Best Practice Guidelines

in the Care and Maintenance of Pediatric Central Venous Catheters

SECOND EDITION

Pediatric Special Interest Group™

Created by
AVA Pediatric Special Interest Group

Association for Vascular Access

Best Practice Guidelines
in the Care and Maintenance of
Pediatric Central Venous Catheters

SECOND EDITION

Created By
AVA Pediatric Special Interest Group

Contributors

Authors

Darcy Doellman MSN, RN, CRNI, VA-BC™
Joan K. Buckner, MA, RN, CIC
J. Hudson Garrett Jr., PhD, MSN, MPN, FNP-BC, CSRN, PLNC, VA-BC™, FACDONA
J. Patricia Catudal RN, BS, VA -BC™
Anne Marie Frey, BSN, RN, CRNI, VA-BC™
Paula Lamagna RN, BSN, VA-BC™, CPUI
Dana A. Runde RN, CRNI
Gregory J. Schears, MD
Melissa Whitehead RN, BSN, CPN, CRNI, VA-BC™

Reviewers

Deborah Campbell MSN, RN-BC, CPHQ
Mary Beth Hovda Davis RN, MSN, VA-BC™
Leslie Gosey MS, RN, VA-BC
Cheryl Kelley RN, BSN, VA-BC™
Stephanie Pitts, MSN, RN, CPN, VA-BC™
Anita Piano, MSN, RN, VA-BC™
Elizabeth Sharpe, DNP, ARNP, NNP-BC, VA-BC™
Kimberly A Sutters PhD, RN, VA-BC™

These guidelines are in honor of Dr Janet Pettit,
our esteemed colleague whose memory lives on in neonatal and pediatric vascular access.

This publication is proudly endorsed by:

Society of Pediatric Nurses

Association of Pediatric Hematology/Oncology Nurses (APHON)

ISBN: 978-0-9966456-1-4

Printed in the United States of America

Preface

PediSIG is the pediatric special interest group of the Association for Vascular Access (AVA). This multidisciplinary group of practitioners is dedicated to best practice in the science of vascular access for children and infants. Membership includes clinicians, educators, and manufacturers. The mission of the pediatric special interest group is to build a community for professional collaboration and evidence based practice for pediatric vascular access with a vision to be the voice of vascular access in pediatrics. Visit www.avainfo.org/PEDISIG for more information.

The Association for Vascular Access (AVA) is an association of healthcare professionals founded in 1985 to promote the emerging vascular access specialty. Today, its multidisciplinary membership advances research, professional and public education to shape practice and enhance patient outcomes, and partners with the device manufacturing community to bring about evidence based innovations in vascular access. The official web site for AVA is www.avainfo.org.

These Best Practice Guidelines in the Care and Maintenance of Pediatric Central Venous Catheters are based upon general conclusions of healthcare professionals who, in developing such Guidelines, have balanced potential benefits to be derived from a particular mode of medical therapy against certain risks inherent in such therapy. The professional judgment of the attending healthcare professional, however, is the primary component of quality medical care. Because guidelines cannot account for every variation and circumstances, the practitioner must always exercise professional judgment in their application. These Guidelines are intended to supplement, but not replace, professional training and judgment. Neither the Association for Vascular Access nor the Pediatric Vascular Access Network are responsible for any adverse effects resulting directly or indirectly from the use of the Guidelines or from the reader's misunderstanding of the Guidelines.

Contents

Pediatric™
Special Interest Group

Author Disclosures

Darcy Doellman: Speaker's bureau for Genentech and Hospira; Consultant to Arrow International; member of INS standards of practice committee

J. Hudson Garrett Jr.: Employed by PDI; Board of Directors of the Vascular Access Certification Corporation (VACC)

Paula Lamagna: Clinical consultant for Medcomp

Dana A. Runde: Educational consultant for Adecco Medial Services for which I have provided contracted education in-services for CareFusion; Member of the CareFusion speakers bureau.

Gregory J. Schears: Paid consultant relative to product development, product problem solving, modeling and general research and development. Companies include B Braun, Beckton Dickenson, CR Bard, Christie Medical Holdings, Insightra, Interrad, IV Watch and Teleflex.

Introduction

Central venous catheters (CVCs) are integral to infants and children requiring intermittent or continuous infusion therapy. In many health care settings, young patients require a reliable CVC for safe delivery of infusion therapy.[1-4] In the past decade, smaller and diverse catheter sizes have emerged to support hemodynamic monitoring and infusion of medications and solutions. Choosing the appropriate device, along with providing meticulous care by competent personnel, is essential for optimizing patient outcomes with a CVC.[5-7] These guidelines specifically address the unique needs of the pediatric patient and result from analysis by a working group of pediatric clinicians, who evaluated the published evidence and developed successful strategies for CVC care and management.

CVC Overview

A CVC is defined as a catheter with the distal tip terminating in the lower third of the superior vena cava (SVC) or cavoatrial junction,[8-11] or in the inferior vena cava (IVC) above the diaphragm and below the right atrium for lower extremity insertions.[12-14] A catheter tip placement in the SVC or IVC provides optimal hemodilution of infusates and prevents complications that are associated with catheter tips terminating in smaller veins outside the SVC or IVC.[13,15] High-risk infusates (eg, vesicants, irritants, chemotherapy, and hyperosmolar solutions > 600 mOsm/L) can be administered safely without vessel irritation or damage if the CVC is positioned appropriately in the IVC or distal SVC.[16,17] Radiographic imaging is required to confirm tip placement of a CVC prior to use of the device.[15,18] Navigational and tip location devices are being used for catheter tip confirmation in the adult population and are likely to increase in use for pediatric patients as research evolves. Ultrasound, echocardiogram, and contrast injections can be used to confirm ambiguous CVC tip location placements.[12,13,19]

Advantages of the CVC over the peripheral intravenous cannula (IV) in the pediatric patient have been validated.[16,17] Often, more than one venipuncture attempt is necessary for successful IV placement.[20,21] Central venous catheters promote vein preservation by avoiding repeated attempts and use of multiple peripheral veins and avoid the pain and associated anxiety of repeated venipunctures for young patients.[22]

Assessing patients for the appropriate device upon admission or early in their hospital course leads to improved patient outcomes and is cost-effective.[17,23] Longer survival of chronically ill children, or prolonged hospitalizations, often leads to repeated need for venous access. In a study by Yang et al,[24] an increase in procedural complexity and complications in pediatric patients was found with successive peripherally inserted central catheter (PICC) insertions. One device may not meet the vascular access needs of every pediatric patient, necessitating the use of several devices throughout therapy. Institutional protocols may limit the number of attempts by a clinician for both IV and CVC insertion, with the goal of preserving and minimizing vessel trauma.[25] Imaging technology enhances access when suitable veins are not easily palpated or visualized and significantly improves the success rate and safety of CVC insertions.[12,13,19,26]

Types of CVCs

CVCs used in the pediatric population include the PICC, nontunneled CVC, tunneled CVC, implanted port, hemodialysis catheter, and apheresis catheter. Appropriate CVC selection should be based on diagnosis, previous history of vascular access devices, anatomical variances, and type and length of therapy, along with the patient and/or caregiver's preference.[11, 25] CVCs for long-term use are commonly inserted in the chest or upper extremities.[27]

CVCs are available in a variety of French sizes, lengths, number of lumens, catheter compositions, and hub designs. Determination of the number of lumens the patient requires is based on number of infusates required, compatibility of medications, blood sampling, and vessel size.[17, 23] Matching the most appropriate catheter size to the patient is crucial.[28] In the clinical setting, the catheter-to-vessel ratio used is 50% and this is based on expert opinion, not clinical evidence. The vein is measured by ultrasound and without a tourniquet.

Catheter material includes polyurethane or silicone, and CVCs can be open-ended or valved. The valved design may be internal, or incorporated into the distal (near the tip) or proximal (near the catheter hub) end in PICCs, tunneled CVCs, and ports. Power injectable devices are now available in CVCs as small as a 3F catheter; advantages include avoiding an IV insertion for a pressure injectable contrast study.[29]

Antibiotic-impregnated catheters have surfaced in the pediatric population as a measure of providing additional benefits to minimize catheter infections.[11,30,31] Catheter coatings and integrated catheter materials include both antimicrobial and antithrombogenic properties. In addition, polymers are being integrated into catheter materials to prevent the adherence of blood components to the device.

Peripherally Inserted Central Catheter

A peripherally inserted central catheter (PICC) is a catheter that is inserted in a peripheral vein and threaded to the SVC or IVC.[8-10] PICCs are less invasive and are economically feasible compared with surgically placed CVCs.[32] The development of smaller introducers, wires, and needles for catheter insertion; the use of ultrasonic imaging guidance; and the development of pediatric vascular access teams has resulted in the growing use of PICCs in infants and children.[26]

PICCs are indicated for therapies of 5 to 7 days or more; infusion of vesicants, irritants, or hyperosmolar solutions; patients with poor peripheral access; blood sampling; and patient and/or caregiver preference.[17,23,33] In home care, PICCs are popular because of their reliability and ease of care by the caregiver or clinician.[1,2]

For patients with chronic renal failure, alternative access options should be discussed with the primary care provider, as PICCs may be contraindicated in this patient population.[11,34] PICCs cannot always be threaded to the SVC or IVC because of venospasm, vessel tortuosity, thrombosis, or the presence of venous

valves. For failed attempts, threading difficulties, or complex venous access patients, an interventional radiology consult may be necessary.[11]

Pediatric patients typically have fewer veins to choose from than adults because of their smaller body size. Guidance imaging may be helpful for locating appropriate veins to access.[13,25] Common sites for PICC insertion include the arm and the lower extremity if the patient is nonmobile. The vein of choice in the upper arm is the basilic vein because of its larger diameter and fewer valves.[17,25,26] The cephalic and brachial veins in the upper arm are also an option but have a higher risk of insertion-related complications. The cephalic vein can be tortuous and lead to catheter tip malposition. The brachial veins are in close proximity to the artery and median nerve.[25]

Infants have the advantage of additional sites for PICCs such as the scalp, internal jugular vein, and lower extremities.[35-37] Scalp veins can be used for insertions in children up to 18 months of age.[25] For lower-extremity PICCs, the saphenous or popliteal vein can be used.[12-14] Inserting a PICC in young patients can be especially difficult because of the small vessels, limited vessel options, and possible venous damage from previous venipunctures.[37] A thorough assessment of the vein(s) by using ultrasound is recommended for choosing the appropriate vein, predicting vessel patency, and determining the most appropriate catheter size.[12, 28]

PICCs can eliminate potential life-threatening insertion complications such as pneumothorax and hemathorax.[38] As compared with insertion attempts in the chest or neck, peripheral veins can easily be compressed to control bleeding in patients with a bleeding disorder or if an artery is inadvertently punctured during insertion.[39]

PICCs can dwell for months to years in patients requiring extended therapies; however, a tunneled CVC or port may be more appropriate.[11] The risk of thrombosis can increase with long-term placement of PICCs in the pediatric oncology patient.[11,35,40] Over time, the child's growth can render the catheter tip inappropriate. Use of a PICC has many advantages because of the relative ease of caring for this type of device.[17]

Nontunneled CVC

A nontunneled or acute-care CVC is designed for short-term therapy (< 7 days) in the critically ill patient or following failed attempts at placement of other vascular access devices.[41] This type of CVC can be single or multilumen and is inserted at the bedside or in the operating room into the internal jugular, subclavian, or femoral veins.[42] Insertion of the CVC in the subclavian vein in children < 1 year of age is more difficult because of a significant superior arch.[18]

Although there is evidence of femoral CVCs presenting a higher risk for infection in the adult population,[43] studies in pediatric patients have shown lower rates of infection compared with catheters inserted into jugular veins. The femoral site for nontunneled CVCs is commonly used in the critical care

setting because of easy access during emergent situations.[41,42] As a result of the high risk of central line–associated bloodstream infection (CLABSI) with nontunneled CVCs and contamination risks, there has been a growing trend to insert PICCs in nonemergent patients in critical care units.

Tunneled CVC

A tunneled CVC is indicated for patients requiring frequent or long-term venous access, such as those requiring chemotherapy, total parenteral nutrition (TPN), factor therapy, and repeated blood sampling.[11] Patients with chronic diseases may retain this catheter for years.[44] CLABSI rates are lower with tunneled catheters than with nontunneled CVCs.[45]

Tunneled CVCs require a surgical procedure for insertion and removal.[41] Anesthesia and the invasiveness of the procedure are disadvantages. Infusion therapy through tunneled CVCs are pain free and may be advantageous in children who have limited coping abilities or low pain thresholds as opposed to accessing an implanted port.[22]

A Dacron cuff, present on the catheter below the skin surface, becomes incorporated in the tract by scar tissue. Adhesions form a seal around the cuff, which helps stabilize the catheter and reduces the risk of infection by preventing entry of microorganisms along the subcutaneous tract.[11] Some tunneled CVCs also have a secondary antimicrobial cuff. Tunneled catheters have larger lumens than PICCs and can deliver a higher volume of fluid.[35]

Tunneled CVCs are inserted into a central vein, commonly via the subclavian or internal jugular veins, are tunneled under the skin through subcutaneous tissue, and typically exit at the chest area.[44] Tunneled CVCs may be inserted in nontraditional locations such as the scapular region on the back, depending on the activity level of the young patient or the veins available for cannulation.[44] Inserting a tunneled CVC in a pediatric patient requires clinical expertise in order to minimize complications.[11]

Implanted Port

The use of implanted ports has grown tremendously since their introduction in the early 1980s as an alternative to tunneled CVCs and is the preferred device for frequent or long-term access. Ports provide a convenient and comfortable way for children to receive long-term therapy.[46]

Port designs have evolved to include smaller, lower profile devices that allow placement in the arm, chest, abdomen, or thigh. Most ports are inserted in the chest area for ease of access.[47] The port body is composed of a small metal or plastic reservoir that contains a silicone rubber septum, which is implanted under the skin, allowing the patient freedom from any external lumens or connectors.[46] Insertion of the port is commonly achieved by cannulating the external jugular, internal jugular, or cephalic veins. Placement of

the port away from the incision site minimizes skin erosion.[47] One of the primary advantages of a port is the lower risk of infection compared with that of other CVCs.[46] Complications unique to ports are damage to the reservoir and skin breakdown over the port septum.[47]

Solutions and medications are administered intermittently by inserting a small non-coring needle through the skin, which pierces the silicone septum and goes into the reservoir.[48] When the needle is withdrawn, the silicone septum reseals. For patient comfort, the use of topical anesthetics prior to accessing the port should be considered, although the possibility of pain remains because of the puncture of superficial and deep layers of skin.[22] Distraction and relaxation may also be beneficial in reducing anxiety and pain.[49] An external dressing is not required if the port is not accessed, which allows for more independence. The port must be accessed monthly and flushed to decrease the risk of occlusion.[50]

Hemodialysis Catheter

Hemodialysis catheters are large-bore, dual-lumen catheters used in patients requiring hemodialysis. These catheters also serve as a bridge for patients awaiting a renal transplant or transitioning to peritoneal dialysis.[51] Hemodialysis catheters can be for temporary or long-term use.

Cuffed hemodialysis catheters are commonly tunneled via the internal jugular vein, with the tip terminating in the right atrium.[34] Avoidance of the subclavian vein is necessary because of the risk of subclavian stenosis, which occurs in up to 80% of pediatric patients. Femoral access can be used when upper-anatomy venous access is not an option.[34] According to the National Kidney Foundation's Kidney Disease Outcomes and Quality Initiative (KDOQI) guidelines, 2 single lumen catheters may improve performance over a dual-lumen catheter in the appropriately sized patients.[34] Hemodialysis catheters have proven reliability and low infection rates and are appropriate for patients weighing more than 15 kg who are awaiting transplant or permanent device placement, or who have changes in treatment modality.[52] Alternative options include arteriovenous fistulas (AVFs) and arteriovenous grafts (AVGs), although these are more common in adults because of the challenges in creating them in young patients. Maturation of fistulas/grafts in pediatric patients can take up to 4 to 6 months, making routine permanent access placement impractical in many situations. Both AVFs and AVGs are recommended in all patients because of the lower infection, lower failure, and lower central vessel thrombosis rates than occur in CVCs. The KDOQI guidelines recommend a 50% AVF rate in all hemodialysis patients, including pediatric patients.[51]

Apheresis Catheter

Apheresis catheters are large-bore, dual- or triple-lumen catheters whose tips are advanced to the lower third of the SVC. Short-term catheters are inserted in the internal jugular or subclavian vein, whereas

long-term catheters are surgically placed and tunneled.[53] Apheresis procedures can also be initiated via 2 large-bore IVs when central access is not available.

Complications

Although catheters are an indispensable component of infusion therapy, they are associated with a variety of complications that require prompt attention to prevent serious sequelae.[52] A study of 279 pediatric patients (age 7 days to 21 years) with a PICC demonstrated a complication rate of 27%.[39] The type and frequency of complications may be influenced by the smaller vessel size inherent in children and the length of therapy.[4] Occlusion, migration, thrombosis, and infection are the most commonly occurring serious complications associated with pediatric CVCs.[25,39,44] Complications can have enormous human and economic costs.[11]

Occlusion

The definition of a functioning CVC is a catheter that flushes easily, infuses without difficulty, and has a free-flowing blood return.[38,54,55] The quality of flushing and the ability to aspirate a brisk blood return depends on the size of the catheter lumen. With the smaller catheter sizes, lower infusion rates, and significantly smaller lumen volumes in pediatric patients, the risk of occlusion is higher.[38,56]

A dysfunctional CVC can be defined as a complete occlusion, a partial occlusion, or a sluggish catheter. A complete occlusion is the inability to infuse or aspirate blood from a CVC.[55,57,58] A partial or withdrawal occlusion is the ability to infuse but not aspirate from a catheter.[55,56] A sluggish CVC is difficult to flush and has a slow or intermittent blood return.[57]

Occlusion is a common complication and occurs in up to 36% of CVCs within 2 years of placement.[27] Although occlusions are not without clinical significance, published occlusion rates vary widely.[38,58] The discrepancy may be related to events being underreported, lack of standardized methods for defining and quantifying occlusion rates, and differentiating between the types of occlusion.[59] Additional factors may be the patient's diagnosis, the severity of illness, the frequency of catheter manipulation, and differences in catheter type, size, and care.[58]

Occluded catheters may be responsible for interruptions in therapy, delays in discharge, or additional procedures such as catheter replacement.[57,58] Occlusions can be acute, gradual, or intermittent.[27] Management and resolution of occluded catheters can be time-intensive and have a fiducial impact on the patient and facility.

