

Heparin Locking for Central Venous Catheters

Lynn Hadaway, MEd, RNC, CRNI

Abstract

Traditionally, heparin-lock solution has been used with all central venous catheters. The introduction of new technology calling for the elimination of heparin and the growing concerns about the use of heparin have caused many health care professionals to question its continued use for this purpose. This literature review attempts to answer the most common questions using available research; however, there continues to be more questions than answers. At present, it appears that some form of anticoagulant will produce more patent catheters, and heparin-lock solution is the only product commercially available. This situation drives the need for a careful assessment of patients' needs prior to abandoning the use of heparin.

The use of a dilute heparin solution has been the most common method of "locking" a catheter since the use of intermittent catheters began in the early 1970s. The inception of this practice brought many questions about the heparin concentration, volume required, and frequency of flushing, and practitioners continue to struggle with these questions today. Innovation in peripheral and central venous catheter design, as well as add-on devices, has led to more confusion and concern about the use of heparin. Although some catheter and needleless injection technology allows the elimination of heparin, the standard of practice for catheter flushing continues to include heparin when these technologies are not used. Even with the use of these technologies, heparin may still be indicated for its anticoagulant properties.

Patency of vascular access devices is a common problem in all health care settings. Lack of lumen patency disrupts patient care, threatens achievement of treatment goals, adds to the burden of limited nursing resources, and increases cost of care. Catheters that do not produce a brisk blood return on aspiration are considered to be nonfunctioning catheters and require further assessment to ensure that the fluid or medication will not leak into extravascular areas.^{1,2} Catheters occlude due to multiple reasons; however, thrombotic occlusion is the most common cause.³

Causes of blood reflux into the catheter lumen are described in Table 1. Flushing procedures can ameliorate the first three problems listed in the table. Another critical aspect of catheter patency is the fact that lumen occlusion problems may be caused by fibrin and thrombosis development inside the vein around the catheter tip, where the flushing solution or procedure has no effect.

At the present time, there are no alternative locking solutions commercially available in the United States that can substitute

for heparin-lock solution. Ongoing clinical research with other flush solutions may bring about future changes; however, practitioners must understand the current issues with heparin and the issues that must be considered before heparin is eliminated.

How Did We Get to This Point?

Physicians at the Cleveland Clinic (Cleveland, OH) caring for cystic fibrosis patients developed the original concept of "heparin lock" by first adding a stopcock to plastic tubing on a winged needle infusion set.⁴ Soon, several products were commercially available such as the Butterfly-INT from Abbott Laboratories (Abbott Park, IL) and the Minicath-PRN from Deseret Pharmaceutical (Sandy, UT). By the mid-1970s, the heparin-lock concept included the use of a plastic catheter with a male adapter plug or injection cap added to the hub.⁵

A "weak heparin" solution was made by adding 1.5 mL of 1000 units per mL to a 30-mL vial of saline, with 0.2 to 0.5 mL used to flush the set. A survey of 36 hospitals reported in 1976 that heparin concentration varied from 5 to 1000 units per mL. Three hospitals reported the use of saline only, causing the authors to question the necessity for heparin.⁶ A 1974 report compared the activated partial thromboplastin times (APTTs) drawn after inserting and flushing a heparin-lock device with 1000 units of heparin to patients with the APTTs drawn before exposure to the heparin-lock solution. The concern was the effect of the heparin-lock solution on therapeutic heparin doses.⁷ Two years later, another study reported successful use of 10 units of heparin in 1 mL of normal saline.⁵

By 1978, the intermittent infusion of antibiotics through peripheral heparin-locked catheters had moved into the home.⁸ The concept of intermittent home parenteral nutrition originated in Seattle in 1970 by using a tunneled, cuffed, central venous catheter.⁹ In 1979, a published report showed successful long-term infusion of parenteral nutrition in children by using silicone central venous catheters that were heparin locked during the day-time.¹⁰ Early procedures of intermittent home parenteral nutri-

Correspondence concerning this article should be addressed to lynn@hadawayassociates.com
DOI: 10.2309/java.11-4-17

Table 1. Causes of intraluminal blood.

