized; rtPA, recombinant tissue plasminogen activator; tPA, tissue plasminogen activator.

In a number of the 34 trials referred to above, baseline HD-CLABSI rates were relatively high (more than 3 cases per 1,000 CDs) by today's standards, which may have made it easier to show a reduction by using an antimicrobial lock solution. However, it is worth noting that the observational study by Abbas et  $al^{27}$  found a substantial reduction in CLABSI rates even though the baseline rate was low (0.9 cases

per 1,000 CDs). Similarly, the recent RCTs of antimicrobial lock solutions by Maki et al<sup>35</sup> and Moran et al<sup>36</sup> documented statistically significant reductions in CLABSI rates despite the fact that baseline CLABSI rates were quite low (0.82 and 0.91 cases per 1,000 CDs, respectively). Maki et al<sup>35</sup> also pointed out that they found a strong trend toward reduced all-cause mortality in the trial. As a result, these recent trials dem-

onstrate that antimicrobial lock solutions can achieve significant reductions in CLABSI rates even in dialysis centers that have low baseline CLABSI rates.

The major concerns regarding the use of antibiotics or antiseptic lock solutions include the potential for side effects, including toxicity, allergic reactions, hemorrhage, and emergence of resistance to the antimicrobial agent used. Of interest, none of the trials reviewed in the above-cited metaanalyses found any evidence that use of an anti-infective lock solution promoted antimicrobial resistance. More recently, a hemodialysis program reported that use of a gentamicinheparin lock solution in a hemodialysis network was associated with the emergence of gentamicin resistance among coagulase-negative staphylococci and enterococci.29 However, there are several aspects of the methods and definitions used in the study that make it difficult to interpret the results. Venditto et al<sup>59</sup> reported that use of a gentamicin-heparin lock for several years was associated with an increase in gentamicin resistance among Enterobacteriaceae but not among S. aureus isolates. A hemodialysis program in New Zealand reported some increase in gentamicin resistance among coagulase-negative staphylococci recovered from CLABSIs after use of the gentamicin lock for a 3.5-year period, although the increase was not statistically significant.<sup>27</sup> In the study by Moran et al,<sup>36</sup> blood culture isolates from the study population did not reveal emergence of gentamicin resistance during the trial or in the 3 years following universal usage of the gentamicin-citrate lock in all patients with tunneled catheters in their facilities, a finding consistent with an earlier study that found no emergence of gentamicin resistance over a period of 7 years.<sup>60</sup>

The main concern regarding the use of high concentrations of citrate is that if it is inappropriately injected into the systemic circulation it can cause serious hypocalcemia, cardiac dysrhythmias, and death. However, the lower concentrations of citrate used in recent studies make these serious side effects less likely.

### SUMMARY

Given the dramatic reductions in CLABSI rates achieved nationally in ICUs, prevention measures similar to those used in ICUs should be utilized in both inpatient and outpatient hemodialysis units. The concept that such infections are an inevitable consequence of complex care and that a certain level of HD-CLABSIs is acceptable is no longer tenable. On the basis of the evidence cited above, the policies and procedures listed below should be adopted and implemented in hemodialysis units.

# **General Recommendations**

• Adopt CDC-recommended core interventions for prevention of dialysis-related bloodstream infections.<sup>14</sup>

## Specific Recommendations

- Continue efforts to reduce the use of catheters for hemodialysis to a minimum.<sup>15</sup>
- When temporary use of a catheter is needed (eg, for institution of hemodialysis), use a tunneled catheter if the expected duration of catheter use is more than 3 weeks.<sup>16</sup>
- Periodically have vascular access managers review with patients the indications for continued use of a dialysis catheter.<sup>61</sup>
- Use maximal barrier precautions when inserting hemodialysis catheters. These include wearing a sterile cap, mask, gown, and gloves and use of a large patient drape during the procedure.<sup>18</sup>
- Use a chlorhexidine-containing antiseptic for prepping the skin at the anticipated catheter site. The preferred type of product contains chlorhexidine in approximately 70% alcohol.<sup>62</sup>
- Have nurse complete checklist during procedure to record compliance with insertion policies.<sup>17</sup> Consider developing a system to determine the frequency and accuracy of checklist completion.<sup>63</sup>
- Use a chorhexidine-containing antiseptic for dressing changes.<sup>18</sup>
- Apply triple-antibiotic ointment to exit site at the end of each dialysis session.<sup>19,20</sup> Povidone-iodine ointment is an acceptable alternative. Mupirocin ointment is no longer considered a recommended alternative because of concerns regarding emergence of resistance when applied to dialysis catheters.<sup>18,64-66</sup>
- Educate personnel regarding current hand hygiene practices. Periodically monitor compliance of heathcare workers with hand hygiene policies and provide them with feedback regarding their performance.<sup>67,68</sup>
- When obtaining blood cultures during a dialysis session is indicated, use careful aseptic technique to minimize the risk of contamination of blood cultures.
- When obtaining blood cultures is indicated and the patient is not being dialyzed, obtain 2 blood cultures from peripheral veins whenever possible. If phlebotomists cannot obtain blood for culture, consider having members of an intravenous team attempt to obtain blood cultures from peripheral veins. If blood cultures must be obtained from hemodialysis catheters during interdialytic periods, have trained nurse or technician obtain blood cultures from the catheter using careful aseptic technique. Consider developing a specific kit that contains all the equipment that personnel will need to aseptically draw blood cultures directly from the dialysis catheter.
- Implement routine use of an antimicrobial lock solution for patients receiving hemodialysis through a catheter.<sup>13,21-25</sup> Consider one of the following antimicrobial lock solutions: (a) 320 μg/mL gentamicin in 4% sodium citrate or (b) C-MB-

P. Avoid lock solutions containing high (more than 30%) concentrations of sodium citrate.

• Continue performing surveillance for CLABSIs among hemodialysis patients. Ideally, the surveillance system should detect CLABSIs in those treated as outpatients as well as those treated as inpatients at area hospitals. Express CLABSI rates as new cases per 1,000 CDs.

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