Catheter occlusions are categorized as thrombotic or nonthrombotic, and an accurate diagnosis of the type of occlusion is essential for appropriate treatment.[55] A nonthrombotic or mechanical occlusion can

be related to a kinked or clamped catheter, tubing, or add-on device; needleless connector malfunction; port access needle dislodgement; catheter tip malposition; or precipitation of infusates.[55,57] Precipitation of infusates may involve parenteral nutrition constituents and/or solutions with alterations in pH.[55,57,60] Although uncommon, pinch-off syndrome occurs when an implanted port or tunneled catheter is compressed between the clavicle and first rib; this occurs in approximately 1% of patients.[61] However, up to 40% of pinch-off syndrome results in fragmentation and subsequent embolization of the catheter tip into the central venous system.[55]

A thrombotic occlusion is the presence of a thrombus in or around the catheter or vessel wall that may impede or disrupt flow through the catheter.[55,57] Fibrin attachment occurs because of the presence of the catheter, creating vessel irritation that may be provoked by a traumatic insertion, large needle size, rapid threading of the catheter, cephalic vein insertion, left-sided insertion, catheter tip malposition, or inadequate catheter-to-vessel ratio.[28,38,62] The risk of catheter-related thrombosis, a potentially serious complication, is increased with thrombotic occlusions.[63]

Fibrin can also develop intraluminally with inadequate or improper flushing techniques or increased intrathoracic pressure.[55] Meticulous flushing and care is vital to decrease the risk of catheter occlusion.[2,50,58,63] In a multilumen CVC, when one or more of the lumens is occluded, leaving it untreated is not recommended, even though another lumen remains functional, as prolonged fibrin formation is a risk factor for CLABSI.[64] Implanted ports with an occlusion do not resolve as readily with thrombolytic therapy as external catheters do.[55]

Thrombotic occlusions are responsible for most catheter occlusions and include intraluminal thrombus, fibrin tail, fibrin sheath, and mural sheath.[62] An intraluminal thrombus is the accumulation of fibrin and blood components that may result in a complete or partial occlusion, or sluggish flow. This type of occlusion occurs in 5%-25% of CVCs.[27]

A mural thrombus forms on the vessel wall and is initiated by irritation of the catheter or infusate.[27] Although a thrombus may adhere to the catheter and bind with the vessel fibrin, it can partially occlude the vein and progress to a thrombosis.[55] A fibrin sheath may form around a catheter at the insertion site or near the catheter tip within 2 weeks after insertion and occurs in up to 47% of patients with CVCs.[55] The fibrin sheath may impede the ability to aspirate a catheter or may lead to retrograde flow of the infusate along the vessel and into the subcutaneous tissue if there is a gap along the sheath.[65] Depending on the type of infusate, a fibrin sheath may lead to an infiltration or extravasation.[66] Fibrin and blood cells can develop at the tip of the catheter, which is also known as a fibrin tail.[65] Flushing or infusing fluid into the catheter displaces the tail away from the catheter tip, allowing the catheter to flush or infuse easily, but the fibrin tail closes over the tip of the catheter and obstructs flow during aspiration.[57] A fibrin tail can become larger as more cells and fibrin are deposited and may eventually occlude the catheter tip. The presence of fibrin on indwelling catheters can be a medium for pathogen growth.[38]

Symptoms

A dysfunctional catheter occurs when there is an inability to freely flush or obtain a brisk blood aspirate. Common clinical symptoms include visible clots or precipitate in the catheter, leaking at the access site, or pain.[38] In a pediatric catheter occlusion study of 310 patients, a partial occlusion was defined as the inability to withdraw 3 mL of blood from the central line in patients > 10 kg and 1 mL in patients < 10 kg.[56] There may be subtle signs of an impending occlusion such as a change in the ability to flush or aspirate, or frequent pump occlusion alarms.[57] Symptoms of pinch-off syndrome include intermittent occlusions that can be relieved by the patient changing position (eg, raising the arm, laying supine). A CVC that exhibits any of these symptoms requires further assessment and possible treatment.[61]

Treatment

Early recognition and intervention will increase the likelihood of restoring catheter patency, thus decreasing the risk of more serious complications, or the need for catheter replacement.[56,58] Treating occlusions is time effective and less costly than replacing a catheter. If a CVC becomes dysfunctional, further assessment of the catheter is warranted to rule out mechanical factors.[57] Mechanical factors can be assessed through visualization of the infusion tubing or catheter for kinks, closed clamps, or change in the external length of the catheter. Removal of any add-on devices (extension piece or needleless connector) is recommended, along with an attempt to flush the catheter at the hub. If a catheter tip malposition is suspected, repositioning the extremity and attempting to aspirate or flush the CVC may resolve the problem.[38] Catheter replacement is recommended for pinch-off syndrome as a measure to prevent catheter fracture or embolization.[61]

If a precipitation is suspected, it is important to obtain a list of medication recently infused through the CVC.[57] Treatment for drug precipitation is to use the appropriate clearing agent, such as ethanol, hydrochloric acid, or sodium bicarbonate (see Table 1).[27,38]

Table 1. Occlusions Caused by Drug Precipitations and Their Treatment

Occlusions Caused by Drug Precipitates	Clearing Agents
Lipid occlusion	70% Ethanol[55,57]
Drugs with a low pH	Hydrochloric acid[55,57]
Drugs with a high pH	Sodium bicarbonate[55,57]
Calcium-phosphate imbalance	Hydrochloric acid[55,57]

Most catheter occlusions are thrombotic and can be treated after ruling out mechanical factors.[27] If catheter patency is not established after thrombolytic therapy, radiographic imaging of the CVC or a contrast study to evaluate for catheter tip malposition, pinch-off syndrome, extensive fibrin formation, or thrombosis should be considered.[38,57] If a thrombotic occlusion is suspected, the treatment is timely administration of alteplase, a thrombolytic that is the only Food and Drug Administration (FDA)-approved agent for the treatment of dysfunctional catheters.[63] Alteplase is a tissue plasminogen activator

that converts plasminogen to plasmin, resulting in local fibrinolysis.[27] The dose of the thrombolytic is based on patient weight. For patients ≥ 30 kg, the dose is 2 mg/2 mL. For patients < 30 kg, the dose is 110% of the catheter priming volume.[56] The priming volume of the CVC depends on catheter size and length, taking into consideration whether the catheter was trimmed. The priming volume of the CVC is not always known and may be located on the catheter lumen, insertion tray, or webpage of the catheter manufacturer.[56,57]

The dwell time of alteplase is 30 minutes and up to 2 hours, with a repeat dose if necessary after 2 hours, for a total dwell time of up to 4 hours.[55,56] The catheter is considered patent upon confirmation of a brisk blood aspirate. Efforts should be made to withdraw the alteplase and discard if possible. In a Cathflo Activase Pediatric Study, 310 patients were treated with alteplase. Catheter function restoration rates of 2 doses and up to a 2-hour dwell time for each dose were 83% among all patients and 80% among the cohort of patients younger than 2 years.[56] Despite several studies having reported safety and efficacy in the pediatric patient, clinical variance occurs with dosage and dwell time of alteplase.[55,56,58]

For frequent or ongoing episodes of catheter occlusion, or if the CVC remains dysfunctional after 2 doses of a thrombolytic, radiographic evaluation of the catheter tip should be considered.[57] The technique for administering the thrombolytic depends on the type of thrombotic occlusion. For a partial occlusion or sluggish catheter, the agent can be instilled with a single syringe attached to the hub of the catheter. With complete occlusions, instillation is best accomplished by using negative pressure. A vacuum can be created with a 3-way stopcock or a 10-mL syringe. On the basis of clinical practice, a 3-way stopcock is preferred in 3F CVCs or smaller because of ease of use and small dose volumes.[57] Flushing against resistance is not recommended because of the risk of catheter rupture.

Preventive Strategies

A primary goal is to avoid catheter occlusion.[57,58,63] The ability to prevent occlusion or salvage a dysfunctional CVC is critical in minimizing delays in therapies and avoiding catheter replacement.[27,56] Unnecessary CVC replacements decreases the number of sites available for future venous access and subjects the patient to additional painful, invasive procedures.

Preventive strategies for intraluminal catheter occlusion include assessing for compatibilities of co-infusing medications and IV solutions, standardized flushing protocols, and having knowledge of the type of clamping sequence for the needleless connector that is in use.[50,57,59,63] Minimization of blood reflux into the catheter can be achieved by promptly responding to alarming infusion pumps and using Luer-lock add-on devices to prevent inadvertent disconnections. Antithrombotic properties have shown benefit in the reduction of catheter occlusion.[67] Blood reflux can also be caused by patient conditions such as increased intrathoracic pressure.

For smaller gauge catheters, an adequate hourly infusion rate of at least 1 to 2 mL minimizes the risk of occlusion.[36,68] Furthermore, the risk of thrombotic catheter occlusion in neonates or small-gauge catheters may be decreased with the prophylactic use of heparin in an infusate. A systematic review analyzing the cumulative results of 2 randomized controlled trials of 267 neonates concluded that patients receiving

heparin were less likely to experience catheter occlusion than were placebo-treated patients (relative risk, 0.28; 95% CI, 0.15-5.3).[58] In a study of 200 pediatric patients from newborn to 16 years of age, patients were randomized to receive either heparin-bonded catheters (HBCs) or standard uncoated catheters. After the first week of catheter placement, the risk of catheter occlusion was lower in the HBC group (relative risk, 0.22; 95% CI, 0.07-0.72).[58] In contrast, in a study of 87 patients less than 1 year of age with congenital heart disease, 44.7% of the patients randomized to the HBC arm experienced a thrombotic event, compared with 42.5% of patients in the standard catheter group.[69] Although current data support the use of heparin as an infusate for the prevention of catheter occlusions in neonatal patients, data regarding the efficacy of the prophylactic use of HBCs in this population are equivocal.[62,63] Considerations for selecting an HBC include cost and ongoing surveillance of patient outcomes.

Risk factors for catheter occlusion include suboptimal catheter tip placement, pump failure, calcium-phosphate imbalance of TPN, lipid residue, fungal infection, and inadequate education of staff caring for the CVCs.[38,62,68] Prior to administering an infusate or solution, the CVC should be assessed for patency. This includes flushing and aspirating the lumen of the CVC for a brisk blood return for 3F or larger CVCs.[54,57] If a thrombotic catheter occlusion is confirmed, prompt treatment with a thrombolytic is recommended. Table 2 shows common types of thrombotic occlusions.

Table 2. Types of Thrombotic Occlusions

Types of Thrombotic Occlusions	Definition	Types of Dysfunctional Central Venous Catheters
Intraluminal thrombus	Fibrin forms within the lumen	Partial occlusion, complete occlusion, or sluggish lumen
Fibrin tail	Fibrin extends past the catheter tip and acts as a 1-way valve	Partial occlusion
Fibrin sheath	Fibrin forms and encases the catheter tip	Partial occlusion or complete occlusion
Mural thrombus	Fibrin from vessel wall injury binds to fibrin that has accumulated around external catheter surface	Complete occlusion

Catheter-Related Vessel Thrombosis

Thrombosis is the formation of fibrin along the internal wall of the vein and may partially or totally occlude the vessel.[4,18,24,70] Thrombosis is a serious complication in pediatric patients and the presence of a catheter is a primary risk factor.[4,71-73] Fibrin production is stimulated by vessel injury or contact between the vessel wall and catheter that occurs with CVC insertion, catheter tip malposition, vessel irritation,

trauma, or underlying hypercoagulability.[71,73] The subendothelial layer of the vein can be exposed with trauma or damage, leading to the activation of the coagulation cascade, which may result in a thrombosis. Thrombosis can cause local or systemic complications and may begin as early as 24 hours after CVC insertion.[18,27,38] Depending on the type of vascular access device, thrombosis rates can vary; substantial variabilities occur in identifying, treating, and preventing thrombosis as well.[27,71]

Etiology

During insertion of a CVC, the catheter surface becomes covered with fibrin, platelets, and plasma proteins, triggering a tail or sheath that leads to the formation of a thrombosis.[71] Thrombosis can cause partial or total obliteration of major vessels and can negatively affect future vascular access options.[38,70,74] Virchow's triad describes 3 broad categories of factors that may contribute to thrombosis formation.[75] The triad consists of the following:

- Changes in normal blood flow (disproportionate ratio of the catheter diameter to the vessel size, use of the cephalic vein, immobility, dehydration)
- Injuries to the vascular endothelium (catheter tip malposition, CVC dwell time > 2 weeks, catheter movement within the vessel, left-sided insertion, traumatic insertion, presence of phlebitis)
- Alteration in coagulability (hypercoagulability, malignancy, sepsis, history of previous thrombosis, renal disease, sickle cell disease, males with hemophilia, trauma, congenital heart disease)

Infants with congenital heart defects and asphyxia are at higher risk for thrombosis because of hemostatic imbalance and small-caliber vessel size.[3,72,76] One study showed that 31% of pediatric patients with single ventricle physiology who underwent palliative corrective surgery developed a thrombosis.[76] The presence of thrombus in central veins, including the femoral vein, presents challenges for the placement of future CVCs and cardiac catheterization.[76] Clotting may be activated by an infection and the presence of fibrin on the catheter, as supported by evidence of a correlation between catheter-related thrombosis and CLABSI.[72]

The incidence of thrombosis may be increased by features of a CVC such as its type, size, and material; endothelial damage during catheter insertion; turbulent flow; previous history of CVC occlusions; and long-term administration of TPN.[72] In a prospective randomized controlled study of 332 adult patients that examined the significance of a PICC with and without a reverse taper, thrombosis rates were not higher in the reverse taper group.[77] PICCs have a higher rate of thrombosis in pediatric oncology patients who are hypercoagulable.[73]

With incidences of venous thrombosis in children, post thrombotic syndrome can occur. It is defined as chronic venous insufficiency following deep vein thrombosis.[78] Risk factors include recurrent ipsilateral thrombosis and extension of the initial thrombosis. Symptoms are typically mild and include the presence of collateral veins, swelling, and pain.[78] In 13% of pediatric patients with post thrombotic syndrome, moderate symptoms occur such as collateral veins, pigmentation of the skin, and pain or heaviness in

the affected leg while ambulating.[79] Persistent vessel occlusion can occur in patients with a history of catheter-related thrombosis.[27,71,75]

Pulmonary embolus is a known complication of thrombosis. The incidence varies significantly in the pediatric population and is a primary cause of morbidity.[76] Clinical symptoms of pulmonary embolus include pleuritic pain, dyspnea, tachypnea, and cyanosis.[80] Pulmonary embolus may likely go undiagnosed in young patients because of their inability to verbalize symptoms. Pulmonary embolus should be considered in the event of unexpected respiratory symptoms in a patient with a CVC.[80]

Symptoms

In pediatric patients, thrombosis may be undiagnosed because of the variation in clinical presentation. The patient may also be asymptomatic.[4,72,75] Newborns have the highest rate of symptomatic thrombosis compared with pediatric patients.[72] Indications of symptomatic thrombosis include the inability to aspirate or infuse through the CVC, leaking at the insertion site, erythema, pain, numbness, swelling above or below the catheter insertion site, limb discoloration, and pulmonary embolus.[4,38,75] Thrombosis often develops over time and collateral circulation may mask overt symptoms.[4,71]

The type of diagnostic study used depends on the location of the presumed thrombosis.[72,75,81] Methods include ultrasound imaging for diagnosing an upper or lower extremity thrombosis and a venogram for intrathoracic vessels. A venogram is the common diagnostic study for detecting vessel occlusion and identifying collateral veins.[25] However, the procedure is invasive, costly, and may be difficult to interpret.[27] Less common methods include computed tomography venography and magnetic resonance venography.[27]

Treatment

Treatment options for catheter-related thrombosis range from catheter removal to systemic anticoagulant therapy to no treatment and are generally based on the location of the thrombus and the patient's condition.[18,72,75] Recent evidence-based treatment guidelines for thrombosis include the use of low-molecular-weight heparin (LMWH) or unfractionated heparin IV and allowing the CVC to dwell if it is functioning.[4,24]

According to the American College of Chest Physicians consensus conference, CVCs should be removed in patients with a confirmed thrombosis after 3 to 5 days of therapeutic anticoagulation.[82] If the CVC cannot be removed because of critical therapies, treatment with either LMWH or warfarin prophylactically is done until the CVC is removed.[24,27] The goal of treatment is to limit the extension of the thrombus and to prevent pulmonary embolus.[4] Treatment may last up to 3 months and consultation with a hematologist is recommended for patient-specific treatment.[72,81]

Coated or impregnated catheters with antimicrobial or antibiotic agents may play a role in reducing microbial migration, catheter-associated thrombosis, and CLABSI.[11,83] The long-term impact on health and quality of life is unknown; further clinical trials are needed to determine the optimal treatment and screening for thrombosis.

Preventive Strategies

Ongoing assessment of the need for the CVC and prompt removal upon completion of therapy is a primary strategy for reducing the risk of thrombosis, as the mere presence of a catheter is the highest risk factor for thrombosis in young patients.[38,72] Pre procedural assessment for CVC insertion is important in identifying these risk factors. The assessment should include a review of underlying medical conditions, the prescribed length and type of therapy, previous history of thrombosis, and appropriate vessel selection; the smallest catheter that meets the vascular access needs should then be chosen.[58] For PICC insertions, ultrasound can be used for identifying preferred vessels, location, patency, and size. Use of small-gauge needles for insertion may also decrease vessel trauma.[17,26] For high-risk and chronic patient populations, screening for thrombosis may be advantageous, as it is unclear whether recannulization will occur in the involved vessel.[11]

Preventive measures for minimizing catheter dysfunction may also prevent thrombosis; these measures include routine flushing of CVCs, catheter securement, avoidance of a restrictive wrap around the affected extremity, appropriate tip placement, aseptic technique, and daily assessment of the CVC site and surrounding areas.[17]

Phlebitis

Phlebitis is defined as inflammation of the vessel wall and is a known complication of PICCs.[25] The inside layer of the vessel can be damaged by irritation, catheter presence, and catheter motion. Types of phlebitis include chemical phlebitis, bacterial phlebitis, and mechanical phlebitis.[38]

Etiology

Chemical phlebitis is caused by the infusion of vesicants, irritants, or hyperosmolar solutions in a noncentral vein, leading to vessel irritation or damage.[84] Solutions with an osmolarity greater than 600 mOsm/L are deemed high risk and central access should be considered.[54,85] Chemical phlebitis occurs most commonly with peripheral intravenous cannulas (IVs), midlines, and malpositioned CVCs with repeated infusions of offending agents.[85,86] Bacterial phlebitis can be related to any break in aseptic technique during insertion or maintenance procedures of the CVC.

Mechanical phlebitis is more common with PICCs than other CVCs and is an inflammatory reaction of the vessel wall due to the presence of the catheter, inadequate catheter-to-vessel ratio, repeated catheter manipulations during insertion, threading difficulties, tortuous vessels, or catheter tip malposition.[38,39] Mechanical phlebitis can occur at any time but typically occurs within the first 72 hours after insertion.

Symptoms

Symptoms include redness, swelling, tenderness, erythema, fever, palpable venous cord, and purulent drainage.[38,87,88]

Treatment

Early identification and treatment is paramount in reducing symptoms. The most effective treatment measures remain unclear, however, and are guided by anecdotal reports. Treatment depends on the type of phlebitis and ranges from conservative monitoring to discontinuing the CVC if symptoms persist.[88] CVC removal is warranted with chemical phlebitis, as vessel damage will continue with subsequent infusions.[86] Warm compresses, elevation of the extremity, and anti-inflammatory agents may resolve a mechanical phlebitis if identified early in its course.[39] In the presence of bacterial phlebitis or if the phlebitis is refractory to treatment, removal of the CVC may be required.[88] Blood or site cultures may be necessary, depending on the symptoms.

Preventive Strategies

Appropriate skin antisepsis, an intact dressing, hand hygiene, and adherence to aseptic technique will minimize the risk of bacterial phlebitis.[38,39] Treatment for mechanical phlebitis begins with prevention, which includes thoroughly assessing the vessel prior to inserting the PICC, as well as avoiding areas of flexion.[17,26] The assessment includes choosing the appropriate vessel and catheter type and size, along with ensuring tip placement in the superior vena cava (SVC) or inferior vena cava (IVC).[11] Performing an atraumatic insertion technique is paramount for decreasing mechanical phlebitis.[89] For upper extremity insertions, the catheter tip should lie parallel to the SVC to prevent vessel irritation.[8-10] Vessels carrying a higher risk for phlebitis include the cephalic and saphenous veins. Appropriate catheter stabilization will help eliminate catheter movement in the vessel. Part of the routine assessment should include palpating along the vein path, observing for edema or erythema, and questioning the patient about pain in the extremity.[89]

Catheter Tip Malposition

Catheter malposition is defined as a CVC tip that has changed or migrated from the original catheter tip placement location. An optimal catheter tip location for CVCs is the distal one-third of the SVC, the cavoatrial junction, or between the diaphragm and the right atrium in the IVC. Complications such as thrombosis, pleural effusion, arrhythmias, pericardial effusion, and tamponade can evolve from catheter tip migration. In a study of 980 neonatal PICCs, the complication rate for PICCs with noncentral tip placement was twice that of PICCs inserted in a central vein.[10]

Etiology

Malposition of the catheter tip occurs when the catheter tip changes from the original tip placement.[10,38] Insertion-related factors may be the result of a tortuous vein path, vessel occlusion, venospasms, or inadequate catheter length. Post insertion malposition can be attributed to increased intrathoracic pressure seen with coughing, crying, vomiting, or high-frequency ventilation.

Symptoms

Symptoms of catheter malposition may be vague or clinically significant, depending on the resultant catheter tip location. Common symptoms include the inability to obtain a blood return, sluggish flow

with flushing, and excessive alarming of infusion pumps.[10] A catheter malpositioned in the jugular veins may cause a child to complain of hearing rushing water or unusual sensations with flushing and/or infusions. Malposition of a catheter into a small vein may evoke signs of pain during infusions. Symptoms associated with vein or organ perforation are specific to the location of the structure involved; for example, perforation of the catheter through the subclavian vein may lead to respiratory distress due to pleural effusion.[38]

If a CVC tip migrates to the cardiac chambers, life-threatening complications such as arrhythmias, pericardial effusion, and/or cardiac tamponade can occur.[18,90]

Treatment

Treatment for catheter tip malposition varies, depending on the cause. During insertion, navigational systems, radiographic imaging, or injection of contrast media may rule out an anatomical anomaly. An alternative CVC may be necessary for aberrant anatomy. If catheter tip malposition is a result of inadequate catheter length, a catheter exchange may be necessary.

A CVC malposition into the jugular or contralateral brachiocephalic or subclavian veins may spontaneously reposition into the SVC.[10] Infusion of fluids, gravity, or raising the head of the patient off the bed or positioning the patient so that the side opposite the catheter tip is down may assist the catheter to the SVC. Catheter removal or exchange should be considered if catheter malposition persists.[8]

Preventive Strategies

With CVC insertion, malposition of the catheter tip can be minimized by selecting appropriate veins for CVC insertion and placing catheter tips deep in the SVC near the cavoatrial junction.[38] For PICC insertions, the basilic vein is larger, has fewer valves, and provides a direct route of threading to the SVC as compared with the cephalic vein. Threading a PICC slowly is recommended, as blood flow may direct the catheter to the SVC or IVC. It is important to review the patient's history of vascular access devices and past complications when planning for the appropriate CVC.[11]

Providing additional support for young patients during dressing changes may avoid retraction of the catheter.[44] It is important to assess and document the external catheter length prior to the dressing change procedure and to monitor for any changes.[33] If any changes in the function of the CVC or frequent alarming of the infusion pump occurs, further assessment of the catheter is warranted. Periodic radiographic imaging may be beneficial.[90] If a PICC is retracted back to make it a midline catheter, this must be documented to ensure that the catheter is labeled properly.