Cause	Description	Prevention
Syringe plunger	Compression of the gasket on the plunger rod of a traditional syringe; release of pressure on plunger rod causes expansion of gasket drawing blood into catheter lumen.	Leave 0.5 to 1 mL of fluid in syringe to avoid gasket compression. Use a prefilled syringe for catheter flushing that is designed to overcome this problem.
Disconnection	Blood drawn into catheter lumen when the Luer tip of the administration set or syringe is disconnected from a negative-displacement needleless device.	Use a positive-pressure flushing technique with a negative-displacement needleless system. Use a positive or a neutral needleless system.
Empty IV fluid container	Venous pressure is greater than infusion pressure of an empty container infusing by gravity, allowing blood to backflow into catheter lumen.	Disconnect and flush immediately when medication is infused. Use a “carrier” fluid (eg, normal saline) for piggybacking all medications. Use an infusion-controlling device with an automatic keep-open rate.
Intrathoracic venous pressure	Changes in venous pressure due to coughing, vomiting, sneezing, or congestive heart failure; normal heart contractions due to the absence of a valve at the junction of the superior vena cava and right atrium.	Maintain a closed catheter lumen between infusions. Ensure infusion pressure is always greater than venous pressure.
Catheter compression	Excessive or forceful arm muscle contraction in the arm with a PICC; compression of the external catheter segment; compression between the clavicle and first rib with insertion into the medial aspect of subclavian vein. Fluid locking the catheter lumen is forced out the internal tip and blood moves into the lumen when the compression is relieved.	Avoid excessive or repetitive physical activity or heavy lifting with a PICC. Ensure that the external catheter segments are not pinched or compressed by stabilization or dressing. Warn patient to avoid unnecessary manipulation of the external catheter segment (ie, Twiddler’s syndrome). Use jugular insertion site.

tion included soaking the male Luer-lock cap for a minimum of two hours in formaldehyde solution, then three minutes in alcohol, followed by handling with sterile forceps. Heparin-lock solution was 1.5 mL of 1000 units per mL. At that time, intermittent catheter use with heparin locking had reported patency for two weeks and “it is theoretically possible to maintain catheter patency in this manner indefinitely.”¹¹

During the late 1980s, many studies reported successful use of saline only for flushing short peripheral catheters. Two meta-analyses were published in 1991 confirming that there was no difference in peripheral catheter patency when flushed with saline only.^{12,13} Practice quickly changed to eliminate the use of heparin-lock solution in these catheters.

Catheters designed with an integral valve were first introduced in the mid-1980s (Groshong, Bard Access Systems, Salt Lake City, UT). The PASV catheters (Boston Scientific Corp., Natick, MA) and LifeValve implanted ports (Rita Medical, Inc., Atlanta, GA) are other catheter designs with an integral valve. All brands have instructions that allow for saline-only flushing. Because the opening pressure for the valve is greater than normal intrathoracic venous pressure, these valves remain closed until pressure is applied for infusion or aspiration.

Needle-based injection caps for catheter hubs changed with the introduction of needleless devices in the early 1990s because of concern about occupationally acquired diseases resulting from needlestick injuries. The Bloodborne Pathogen Standard from the

Occupational Safety and Health Administration (OSHA) became effective in March 1992; it required engineering controls to reduce needlestick injuries. In April 1992, the U.S. Food and Drug Administration (FDA) issued a safety alert on the use of hypodermic needles used to connect piggybacked and intermittent administration sets to primary administration sets and the catheter hub. This alert “strongly urged that needleless systems or recessed needle systems replace hypodermic needles for accessing I.V. lines.”¹⁴ This report highlighted the issue of needlestick injuries with these needles along with needles breaking off inside the injection port. After the release of these documents, the use of needleless connectors or injection systems increased significantly.

Issues and concerns continued to grow as needleless injection systems advanced. Large, blunt cannulas and moving mechanical valves appeared to encourage catheter lumen occlusion because of blood reflux into the catheter lumen. This concern led to the development of positive-displacement needleless devices, although the evidence for this need was based on in vitro demonstrations instead of clinical studies. The desire to eliminate heparin from flushing protocols for central venous catheters led to saline-only flushing instructions for some needleless system. The relationship between needleless systems and bloodstream infection is currently receiving the most attention.¹⁵

Heparin: What Is It?

Unfractionated heparin (UFH) is a mixture of glycosamino-

glycans, which are long unbranched polysaccharides, that act as a potent anticoagulant. UFH does not break down existing blood clots but allows the body's natural fibrinolytic system to act. It prevents additional clots from forming or existing clots from getting larger.