Catheter Fracture

The incidence of catheter fracture is not known. In a study by Matsuzaki et al[91] on PICCs in oncology patients, over half of the catheter breakage occurred 90 days after PICC placement.

Etiology

Predisposing factors for CVC fractures include catheter damage from flushing against resistance, use of small-volume syringes, use of silicone catheters, stress on the catheter due to clamping, high-pressure injections on catheters not indicated for power injection, patients pulling on the external segment of the catheter or other external pulling forces, and difficult catheter removal.[92] Catheters can fracture because of manufacturing designs or improper handling during care of the CVC.[18]

Less commonly, tunneled catheters can fracture with pinch-off syndrome. Pinch-off is defined as a narrowing of the catheter lumen due to compression between the clavicle and first rib and may lead to catheter fracture and embolization.[61] Fragments from a catheter fracture may lead to pulmonary embolism.

Symptoms

Patients may be asymptomatic or experience respiratory distress or arrhythmias. Symptoms include visible catheter or hub fracture, leaking at the insertion site, frequent infusion pump alarms, or radiographic findings.[92] External fracture of a catheter must be clamped or pinched off immediately to avoid air and catheter embolism.

Treatment

Catheter fragments can lodge in the vena cava, right atrium or ventricle, pulmonary artery, or its branches. Attempts are typically made to remove the catheter fragment by using loop snares, baskets, or guidewires via the femoral vein, but a surgical procedure may be necessary.[91] Fractured catheter hubs or external lumen(s) may be repaired if allowed by the manufacturer's recommendations. The decision to repair a catheter should be based on the length of time the catheter will be needed, the availability of alternate veins, and exposure to microorganisms caused by the breakage.[92] Repair of a broken CVC is associated with a 2- to 4-fold higher risk of developing CLABSI within 30 days of the repair.[93] Unless the damage is immediately identified, repairs pose a risk of infection. Discussion of risks and benefits related to repairing a CVC is necessary.

Preventive Strategies

Strategies include flushing with a 10-mL or larger syringe size, avoiding flushing against resistance, maintaining a secure dressing suitable for the age of the patient, and limiting contrast power injections to specifically manufactured CVCs intended for this type of study.[29]

Air Embolism

Air embolism is the inadvertent entry of air into the circulatory system, causing obstruction of blood flow and hypoxia.[94] Air embolism is a rare but potentially devastating complication with vascular access devices, and death can occur if cardiac output is diminished or lifesaving interventions are lacking.[94,95]

Etiology

Air embolism can occur during placement, maintenance, and removal of a CVC; catheter fracture; and unprimed or inadvertent tubing disconnection.[18,80] Because of the rapid transit time of air through the circulation, the diagnosis is typically made after ruling out other potential causes.

Symptoms

Symptoms include acute dyspnea with hypoxia, tachypnea, tachycardia, and altered mental status.[80] The symptoms depend on the volume of air in the system.

Treatment

Timely recognition of air embolism can minimize complications, including death.[94] The most appropriate intervention is to place the patient on the left side in the Trendelenburg position and provide 100% oxygen and cardiorespiratory support.[80,95]

Preventive Strategies

Preventive strategies include using infusion pumps with appropriate alarms to alert clinicians to the presence of air and using Luer-lock tubing to minimize accidental tubing disconnection.[80] It is important to ensure that the catheter is clamped with tubing and needleless connector changes. During CVC removal, the patient should be placed in the Trendelenburg position, and the Valsalva maneuver should be used, if possible.[18] When removing the catheter, it is important to apply digital pressure at the insertion site followed by the application of an occlusive dressing with ointment for 24 to 48 hours.[18,94]

Infiltration and Extravasation

Infiltration and extravasation can cause significant tissue damage and long-term morbidity.[66,96] Infiltration is defined as the inadvertent administration of a nonvesicant solution or infusate into the tissue, whereas an extravasation is the inadvertent administration of a vesicant into the tissue.[25]

Etiology

With IVs, infiltration and extravasation can occur with dislodgement of the cannula into the tissue, puncturing of the vessel wall during insertion, or trauma or irritation from infusates.[97] With CVCs, infiltration and extravasation can occur with catheter rupture, catheter tip migration or malposition, perforation through the vein or organ with infusate leakage into the tissue, fibrin sheath formation, or improperly implanted port access.[98] Nonverbal children are at increased risk for infiltration and extravasation because of their inability to describe pain or changes in sensation, which can result in disastrous outcomes.[66] Quality of life can be affected by significant tissue damage and altered limb function.[86,99]

Symptoms

Symptoms of infiltration include redness, swelling, and pain at the site of injury. Extravasation injuries include the symptoms above, along with blistering, tissue sloughing, compartment syndrome, and

nerve damage.[66] Superficial injuries may be obvious; however, extensive injuries may not be recognized immediately.[85] Although these types of injuries occur less frequently with CVCs, morbidity is higher. If a CVC is dysfunctional, the catheter should be evaluated prior to administering the therapy.[98] Assessment includes visual inspection of the catheter to rule out any mechanical complications, flushing the catheter, and, if indicated, initiation of thrombolytic therapy.[100] A chest radiograph or venogram may be necessary.[85]

Treatment

Treatment is based on the type, amount, and location of the tissue injury and includes stopping the administration of medication and, if possible, aspirating the residual medication.[86] Antidotes are available for some types of infusates; medication package inserts or institutional policies will direct administration.[66] An appropriate antidote, if available, should be administered around the injury to aid in reabsorption of the infusate or vesicant.

Preventive Strategies

Preventive strategies include a thorough hourly assessment of the CVC site and surrounding area for evidence of swelling or tissue damage during infusions.[98] Nurses play a critical role in assessing and providing early intervention if infiltration or extravasation occurs. Extreme vigilance must be practiced with administration of vesicants.[85,86]

Central Line-Associated Bloodstream Infection

Although CVCs provide necessary vascular access in the pediatric patient, CLABSI remains an inherent risk and can be difficult to treat.[101-103] CLABSIs are major contributors of morbidity, mortality, exposure to antibiotics, increased length of stay, and hospital costs. Children are especially vulnerable.[104,105] Moreover, morbidity and mortality from CLABSI may have a greater effect in a pediatric population in terms of productive life-years lost because of the infection occurring at a younger age.[106]

CLABSIs are the most common hospital-acquired infections in critically ill children, and CLABSI prevention is integral to patient safety.[107] In 2010, a consortium of professional societies and government groups issued a call to action to move toward the elimination of hospital-acquired infections.[108] The Centers for Medicare & Medicaid Services no longer reimburse hospitals for the costs of treating CLABSIs and require reporting of CLABSI rates for inpatient units to receive payment increases.[109] Institutional rates are publicly reported to the Centers for Disease Control and Prevention's (CDC's) National Healthcare Safety Network (NHSN) and state specific CLABSI rates; nationally pooled data are published by NHSN.[110]

Various agencies use the terms catheter-related bloodstream infection (CRBSI), CLABSI, and catheter-associated bloodstream infection (CABSI) interchangeably. Clinicians need to understand the differences among the terms, as confusion affects plans that are being developed for measuring and eliminating bloodstream infections. CRBSI is a rigorous clinical definition, used to determine diagnosis, treatment, and possibly epidemiology of bloodstream infections in patients with a CVC.[33] It is not typically used

for surveillance purposes and there are little data available for comparison. The CDC criteria for CRBSI include one of the following:

A positive semiquantitative (> 15 colony-forming units/catheter segment) or quantitative (> 10^3 colony-forming units/catheter segment) culture whereby the same organism (species and antibiogram) is isolated from the catheter segment and peripheral blood

Simultaneous quantitative blood cultures with a ≥ 5:1 ratio of organisms in the CVC vs peripheral blood

A differential period of CVC culture vs peripheral blood culture positivity of > 2 hours

The NHSN definition of a CLABSI is a recognized pathogen cultured from one or more blood cultures, with the organism not related to an infection at another site, in patients with a CVC in place within 48 hours before detection.[33] If a common skin contaminate is cultured, then 2 or more blood cultures drawn on separate occasions are required, along with specific symptoms.[33]

In January 2013, NHSN released revised CLABSI criteria termed "mucosal barrier injury laboratory confirmed bloodstream infection" in response to clinical demonstrations that the CLABSI surveillance definition lacked specificity in certain populations, primarily oncology patients.[33] In these patients, bloodstream infection can result from other mechanisms, such as the translocation of bacteria through nonintact mucosa in patients with oral or gastrointestinal (GI) mucositis, and it may not be related to the CVC.[111] Distinguishing bloodstream infections that occur through translocation from those related to the catheter improves reliability of interfacility comparison of CLABSI rates and may help guide prevention efforts.[111]

Risk Factors

Most bloodstream infection data are derived from critical care units because of the high volumes of patients having a CVC.[104] Pooled data from 51 children's hospitals nationwide showed that, with the exception of bone marrow transplant and rehabilitation units, pediatric intensive care units (PICUs) have the highest mean CLABSI rates.[112] Catheters are often inserted in urgent situations in which optimal attention to aseptic technique may not be feasible. Infections are higher in ICUs for multiple reasons: access might be needed for extended periods of time, patients may be colonized with hospital-acquired organisms, and CVCs may be manipulated multiple times per day for the administration of fluids, drugs, and blood products or for obtaining blood sampling. Advani et al[102] reported that children with PICCs who had PICU exposure during their hospitalization experienced a significantly shorter time to development of CLABSI compared with patients who were not in the PICU.

In a case-control study conducted in patients admitted to a medical-surgical PICU or cardiac ICU, independent predictors of CLABSI included duration of PICU CVC access for 15 or more days and receipt of blood products.[106] Duration of central venous access is consistently recognized as a risk factor and prompts consideration of line necessity and early line removal. The largest cohort PICU study to date demonstrated a low risk of CLABSI in the first week of catheterization, but the risk doubled thereafter.[113]

Longer duration of CVC access associated with increased risk of CLABSI is further supported by reports of biofilm formation increasing with catheter age.

Blood product transfusion has been described as a risk in previous studies; the proposed mechanism to account for the risk includes immune suppression, increased frequency of CVC access, and promotion of pathogen proliferation.[106,113] Platelet transfusion within the week prior to infection was found to be an independent predictor of CLABSI in hospitalized pediatric oncology patients and was associated with neutropenia.[114] Newly identified risk factors in the PICU population that were also reported as independent predictors of CLABSI by Wylie et al[106] include the presence of a gastrostomy tube, nonoperative cardiovascular disease, and PICU placement of a CVC. The authors suggest that the presence of a gastrostomy tube may be a marker for chronic comorbid illness or poor nutritional status and be more susceptible to the possible transfer of enteric pathogens to their CVC. The increased risk in patients with medical cardiovascular disease may be attributed to chronic low cardiac output, which may make tissues more susceptible to proliferation of pathogenic bacteria.[106]

Children with a primary GI or oncologic diagnosis demonstrated a higher CLABSI risk in the multicenter PICU quality improvement CLABSI collaborative.[113] A potential explanation for the higher risk in patients with a GI diagnosis is that they may be more likely to receive therapies such as parenteral nutrition or blood products that increase CLABSI risk. Some of these patients may be more prone to chronic diarrhea, which may increase the risk of contamination of the CVC and add-on device[113] Compared with immunocompetent patients, immunocompromised children are more susceptible to pathogens and less virulent organisms (eg, *Staphylococcus epidermidis*) and may be less tolerant of microcontamination. Furthermore, bacterial translocation may be more persistent in an immunocompromised patient with mucositis.[113]

Significant proportions of non-ICU patients are discharged with a CVC in place.[1,114] These patients are also at risk for serious CLABSI, although the incidence of infection is lower in these patients than in those with catheters in the ICU. [112] Additional risk factors for the pediatric patient include weight, immune dysfunction, lack of physical barriers between bed spaces, multiple attempts at CVC insertion, involvement of multidisciplinary teams, and inadequate hand hygiene and skin antisepsis.

The significant differences between children and adults include age, underlying medical conditions, process of care, and type and distribution of pathogens. These factors present obstacles in extrapolating the substantial amount of data in the literature regarding adult CLABSI and applying it to children.[115] Risk factors for CLABSI include the presence of arterial catheters, frequent collection of specimens, and extracorporeal and renal replacement therapy.[115] Other examples of process of care include procedures performed in the PICU and transport of the patient out of the PICU to the radiology department or the operating room, where a potential breach of sterile or aseptic technique may predispose the patient to infection.

Total parental nutrition is associated with higher rates of infection because the nutrients support microbial growth.[106] During long-term catheter use for TPN, an intraluminal biofilm, catheter-tip fibrin sheath

or tail, and thrombosis create sites for microbial seeding and infection. Further, lipid contamination, glycemic changes, and breakdown of GI mucosa related to lack of enteral feeding have been suggested as possible contributors to the risk of CLABSI in patients receiving TPN.

CVC site selection can be a potential risk for CLABSI, although data are limited in the pediatric population. A multicenter PICU cohort study observed a significantly lower risk in patients with CVCs in the jugular vein than in other sites but no significant association with the number or type of CVCs.[113] Femoral CVCs have a lower incidence of mechanical complications and may have an equivalent incidence of infection to that of catheters in alternative sites. Femoral veins are a common location for CVCs in the critically ill pediatric patient, as the landmarks can be easily identifiable and complications such as pneumothorax can be avoided. An additional advantage is avoidance of the head and neck for the patient with respiratory or airway compromise.

Dedicating a lumen of a multilumen CVC for TPN infusions is a common practice, although not evidence based. The risk of infection is increased in hospitalized patients because of malnutrition-associated immunosuppression, hyperglycemia exacerbated by dextrose infusion, and microbial colonization/contamination of the catheter hub and the skin surrounding the insertion site. Children undergoing cardiac surgery may be at increased risk for developing CLABSI because of their young age, frequent use of multiple invasive devices, and common exposure to the immunosuppressive effects of cardiopulmonary bypass.[116,117]

In a study of the pediatric hematology oncology population, Rinke et al[118] found that CLABSI rates decreased by 48% after a CVC maintenance bundle was implemented for outpatients. Higher CLABSI rates were attributed to therapies requiring frequent CVC access such as blood sampling, TPN, and the administration of blood products. Wagner et al[119] identified a significant association between device and risk of CLABSI, the lowest risk occurring with an implanted port, most likely related to less exposure to microbial contamination. The pediatric hematology/oncology 36 multicenter CLABSI collaborative reported no significant association with type of CVC, although double-lumen tunneled catheters were present in 46% of patients at the time of the first positive blood culture results.[7] This prospective study reported 576 CLABSIs, in which 60% of CLABSI events occurred in patients with leukemia, 60% of whom had acute myeloid leukemia and 35% of whom had acute lymphoblastic leukemia. Eighty percent of events occurred in patients who were extremely neutropenic (absolute neutrophil count < 100) and 25% in those had undergone stem cell transplantation within 100 days prior to the CLABSI.[7]

Frequent sampling through a stopcock may lead to an increased opportunity for microorganisms to enter the catheter.[120] Creation of a closed system by capping the opening of a stopcock with a needleless connector rather than a dead-end cap or a syringe may decrease colonization.

Etiology

Microbial contamination of catheter hubs and subsequent intraluminal migration and colonization of the catheter tip is an important portal of entry for microorganisms and is recognized as a frequent cause of CLABSI, particularly in CVCs used for long-term venous access.[113] Extraluminal infections begin in

the soft tissues and spread along the external surface or subcutaneous tunnel of the CVC directly into the bloodstream. Extraluminal infections usually develop within 7 days after catheter insertion because of heavy colonization of the external catheter surface, most likely after insertion through inadequately disinfected skin.[121] Intraluminal infections generally occur after 7 to 10 days and are related to microorganisms contaminating the catheter hub, lumen, or needleless connectors during manipulations of the catheter (eg, catheter exchanges).[121]

Biofilm formation is a process whereby microorganisms attach to and grow on the external and internal surface of the catheter in a microbial community and produce a 3-dimensional structure called an extracellular polymer substance matrix.[122] Biofilms have been reported to form within days of catheter insertion, and they play a crucial role in the pathogenesis and treatment of CLABSI. Organisms in a biofilm may serve as a persistent source of infection, act as a physical barrier to antibiotic penetration, and promote antimicrobial resistance.[122]

Diagnosis

The diagnosis of CLABSI remains a major challenge. Fever associated with infection is not always present in infants; therefore, microbiologic evidence is necessary for the diagnosis. Central venous catheter cultures have a good negative predictive value but a poor positive predictive value as a result of potential contamination.[123,124] Differential time to positivity and semiquantitative superficial blood cultures were found to be the most accurate diagnostic tests of CLABSI in critical care patients.[125] However, the use of these tests is limited, as they are labor intensive and costly and can contribute to iatrogenic anemia in infants.

Differential time to positivity uses paired qualitative blood cultures obtained simultaneously from the CVC and peripherally. The CVC is considered the source of infection when the CVC blood culture becomes positive for an organism < 120 minutes earlier than the peripheral blood culture does.[125]

Treatment

The Infectious Diseases Society of America (IDSA) published practice guidelines for the management of CLABSI in 2014.[126] According to the guidelines, empiric systemic antibiotic regimens should be based on the institution's commonly isolated organisms, the severity of the patient's clinical symptoms, the risk factors for infection, and the pathogens that are likely associated with specific devices; regimens are modified on the basis of the antibiogram and symptoms.

Depending on the microorganism, the patient's condition, and availability of alternative access sites, CVCs with a positive blood culture may be removed or the lumen(s) may be treated with antibiotics. Specific bacterial infections and all fungal infections in CVCs usually warrant removal of the device, resulting in difficult management issues, especially for patients who are CVC dependent.[126] Catheter removal is not always feasible and the decision must be weighed against potential loss of a CVC in the future and the impact on treatment.[127] Ethanol instillation and systemic antibiotic therapy has resulted in a decrease in the length of stay for pediatric patients.[122]

Antibiotic lock therapy (ALT) and ethanol lock therapy (ELT) are thought to be effective in conjunction with systemic antibiotics for treatment of CLABSI in long-term CVCs in which the pathogenesis is usually intraluminal.[122,127] Treatment success varies and catheter salvage is not recommended in tunnel or pocket infections. IDSA recommends ALT in patients with CLABSI in long-term catheters without these infections and for whom catheter salvage is the goal.[126] Concerns with the use of ALT include potential toxicity as a result of inadvertent flushing of the solution systemically and the possible development of antimicrobial resistance.[127] In a small study of 7 pediatric patients receiving ethanol, the rate of CLABSI decreased; however, repair rates of the tunneled CVCs increased.[71]

As a bactericidal and fungicidal disinfectant, ethanol denatures cell membrane proteins and is less likely to promote antimicrobial resistance as a result of this mechanism of action.[128] Ethanol is an antifibrinolytic and has the ability to penetrate established biofilms.[128,129] Although most studies and case reports reveal tolerable adverse effects, limited concern for resistance, and relative safety with the use of ELT, reported concerns are as follows:

1. Ethanol is incompatible with heparin and can precipitate if exposed to heparinized saline; documented case reports of catheter occlusion exist.

2. Ethanol may be associated with plasma protein precipitation in solutions with an ethanol concentration above 28%.

3. Ethanol may weaken silicone catheters; the American Pediatric Surgical Association does not recommend ELT for use in polyurethane catheters because of the risk of damaging the integrity of the catheter.

4. Ethanol lock therapy can theoretically cause ethanol intoxication, although there are no reports of it doing so.[127,130]

Ethanol lock therapy shows promise as an adjunctive therapy considering the available data, relatively low cost, and pathogenesis of CLABSI. Pediatric trials of ELT as an adjunctive therapy in the treatment of CLABSI are summarized in Table 3.

Table 3. Overview of Trials with Ethanol Lock Therapy

Author and Year Study Design	Population	Type of CVC	Ethanol Dwell Time	Treatment	Results
Onland et al,[46] 2006 Retrospective	28 patients 2-18 years old Hematology and oncology 39 episodes CLABSI Gram +/gram - bacteria	Multilu-men tunneled CVCs	2.3 mL for 20-24 hours between each lumen every 3 days	74% ethanol plus systemic antibiotics (n=18) vs systemic antibiotics (n=13) Ethanol flushed after dwell time	67% of infections cleared without recurrence in ethanol group vs 47% with antibiotics alone 1 catheter removed in each group because of infection Adverse effects: fatigue, headaches, dizziness, nausea, light-headedness; mild LFT changes
Onland et al,[46] 2006 Retrospective	40 patients > 6 months Hematology, oncology, bone marrow transplant, small-bowel transplantation, metabolic, gastroenterology disorders 51 episodes CLABSI Gram +/gram – bacteria; *Candida*	Multilumen tunneled CVCs, ports	1.4 mL for 12-24 hours for 5 days in single lumen CVC or 10 days alternating double lumens	70% ethanol discarded after dwell time	88% of infections cleared of same pathogen within 30 days 3 patients had recurrence of infection within 30 days of same pathogen No catheters removed No adverse effects reported
Rajpurkar et al,[132] 2009 Retrospective	3 patients 3-13 years old Hemophilia 4 episodes CLABSI Gram +/gram – bacteria Candida	Port	0.5 mL for 24-72 hours	70% ethanol flushed after dwell time	100% of infections cleared; results of blood cultures drawn after ethanol lock therapy were negative; patients asymptomatic for 9 months, 6 months, and 9 months No adverse effects reported
Blackwood et al,[133] 2011 Retrospective	3 patients 8 months to 5 years 3 episodes CLABSI *Candida* infection	Long-term CVC	CVC volume for 2-24 hours	70% ethanol aspirated after dwell time	100% of infections cleared No reported adverse effects

McGrath et al,134 2011 Retrospective	59 patients 2 months to 19 years Hematology, oncology, solid tumor, bone marrow transplant, short bowel, congenital syndromes 80 episodes CLABSI Gram +/gram – bacteria Candida, Cryptococcus	PICCs, tunneled CVCs, ports Silicone and polyure-thane catheters	1-5 doses 4-25 hours	70% ethanol 0.3-1.0 mL	86% - negative blood culture obtained from CVC ~ 25 hours after initial ethanol 95% - negative blood cultures obtained from CVC after ≤ 4 doses of ethanol 75% - negative repeat blood cultures obtained after ≤ 4 doses of ethanol and ≥ 30 days after ethanol 2.5% line dysfunction - both resolved, 1 required alteplase Adverse effects: mild transaminase elevation
Valentine,[135] 2011 Retrospective	20 patients 6 months to 20 years Sepsis, cardiomyopathy, heart transplant, malignancy, congenital heart surgery, chronic respiratory failure, neuromuscular 26 episodes CLABSI Gram +/gram – bacteria Candida	Long and short-term CVCs	0.1 mL plus CVC volume for 4-48 hours	70% ethanol flushed after dwell time	92% of infections cleared with negative blood cultures within 48 hours of initiating ethanol All sterilized CVCs salvaged remained infection free for a minimum of 30 days or until no longer needed No serious adverse events; mild LFT increases
Wong et al,[81] 2012 Retrospective	2 patients 10, 11 years Intestinal failure on home TPN, gastroschisis, NEC	Long-term CVCs	CVC volume for 2-12 hours for 10-14 days	70% ethanol aspirated after dwell time	Both patients developed thrombosis in CVC; 1 difficult to flush after 3 days of ethanol; 1 visible thrombosis on aspiration of ethanol Ceased ethanol therapy; 1 CVC became patent again

Abbreviations: CLABSI, central line-associated bloodstream infection; CVC, central venous catheter; LFT, liver function test; NEC, necrotizing enterocolitis; PICC, peripherally inserted central catheter; TPN, total parental nutrition.

Preventive Strategies

Preventing CLABSIs is a national priority, and efforts to reduce CLABSI are at the forefront of patient safety initiatives.[110] The risk of CLABSI may be reduced by preventing contamination of the CVC both intraluminally and extraluminally.[125] Implementation of evidence-based infection control guidelines that focus on insertion and maintenance of the catheter, including the CVC site, can substantially reduce or prevent CLABSIs.[2,6]

Multifaceted interventions, known as bundles, are necessary to ensure that evidence-based infection control guidelines to prevent CLABSI are followed.[2,6] According to the Institute for Healthcare Improvement (IHI), care bundles are groupings of best practices that individually improve care regarding a disease process, but when applied together result in substantially greater improvement. The science supporting the bundle components is sufficiently established and considered a standard of care. To improve compliance with evidence-based recommended practices, the CDC's latest guidelines recommend the use of hospital-specific or collaborative bundles.[33]

A CVC insertion bundle was successfully implemented several years ago; multicenter and single-institution pediatric collaborative efforts that emphasize the use of these best practices have resulted in decreases in CLABSI rates. The largest 36 multicenter PICU collaborative supported by the National Association of Children's Hospitals and Related Institutions has successfully implemented pediatric-specific central line care bundles.[113] During the first year of the project, the incidence of CLABSI in PICUs decreased by 43% (from 5.4 to 3.1 per 1000 catheter days).[113] Analysis demonstrated that this decrease was related to the initiation of a reliably implemented standardized maintenance care bundle.[113,136] The authors suggest that "the most important risk factors for CLABSI in the PICU have been catheter care practices and the healthcare systems that promote adherence to best practice."[113] Another large 26 multicenter pediatric PICU collaborative demonstrated a 32% reduction in CLABSI with standardization of CVC insertion and maintenance bundles; 35% of institutions achieved or surpassed the goal of at least a 50% CLABSI reduction.[137] Wheeler et al[107] describe a pediatric hospital-wide collaborative that successfully reduced CLABSI rates from a baseline of 3.0 to < 1.0 per central line days after implementation of CVC insertion and maintenance bundles.

Maintenance care bundles have also been successfully implemented in the outpatient setting. An interrupted time-series study in outpatient pediatric oncology patients compared baseline CLABSI rates before implementation of a standardized maintenance bundle with CLABSI rates after implementation and reported a 48% decrease and a 54% decrease in bacteremias.[118]

Adjunctive Strategies

In addition to the evidence-based strategies described throughout these guidelines, other adjunctive interventions have been shown to be effective in the prevention of CLABSI. The CDC recommends the use of prophylactic antimicrobial lock solution in patients with long-term catheters who have a previous history of multiple CLABSIs.[33]

Taurolidine citrate has been shown to have broad-spectrum antimicrobial and fungal activity with no reported resistance. It prevents bacterial adhesion to biological surfaces, thereby prophylactically minimizing catheter colonization.[138] In Germany, a randomized controlled trial of taurolidine citrate vs heparin as a catheter lock solution in pediatric hematology/oncology patients demonstrated a significantly lower CLABSI rate in the taurolidine group compared with the control group.[138] Children receiving home TPN were also found to have a significantly reduced CLABSI rate when taurolidine citrate was used as a catheter lock.[139]

Ethanol has also demonstrated effectiveness in preventing CLABSI when used prophylactically. Table 4 summarizes studies of prophylactic ELT in the pediatric population to prevent CLABSI.

Table 4. Pediatric Case Reports and Trials of Prophylactic Ethanol Lock Treatments for the Prevention of CLABSI

Author and Year Study Design	Age	Type of CVC	Definition of CLABSI	Ethanol Dwell Time	Treatment and Duration of Prophylaxis	Results
Mouw et al,[140] 2008 Retrospective	10 patients 7 months–to 2 years Receiving home TPN; short bowel	Tunneled CVC Silicone	Not reported	Initial: 2 mL for all CVCs, decreased to CVC volume plus 0.5-1 mL 4-14 hours daily	70% ethanol flush not reported 36 months	CLABSI rate reduced from 11.2 to 2.1/1000 catheter days 2 CVCs removed because of CLABSI No adverse effects reported
Cober et al,[141] 2011 Retrospective	15 patients < 25 y Home TPN, short bowel, intestinal failure, high risk with any one of the following: (1) 2 previous CVCs replaced because of infection in the past 18 months. (2) Previous history of CLABSI in current CVC	Tunneled CVC, port Silicone	CDC 2002	CVC volume plus 0.1 mL for patients < 15 kg and 0.2 mL plus CVC volume for patients > 15 kg ³ 2 hours daily	70% ethanol discarded after dwell time 22 months	73% of patients remained infection free throughout study period CLABSI rate reduced from 8.0 to 1.3 per 1000 catheter days Adverse effects: 1 patient developed DVT requiring CVC removal; 7 patients developed CVC leakages or disruption requiring CVC repair (incidence 3.1 vs 6.4/1000 catheter days).

Jones et al,[142] 2010 Retrospective	23 patients 3 months to 18 years old receiving home TPN, intestinal failure	Tunneled CVC, PICC	Not reported	CVC volume ³ 4 h daily	70% ethanol aspirated after dwell time 22 mo	CLABSI rate reduced from 9.9 to 2.1/1000 catheter days; median CVC replacement rate 8.2 to 0/1000 catheter days. Motility disorders associated with significantly higher CLABSI rates. No adverse effects reported.
Kayton et al,[143] 2010 Prospective Open label	12 patients £ 6 months Neuro-blastoma on IV antibody treatment	Port (no titanium) Silicone or polyure-thane	Positive blood culture result from CVC	CVC volume overnight 4 days/ month	70% ethanol aspirated after dwell time 6 months	Positive blood culture in 1 patient; 3 patients developed thrombosis; 1 of these developed fracture All 3 catheters removed; examination revealed catheter intraluminal thrombosis Adverse effects: abdominal pain, vomiting, sneezing, slurred speech, sleepiness, puffy cheeks, personality change, pain on inspiration
Wales et al,[144] 2011 Retrospective	12 patients £ 6 months Neuro-blastoma on IV antibody treatment	Port (no titanium) Silicone or polyure-thane	Positive blood culture result from CVC	CVC volume overnight 4 days/ month	70% ethanol aspirated after dwell time 6 months	Positive blood culture in 1 patient; 3 patients developed thrombosis; 1 of these developed fracture All 3 catheters removed; examination revealed catheter intraluminal thrombosis Adverse effects: abdominal pain, vomiting, sneezing, slurred speech, sleepiness, puffy cheeks, personality change, pain on inspiration
Wong et al,[81] 2012 Retrospective	2 patients 4 and 11 years Home TPN, intestinal pseudoob-struction, Hirsch-sprung disease	Long-term CVC	Not reported	CVC volume for 12 hours, 3 times per week	70% ethanol aspirated after dwell time	Both patients developed thrombosis in CVC. In first patient, ethanol ceased after 413 days - visible thrombosis on aspiration of ethanol by parents. In second patient, ethanol ceased after 168 days - thrombosis in line with aspiration of ethanol by treating clinician

Pieroni et al,[128] 2013 Retrospective	14 patients average age 4.3 years Home TPN, intestinal failure, history of at least 2 CLABSIs	Tunneled CVC Silicone	At least 1 positive blood culture result from CVC without other confirmed source of infection that could lead to bacteremia or fungemia	1 mL in patients < 30 kg; 2 mL in patients > 30 kg 2 hours once a wk	70% ethanol aspirated after dwell time 47 months	Significant reduction (73%) in CLABSI (9.8 -2.7/1000 catheter days); 77% reduction in catheter removal rate (4.3 - 1/1000 catheter days) Adverse effects: 1 patient with facial flushing and irritability while receiving ELT. No thrombotic events

Abbreviations: CLABSI, central line-associated bloodstream infection; CDC, Centers for Disease Control and Prevention; CVC, central venous catheter; DVT, deep vein thrombosis; ELT, ethanol lock therapy; IV, intravenous; PICC, peripherally inserted central catheter; TPN, total parental nutrition.

Maintenance Bundles

Hand Hygiene

Hand hygiene is recognized by infection prevention and control experts as the single most important intervention to decrease the spread of infection in both health care and community settings.[145] Because the hands are vectors for transmission between people as well as between inanimate objects such as environmental surfaces, it is critical to practice frequent hand hygiene with all CVC encounters by using the traditional soap and water or an alcohol-based product as appropriate.[145]

The CDC and World Health Organization (WHO) maintain extensive hand hygiene guidelines with quality and patient safety organizations such as the IHI and The Joint Commission.[146] A solid hand hygiene program with documented compliance will reduce risk for transmission of microorganisms in patients and clinicians with the goal of decreasing the cost and risks of CLABSI.[145,147]

Transmission of Microorganisms via the Hands of Health Care Workers

The 2009 *WHO Guidelines on Hand Hygiene in Health Care* identified 5 steps for the nosocomial transmission of pathogens from one patient to another via the clinician's hands.[146]

1. Microorganisms must be present on the patient's skin or have the ability to shed onto inanimate objects such as the bedside table.

2. The microorganisms must be transferred to the hands of the clinician.

3. The microorganisms that have contaminated the clinician's hands must be able to survive.

4. The clinician has either omitted hand hygiene or inadequately performed it.

5. The clinician's contaminated hands must come in direct contact with either another patient or with an inanimate object that will then come in contact with a patient.

Factors Influencing Adherence to Hand Hygiene Practices

According to published studies, several factors influence compliance for hand hygiene practices, such as male gender and working in a critical care setting.[148] Self-reported factors for poor hand hygiene adherence include dryness of skin from soap, sinks not being located in convenient locations, and a high nurse-patient staffing ratio.

Indications for Hand Hygiene in Health Care Settings

The goal of hand hygiene is to remove microorganisms from the hand to avoid transmission.[147] The skin flora can be transient or resident flora. According to the WHO guidelines, clinicians should concentrate their hand hygiene efforts on all aspects of CVC care, after touching inanimate objects, and after exposure to bodily fluids.[146] Alcohol-based agents may be used when hands are not visibly soiled, before and after patient contact, and after removing gloves.

Availability of Hand Hygiene Agents

Hand hygiene products are available in a wide variety of forms to meet the clinical needs of the health care environment. Typical agents include plain soap, alcohols, chlorhexidine, chloroxylenol, hexachlorophene, iodine and iodophors, quaternary ammonium compounds, or triclosan.[146] Most alcohol-based products have significant activity against a wide variety of bacteria and viruses. The Food and Drug Administration (FDA) classifies health care antiseptic drug products into 3 unique categories that include surgical hand scrub, antiseptic hand washing, and preoperative skin preparation.[149]

Selection of Hand Hygiene Agents

Hand hygiene agents must be carefully selected in order to ensure compliance, efficacy, and safety.[148] Factors that should be taken into consideration are the cost, ease of use, accessibility, and potential skin reactions. Adjuncts to prevent contact dermatitis such as hospital-grade lotions should be considered.

Technique for Hand Hygiene for Clinicians

Soap and water is still considered the gold standard for hand hygiene but, if not available, alcohol-based hand rubs (wipes, gels, or foams) with alcohol concentrations between 60% and 90% should be used. When using soap and water, it is important to wet the hands first, and then apply to 3 to 5 mL of soap.

Next, rub the hands together for a minimum of 15 seconds, covering all surfaces of the hands and fingers. Finally, rinse the hands off with water, dry thoroughly, and turn off the faucet with the paper towel.[146]

When using an alcohol-based product, follow the manufacturer's label to ensure that the desired efficacy is reached and allow the agent to completely dry prior to using gloves. The pediatric patient should be encouraged to practice hand hygiene; this is an excellent way to decrease colonization of the patient's hands and the health care environment.

Strategies for Compliance

Monitoring hand hygiene is a key component for improving compliance.[148] Secret shoppers have proven to be an effective measurement tool for some facilities. Monitoring should be conducted and recorded on a routine basis, and noncompliant personnel should be immediately counseled.

Resources for Success

Several organizations provide resources to health care providers on hand hygiene standards. The IHI resource guide focuses on proper hand hygiene and compliance, WHO includes hand hygiene educational materials, and the CDC has a dedicated web course on hand hygiene.[146,149] The impact on the patient and health care delivery system when proper hand hygiene does not occur can be significant.

Environmental Hygiene and Surface Disinfection

Every day, clinicians face significant challenges because of evolving technology and time constraints. Choosing the correct disinfectant products from among new or revised products can be similarly challenging. A methodical approach for evaluating disinfectants includes the following:

1. Understanding product labels
2. Evaluating broad-spectrum efficacy claims
3. Adhering to overall contact time
4. Educating staff to improve compliance

Components of Health Care Disinfectant Labels

In the United States, all disinfectants must be registered with the Environmental Protection Agency (EPA), which is responsible for approval of products containing ingredients that enter the environment.[150] Upon approval of a specific product, the manufacturer will receive an EPA registration number for it that dictates the necessary information that must be included on the product label.

For health care disinfectant labels, this information includes product name, ingredient statement, the signal words "Keep Out of Reach of Children," first aid instructions, net contents/net weight, EPA registration

number, EPA establishment number, precautionary statements, directions for use information, storage and disposal statement, and any product-specific marketing claims and graphics.[150]

Criticality of Broad-Spectrum Efficacy Claims

When evaluating a new or existing health care disinfectant, review the efficacy claims available from the manufacturer, the material safety data sheet, and instructions for use. Product labels generally list efficacy claims by class of microorganism, including bacteria, viruses, fungi, and mycobacterium (tuberculosis). When evaluating microorganism efficacy claims, it is important to review the facility's infection prevention risk assessment and infection control plan, as well as the pharmacy's antibiogram, for proper selection of a product with relevant pathogenic efficacy claims.[146]

The broader spectrum a product's efficacy, the more effective it will be against a wide variety of gram-positive and gram-negative bacteria. With new and existing multidrug-resistant organisms, infection preventionists should seek products with broad bactericidal efficacy and effectiveness against organisms such as multidrug-resistant *Acinetobacter baumannii*, extended spectrum beta-lactamase-producing organisms such as *Escherichia coli*, and carbapenem-resistant organisms such as *Klebsiella pneumoniae*.[146]

Products with efficacy against resistant pathogens will assist the infection preventionist with the daily threats of these microorganisms. Viruses, particularly the blood-borne pathogens and those causing outbreaks (eg, norovirus, influenza, and rotavirus), are concerning to the users of health care disinfectants. Efficacy claims against blood-borne pathogens such as human immunodeficiency virus (HIV), hepatitis B, and hepatitis C should be required for any product that will be used in the health care environment. Products may have different contact times for viruses than for bacteria. Products that are effective against mycobacterium are considered intermediate-level disinfectants. Tuberculosis is not specifically tested in the laboratory setting because of its high pathogenicity and potential transmission to the laboratory technician. A surrogate organism, typically *Mycobacterium bovis*, is used for testing procedures. It is not uncommon for fungal organisms such as *Candida albicans* and *Aspergillus* to be in the health care environment. When evaluating fungal efficacy claims, it is important to seek products that are effective against pathogenic fungal organisms.

It's All About the Time: Importance of Overall Contact Time

Manufacturers of disinfectants are required to list detailed information regarding efficacy claims and contact time for each class of microorganism. This includes the classes of bacteria (both gram positive and gram negative), viruses, mycobacterium, and fungi. In accordance with the current requirements from the EPA, labels must also provide detailed information on the product's effectiveness against blood-borne pathogens and viruses, including HIV, hepatitis B, and hepatitis C.[150]

Many manufacturers provide several contact times for bacteria, viruses, mycobacterium, and fungi. These contact times may vary from 1 to 10 minutes. Because it is impossible for the user of the product to determine the type of potential contamination that exists on the surface, users are recommended to always disinfect the surface according to the longest contact time found on the product label to ensure full efficacy of the solution.

Use of Maintenance Kits or CVC Carts

Use of customized kits for maintenance therapies ensures the availability of proper supplies, increases compliance, and saves time.[2] Customized maintenance kits include dressing change, needleless connector change, and CVC removal. Central venous catheter maintenance checklists can be attached to kits as an educational tool for those unfamiliar with the procedure.[151] Procedure carts can be stocked with the necessary supplies for CVC maintenance care. The availability of carts on all inpatient units supports easy access to supplies.

Daily Assessment of the Need for the CVC

In addition to assessing the site and the device, designated medical providers should evaluate the need for the continued use of the CVC daily.[152] Prompt removal of the CVC is recommended when the device is no longer required for patient care, as CLABSI rates increase with longer catheter dwell times. Evaluation is recommended if the frequency of ordered laboratory test results can be decreased, or if the current IV medications can be given orally. When patients are receiving TPN, a discussion about the appropriateness of oral feedings can be implemented.

Considerations for continued use of the CVC:

- Patient receiving the following: hyperosmolar therapies (eg, TPN), chemotherapy, vesicants, irritants, vasopressor drips, central venous pressure monitoring, and frequent blood sampling

- Patient conditions: hemodynamically unstable, critical airway, poor access, and need for frequent or long-term access

Skin Antisepsis

Proper skin antisepsis for CVC insertion and dressing changes is a key component for the prevention of infection. Many CLABSIs are caused by the patient's own microbial flora contaminating the catheter as a result of improper skin antisepsis.[153] The role of a skin antiseptic is to remove as much microbial contamination from the patient's skin as possible.