Pharmaceutical-grade heparin is most often obtained from porcine intestine or bovine lung. Heparin is one of the oldest drugs in clinical use and actually predated the creation of the FDA.

Heparin interacts with antithrombin III, causing the inactivation of several normal clotting factors. Heparin also interacts with platelets and endothelial cells, possibly contributing to heparin-induced bleeding by a noncoagulant mechanism. It increases vascular permeability, restrains the proliferation of smooth muscle cells and promotes bone loss by suppressing osteoblast formation. There may also be variation in anticoagulant activity because of heparin binding with plasma proteins, producing inconsistency in response from patients with thromboembolic events.¹⁶ Heparin has been shown to produce vasodilation in human hand veins through a direct relaxing effect, and other reports have shown that long-term heparin administration lowers blood pressure in hemodialysis and cardiac surgery patients.¹⁷

The average half-life of heparin is between 30 and 150 minutes, with larger doses producing a longer half-life. The reason for this dose-dependent difference is thought to be caused by large amounts of the drug binding to endothelial cell receptors and macrophages.¹⁶

The therapeutic effect of heparin is measured by the aPTT, and values between 1.5 and 2.5 are considered to be the traditional therapeutic range. A wide variety of laboratory methods, reagents, and instruments in use require that the therapeutic range for aPTT be calibrated for each reagent lot and coagulometer being used.¹⁶

Heparin resistance is seen in patients who require very high doses to achieve a therapeutic range of the aPTT. Causes include antithrombin deficiency, increased heparin clearance, or elevations in heparin-binding proteins, factor VIII levels, and fibrinogen.¹⁶

Low-molecular-weight heparins (LMWHs) are made from unfractionated heparin and have better pharmacokinetic properties. Although there are European studies using LMWH for catheter locking, these drugs are not labeled for intravenous use in the United States and are given by the subcutaneous route.

Issues With Heparin Use

Volume and Concentration

The volume of heparin required to properly lock the catheter depends on the priming volume of the catheter plus any add-on devices. The Infusion Nurses Society (INS) *Standards of Practice*¹ call for the minimum volume to be equal to twice the internal volume of the catheter system. This overflow should allow for properly filling the entire system.

Leakage or spillage of the locking fluid has been documented in several in vitro studies of hemodialysis catheters. Some report this as a positive aspect to ensure that the entire catheter lumen is properly filled, whereas others report it as a negative aspect because of the high concentrations of heparin used to routinely lock hemodialysis catheters, thus increasing the risk of bleeding and skewing

coagulation laboratory values.¹⁸ Polaschegg and Shah¹⁹ found that the locking volume must be more than 120% of the catheter priming volume to achieve the full strength of the locking solution at the catheter tip. This in vitro experiment used dialysis catheters with and without side holes near the internal tip and found that 15% of the locking solution spills from the catheter tip when an amount equal to the catheter's priming volume is used.¹⁹

Another in vitro study by Polaschegg²⁰ revealed that the density of the locking solution alters the fluid spilled from the catheter. Locking the catheter with a high-density or heavier fluid causes additional fluid to spill from the catheter because the weight of the locking solution is greater than blood. Fluids used in this study were water and saline with red dye to simulate blood and citric acid and polyvinyl pyrrolidone to represent a high-density fluid. Heparin was not included. This study discussed the position of the catheter in relation to the fluid spilled. When the tip is higher than the catheter hub, such as when the patient is lying down, lower density fluid may spill out of the lumen, but when the hub is higher than the tip, higher density fluid will leak out of the lumen. These authors also disputed the idea that diffusion is the cause of fluid spill, citing diffusion as a process too slow to account for the rapid fluid movement seen in their experiments.²⁰

Several studies have examined heparin-locking procedures, but the studies' methods varied greatly, making it impossible to compare results in a meaningful way. In a retrospective study using peripherally inserted central catheters (PICCs), Andersen and Holland²¹ reported on the use of 10 units of heparin per mL in 26 patients, and 20 patients who received 100 units of heparin per mL. In the 10-units-per-mL group, four catheters occluded, whereas only two occluded in the 100-units-per-mL group. In both groups, the majority of catheters tips were placed in the midclavicular tip location, a position with a higher rate of vein thrombosis that could also produce catheter occlusion.²¹