Many choices for skin antiseptics are available, including povidone iodine, isopropyl alcohol, and, more recently, chlorhexidine gluconate (CHG) solutions. Clinicians should consider a variety of factors when selecting a skin antiseptic:

1. Is the skin antiseptic broad spectrum?

2. Is the product quick and easy to use?

3. Is the product's effect persistent?

4. Will the product maintain its antimicrobial activity in the presence of blood?

5. Is the antiseptic nonirritating to the patient's skin?

The most common skin antisepsis for site care is a CHG/alcohol combination solution.[153] For patient's < 2 months of age, the FDA states that chlorhexidine-based antiseptics should be used with caution.[149] In one of the early studies of chlorhexidine-based antiseptics by Garland et al,[154] a CHG/alcohol combination for skin antisepsis reduced catheter tip colonization compared with povidone iodine in 705 neonatal patients, although there were no differences in CLABSI rates.[154] In a survey of practice for neonatal ICUs, CHG was the primary skin antisepsis for CVCs.[36]

Chlorhexidine gluconate preparations have residual antibacterial activity between 48 and 72 hours.[153] For sufficient antisepsis, it is recommended that CHG be applied by using a repeated back-and-forth and side-to-side motion with friction for 30 seconds.[155] Minimization of skin irritation can be achieved by allowing the CHG to dry completely before applying the dressing. A meta-analysis of hospitalized patients with CVCs showed a 49% reduction of CLABSIs when CHG was used as compared with povidone-iodine solution. For patients with a chlorhexidine allergy or sensitivity, the use of povidone iodine should be considered. Povidone iodine is applied using concentric circles, beginning at the point of insertion. Povidone iodine should be allowed to dry completely (minimum of 2 minutes) prior to applying the dressing.[156]

CVC Dressing: Assessment and Change

A CVC dressing has dual functions: to protect the site from microorganisms and to secure the device.[157] Dressings that are dry and intact decrease the risk of catheter migration, dislodgement, catheter damage, phlebitis, thrombosis, and CLABSI.[105] Although the CDC guidelines state that healed tunneled CVCs sites may not require a dressing, a dressing is commonly used in the pediatric population to minimize the risk of catheter migration or unplanned catheter removal.[33] Topical ointments are not recommended for CVC sites, with the exception of hemodialysis catheters because of the potential for antimicrobial resistance and fungal overgrowth.[158]

CVC dressing choices include transparent semipermeable dressing, transparent dressing with gauze, and a tape and gauze dressing. There is no significant difference in the relationship between infection prevention and the type of dressing used. Choosing the appropriate dressing is based on the type of CVC, bleeding risks, skin condition, known allergies or sensitivities, patient size, patient preference, and institutional protocols. Additional factors to consider for choosing a dressing include sterility, cost, wear time, ease of application, and removal.[157]

Transparent semipermeable dressings are advantageous for visualizing the site, securing the catheter, and reducing the frequency of dressing changes.[84] Transparent semipermeable dressings are changed every 7 days and more frequently in the presence of moisture, blood, or drainage, or if the dressing in not intact.[84] Moisture under the CVC dressing proliferates the growth of microorganisms. Purulence at the CVC site is uncommon, but has been found to be highly predictive of CLABSI. Gauze dressings are appropriate for patients with blood or drainage at the site, but not for routine use, as this type of dressing should be

changed at least every 48 hours.[33] Evolving practices include the use of a hemostatic agent at the CVC site if bleeding occurs, or as a strategy to prevent bleeding.

Depending on the developmental level of the patient and underlying diagnosis, the procedure for changing the CVC dressing can be challenging because of anxiety or patient activity. A child life specialist can provide distraction and support during the procedure. Appropriate planning and support is needed to prevent the risk of catheter dislodgement, migration, and damage, as well as site contamination or epithelial stripping.[159] Performance of CVC dressing changes by a specialized team promotes a standardized approach and may minimize catheter complications.[33]

Procedural documentation for the dressing change should include the following:

- Indication for the dressing change
- Site assessment
- Type of antimicrobial agent
- External measurement of the catheter (PICCs)
- Evidence of complication (eg, erythema, edema, drainage, leaking, or catheter damage)
- Type of dressing and securement device

Catheter Securement Methods

The technique of securing the catheter is determined at the time of CVC insertion on the basis of type of catheter, manufacturer's recommendations, patient-specific indications, and institutional policy. Securement techniques are critical and directly influence catheter motion, which contributes to known complications such as catheter migration and dislodgement.[160] Catheter securement devices include specially designed securement devices such as suturing the catheter to the skin, application of securement tape strips to the catheter hub, or securement disk and application of a transparent semipermeable dressing. Education for clinicians that emphasizes proper use of the securement products is vital for positive outcomes.[160]

Suturing the catheter was found to be superior to using tape as a securement technique, with fewer complications in children, particularly migration, occlusion, and leaking (5.8% for sutured vs 32.4% for taped catheters).[161] Independent risk factors for dislodgement of tunneled catheters that failed within the initial 7 weeks include the use of multilumen CVCs, absence of exit site sutures, low platelet counts, and patients < 2 years of age.

Historically, securing the CVC, with the exception of nontunneled catheters, with suturing and tape was standard, preventing catheter pistoning and facilitating catheter stabilization.[161] Disadvantages of suturing include patient discomfort, scarring, increase in the risk of CLABSI, and risk of needlestick

injuries for the clinician. Suturing is no longer recommended by the Occupational Safety & Health Administration and the CDC.[33,161] Failure of the broad acceptance of needleless securement devices for CVCs has perpetuated unnecessary needlestick injuries.[162,163] The site of sutured CVCs should routinely be assessed for signs of irritation or infection. Sutures may require replacement if they become loose.

The use of tape or sterile skin closure strips over a PICC can lead to catheter damage and may not prevent catheter dislodgement. However, tape may be used on catheter hubs or securement disks as directed by the manufacturer and is most commonly used in the neonatal population.[36]

Securement devices are commonly used with PICCs and have been proven to be superior to sutures and tape by reducing CLABSIs and catheter dislodgement.[160] Securement devices should be replaced per manufacturer's guidelines or in the presence of drainage, blood, or compromised integrity.

A novel insertion site anchoring system with nitinol wire and a catheter clamp system has been introduced to the market.[164,165] Single-device securement may be possible by using this for the duration of the catheter, although removal of the device may be more difficult with prolonged dwell times.

Use of an Antimicrobial Product at the CVC Insertion Site

The use of a CHG/alcohol combination solution as an effective skin antiseptic prompted the development of CHG-impregnated dressings and disks. This type of technology helps protect the extraluminal pathway by reducing heavy cutaneous colonization at the site.[154] The impregnated dressings and disks cover the CVC insertion site and release chlorhexidine for up to 7 days; they require replacement per the manufacturer's recommendation. In a prospective randomized controlled study conducted in a pediatric cardiac surgical unit, the CHG-impregnated sponge was safe and significantly reduced the rates of CVC colonization when compared with a polyurethane dressing.[166] Local redness developed in 4 (5.4%) of the study patients and 1 (1.5%) of the control patients. Another retrospective study of pediatric chronic dialysis patients also showed no difference in CLABSI rates in patients using the CHG disks compared with the control group, although it demonstrated a significant reduction in exit site infections.[167] These studies may suggest that current insertion site asepsis and care may be adequate and that more emphasis needs to be placed on the intraluminal causes of CLABSI.[166,167] The data demonstrating reduction in CLABSI rates with these products are mixed; their recommendations may still hold true to target use of these products in units with a high CLABSI rate or in patients with limited access or with a history of previous infection.[126] A recent meta-analysis of chlorhexidine-integrated dressings and sponges favored their use to help reduce CLABSI, but emphasized the need to consider them as adjuncts to overall preventative measures.[105] Careful monitoring of the skin of pediatric patients is necessary when using the chlorhexidine-integrated dressings because of reports of erosive dermatitis.[168]

Daily Bathing With CHG/Alcohol Combination Solutions

Daily bathing with chlorhexidine-impregnated washcloths has been shown to reduce microbial density on the skin and to decrease transmission of microorganisms; it is a practice being advocated in the quest to reduce the risk of CLABSI.[169] In a 6-month study of pediatric ICU patients, daily bathing with a CHG/

alcohol combination showed a lower incidence of bacteremia compared with those patients receiving a standard bath.[169]

To reduce colonization and CLABSI, health care workers should consider daily bathing with chlorhexidine-impregnated washcloths for critically and chronically ill pediatric patients who have a CVC. When using chlorhexidine-impregnated washcloths, it is important to exclude the head, nonintact skin, and mucous membranes.

Use of Needleless Connectors

Needleless connectors, also known as caps, provide a safe means of CVC access.[170] Originally introduced to reduce needlestick injuries to health care workers, needleless connectors differ significantly in design from other types of connectors. These devices are classified as having either a split septum, a neutral, or a negative mechanical valve and zero fluid displacement offering neutral, negative, or positive displacement of the infusate upon locking.[170,171] Antimicrobial coatings are available on some devices.[172] In an in vitro evaluation of 3 silver-impregnated/coated needleless connectors in 2013, Chernecky et al[173] reported that routine exposure of blood impaired the efficacy of the agent.

Needleless connectors are generally the port of entry for microbial colonization with CVCs.[170] Specific needleless connector designs have been linked to an increase in CLABSI rates.[173-175] Recent data on post market surveillance of a positive displacement needleless connector showed no evidence of higher infection rates as compared with other neutral or negative needleless connectors.[176] Alterations in practice initiated with device change, staff education, and compliance regarding the use and acceptance of the new connector are factors that could have contributed to the change in CLABSI rates.[173] The flushing sequence can vary with the type of device.[172] Children, particularly young infants, require special consideration relative to the selection of needleless connectors. Important features of these devices to consider during the selection process include the following:

- **Size and profile**: The large size and bulk of some connectors makes securement to the child difficult and may also be uncomfortable.
- **Internal**: Internal fluid volumes of connectors vary by design. Priming volume is not always indicative of flush clearance. Careful attention needs to be given when administering small-volume medication.
- **Color**: The device may be transparent or clear, opaque, or colored.
- **Surface features**: Irregular, raised, or concave surfaces or gaps may affect the ability to adequately disinfect the surface.[1,175]
- **Internal parts**: Movable parts inherent in mechanical valves may alter the path of fluid flow, thereby creating stagnation and potential reservoirs for microbial growth.

- **Flushing**: The ability to adequately flush blood cells from the fluid path within the device, specific priming volume and design determine flush and lock techniques and protocols for the device.

- **Locking ability**: Use of a Luer-lock for the connector on the catheter hub or tubing is an important consideration in children.

- **Flow rate**: Restrictions of flow through the device may limit its use in patients requiring high infusion rates and these vary by design.

- **Fluid displacement**: The pattern of fluid movement (positive, negative, or neutral) upon disconnection of a syringe needs to be identified.

Antisepsis of Needleless Connectors and Catheter Hub

Disinfection of the needleless connector or catheter hub prior to entry is a critical step in decreasing the transmission of organisms acquired from the patient's skin, respiratory and oral secretions, or wounds; the clinician's hands; or during CVC maintenance, especially when higher bacterial counts are present on the surface.[172,175] Adequate disinfection of the device hinges on the concentration of organisms on the surface, use of and type of antiseptic agent, contact time of the agent, method of application, and design of the needleless connector.[175] The current National Patient Safety Goals published by the Joint Commission require health care organizations to implement and document a standardized protocol to disinfect catheter hubs and injection ports before accessing them.[177]

The needless connector, including the surface and sides of the device, must be disinfected each time the device is entered with a syringe or tubing connection; this requires training, as the CVC may be accessed several times per day in the critical care setting.[126,172,175]

To reduce contamination of the catheter hub or needleless connector, health care workers are recommended to use 70% alcohol, povidone iodine, or a CHG/alcohol combination supplied in single-use packages.[33,126] Recommendations for the type and duration of needleless connector disinfection are unknown because of lack of evidence.[33,126,178] In an in vitro study, a combination of povidone iodine and CHG/alcohol showed that it may enhance skin disinfection; however, the effectiveness may be reduced if the needleless connector is contaminated with blood or serum.[178]

Five seconds of cleaning with 70% alcohol was shown to be effective for split-septum needleless connector disinfection[175] if the needleless connector possesses heavy colonization; however, application of more than 15 seconds with the use of friction and drying was found to prevent transfer of microorganisms on 4 needleless connectors.[179] Currently, there is no recognized national standard for needleless connector disinfection.[175] Targeted education to clinicians for proper needleless connector disinfection is paramount to minimize device colonization and risk for CLABSI.[172,175,180]

Passive disinfection products (eg, port protectors) for needleless connectors have entered the market. The plastic port contains 70% isopropyl alcohol and remains on the needleless connector until the connector is accessed. This type of device provides continuous protection to the needleless connector and is for

1-time use, not to be confused with the Infusion Nurses Society's standard of disinfecting needleless ports prior to each access.[54] In a study by Sweet et al,[180] CLABSI rates significantly decreased by changing the needleless connector disinfection practice from alcohol wipes to a port protector. Minimum dwell times vary based on the manufacturer's instruction for use.[172]

Needleless Connectors and Administration Set Changes

Administration sets include infusion tubing (primary and secondary sets) and extension tubing. Recommended replacement of administration sets for patients receiving lipids and blood is every 24 hours, as these infusates may serve as a growth medium for microorganisms[33]; however, in a study of pediatric stem cell patients, the CLABSI rate increased when the needleless connector was changed every 24 hours.[5]

Administration sets for intermittent infusions should be changed every 24 hours because of the high risk of contamination.[33] Time intervals for changing administration sets for solutions containing dextrose and parenteral nutrition solutions not containing lipids is every 96 hours. Strict adherence to needleless connector and hub disinfection must be followed, along with the number of times the device is accessed.[126] Continuous infusions do not require a needleless connector.[172]

It is important to assemble infusion tubing consistently for each type of CVC or therapy by using an aseptic or sterile technique. Reducing the number of manipulations of needleless connectors and infusion tubing decreases the risk of a CLABSI.[126] An add-on device should be changed with administration set changes. Needleless connectors should be changed at least as frequently as the administration set.[33,54] When CVCs are locked, they should not be changed more frequently than every 96 hours.[33] Administration sets and needleless connectors should be changed immediately for any suspected break in sterile technique or visible soiling.[33,175]

Blood Sampling From CVC

Little scientific evidence exists defining the optimal methods for obtaining blood samples from CVCs in children, and clinicians use a variety of unproven techniques.[181] Concerns related to obtaining laboratory specimens from pediatric CVCs include risks of volume depletion, skewing of laboratory test results, catheter occlusion, catheter colonization, and CLABSIs.

As a result of these concerns, children often undergo multiple venipuncture procedures before clinicians are able to obtain blood samples. Multiple needle puncture attempts often result in pain, fear, anxiety, and dissatisfaction with care by children and family members.[22] The presence of a CVC enhances the ability to easily obtain blood samples, eliminating the need to perform repeated venipunctures, thus decreasing one of the most commonly identified sources of trauma in pediatric patients. The Infusion Nurses Society *Standards of Practice* state that "benefits include avoidance of anxiety, discomfort, and dissatisfaction associated with venipuncture in patients who require frequent blood tests and/or those with difficult vascular access."[54]

General Guidelines

The use of a CVC for obtaining blood specimens necessitates the need to remove lumen content such as fluids or recently infused medications, or indwelling saline or heparinized saline flush solutions. Inaccuracy of laboratory results can directly affect the treatment plan, and conflicting reports have been published on the accuracy of laboratory results obtained from CVCs that have been flushed or used for infusion. Prior to blood sampling from a CVC, the infusions should be stopped and the CVC flushed with preservative-free 0.9% sodium chloride or other compatible solution. For multilumen catheters, the largest lumen should be used and gentle withdrawal pressure exerted.[25] When a CVC has staggered lumen exit holes, the sample should be drawn from the distal hub or the hub port that coincides with the opening deepest in the superior vena cava.[54] Multiple entries into the CVC should be limited by consolidating blood sampling to once per day and by using low-volume blood collection tubes or Microtainers for specimens to avoid depleting blood volume.[25]

Many inconsistencies exist in clinical practice regarding the most appropriate method for obtaining blood specimens from pediatric CVCs.[182] Three techniques for obtaining blood specimens from CVCs are described in the literature, although there are few scientific studies to support their use: the discard method, the reinfusion method, and the push-pull or mixing method.[181]

Discard Method

The purpose of the discard method is to remove flush solutions from the catheter such as normal saline or heparin, to remove potential contaminants, and to facilitate obtaining accurate laboratory specimens.[181] The discard method is recommended by many national organizations, and it is the method most commonly reported in existing literature. Disadvantages include the potential for significant blood loss, risk of blood exposure for the clinician, and the potential to confuse a discard specimen with the blood sample. A currently unsolved question is the most appropriate amount of discard volume to remove for efficacious results. In 1996, a discard volume of 1.5 mL (3 times the dead space volume) was shown to be sufficient for accurate hemoglobin measurements from IVs.[183] A 2010 study by Berger-Achituv et al[184] supported 3 times the catheter dead space as discard volume for blood sampling from IVs, and this guideline may be useful for extrapolation in calculating CVC discard volume. Caution is advised when obtaining and interpreting drug levels from CVCs, as some studies have shown skewed results, especially for samples from implanted ports, silicone catheters, and the same catheter lumen used to administer the drug.[185] A 2002 study by Hinds et al[186] examined the accuracy of coagulation studies drawn from CVCs and concluded that not a 6-mL, a 9-mL, or a 12-mL discard from a heparinized CVC was sufficient to yield clinically trustworthy prothrombin time, activated partial thromboplastin time, or fasting blood glucose values and that this research-based information makes it unreliable and potentially unsafe to sample blood from a CVC to assess coagulation. The Infusion Nurses Society Standards do not support blood sampling for coagulation levels with heparinized CVCs.[54] Table 5 reviews blood sampling techniques for CVCs.

Table 5. Blood Sampling Techniques

Recommendations for Practice: Discard Method	Reference
Flush catheter prior to obtaining specimen and use a discard specimen when obtaining drug levels. Drug concentrations were present in catheters with no flushing after dose and/or when no discard was taken. Use a new syringe for the final sample, not the discard syringe.	Wanwimolruk and Murphy,[187] 1991
Consider removal of at least 3 times the catheter volume to clear the catheter of infusate.	Yucha and DeAngelo,[183] 1996; Berger-Achituv et al,[184] 2010
Consider use of a larger saline flush (10-20 mL; normal saline based on patient weight) prior to drawing aminoglycoside levels from the CVC, as this practice was shown to greatly improve the accuracy of results.	Mogayzel et al,[188] 2008
Use discard technique for obtaining blood cultures, drug levels, and coagulation studies. Consider using push-pull method for hematology and chemistry testing.	Adlard,[189] 2008

Reinfusion Method

The reinfusion method aspirates the discard volume into a syringe that is set aside while the samples are drawn, and then is reinfused into the patient.[190] The advantage of reinfusing the discard blood specimen is that this method is thought to limit depletion of blood volume.[182,191] A distinct concern regarding reinfusion of discard specimens is the condition of the blood being returned to the patient. Half of discard specimens sampled contained clots when evaluated for this risk.[181] Current *Standards of Practice* do not recommend the reinfusion method of blood sampling because of the risk of contamination and blood clot formation when the discard specimen is reinfused (see Table 6).[54]

Table 6. Reinfusion Method for Blood Sampling

Recommendations for Practice: Reinfusion Method	Reference
Methods of drawing blood requiring reinfusion of discard may introduce clots into the system, although whether the clots present in the catheter and their reinfusion represent a significant risk to the patient outcome is unclear.	Cosca et al,[181] 1998

Push-Pull or Mixing Method

The push-pull or mixing method for obtaining blood specimens from the CVC requires mixing the blood back and forth in the same syringe several times, theoretically to eliminate IV fluids or to flush solutions from the catheter lumen.[181] In 1998, Holmes[192] described the push-pull method in a study that was done in the adult oncology population. The CVC was flushed with 5 mL of normal saline by using a 10-mL syringe, and then without removing the saline syringe, 6 mL of blood was aspirated and then flushed back into the catheter. This process was repeated 3 times. The empty syringe was then removed and a new syringe or Vacutainer was attached to obtain laboratory samples. The catheter was then flushed with 20 mL of normal saline and heparinized normal saline.

The first pediatric study comparing the push-pull and discard methods was conducted by Barton et al[193] in 2004. This study of paired blood samples, using push-pull and 4-mL discard methods via a stopcock, was conducted in 28 pediatric oncology inpatients, who were 6 months to 12 years of age. The laboratory values compared were hologram, glucose, and electrolytes. Results demonstrated statistically significant, but not clinically significant, differences in paired samples and no reported catheter infections in children enrolled in the study during data collection.[193] In 2008, Adlard[189] studied 30 pediatric oncology patients (8 months to 17 years) with tunneled or implanted ports. This study compared the laboratory values of paired samples obtained by using the push-pull and discard methods to determine the level of agreement. Results were similar to those of the Barton et al study.

Although additional studies are needed, this method appears to be one answer to the issue of iatrogenic anemia from laboratory draws. In addition, the push-pull method uses less equipment and reduces the risk of catheter contamination or blood exposure. Even though there is an evolving body of evidence to support the push-pull method, some limitations include difficulty in obtaining enough blood for 3 to 4 push-pull sequences from small catheters, possible risk of clots being reinfused, and potential hemolysis with the agitation of the blood (Table 7). The amount of blood obtained for blood sampling, including discard and laboratory assay amounts, should be documented in the patient's medical records.

Table 7. Push-Pull or Mixing Method for Blood Sampling

Recommendations for Practice: Push-Pull or Mixing Method	References
Use a new sterile syringe (other than the mixing syringe) to obtain the specimen.	MacGeorte et al,[190] 1998; Holmes,[192] 1998
Consider removal of at least 3 times the catheter volume to clear the catheter of infusate.	Pinto,[194] 1994
Consider using the push-pull method for hematology and chemistry testing. Use the discard technique for obtaining blood cultures, drug levels, and coagulation studies.	Adlard,[189] 2008

Flushing

Flushing is defined as the "act of moving fluids, medications, blood, blood products, and nutrients out of a vascular access device into the bloodstream, ensuring delivery of those components and verifying device patency."[54] CVC flushing is the primary intervention used to verify patency and theoretically clear the lumen(s) between doses of medications that could cause potential occlusion by formation of a precipitate or thrombus. Central venous catheters are generally flushed before and after medication administration, before and after blood sampling, after an infusion is discontinued, and when the catheter is not being used for infusion and is locked. Locking the CVC prevents blood reflux and minimizes catheter occlusion.