A multicenter German study examined the use of subcutaneous LMWH and heparin flushing to prevent catheter-related thromboses in patients with implanted ports. The heparin-locking solution ranged from 0 to 250 units per mL in 108 patients, whereas 65 patients received from 500 to 2500 units per mL. The group with 250 units or less had eight thromboses (7.4%), whereas the group with higher heparin doses had no reported thromboses. This study made no attempt to distinguish between occlusions inside the vein versus the catheter lumen and was limited by the observational study design.²²

A randomized, double-blind trial in pediatric patients compared the use of saline infusion with the infusion of saline with 1 unit of heparin per mL through arterial and central venous catheters. The trial was stopped prematurely because of the high incidence of nonpatent arterial catheters receiving saline-only infusions. The endpoint of the study was *loss of patency*, which was defined as the inability to flush the catheter with 1 mL of saline from a 10-mL syringe without resistance. For the central venous catheters, three of 66 (4.5%) patients in the saline-only group were nonpatent and all patients in the heparin group of 72 patients remained patent. Although a trend toward nonpatency in the saline-only group was noticed, the study would require more patients to achieve statistical significance.²³

A study of 86 double-lumen tunneled and cuffed catheters

used for apheresis compared the use of saline-only locking with locking with 5 mL of heparin 100 units per mL. Study endpoints were inadequate blood flow rates for the apheresis procedure, use of urokinase, and radiographically confirmed thrombosis. Catheters in both groups experienced all three problems, and there were no significant differences between the saline-only group and the heparin group; however, the power of this study is limited by the lack of randomization.²⁴

Systematic reviews from the Cochrane Database found that prophylactic use of heparin infusion in neonates with PICCs had been studied in one eligible randomized trial. There were no significant differences in thrombosis, occlusion, or catheter patency, and the reviewers could not recommend heparin use on the basis of this limited data.^{25,26}

To the contrary, a meta-analysis of randomized trials of heparin use in central venous catheters and pulmonary artery catheters found a “strong trend” for reducing catheter thrombosis and bacterial colonization of the catheter. Heparin doses included 1 and 3 units per mL infusions, 50 units every 12 hours, 5000 units every 6 and 12 hours, and 2500 units LMWH subcutaneously once per day.²⁷

A literature review of flushing protocols for tunneled, central venous catheters examined six published studies and made recommendations for practice. These recommendations were for the use of heparin 5 mL of 10 units per mL (50 units) flushed once or twice weekly. This review revealed that the incidence of thrombosis was no greater with larger or more frequent doses of heparin-lock solution.²⁸

A Japanese study of a unique dialysis catheter containing urokinase on the catheter surfaces compared locking with normal saline-only versus heparin 2 mL of 1000 units per mL after each use. The researchers reported no significant differences in catheter survival and one thrombotic occlusion in each cohort of patients in this randomized trial. This catheter is not available in Europe or the United States, so duplication of the study is not possible at the present time.²⁹

Over the past 30 years, practitioners have seen a steady increase in use of many types of central venous catheters. Although it appears that an anticoagulant is needed, there continues to be a lack of answers to the questions of heparin concentration, volume, and frequency of flushing. Study design becomes a challenging proposition because of numerous variables, such as different catheter designs, insertion sites and tip location, intermittent flushing versus continuous infusion of heparin, and the patient-related factors affecting coagulability.

Flushing Techniques

Catheter flushing techniques may be equally as important as the solution itself. The use of a needleless injection device that produces a negative fluid displacement or blood reflux into the catheter lumen requires the use of positive-pressure techniques to ensure no blood remains inside the catheter lumen. Although infusion and vascular access specialists understand and apply these techniques, the majority of primary care nurses may have never been taught these flushing techniques or the reason for their use. The use of positive- and neutral-displacement injection systems eliminates the need for these flushing techniques; how-

ever, it is often difficult, if not impossible, to determine which type of device is being used. In addition, the use of positive-pressure flushing techniques with a positive-displacement device negates the displacement mechanism and promotes blood reflux. This may give the impression that the product has failed to perform adequately when the issue is one of technique.

The “turbulent” flushing technique has gained widespread clinical acceptance. Although some nurses have reported success anecdotally, there are no published data on clinical outcomes. This technique calls for a rapid stop–start or push–pause method to inject the fluid into the catheter and is based on the concept of laminar and turbulent fluid flow. Laminar fluid flows in undisturbed layers, with the fastest current in the center of the lumen. Turbulent flow moves in swirls and eddies. Theoretically, turbulent flow should remove blood components that attach to the catheter’s internal wall, creating less chance for lumen occlusion.