The most frequently used flush solution for assessing line patency and clearing the catheter lumen prior to or between medication administration is normal saline, or 0.9% sodium chloride, except in cases where sodium chloride is incompatible with the medication being administered (eg, amphotericin B). In

children, medication administration systems include large volume pumps, gravity sets, syringe pumps, and IV push; therefore, the unique tubing configurations used in the pediatric population and volume contained therein are considered when calculating flush volumes.

Sodium chloride alone did not prove efficacious for maintaining catheter patency, except when used in valve catheters. In 2009, Cesaro et al[195] conducted a randomized trial of 203 oncology patients with newly inserted tunneled, cuffed catheters for more than 75,000 catheter days. The researchers compared one cohort with heparin flushing and a "standard cap" to another cohort with saline-only flushing and a positive displacement needleless connector. The saline cohort demonstrated twice the rate of catheter occlusion and almost triple the rate of bacteremia as the heparin cohort did.

Heparin remains the recommended locking solution for intermittent flushing of CVCs in the pediatric population. Heparin is an anticoagulant that is instilled in the catheter lumen to maintain patency and prevent occlusions; however, occlusions may still occur from the formation of fibrin extraluminally. The use of heparin in pediatric and neonatal populations has been associated with significant risks. The clinician must be aware of side effects of heparin, which can include iatrogenic hemorrhage, heparin-induced thrombocytopenia, heparin-induced thrombosis, and thrombocytopenia syndrome.[196] Heparin comes in different strengths and is packaged in vials with similar labeling, factors that can increase the risk of error.[50] According to the FDA, "Pediatric patients, including neonates, have died as a result of medication errors in which heparin sodium injection vials have been confused with 'catheter lock flush vials." [149] Medication dosing errors represent a significant risk of overheparinization of children. In addition, many IV-administered medications are incompatible with heparin, including gentamycin, tetracycline, methicillin, vancomycin, erythromycin, codeine, and morphine.[196]

Although multiple publications have reviewed the efficacy of heparin flush for IVs, as well as compared various concentrations, flushing schedules, and flush delivery technique, few randomized controlled studies exist for flushing of CVCs in children. Studies available prior to 2000 reported conflicting practice recommendations. In 1972, the "heparin lock" was described for patients treated with IV antibiotics for cystic fibrosis exacerbation.[197] A later study in 1976 reported success with the use of 10 U of heparin in 1 mL of normal saline to maintain patency of IV devices.[198] In 1979, Goldberger et al[199] published a report demonstrating that cycled infusions of parenteral nutrition in children via silicone CVCs were kept patent during periods of noninfusion by using a heparin lock. In 1991, Smith et al[200] reported no significant difference in the incidence of occlusions between the use of heparin flush solution twice daily and a flushing protocol using an isotonic saline flush once a week. Conversely, in 1998, Randolph et al[201] completed a meta-analysis and reported that prophylactic heparin decreases catheter-related venous thrombosis and bacterial colonization of CVCs and may decrease catheter-related bacteremia. Published reports of outcomes with PICCs described intermittent flushing with heparinized saline in strengths ranging from 10 to 100 U/mL once or twice daily. Reported concentrations of heparin flushes in the neonatal and pediatric population range from 1 to 100 U/mL and published standards recommend that CVCs be flushed at established intervals.[54]

Few randomized controlled studies exist for pediatric CVC flushing/locking solution volume, type, and frequency; anecdotal reports and descriptive studies most commonly report the use of various amounts of heparinized saline.[202] The exception to using heparinized saline is a valved catheter, as saline is the recommended flushing/locking solution.[202] In 2011, Marshall et al[203] collected data on more than 500 CVCs at the Children's Hospital of Michigan to establish a scientific basis for heparin dosing in pediatric patients. The researchers measured catheter volumes and found that intraluminal volumes did not exceed 1 mL for PICCs, nontunneled CVCs, and tunneled CVCs and were less than 2 mL for ports and apheresis catheters. The results gave support for changes in the volumes needed for heparinization.[203] After a review of the literature and standards published by organizations, this report recommended guidelines categorized by catheter type and size, decreasing heparin doses by half, and using a continuous infusion rather than intermittent flushing for PICC lines 2Fr or smaller.[50] Ranges of heparin concentration reported in multiple publications are outlined in Table 8. Since heparin is not an innocuous medication, as noted previously, maximum daily dosage can be a concern. In one study of pediatric patients receiving cycled home parenteral nutrition, the authors recommended not exceeding a maximum dose of 50 U/kg/day to maintain the patient well below the dose for systemic heparinization.[204]

Although heparinized saline is the most commonly reported solution for flushing CVCs, other solutions have been reported for locking catheters to maintain patency, or to inhibit or treat CVC infection. These solutions may be used alone, prophylactically, in conjunction with systemic antibiotics, or combined with heparin or other agents with antimicrobial or anticoagulant activity. Published reports, including some on neonatal and pediatric populations, include the use of ethanol, antibiotics, amphotericin B, citrate/taurolidine and minocycline, and EDTA.[46,131,140,205]

The goal of fibrinolytic agents is to decrease the risk of thrombosis and related infection, while antibiotic lock solutions are used to extend the life of the catheter and to decreased morbidity and the financial burden of managing CLABSIs.[205] The ethanol-lock technique, although contraindicated for use with catheters made of material not compatible with ethanol, appears to be a safe, well-tolerated, and effective way to treat CVC infections, even in small children.[131,140] Ethanol lock has been demonstrated as being efficacious for preserving catheter life in children who have long-term or life-time need for central venous access with limited sites for CVC placement, such as children with short-bowel syndrome who are dependent on parenteral nutrition.[140]

Antibiotic lock describes a solution that is usually a combination of heparin and one or more antibiotics; this solution is then allowed to dwell within the internal lumen of the catheter.[127] There is evidence of potential efficacy of antibiotic lock solutions containing vancomycin used for short periods of dwell time in pediatric patients.[130] Use of prophylactic antimicrobial lock solution is recommended in patients with long-term catheters who have a history of multiple catheter infections despite optimal maximal adherence to aseptic technique.[33] Henrickson et al[206] published a pediatric study comparing heparin, vancomycin and heparin, and heparin-vancomycin-ciprofloxacin to evaluate the effectiveness of each against CLABSI rates. The results of the study demonstrated that either the vancomycin-heparin combination or the heparin-vancomycin-ciprofloxacin combination significantly decreased the incidence of CLABSI.

A prospective cohort study, published in 2003, evaluated the effectiveness of methicillin/EDTA as a prophylactic lock solution with implanted ports in pediatric oncology patients. This study compared a control group whose ports were flushed monthly with heparinized saline to the experimental group, whose ports were flushed weekly with 2 mL of 3 mg minocycline and 30 mg EDTA for 6 months. There was no evidence of CLABSI or thrombosis in the experimental group, leading the researchers to state that this combination of antibiotic flushing solution is efficacious in preventing CLABSI in children with cancer without causing adverse events.[207]

Other agents have been studied, but not in children. Taurolidine is an antimicrobial agent that demonstrated broad antibacterial activity and was found to prevent biofilm formation on dialysis catheters. It is rapidly metabolized into 2 harmless products: taurine and carbon dioxide.[208]

Although initial data are promising, particularly for patients who are CVC dependent, prospective randomized studies are needed to compare antibiotic-lock, ethanol-lock, and locking techniques with other agents, using these agents as prophylaxis alone or combined with systemic antimicrobials in the prevention and/or treatment of CLABSI. Along with the solution used, volume is an issue of concern, particularly for pediatric patients, who may be volume restricted because of their size or the disease state.

Flushing Techniques

The technique for flushing catheters can vary by institution, equipment, and clinician. The syringe size used for flushing may cause pressure gradients that can damage catheters.[195] Catheters should be flushed by using prefilled, single-use syringes to prevent contamination. In an effort to decrease catheter fractures that may occur from high pressure generated by small syringes, particularly when forced against resistance, many manufacturers recommend the use of 10-mL syringes for flushing. However, when small doses of medications are administered, often a small syringe must be used for accuracy. A safe practice is to check the patency of the CVC first by using a 10-mL syringe filled with a compatible flush solution, such as normal saline, followed by the medication delivery in the smaller syringe.

The pulsatile flushing technique has gained popularity in the clinical arena and is effective for reducing catheter bacterial colonization.[209] This technique calls for a rapid push-pause method to inject the flush solution into the catheter; it is based on the theoretical concept that the turbulent flow of the flush solution clears blood components that attach to the catheter's internal wall, creating less chance for catheter occlusion. Procedures for locking pediatric CVCs must be safe, efficacious, and evidenced-based in order to provide optimum care for these fragile lines (see Table 8).

Table 8. Locking Guidelines for Pediatric CVCs [25,50,203]

Device	Locked device (volume, solution, and frequency) Add volume for add-on devices to priming volume.
PICCs: Device priming volume ranges from 0.06 to 0.6 mL. Check manufacturer guidelines.	2Fr and smaller: continuous infusion preferred or 1 mL heparinized saline (10 U/mL) every 6 hours 2.6Fr and larger: 1-2 mL heparinized saline (10 U/mL) every 12 hours
Tunneled and nontunneled: Device priming volume ranges from 0.12 to 1.3 mL. Check manufacturer guidelines.	1-3 mL heparinized saline (10-100 U/mL) every 24 hours
Implanted port: Device priming volume ranges from 0.8 to 2 mL. Check manufacturer guidelines.	If used for more than 1 medication daily: 3-5 mL heparinized saline (10 U/mL) Monthly maintenance flush: 3-5 mL heparinized saline (100 U/mL)

Abbreviation: PICC, peripherally inserted central catheter.

Management of Occluded CVCs

The inability to freely flush or aspirate a CVC can be categorized as a nonthrombotic (mechanical) or thrombotic occlusion. The CVC must be carefully assessed to determine the type of occlusion, as interventions or treatment may vary. The CVC catheter must be thoroughly assessed to rule out a kinked or clamped catheter or infusion tubing, precipitate, or catheter tip malposition. Repositioning the patient's extremity or assessing for a catheter kink under the dressing may help alleviate a nonthrombotic occlusion. Precipitation of medication can be dissolved with the appropriate clearing agent. If a catheter tip malposition is suspected, an x-ray may be necessary.

Restoring catheter function is preferred over CVC replacement to preserve the patient's vasculature. For thrombotic occlusions, a fibrinolytic is indicated. Prompt treatment of the catheter occlusion leads to improved outcomes.

Use of Antimicrobial- or Antibiotic-Coated Catheters

Catheters impregnated with or coated with antibiotic or antimicrobial agents have been clinically effective in reducing CLABSIs in adult patients. However, a dearth of literature exists in the pediatric population and the efficacy of these catheters remains unclear.

A prospective observational trial of coated catheters in 225 PICU patients was studied over a 13-month period. Patients were randomized to either a noncoated (NC) CVC or a minocycline–rifampin-coated (MR) CVC. Of the 225 patients, NC CVCs were inserted in 156 patients and MR CVCs were inserted in 69 patients. The incidence of CLABSI was not significantly different between the 2 groups: 7.53 per 1000 catheter days with MR CVCs and 8.64 per 1000 catheter days in the NC CVCs. The trial demonstrated that the median time to onset of infection in children with the MR CVCs was 3-fold longer than that in children with the NC CVCs.[31]

Impregnated catheters are cost-effective; consideration should be given to the use of an antibiotic-coated catheter as a strategy to decrease CLABSI rates. High-risk patients are defined as those:

- who are receiving TPN
- who are critically ill
- have a history of CLABSI
- with multiple vascular access devices (CVCs, arterial line)
- with limited veins for future vascular access devices

Replacement of CVCs

Routine replacements of CVCs are not recommended as a measure to decrease CLABSI rates. Catheter exchange is indicated for catheter tip malposition, fractured catheters in patients requiring additional therapy, and patients who have limited access sites. Risks vs benefits should be discussed with the medical provider prior to exchanging a CVC.

Education

All clinicians caring for children who have an indwelling CVC or in whom one is anticipated should be knowledgeable about catheter choices, procedures planned for catheter placement, ongoing assessment of the patient and the device, identifying and targeting prevention of potential complications, and care strategies within the medical care facility and in the home situation. Raising the awareness of clinicians of their role in reducing infection has been shown to decrease the rate of CLABSIs. The health care facility or agency bears responsibility for ensuring adequately educated and prepared staff and for maintaining compliance with facility protocols for care. Educational programs need to reflect the dynamic environment of pediatrics and should be updated on an ongoing basis. The clinician should be knowledgeable of developmental stages, procedural preparation for the pediatric patient, and pain management. Approaches to educational programs vary from a focused 1-day program to a comprehensive ongoing endeavor that addresses appropriate care and maintenance of all types of CVCs. Competencies should be evaluated on an ongoing basis and be integrated in CVC policies and procedures.

Staff education has been identified as one of the strongest predictors of long-term success with PICCs. Earlier identification of catheter-related complications has being attributed to staff knowledge. An increase in knowledge and self-efficacy, along with a significant decline in the rate of PICC occlusion, has been demonstrated following targeted educational programs.

One of the most studied areas of success is in the reduction of CLABSI. Improved catheter care is closely related to infection prevention. Successful clinician educational programs include lectures, web-based

training modules, hands-on demonstration, and provision of feedback to staff hospital-wide as patients move between departments. Posters and fact sheets related to CVC education can be placed on units as well.

Ongoing education and feedback to clinicians about CLABSI has been shown to increase staff compliance to bundle elements and to adhere to strict aseptic technique during catheter maintenance.[210] CLABSI rates significantly decreased following revision of catheter care protocols and intensive staff education in a children's hospital. However, education may not lead to sustained improvement and needs to be further investigated. Modest compliance with a previously successful program to decrease the rate of CLABSI in a surgical ICU 18 months later stressed compliance with best practices of CVC maintenance and insertion.[210]

Initial and ongoing competencies for catheter care should be monitored. Evidence-based educational programs with a strong emphasis on aseptic technique can reduce CLABSIs. Clinicians should be educated on the benefits and use of the catheter maintenance checklist. Education of clinicians responsible for managing central lines should include care and maintenance strategies, along with identification and management of complications.[44]

Administrative support for infection prevention efforts should minimally include oversight of educational efforts and competencies, revision of policies and procedures based on evidence-based practice, and implementation of checklists.[118] It is essential that those clinicians caring for central lines are not only knowledgeable about evidence-based practices for reducing CLABSI, but that they also consistently practice the guidelines. In addition, scheduled reviews of unit-specific CVC outcome data can assist in communicating CLABSI rates (eg, posting the number of days since the last CLABSI). Unit and institutional successes can be celebrated to acknowledge team efforts in reducing CLABSI rates.

Development of Specialty Teams or Competent Trained Clinicians for CVC Maintenance Procedures

Several studies support the use of specialized teams in decreasing CVC complications by standardizing practices and products, monitoring catheter sites, and being a resource to less experienced staff. Central venous catheter complications can be minimized by a dedicated nursing team.[151] For a vascular access team to be effective, a collaborative approach between the stakeholders is imperative, along with CVC competencies encompassing all aspects of catheter care. Structured house-wide CVC educational programs enhance the nurses' knowledge of CVC care, identification and treatment of complications, and adherence to aseptic technique. Compliance with institutional CVC policies is linked with targeted educational programs. A team can be involved with oversight of policy and procedures, education, process improvement, and safety and efficacy of vascular access devices, as well as routine performance of dressing changes, infusion tubing change, catheter clearance, and catheter repair. The benefits of a dedicated team of highly skilled clinicians for PICC placement can reduce the need for multiple vascular access device insertions, which can have significant cost savings for an institution.

Routine Surveillance of CVCs and Other Vascular Access Devices and Procedures

Collecting and benchmarking outcome data with the National Healthcare Safety Network (NHSN) assists with comparing current and historical data. Compiling and evaluating complication rates can aid prioritization of changes for policies and procedures. Multiple vascular access devices are not uncommon for pediatric patients. Surveillance of other vascular access devices (eg, peripheral arterial catheters) is critical, as many of these devices have been shown to be a relative risk factor for increasing CLABSI rates.

Standardizing insertion and maintenance practice with peripheral arterial catheters and CVCs has the potential to lower CLABSI rates.[151] Developing and implementing documentation, along with a procedure note that incorporates the checklist, ensures elements of sterile technique and ensures that CVC maintenance procedures are consistently followed. Staff members who serve as monitors can be educated on appropriate CVC procedures and can be empowered to stop the procedure if sterile technique is not followed.

Development of a Process Improvement Plan for CVCs

Growing evidence suggests that hospitals participating in collaborative quality improvement efforts to reduce CLABSI are successful.[151] The collaborative process for clinical quality improvement can result in effective change through the sharing of best practices, learning from the success of others, and achieving a friendly competitive spirit. The CDC recommends surveillance in critical care areas and other patient populations to collect data on CLABSI rates and to identify trends and potential lapses with infection control practices. Collaboratives also assist in prioritizing infection prevention efforts and outline insertion and maintenance bundles, pool data, and provide guidance and peer support.

For confirmed CLABSIs, a root cause analysis is recommended. This type of approach enables clinicians and leaders to examine all care aspects of the CVC and potential risk factors. From the information obtained, a process improvement plan can be implemented. Surveillance on care processes can be performed to identify areas of improvement, including:

- Hand hygiene
- Sterile or aseptic technique
- Use of clean gloves with CVC access
- Proper skin disinfectant
- Catheter access technique
- Needleless connector/infusion tubing change technique

- Dressing change technique
- Adherence to CVC maintenance bundle
- Complication rates

Conclusion

CVCs in pediatric patients are not without risk of complications. Some CVCs carry more risks than others. Infection is a known complication that at times necessitates removal and replacement of CVCs in pediatric patients who have limited access sites. Central venous catheter risk factors include catheter dwell time, location of CVC, multilumen catheters, patient location, and patient condition. Proven technology and procedures should be used to decrease the incidence of infection, and future research should focus on decreasing entry of microorganisms.

Prioritizing care for pediatric vascular access includes early assessment and preserving indwelling CVCs, with a primary focus on prevention strategies.[180] Vigilance, ongoing education, competencies, and checklists can improve central line care by providing repetitive attention to detail regarding CVCs.[2,151] Clinicians have a responsibility to review and integrate evidence-based guidelines to improve patient outcomes. Successful approaches to achieving CLABSI rates of zero parallel meticulous CVC care, ownership, teamwork, and explicit support from leadership.[2]

References

1. Kramer N, Doellman DD, Curley M, Wall JL. Central vascular access device guidelines for pediatric home-based patients: driving best practices. *J Vasc Access*. 2013;18(2):103-113.

2. Rinke ML, Chen AR, Bundy DG, et al. Implementation of a central line maintenance care bundle in hospitalized pediatric oncology patients. *Pediatrics* 2012;130(4):e996-e1004.

3. Revel-Vilk S, Ergaz Z. Diagnosis and management of central-line associated thrombosis in newborns and infants. *Semin Fetal Neonatal Med*. 2011;16(6):340-344.

4. van Ommen CH, Tabbers MM. Catheter-related thrombosis in children with intestinal failure and long-term parenteral nutrition: how to treat and to prevent? *Thromb Res*. 2010;126(6):465-470.

5. Sandora TJ, Gerner-Smidt P, McAdams AJ. Impact of needleless connector change frequency on central line-associated bloodstream infection rate. *Am J Infect Control*. 2014;42(5):485-489.

6. Billett AL, Colletti RB, Mandel KE, et al. Exemplar pediatric collaborative improvement networks: achieving results. *Pediatrics*. 2013;131(S4):S196-203.

7. Gaur AH, Bundy DG, Gao C, et al. Surveillance of hospital-acquired central line-associated bloodstream infections in pediatric hematology-oncology patients: lessons learned challenges ahead. *Infect Control Hosp Epidemiol.* 2013;34(3):316-320.

8. Dzierzega M, Ossowska M, Chmiel D, Wieczorek A, Balwierz W. The malposition of central venous catheters in children. *Pol J Radiol*. 2014;25(79):275-278.

9. Kim H, Jeong CH, Byon HJ, Shin HK, Yun TJ. Predicting the optimal depth of left-sided central venous catheters in children. *Anaesthesia*. 2013;68(10):1033-1037.

10. Colacchio K, Deng Y, Northrup V, Bizzarro MJ. Complications associated with central and non-central venous catheters in a neonatal intensive care unit. *J Perinatol*. 2012; 32:941-946.

11. Baskin KM, Hunnicutt C, Beck ME, Cohen ED, Crowley JJ, Fitz CR. Long-term central venous access in pediatric patients at high risk: conventional versus antibiotic-impregnated catheters. *J Vasc Interv Radiol.* 2014;25(3):411-418.

12. Gaballah M, Krishnamurthy G, Keller MS, McIntosh A, Munson DA, Cahill AM. US-guided placement and tip position confirmation for lower-extremity central venous access in neonates and infants with comparison versus conventional insertion. *J Vasc Interv Radiol.* 2014;25(4):548-555.