Many questions about this technique come to mind. How rapid should the stop–start action be applied? How much turbulence is actually created inside the catheter lumen? Will this manually created turbulence be enough to remove blood components that have attached to the catheter wall? What impact will this technique have on the biofilm that is present in virtually all central venous catheters? What are the clinical outcomes with its use regarding catheter lumen occlusion and bloodstream infection? Because of the absence of research on this flushing technique, no recommendation for or against its use can be made.

Impact on Coagulation

Concern about heparin’s effect on coagulation comes from two aspects of care: overflow of large doses of heparin from hemodialysis catheters and drawing blood samples for coagulation studies from a catheter that has been exposed to heparin.

Hemodialysis catheters are locked with very large doses of heparin, frequently as high as 5000 units per lumen. A French study of hemodialysis catheters found normal aPTT values immediately after dialysis, yet all patients had elevated values 10 minutes after locking each lumen with 2 mL containing 5000 units of heparin (a total of 10,000 units of heparin). This study also determined the priming volume of each lumen to be significantly less than the 2-mL volume used for locking each lumen.³⁰ Other studies have found similar results that were primarily related to two causes: the volume of heparin is greater than the catheter lumen will hold or there are side holes in some catheters, allowing injected heparin to leak out. The other issue is failure to aspirate the catheter lumen to remove the residual heparin before it is used.^{31,32}

A small study in oncology patients compared prothrombin time (PT) and aPTT results taken from a central venous catheter and a peripheral venous site. Catheters were flushed with heparin 100 units per mL, and blood equal to six times the interval volume of the catheter was discarded before the laboratory sample was drawn. There were significant differences between the central and peripheral samples, which could lead to incorrect interventions on the basis of the distorted laboratory results.³³ Mayo et al³⁴ reported that 25 mL of blood must be discarded before obtaining the laboratory sample for coagulation studies. This discard volume results in clinically useful PTs and fibrino-

gen levels in all samples and 95% of the aPTTs.³⁴ This volume of discard could compromise the patients' circulating blood volume for many hospitalized patients.

In yet another study, four sequential blood samples were drawn from heparinized tunneled catheters in pediatric oncology patients and compared with peripheral samples. Discard volumes of 6 mL, 9 mL, and 12 mL were not sufficient to obtain correct values for PT, fibrinogen levels, and aPTT. Although there were statistical differences for all three blood tests, clinical experts thought that there was enough difference in the aPTT values to incorrectly influence clinical decisions.³⁵

Drug Compatibility

The list of drugs that are incompatible with heparin is long; however, there have been very few studies assessing compatibility of a drug inside the catheter lumen that is followed by a heparin-locking solution. Trissel's *Handbook of Injectable Drugs* reported precipitate formation when meperidine, promethazine, hydroxyzine HCl, gentamicin sulfate, tobramycin sulfate, metilmicin sulfate, and amikacin sulfate were given into a heparinized catheter.³⁶

This list could be longer if the studies were available on all intravenous medications. In the absence of the compatibility data, the safest approach is to assume incompatibility. To avoid drug contact and any possible problems with drug precipitate that could occlude the catheter lumen, all catheters require flushing with normal saline before and after each dose of medication.

Heparin-Induced Thrombocytopenia

The most alarming issue with heparin-lock solution may be heparin-induced thrombocytopenia (HIT), an antibody-mediated reaction known to cause arterial and venous thromboses. The reaction occurs from heparin-associated antiplatelet antibodies created from previous exposure to heparin, especially within the past 100 days.³⁷

The true incidence of HIT caused by heparin-lock solution is unknown; however, in 1999, Kadidal et al³⁸ reported on three cases and found 29 previously reported cases. During the period when the three cases were identified, there were 150 tunneled catheters inserted and flushed daily with heparin-lock solution, thus indicating a relatively low rate of HIT.³⁸

This group of researchers also reported on serological testing for heparin sensitization in cancer patient with catheters being flushed with heparin. Forty-nine oncology patients had blood samples taken at the time of catheter insertion and at three to five weeks and seven to nine weeks postinsertion. In 33% (16 of 49) of patients, tests were either positive or indeterminate for heparin-related antibodies, although nine patients had elevated antibodies before heparin-lock solution was administered. None of these patients developed clinical evidence of HIT; however, sensitization did occur. HIT should be considered in symptomatic patients despite the fact that heparin-lock solution may be the only exposure to heparin.³⁹

Hong et al⁴⁰ studied 260 antibody-positive HIT patients and the location of thromboses. HIT patients with a central venous catheter had more upper-extremity deep vein thromboses (9.7%) than HIT patients without a central venous catheter (0%). All

thromboses occurred at the location of the catheter, probably due to the vascular injury from catheter insertion.⁴⁰

Heparin and Catheter-Related Infection

Research published in 1980 showed that, in laboratory tests, heparin concentrations less than or equal to 500 units per mL inhibited the growth of many microorganisms in a brain-heart infusion broth.⁴¹ This study has been used to support the use of heparin-lock solutions; however, this research assessed the impact of heparin contamination on laboratory samples only.

The results from two in vitro studies suggested that any antimicrobial activity related to heparin may be due to the preservative in the heparin-lock solution, which thereby might reduce catheter-related infection.^{42,43} Two reports of clinical studies revealed a trend toward reduction of catheter-related bloodstream infection (CRBSI) when catheters were locked with heparin; however, there were limitations due to varying definitions of catheter-related infections and other issues with study design.^{27,44}

In 2005, Shanks et al⁴⁵ reported that heparin actually stimulated the growth of biofilm. Adhesion of *Staphylococcus aureus* and biofilm formation was found with heparin concentrations ranging from 0.1 unit per mL to 1000 units per mL when tested in a polystyrene microtiter plate. The researchers reported that increased cell-cell interactions after primary attachment appeared to be the mechanism for heparin-stimulated biofilm growth.⁴⁵ A recent in vitro study by Shanks et al⁴⁶ compared the formation of biofilm on polystyrene, polyurethane, and silicone elastomer. Biofilm formation was measured after each material was exposed to lepirudin, LMWH, tissue plasminogen activator, sodium citrate, sodium citrate with gentamicin, and sodium ethylene diamine tetra-acetic acid (EDTA) combined with LMWH that has been shown to stimulate the growth of biofilm.⁴⁶

The above reports were all in vitro studies; however, clinical evidence exists demonstrating *Pseudomonas fluorescens* bloodstream infections after patients were exposed to contaminated heparin-flush solution. A multistate outbreak of *P. fluorescens* bloodstream infections was reported in March 2005. The manufacturer voluntarily recalled the contaminated prefilled syringes. *P. fluorescens* was obtained from catheter and/or blood cultures, was confirmed by pulsed-field gel electrophoresis to be the same organisms as that in the contaminated heparin, and scanning electron microscopy confirmed the presence of *P. fluorescens* biofilms in explanted catheter segments. Many of these bloodstream infections were delayed from 84 to 421 days after exposure to the contaminated heparin solution. Delays in the signs and symptoms were related to the colonization of existing biofilm or formation of new biofilm from the contaminated solution combined with subsequent flushes of uncontaminated flush solution that disturbed the biofilm and flushed it into the bloodstream.⁴⁷

Potential Alternative Locking Solutions

Many researchers are working on alternatives to heparin-lock solutions. No alternative solutions are commercially available at the present time, and many questions remain to be answered based on the limited published research to date.

Combinations of various antibiotics and heparin, known as antibiotic lock therapy (ALT), have been suggested as a means

to treat existing CRBSIs. In 2001, the Infectious Disease Society of America released guidelines for the management of catheter-related infections.⁴⁸ The guidelines recommend use of ALT for two weeks in combination with systemic antimicrobial therapy for salvage of tunneled catheters and implanted ports when *S. aureus*, coagulase-negative staphylococci, and gram-negative bacilli caused the bacteremia. The infection should be due to intraluminal colonization of the catheter, and there should be no evidence of a tunnel or port pocket infection. This recommendation was given a category B rating, indicating moderate evidence to support its recommendation, and the quality of evidence was ranked as II, indicating evidence from one or more well-designed clinical trials without randomization.⁴⁸

Since the release of these recommendations, many other studies have examined the use of ALT for long-term catheters in oncology patients and hemodialysis catheters. A Cochrane Database review in 2003 produced a statement that ALT produced a positive overall effect but recommended that it be used cautiously because of the small number of studies.⁴⁹ A recent meta-analysis reported on seven studies using vancomycin and heparin for the ALT in 463 patients with long-term central venous catheters. This report found that ALT reduced the risk of CRBSIs in high-risk patients such as oncology patients and low-birth-weight neonates.⁵⁰ Thus, the remaining unanswered question is whether ALT should be used (1) only for therapeutic or catheter salvage procedures or (2) on a routine basis for prophylactic purposes.