13. Subramanian S, Moe DC, Vo JN. Ultrasound-guided tunneled lower extremity peripherally inserted central catheter placement in infants. *J Vasc Interv Radiol*. 2013;24(12):1910-1913.

14. Sneath N. Are supine chest and abdominal radiographs the best way to confirm PICC placement in neonates? *Neonatal Netw*. 2010;29(1):23-35.

15. Jain A, Deshpande P, Shah P. Peripherally inserted central catheter tip position and risk of associated complications in neonates. *J Perinatol.* 2013;52(5):307-312.

16. Clark E, Giambra BK, Hingl J, Doellman D, Tofani B, Johnson N. Reducing risk of harm from extravasation: a 3-tiered evidence-based list of pediatric peripheral intravenous infusates. *J Infus Nurs*. 2013;36(1):37-45.

17. Bourgeois FC, Lamagna P, Chiang VW. Peripherally inserted central catheters. *Pediatr Emerg Care.* 2011;27(6):556-561.

18. Askegard-Giesmann JR, Caniano DA, Kenney BD. Rare but serious complications of central line insertion. *Semin Pediatr Surg*. 2009;18(2):73-83.

19. Perin G, Scarpa MG. Defining central venous line position in children: tips for the tip. *J Vasc Access.* 2015;16(2):77-86.

20. Goff DA, Larsen P, Brinkley J, et al. Resource utilization and cost of inserting peripheral intravenous catheters in hospitalized children. *Hosp Pediatr.* 2013;3(3):185-191.

21. Myers LA, Arteaga GM, Kolb LJ, Lohse CM, Russi CS. Prehospital peripheral intravenous vascular access success rates in children. *Prehosp Emerg Care*. 2013;17(4):425-428.

22. Uman LS, Birnie KA, Noel M, et al. Psychological interventions for needle-related procedural pain and distress in children and adolescents. *Cochrane Database Syst Rev*. 2013;(10):CD005179. doi:10.1002/14651858.CD005179.pub3.

23. Walker G, Todd A. Nurse-led PICC insertion: is it cost effective? *Br J Nurs.* 2013;22(19):S9-15.

24. Yang RY, Moineddin R, Filipescu D, et al. Increased complexity and complications associated with multiple peripherally inserted central catheter insertions in children: the tip of the iceberg. *J Vasc Interv Radiol.* 2012;23(3):351-357.

25. Alexander M, Corrigan A, Gorski L, Phillips L. *Core Curriculum for Infusion Nursing*. 4th ed. Philadelphia, PA: Infusion Nurses Society; 2013.

26. Doellman DA, Nichols I. Modified Seldinger technique with ultrasound for PICC placement in the pediatric patient: a precise advantage. *J Vasc Access*. 2009;14(2):93-99.

27. Baskin JL, Pui, CH, Reiss, U, et al. Management of occlusion and thrombosis associated with long-term indwelling central venous catheters. *Lancet*. 2009;374(9684):159-169.

28. Nifong TP, McDevitt TJ. The effect of catheter to vein ratio on blood flow rates in a simulated model of peripherally inserted central venous catheter. *Chest.* 2011;140(1):48-53.

29. Chang DH, Kabbasch C, Bovenschulte H, Libicher M, Maintz D, Bangard C. Experiences with power-injectable port systems: complications, patient satisfaction and clinical benefit. *Rofo.* 2013;185(5):454-460.

30. Weber JM, Sheridan RL, Fagan S, et al. Incidence of catheter-associated bloodstream infection after introduction of minocycline and rifampin antimicrobial coated catheters in a pediatric burn population. *J Burn Care Res.* 2012;33(4):439-343.

31. Cheliah A, Heydon KH, Zaoutis TE, et al. Observational trial of antibiotic-coated central venous catheters in critically ill pediatric patients. *Pediatr Infect Dis J*. 2007;26(9):816-820.

32. Westergaard B, Classen V, Waither-Larsen S. Peripherally inserted central catheters in infants and children – indications, techniques, complications, and clinical recommendations. *Acta Anaesthesiol Scand.* 2013;57(3):278-287.

33. O'Grady NP, Alexander M, Burns LA, et al. 2011 Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. http://www.cdc.gov/hicpac/BSI/BSI-guidelines-2011.html. Published 2011. Accessed January 5, 2015.

34. National Kidney Foundation. KDOQI Clinical practice guidelines and clinical practice recommendations for 2006 updates: hemodialysis adequacy, p*eritoneal dialysis adequacy and vascular access*. *Am J Kidney Dis*. 2006;48(suppl 1):S1-322.

35. Cotogni P, Pittiruti M. Focus on peripherally inserted central catheters in critically ill patients. *World J Crit Care Med*. 2014;3(4):80-94.

36. Sharpe EL. Neonatal peripherally inserted central catheter practices and their association with demographics, training, and radiographic monitoring: results from a national survey. *Adv Neonatal Care*. 2014;14(5):329-335.

37. Pettit J. External jugular cannulation in infants and children. *J Infus Nurs*. 2009;32(2):93-97.

38. Jumani K, Advani S, Reich NG, Gosey L, Milstone AM. Risk factors for peripherally inserted central venous catheter complications in children. *JAMA Pediatr.* 2013;167(5):429-435.

39. Levy I, Bendet M, Samra Z, Shalit I, Katz J. Infectious complications of peripherally inserted central venous catheters in children. *Pediatr Infectious Dis J*. 2010;29(5):426-429.

40. Qiu XX, Guo Y, Fan HB, Shao J, Zhang XB. Incidence, risk factors and clinical outcomes of peripherally inserted central catheter spontaneous dislodgement in oncology patients: a prospective cohort study. *Inf J Nurs Stud*. 2013;51(7):955-963.

41. Fallon SC, Kim ME, Fernandes CJ, Vasudevan SA, Nuchtern JG, Kim ES. Identifying and reducing early complications of surgical central lines in infants and toddlers. *J Surg Res*. 2014; 190(1):246-250.

42. Alyagari R, Song JY, Donohue JE, Yu S, Gaies MG. Central venous catheter-associated complications in infants with single ventricle: comparison of umbilical and femoral venous access routes. *Pediatr Crit Care*. 2012;13(5):549-553.

43. Marik PE, Flemmer M, Harrison W. The risk of catheter-related bloodstream infection with femoral venous catheters as compared to subclavian and internal jugular venous catheters: a systematic review of the literature and meta-analysis. *Crit Care Med.* 2012;40(8):2479-2485.

44. McCaskey MS. Preventing catheter-related bloodstream infections: a pediatric case study. *Home Healthc Nurse*, 2009;27(2):124-126.

45. Nurse BA, Bonczek R, Barton RW, LaRose DT. Low rate of bacteremia with a subcutaneously implanted central venous access device. *J Vasc Access.* 2014;15(1):51-55.

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

47. Harish K. Chemoport-skin erosion: our experience. *Int J Angiol*. 2014;23(3):215-216.

48. Callahan MJ, Servaes S, Lee EY, Towbin AJ, Westra SJ Frush DP. Practice patterns for the use of iodinated i.v. contrast media for pediatric CT studies: a survey for the society of pediatric radiology. *Am J Roentgenol.* 2014;202(4):872-879.

49. Sadeghi T, Mohammadi N, Shamshiri M, Bagherzadeh R, Hossinkhani N. Effect of distraction on children's pain during intravenous catheter insertion. *J Spec Pediatr Nurs*. 2013;18(2):109-114.

50. Peterson K. The development of central venous access device flushing guidelines utilizing an evidence-based practice process. *J Pediatr Nurs*. 2013;28(1):85-88.

51. Chand DH, Bednarz D, Eagleton M, Krajewski L. A vascular access team can increase AV fistula creation in pediatric ESRD patients: a single center experience. *Semin Dial*. 2009;22(6):679-683.

52. Lopez PJ, Troncoso B, Grandy J, et al. Outcome of tunneled central venous catheters used for haemodialysis in children weighing less than 15 kg. *J Pediatr Surg.* 2014;49(8):1300-1303.

53. Hunt EA, Jain NG, Somers MJ. Apheresis therapy in children: an overview of key technical aspects and a review of experience in pediatric renal disease. *J Clin Apher*. 2013;28(1):36-47.

54. Infusion Nurses Society. Infusion nursing standards of practice. *J Infus Nurs.* 2011;29:S1-92.

55. Baskin JL, Reiss U, Wilimas JA, et al. Thrombolytic therapy for central venous catheter occlusion. *Haematol*. 2012;97(5):641-650.

56. Blaney M, Shen V, Kerner, JA. Alteplase for the treatment of central venous catheter occlusion in children: results of a prospective, open-label, single-arm study (The Cathflo Activase Pediatric Study). *J Vasc Interv Radiol*. 2006;17(11, pt 1):1745-1751.

57. Doellman DA. Prevention, assessment, and treatment of central venous catheter occlusions in neonatal and young pediatric patients. *J Infus Nurs*. 2011;34(4):251-258.

58. Cortejoso L, Manrique-Rodriguez S, Ferenandez-Llamazares CM, Sanjurjo-Saez M. Treatment and prophylaxis of catheter-related thromboembolic events in children. *J Pharm Sci*. 2012;15(5):632-636.

59. Btaiche I, Kovacevich D, Khalidi N, Papke LF. The effects of a needleless connector on catheter related thrombotic occlusions. *J Infus Nurs.* 2011;34(2):89-96.

60. Pai VB, Plogsted S. Efficacy and safety of using L-cysteine as a catheter clearing agent for nonthrombotic occlusions of central venous catheters in children. *Nutr Clin Pract*. 2014;29(5):636-638.

61. Tamura A, Sone M, Ehara S, et al. Is ultrasound-guided central venous port placement effective to avoid pinch-off syndrome. *J Vasc Access.* 2014;15(4):311-316.

62. Kamphuisen PW, Lee AW. Catheter-related thrombosis: lifeline or pain in the neck? *Hematology Am Soc Hematol Educ Program*. 2012:638-644.

63. Schiffer CA, Mangu PB, Wade JC, et al. Central venous catheter care for the patient with cancer: American society of clinical oncology clinical practice guideline. *J Clin Oncol.* 2013;31(10):1357-1370.

64. Kerner JA, Garcia-Careaga MG, Fisher AA, Poole RL. Treatment of catheter occlusion in pediatric patients. *J Parenter Enteral Nutr.* 2006;30(suppl 1):S73-81.

65. Nayeemuddin M, Pherwani AD Asquith JR. Imaging and management of complications of central venous catheters. *Clin Radiol.* 2013;68(5):529-544.

66. Doellman DA, Hadaway L, Bowe-Geddes LA, et al. Infiltration and extravasation. *J Infus Nurs*. 2009;32(4):203-211.

67. Webb J, Rineair S. Changing the outcome for the pediatric peripherally inserted central catheter patient. Poster presented at: 27th Annual Meeting of the Association for Vascular Access; September 2013; Washington, DC.

68. Can E, Salihoglu O, Ozturk A, Gungor A, Guler E. Hatipoglu S. Complication profiles of central and non-central 1Fr PICCs in neonates weighing <1500g. *J Matern Fetal Neonatal Med*. 2014;27(15):1522-1525.

69. Anton N, Cox PN, Massicotte MP, et al. Heparin-bonded central venous catheters do not reduce thrombosis in infants with congenital heart disease: a blinded randomized, controlled trial. *Pediatr*. 2009;123(3):e453-458.

70. Male C, O'Brien S, Rodriguez V, Mitchell L. Central venous catheter-related thrombosis and thromboprophylaxis in children: a systematic review and meta-analysis: discussion. *J Thromb Haemost.* 2014;13(4):688-690.

71. Abu-El-Haija M, Schultz J, Rahal RM. Effects of 70% ethanol locks on rates of central line infection, thrombosis, breakage, and replacement in pediatric intestinal failure. *J Pediatr Gastroenterol Nutr*. 2014;58(6):703-708.

72. Sellitto M, Messina F. Central venous catheterization and thrombosis in newborns: update on management and treatment. *J Matern Fetal Neonatal Med*. 2012;25(S4):26-28.

73. Revel-Vilk S, Yacobovich J, Tamary H, et al. Risk factors for central venous catheter thrombotic complications in children and adolescents with cancer. *Cancer.* 2010;116(7):4197-4205.

74. Tsai HL, Liu CS, Chang JW, Wei CF, Chin TW. Totally implantable venous access ports via the external jugular vein: safety and effectiveness for young pediatric patients. *J Pediatr Hematol Oncol.* 2008;30(5):366-368.

75. Wilson TJ, Brown DL, Meurer WJ, Stetler WR, Wilkinson DA, Fletcher JJ. Risk factors associated with peripherally inserted central venous catheter-related large vein thrombosis in neurological intensive care patients. *Intensive Care Med.* 2012;38(2):272-278.

76. Tzanetos DR, Yu C, Hernanz-Schulman M, Barr FE, Brown NJ. Prospective study of the incidence and predictors of thrombus in children undergoing palliative surgery for single ventricle physiology. *Intens Care Med.* 2012;38(1):105-112.

77. Itkin M, Mondshein JI, Stavropoulo SW, Shiansky-Goldberg RD, Soulen MC, Trerotola SO. Peripherally inserted central catheter thrombosis-reverse tapered versus nontapered catheters: a randomized controlled study. *J Vasc Interv Radiol*. 2014;25(1):85-91.

78. Revel-Vilk S, Brandao LR, Journeycake J, et al. Standardization of post-thrombotic syndrome definition and outcome assessment following upper venous system thrombosis in pediatric practice. *J Thromb Haemost*. 2012;10(10):2182-2185.

79. Kumar R, Rodriguez V, Matsumoto JM, et al. Prevalence and risk factors for post thrombotic syndrome after deep vein thrombosis in children: a cohort study. *Thromb Res*. 2015;135(2):347-351.

80. Cook, L. Infusion-related air embolism. *J Infus Nurs*. 2013;36(1):26-36.

81. Wong T, Clifford V, McCallum Z, et al. Central venous catheter thrombosis associated with 70% ethanol locks in pediatric intestinal failure patients on home parenteral nutrition: a case series. *J Parenter Enteral Nutr.* 2012;36(3):358-360.

82. Pruthi, RK. Review of the American College of Chest Physicians 2012 for anticoagulation therapy and prevention of thrombosis. *Semin Hematol*. 2013;50(3):251-258.

83. Allan ND, Giare-Paterl K, Olsoen ME. An in vivo rabbit model for the evaluation of antimicrobial peripherally inserted central catheter to reduce microbial migration and colonization as compared to an uncoated PICC. *J Biomed Biotechnol*. 2012:921617. doi:10.1155/2012/921617.

84. Webster J, Osborne S, Rickard CM, New K. Clinically-indicated replacement versus routine replacement of peripheral venous catheters. *Cochrane Database Syst Rev*. 2013;(4): CD007798. doi:10.1002/14651858.CD007798.pub3.

85. Clark E, Giambra BK, Hingl J, Doellman D, Tofani B, Johnson N. Reducing risk of harm from extravasation: a 3-tiered evidence-based list of pediatric peripheral intravenous infusates. *J Infus Nurs*. 2013;36(1):37-45.

86. Amjad I, Murphy T, Nylander-Houshoulder L, Ranfi A. A new approach to management of intravenous infiltration in pediatric patients: pathophysiology, classification, and treatment. *J Infus Nurs*. 2011;34(4):242-249.

87. Wallis MC, McGrail M, Webster J, et al. Risk factors for peripheral intravenous catheter failure: a multivariate analysis of data from a randomized controlled trial. *Infect Control Hosp Epidemiol.* 2014;35(1):63-68.

88. Ray-Barruel G, Polit DF, Murfield J, Rickard CM. Infusion phlebitis assessment measures: a systematic review. *J Eval Clin Pract*. 2014;20(2):191-202.

89. Li J, Fan YY, Xin MZ, et al. A randomized, controlled trial comparing the long-term effects of peripherally inserted central catheter placement in chemotherapy patients using B-mode ultrasound with modified Seldinger technique versus blind puncture. *Eur J Oncol Nurs*. 2014;18(1):94-103.

90. Srinivasan HB, Tjin-A-Tam A, Galang R, Hecht A, Srinivasan G. Migration patterns of peripherally inserted central venous catheters at 24 hours postinsertion in neonates. *Am J Perinatol.* 2013;30(10):871-874.

91. Matsuzaki A, Suminoe A, Koga Y, Hatano M, Hattori S, Hara T. Long-term use of peripherally inserted central catheters for cancer chemotherapy in children. *Support Care Cancer*. 2006;14(2):153-160.

92. Peters JR. Central venous catheter fracture. *J Am Osteopath Assoc*. 2014;114(8):665.

93. Lundgren IS1, Zhou C, Malone FR, McAfee NG, Gantt S, Zerr DM. Central venous catheter repair is associated with an increased risk of bacteremia and central line-associated bloodstream infection in pediatric patients. *Pediatr Infect Dis J.* 2012;31(4):337-340.

94. Gordy S, Rowell S. Vascular air embolism. *Int J Crit Ill Inj Sci*. 2013;3(1):73-76.

95. Von Jurgensonn S. Prevention and management of air in an IV infusion system. *Br J Nurs.* 2010;19(10):S28-30.

96. Tofani BF, Rineair SA, Gosdin CH, et al. Quality improvement project to reduce infiltration and extravasation events in a pediatric hospital. *J Pediatr Nurs.* 2012;27(6):682-689.

97. Paquette V, McGloin R, Northway T, Dezorzi P, Singh A, Carr R. Describing intravenous extravasation in children (DIVE Study). *Can J Hosp Pharm.* 2011;64(5):340-345.

98. Haslik W, Hacker S, Felberbauer FX, et al. Port-a-Cath extravasation of vesicant cytotoxics: surgical options for a rare complication of cancer chemotherapy. *Eur J Surg Oncol*. 2015;41(3):378-385.

99. Chen TK, Yang CY, Chen SJ. Calcinosis cutis complicated by compartment syndrome following extravasation of calcium gluconate in a neonate: a case report. *Pediatr Neonatol*. 2010;51(4):238-241.

100. Ernst FR, Chen E, Lipkin C, Tayama D, Amin AN. Comparison of hospital length of stay, costs, and readmissions of alteplase versus catheter replacement among patients with occluded central venous catheter. *J Hosp Med*. 2014;9(8):490-496.

101. Wilson MZ, Deeter D, Rafferty C, Comito MM, Hollenbeak CS. Reduction of central line-associated bloodstream infections in a pediatric hematology/oncology population. *Am J Med Qual.* 2014;29(6):484-490.

102. Advani S, Reich NG, Sengupta A, Gosey L, Milstone AM. Central line-associated bloodstream infection in hospitalized children with peripherally inserted central venous catheters: extending risk analyses outside the intensive care unit. *Clin Infect Dis*. 2011,52(9):1108-1115.

103. Tsai HC, Huang LM, Chang LY, et al. Central venous catheter-associated bloodstream infections in pediatric hematology-oncology patients and effectiveness of antimicrobial lock therapy [published online October 10, 2014]. *J Microbiol Immunol Infect.* doi:10.1016/j.jmii.2014.07.008.

104. Goudie A, Dynan L, Brady PW, Rettiganti M. Attributable cost and length of stay for central line-associated bloodstream infections. *Pediatrics*. 2014;133(6):1525-1532.

105. Safdar N, O'Horo JC, Ghufran A, et al. Chlorhexidine-impregnated dressing for prevention of catheter-related bloodstream infection: a meta-analysis. *Crit Care Med.* 2014;42(7):1703-1713.

106. Wylie MC, Graham DA, Potter-Bynoe G, et al. Risk factors for central line-associated bloodstream infection in pediatric intensive care units. *Infect Control Hosp Epidemiol*. 2010;31(10):1049-1056.

107. Wheeler DS, Giaccone MJ, Hutchinson N, et al. A hospital-wide quality-improvement collaborative to reduce catheter-associated bloodstream infections. *Pediatr*. 2011;128(4):e995-e1004.

108. Cardo D, Dennehy PH, Halverson P, et al. Moving toward elimination of healthcare-associated infections: a call to action. *Am J Infect Control*. 2010;38(9):671-675.

109. Centers for Medicare & Medicaid Services. Central line-associated blood stream infections (CLABSI). Partnership for patients website. http://partnershipforpatients.cms.gov/p4p_resources/tsp-centralline-associatedbloodstreaminfections/toolcentralline-associatedbloodstreaminfectionsclabsi.html. Accessed January 15, 2015.

110. Huskins WC. Quality improvement interventions to prevent healthcare-associated infections in neonates and children. *Curr Opin Pediatr*. 2012;24(1):103-112.

111. See I, Iwamoto M, Allen-Bridson K, Horan T, Magill SS, Thompson ND. Mucosal barrier injury laboratory-confirmed bloodstream infection: results from a field test of a new National Healthcare Safety Network definition. *Infect Control Hosp Epidemiol*. 2013;34(8):769-776.

112. Dudeck MA, Horan TC, Peterson KD, et al. National Healthcare Safety Network (NHSN) report, data summary for 2010, device-associated module. *Am J Infect Control*. 2011;39(10):798-816.