In vitro studies with trisodium citrate⁵¹ and clinical studies with trisodium citrate⁵² and a citrate and taurolidine combination⁵³ have reported greater antimicrobial activity and decreased rates of CRBSIs. Taurolidine is a derivative of the amino acid taurine, with antimicrobial effects against many organisms.

In a retrospective study of CRBSIs in pediatric patients, ethanol 70% was used to lock catheters for 12 to 24 hours; 88% of the infectious episodes cleared up and did not reoccur over the 30-day study period.⁵⁴

About 15 years ago, EDTA was first suggested as an alternative catheter flushing solution. Minocycline and disodium EDTA combinations were assessed in animal, in vitro, and ex vivo studies and demonstrated effectiveness against both fresh and mature biofilms.⁵⁵⁻⁵⁷ Current research focuses on tetrasodium EDTA 40 mg per mL. Biofilms from numerous organisms were greatly reduced after exposure in catheter segments for 21 hours.⁵⁸ Another recent in vitro study comparing minocycline-EDTA, taurolidine-polyvinylpyrrolidone, and ethanol and several other antibiotic locking solutions reported that many of these solutions offer promising alternatives but require large, randomized clinical trials.⁵⁹

Although the research looks promising, many questions must be answered. Can these alternatives be true replacements for the routine heparin-lock solution? How long must the solution be locked in the catheter lumen to be effective? Will a lengthy exposure time to these solutions in the catheter lumen prohibit their use in hospitalized patients where the catheter must be used for frequent infusions? Will the required exposure time limit the use of these alternatives to those situations where the catheter is only needed once a day or every other day?

Clinical Dilemmas and Decisions

Although this review of the literature appears exhaustive, no concrete answers can be found about the use of heparin for all types of catheters in all clinical settings. Most health care professionals have a strong inclination to eliminate the heparin-lock solution, but this decision requires careful assessment of many factors. Although the available literature can be confusing, it appears that some form of anticoagulation is needed for central venous catheters. The chosen locking solution should keep the catheter lumen patent, reduce the incidence of CRBSI, produce minimal or no side effects, and be cost effective and easy to use. In Europe and Asia, there are alternatives to heparin-lock solution, but none are currently available in the United States.

While practitioners await the clinical evidence to reveal the most effective alternative(s) for heparin-lock solutions and for clearance by the FDA, they must make careful decisions about catheter-lock solutions. Rapid elimination of heparin-lock solutions may not be the best alternative. These decisions must be based on an assessment of many factors in each facility. Is the facility currently using one of the technologies with instructions for heparin elimination? What are the documented outcomes with the use of the catheter or device? What is the frequency of catheter lumen occlusion? What quantity of thrombolytic agents and clotting procedures are required in the patient population? What is the rate of CRBSI in the facility? Has this changed with a recent product change? What are the risk factors presented by the various patients? What are the activity levels of patients with central venous catheters? Have there been complications directly attributed to heparin-lock use? What evidence does the facility have that the complication was related to the use of heparin?

Patient safety is foremost in all health care practice settings today. How will elimination of all heparin-lock solutions affect patient safety? Does the risk of thrombotic catheter occlusion outweigh the risk of HIT in patients? What other interventions can be used to decrease the risk of CRBSI? These and many other questions should be addressed with a collaborative, multidisciplinary approach to determine the most appropriate catheter-locking solution for a facility. Heparin remains the recommended locking solution for intermittent central venous catheters.¹ Hopefully, there will be a point in the near future when these concerns are adequately answered with sound scientific evidence.

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Lynn Hadaway, MEd, RNC, CRNI, has more than 30 years experience as an IV nurse, educator, and consultant. She holds a master's degree in education and certification in professional staff development and infusion nursing. She has published extensively on infusion topics in numerous journals and textbooks.

Received 10/25/2006; accepted 11/1/2006.