113. Niedner MF, Huskins WC, Colantuoni E, et al. Epidemiology of central line-associated bloodstream infections in the pediatric intensive care unit. *Infect Control Hosp Epidemiol.* 2011;32(12):1200-1208.

114. Kelly MS, Conway M, Wirth K, Potter-Bynoe G, Billett AL, Sandora TJ. Moving CLABSI prevention beyond the intensive care unit: risk factors in pediatric oncology patients. *Infect Control Hosp Epidemiol.* 2011;32(11):1079-1085.

115. O'Hanlon M, Dornilkova G, Curran R, et al. Incidence of central line related/associated bloodstream infections in an acute hospital. *Ir Med J.* 2014;107(8):253-254.

116. Blanchard AC, Fortin E, Rocher I, et al. Central line-associated bloodstream infection in neonatal intensive care units. *Infect Control Hosp Epidemiol*. 2013;34(11):1167-1173.

117. Shin AY, Jin B, Hao S, et al. Utility of clinical biomarkers to predict central line associated bloodstream infections after congenital heart surgery. *Pediatr Infect Dis J*. 2014;34(3):251-254.

118. Rinke ML, Bundy DG, Chen AR, et al. Central line maintenance bundles and CLABSIs in ambulatory oncology patients. *Pediatrics*. 2013;132(5):1403-1412.

119. Wagner M, Bonhoeffer J, Erb TO, et al. Prospective study on central venous line associated bloodstream infections. *Arch Dis Child.* 2011;96(9):827-831.

120. Al-Sayaghi KM. Management of central venous catheters at the intensive care units in Yemen. Survey of practices. *Saudi Med J*. 2011;32(3):275-282.

121. Ryder M. Evidence-based practice in the management of vascular access devices for home parenteral nutrition therapy. *J Parenter Enteral Nutr*. 2006;30(suppl 1):S82-93.

122. Chaudhary M, Bilal MF, Du W, Chu R, Rajpurkar M, McGrath EJ. The impact of ethanol lock therapy on length of stay and catheter salvage in pediatric catheter-associated bloodstream infection. *Clin Pediatr*. 2014;53(11):1069-1076.

123. Schoot RA, van Dalen EC, van Ommen CH, van de Wetering MD. Antibiotic and other lock treatments for tunneled central venous catheter-related infections in children with cancer. *Cochrane Database Syst Rev.* 2013;(6):CD008975. doi:10.1002/14651858.CD008975.pub2.

124. Kaasch AJ, Rieg S, Hellmich M, Kern WV, Seifert H. Differential time to positivity is not predictive for central line-related Staphylococcus aureus bloodstream infection in routine clinical care. *J Infect*. 2014;68(1):58-61.

125. Gowardman JR, Jeffries P, Lassig-Smith M, et al. A comparative assessment of two conservative methods for the diagnosis of catheter-related infection in critically ill patients. *Intensive Care Med.* 2013;39(1):109-116.

126. Marschall J, Mermel LA, Fakih M, Infectious Diseases Society of America. Strategies to prevent central line–associated bloodstream infections in acute care hospitals. *Infect Control Hosp Epidemiol.* 2014;35(7):1-20.

127. Wolf J, Shenep JL, Clifford V, Curtis N, Flynn PM. Ethanol lock therapy in pediatric hematology and oncology. *Pediatr Blood Cancer.* 2013;60(1):18-25.

128. Pieroni KP, Nespor C, Ng M, Garcia M, Hurwitz M, Berquist WE, Kerner JA. Evaluation of ethanol lock therapy in pediatric patients on long-term parenteral nutrition. *Nutr Clin Pract.* 2013;28(2):226-231.

129. Oliveira C, Nasr A, Brindle M, Wales PW. Ethanol locks to prevent catheter-related bloodstream infections in parenteral nutrition: a meta-analysis. *Pediatrics*. 2012;129(2):318-329.

130. Huang EY, Chen C, Abdullah F, et al. Strategies for the prevention of central venous catheter infections: an American pediatric surgical association outcomes and clinical trials committee systematic review. *J Pediatr Surg.* 2011;46(10):2000-2011.

131. Dannenberg C, Bierbach U, Rothe A, Beer J, Körholz D. Ethanol-lock technique in the treatment of bloodstream infections in pediatric oncology patients with broviac catheter. *J Pediatr Hematol Oncol.* 2003;25(8):616-621.

132. Rajpurkar M, Boldt-Macdonald K, McLenon R, et al. Ethanol lock therapy for the treatment of catheter-related infections in haemophilia patients. *Haemophilia.* 2009;15(6):1267-1271.

133. Blackwood RA, Klein KC, Micel LN, et al. Ethanol locks therapy for resolution of fungal catheter infections. *Pediatr Infect Dis J*. 2011;30(12):1105-1107.

134. McGrath EJ, Salloum R, Chen X, et al. Short-dwell ethanol lock therapy in children is associated with increased clearance of central line-associated bloodstream infections. *Clin Pediatr (Phila).* 2011;50(10):943-951.

135. Valentine KM. Ethanol lock therapy for catheter-associated blood stream infections in a pediatric intensive care unit. *Pediatr Crit Care Med.* 2011;12(6):e292-296.

136. Miller MR, Griswold M, Harris JM, et al. Decreasing PICU catheter-associated bloodstream infections: NACHRI's quality transformation efforts. *Pediatrics.* 2010;125(2):206-213.

137. Jeffries HE, Mason W, Brewer M, et al. Prevention of central venous catheter-associated bloodstream infections in pediatric intensive care units: a performance improvement collaborative. *Infect Control Hosp Epidemiol*. 2009;30(7):645-651.

138. Dümichen MJ, Seeger K, Lode HN, et al. Randomized controlled trial of taurolidine citrate versus heparin as catheter lock solution in paediatric patients with haematological malignancies. *J Hosp Infect.* 2012;80(4):304-309.

139. Chu HP, Brind J, Tomar R, Hill S. Significant reduction in central venous catheter-related bloodstream infections in children on HPN after starting treatment with taurolidine line lock. *J Pediatr Gastroenterol Nutr.* 2012;55(4):403-407.

140. Mouw E, Chessman K., Lesher, A, Tagge E. Use of an ethanol lock to prevent catheter-related infections in children with short bowel syndrome. *J Pediatr Surg,* 2008;43(6):1025-1029.

141. Cober MP, Kovacevich DS, Teitelbaum DH. Ethanol-lock therapy for the prevention of central venous access device infections in pediatric patients with intestinal failure. *J Parenter Enteral Nutr.* 2011;35(1):67-73.

142. Jones BA, Hull MA, Richardson DS, et al. Efficacy of ethanol locks in reducing central venous catheter infections in pediatric patients with intestinal failure. *J Pediatr Surg.* 2010;45(6):1287-1293.

143. Kayton ML, Garmey EG, Ishill NM, et al. Preliminary results of a phase I trial of prophylactic administration to prevent mediport catheter-related bloodstream infections. *J Pediatr Surg.* 2010;45(10):1961-1966.

144. Wales PW, Kosar C, Carricato M, de Silva N, Lang K, Avitzur Y. Ethanol lock therapy to reduce the incidence of catheter-related bloodstream infections in home parenteral nutrition patients with intestinal failure: preliminary experience. *J Pediatr Surg*. 2011;46(5):951-956.

145. Jeong IS, Park SM, Lee JM, Song JY, Lee SJ. Effect of central line bundle on central line-associated bloodstream infections in intensive care units. *Am J Infect Control*. 2013;41(8):710-716.

146. World Health Organization. WHO guidelines on hand hygiene in health care. http://www.who.int/gpsc/5may/tools/9789241597906/en. Published 2009. Accessed January 6, 2015.

147. Johnson L, Grueber S, Schlotzhauer C, et al. A multifactorial action plan improves hand hygiene adherence and significantly reduces central line-associated bloodstream infections. *Am J infect Control.* 2014;42(11):1145-1151.

148. Stewardson AJ, Iten A, Camus V, et al. Efficacy of a new educational tool to improve handrubbing technique amongst healthcare workers: a controlled, before-after study. *PLoS One.* 2014;9(9):e105866.

149. U.S. Food and Drug Administration. Medical device safety. http://www.fda.gov/MedicalDevices/Safety/default.htm. Accessed December 19, 2014.

150. U.S. Environmental Protection Agency. Guidelines for ensuring and maximizing the quality, objectivity, utility, and integrity of information disseminated by the Environmental Protection Agency. http://www.epa.gov/quality/informationguidelines. Published 2002. Accessed January 10, 2015.

151. McMullan C, Propper G, Shuhmacher C, et al. A multidisciplinary approach to reduce central line-associated bloodstream infections. *Jt Comm J Qual Patient Saf*. 2013;39(2):61-69.

152. Helder O, Kornelisse R, van der Starre C, et al. Implementation of a children's hospital-wide central venous catheter insertion and maintenance bundle. *BMC Health Serv Res*. 2013;13:417.

153. Yamamoto N, Kimura H, Misao H, et al. Efficacy of 1.0% chlorhexidine-gluconate ethanol compared with 10% povidone-iodine for long-term central venous catheter care in hematology departments: a prospective study. *Am J Infect Control*. 2014;42(5):574-576.

154. Garland JS, Alex CP, Mueller CD, et al. A randomized trial comparing povidone-iodine to a chlorhexidine gluconate-impregnated dressing for prevention of central venous catheter infections in neonates. *Pediatrics*. 2001;107(6):1431-1436.

155. Lu SF, Chen JH, Shang WM, Chou SS. Prevention and nursing care of central line-associated bloodstream infections in critically ill patients. *Hu Li Za Zhi*. 2012;59(4):5-11.

156. Tian G, Zhu Y, Qi L, Guo F, Xu H. Efficacy of multifaceted interventions in reducing complications of peripherally inserted central catheter in adult oncology patients. *Support Care Cancer.* 2010;18(10):1293-1298.

157. Pedrolo E, Danski MT, Vayego SA. Chlorhexidine and gauze and tape dressings for central venous catheters: a randomized clinical trial. *Rev Lat Am Enfermagem.* 2014;22(5):764-771.

158. Stefanidis CJ. Preventing catheter-related infections in children undergoing hemodialysis. *Expert Rev Antl Infect Ther.* 2010;8(11):1239-1249.

159. Kampf G, Reise G, James C, Gittelbauer K, Gosch J, Aplers B. Improving patient safety during insertion of peripheral venous catheters: an observational intervention study. *GMS Hyg Infect Control*. 2013;8(2). doi:10.3205/dgkh000218.

160. Gabriel J. Vascular access devices: securement and dressings. *Nurs Stand*. 2010;24(52):41-46.

161. Graf JM, Newman CD, McPherson ML. Sutured securement of peripherally inserted catheters yields fewer complications in pediatric patients. *J Parenter Enteral Nutr*. 2006;30(6):532-535.

162. Occupational Safety & Health Administration. Bloodborne pathogens and needlestick prevention. United States Department of Labor website. https://www.osha.gov/SLTC/bloodbornepathogens. Accessed January 9, 2015.

163. Griswold S1, Bonaroti A, Rieder CJ, et al. Investigation of a safety-engineered device to prevent needlestick injury: why has not StatLock stuck? *BMJ.* 2013;3(4). doi:10.1136/bmjopen-2012-002327.

164. Egan GM, Siskin GP, Weinmann R, Galloway MM. A prospective postmarket study to evaluate the safety and efficacy of a new peripherally inserted central catheter stabilization system. *J Infus Nurs.* 2013;36(3):181-188.

165. Hughes EM. Reducing PICC migrations and improving patient outcomes. *Br J Nurs.* 2014;23(2):S14-18.

166. Levy I, Katz J, Solter E. Chlorhexidine-impregnated dressing for prevention of colonization of central venous catheters in infants and children: a randomized controlled study. *Pediatr Infect Dis J.* 2001;24(8):676-679.

167. Onder AM, Chandar J, Coakley S, Francoeur D, Abitbol C, Zilleruelo G. Controlling exit site infections: does it decrease the incidence of catheter-related bacteremia in children on chronic hemodialysis? *Hemodial Int*. 2009;13(1):11-18.

168. Weitz NA, Lauren CT, Weiser JA, et al. Chlorhexidine gluconate–impregnated central access catheter dressings as a cause of erosive contact dermatitis: a report of 7 cases. *JAMA Dermatol.* 2013;149(2):195-199.

169. Milstone AM, Elward A, Song X, et al. Daily chlorhexidine bathing to reduce bacteraemia in critically ill children: a multicenter, cluster-randomized, crossover trial. *Lancet* 2013;381(9872):1099-1106.

170. Perez E, Williams M, Jacob JT, et al. Microbial biofilms on needleless connectors for central venous catheters: comparison of standard and silver-coated devices collected from patients in an acute care hospital. *J Clin Microbiol.* 2014;52(3):823-831.

171. Chernecky CC, Macklin D, Jarvis WR, Joshua TV. Comparison of central line-associated bloodstream infection rates when changing to a zero fluid displacement intravenous needleless connector in acute care settings. *Am J Infect Control*. 2014;42(2):200-202.

172. Hadaway L. Needleless connectors for IV catheters. *Am J Nurs.* 2012;112(11):32-44.

173. Chernecky CC, Waller JL, Jarvis WR. In vitro study assessing the antimicrobial activity of three silver-impregnated/coated mechanical valve needleless connector after blood exposure. *Am J Infect Control.* 2013;41(3):278-280.

174. U.S. Food and Drug Administration. Letter to infection control practitioners regarding positive displacement needleless connectors. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm220459.htm. Updated August 22, 2013. Accessed December 27, 2014.

175. Rupp ME, Yu S, Huerta T, et al. Adequate disinfection of a split-septum needleless intravascular connector with a 5-second scrub. *Infect Control Hosp Epidemiol.* 2012;33(7):661-665.

176. Centers for Medicare and Medicaid Services. Hospital compare. U.S. Government site for Medicare. http://www.medicare.gov/hospitalcompare/search.html?AspxAutoDetectCookieSupport=1. Accessed November 28, 2014.

177. The Joint Commission. 2014 National patient safety goals. http://www.jointcommission.org/standards_information/npsgs.aspx. Accessed January 5, 2015.

178. Mazher MA, Kallen A, Edwards JR, Donlan RM. An in vitro evaluation of disinfection protocols used for needleless connectors of central venous catheters. *Lett Appl Microbiol.* 2013;57(4):282-287.

179. Kaler W, Chinn R. Successful disinfection of needleless access ports: a matter of time and friction. *J Vasc Access*. 2007;12(3):140-142.

180. Sweet MA, Cumpston A, Briggs F, Craig M, Hamadani M. Impact of alcohol-impregnated port protectors and needless neutral pressure connectors on central line-associated bloodstream infections and contamination of blood cultures in an inpatient oncology unit. *Am J Infect Control*. 2012;40(10):931-934.

181. Cosca PA, Smith S, Chatfield S, et al. Reinfusion of discard blood from venous access devices. *Oncol Nurs Forum*. 1998;25(6):1073-1076.

182. Keller CA. Methods of drawing blood samples through central venous catheters in pediatric patients undergoing bone marrow transplant: results of a national survey. *Oncol Nurs Forum*. 1994;21(5):879-884.

183. Yucha CB1, DeAngelo E. The minimum discard volume: accurate analysis of peripheral hematocrit. *J Intraven Nurs*. 1996;19(3):141-146.

184. Berger-Achituv S, Budde-Schwartzman B, Ellis MH, Shenkman Z, Erez I. Blood sampling through peripheral venous catheters is reliable for selected basic analytes in children. *Pediatrics.* 2010;126(1):e179-186.

185. Boodhan S1, Maloney AM, Dupuis LL. Extent of agreement in gentamicin concentration between serum that is drawn peripherally and from central venous catheters. *Pediatrics*. 2006;118(6):e1650-1656.

186. Hinds PS, Quargnenti A, Gattuso J, et al. Comparing the results of coagulation tests on blood drawn by venipuncture and through heparinized tunneled venous access devices in pediatric patients with cancer. *Oncol Nurs Forum*. 2002;29(3):E26-34.

187. Wanwimolruk S, Murphy JE. Effect of monitoring drug concentrations through lines use to administer the drugs: an in vitro study. *Ther Drug Monit*. 1991;13(5):443-447.

188. Mogayzel PJ, Pierce E, Mills J, et al. Accuracy of tobramycin levels obtained from central venous access devices in patients with cystic fibrosis is technique dependent. *Pediatr Nurs*. 2008;34(6):464-468.

189. Adlard K. Examining the push-pull method of blood sampling from central venous access devices. *J Pediatr Oncol Nurs* 2008;25(4):200-207.

190. MacGeorte L, Steeves L, Steeves RH. Comparison of the mixing and reinfusion methods of drawing blood from a Hickman catheter. *Oncol Nurs Forum*. 1998;15(3):335-338.

191. Dech ZF, Szaflarski NL. Nursing strategies to minimize blood loss associated with phlebotomy. *AACN Clin Issues.* 1996;7(2):277-287.

192. Holmes KR. Comparison of push-pull versus discard method from central venous catheters for blood testing. *J Intraven Nurs*. 1998;21(5):282-285.

193. Barton SJ, Chase T, Latam B, Rayens MK. Comparing two methods to obtain blood specimens from pediatric central venous catheters. *J Pediatr Oncol Nurs*. 2004;21(6):320-326.

194. Pinto KM. (1994). Accuracy of coagulation values obtained from a heparinized central venous catheter. *Oncol Nurs Forum*.1994;21(3):573-575.

195. Cesaro S, Tridello G, Cavaliere M, et al. Prospective, randomized trial of two different modalities of flushing central venous catheters in pediatric patients with cancer. *J Clin Oncol.* 2009;27(12):2059-2065.

196. Schallom ME, Prentice D, Sona C, Micek ST, Skrupky LP. Heparin or 0.9% sodium chloride to maintain central venous catheter patency: a randomized trial. *Crit Care Med*. 2012;40(6):1820-1826.

197. Stern RC, Pittman S, Doershuk CF, Matthews LW. Use of a "heparin lock" in the intermittent administration of intravenous drugs. A technical advance in intravenous therapy. *Clin Pediatr*. 1972;11(9):521-523.

198. Hanson RL, Grant AM, Majors KR. Heparin-lock maintenance with ten units of sodium heparin in one milliliter of normal saline solution. *Surg Gynecol Obst*. 1976;142(3):373-376.

199. Goldberger JH, DeLuca FG, Wesselhoeft CW, Randall HT. A home program of long-term total parenteral nutrition in children. *J Pediatr.* 1979;94(2):325-328.

200. Smith S, Dawson S, Hennessey R, Andrew M. Maintenance of the patency of indwelling central venous catheters: is heparin necessary? *Am J Pediatr Hematol Oncol*. 1991;13(2):141-143.

201. Randolph AG, Cook DJ, Gonzalez CA, Andrew M. Benefit of heparin in central venous and pulmonary artery catheters: a meta-analysis of randomized controlled trials. *Chest.* 1998;113(1):165-171.

202. Marcoux C, Fisher S, Wong D. Central venous access devices in children. *Pediatr Nurs.* 1990;16(2):123-133.

203. Marshall C, Boldt-MacDonald K, McLenon R, et al. A multidisciplinary approach to determine heparin dosing in pediatric vascular devices. *J Pediatr Oncol Nurs*. 2011;28(1):53-57.

204. Moukarzel, AA, Haddad I, Ament ME, et al. 230 patient years of experience with home long-term parenteral nutrition in childhood: natural history and life of central venous catheters. *J Pediatr Surg.* 1994;29(10):1323-1327.

205. Dillon PW, Jones GR, Bagnall-Reeb HA, Buckley JD, Wiener ES, Haase GM. Prophylactic urokinase in the management of long-term venous access devices in children: a children's oncology group study. *J Clin Oncol*. 2004;22(13):2718-2723.

206. Henrickson KJ, Axtell RA, Hoover SM, et al. Prevention of central venous catheter-related infections and thrombotic events in immunocompromised children by the use of vancomycin/ciprofloxacin/heparin flush solution: a randomized, multicenter, double-blind trial. *J Clin Oncol*. 2000;18(6):1269-1278.

207. Chatzinikolaou I, Zapf TF, Hanna H, et al. Minocycline-ethylenediaminetetraacetate lock solution for the prevention of implantable port infections in children with cancer. *Clin Infect Dis.* 2003;36(1):116-119.

208. Handrup MM, Fuursted K, Funch P, Moller JK, Schreder H. Biofilm formation in long-term central venous catheters in children with cancer: a randomized controlled open-labelled trial of taurolidine versus heparin. *APMIS.* 2012;120(10):794-801.

209. Ferroni A, Gaudin F, Guiffant G, et al. Pulsatile flushing as a strategy to prevent bacterial colonization of vascular access devices. *Med Devices.*2014;7:379-383.

210. Smulders CA, van Gestel JP, Bos AP. Are central line bundles and ventilator bundles effective in critically ill neonates and children? *Intensive Care Med*. 2013;39(8):1352-1358.

This publication is proudly endorsed by:

Society of Pediatric Nurses

Association of Pediatric Hematology/Oncology Nurses (APHON)

Association for Vascular Access

Special Interest Group