Central Venous Catheters: Care and Complications

17

Connie Goes

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Abstract

Central venous catheters are an essential component of care in children and adolescents with cancer and allow for safe and compassionate administration of chemotherapy and supportive medications, infusions, and transfusions in an efficient and cost-effective manner. With these benefits also come a host of decisions and potential complications. Catheter choice includes implanted versus external catheter, those meant for short- versus longer-term usage, as well as catheters that may be utilized for hematopoietic stem cell harvesting. Complications are primarily infection and thrombosis. This chapter provides evidence-based graded recommendations from the medical literature regarding choice and care of catheters specific for each patient and provides techniques for prevention, recognition and treatment of the most common complications.

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17.1 Introduction

Central venous catheters (CVCs) are an important component of the supportive care of pediatric oncology patients and allow for the utilization of increasingly intensive and complex therapeutic regimens which has contributed to the increased survival rate in high-income countries. CVCs allow for safe delivery of chemotherapy, antibiotics and other medications, parenteral nutrition, blood products, hematopoietic stem cell infusions, and fluids. Frequent blood sampling, required to monitor side effects of therapy and disease status, can be accomplished comfortably and efficiently through an external CVC. Despite these advantages, challenges exist with the use of CVCs, primarily infection and occlusion. Ongoing research to develop strategies to prevent and treat these problems is needed. Here we review the existing literature and provide graded recommendations based on the evidence as well as consensus and expert opinion when firm evidence is lacking (Table 17.1).

17.2 Types of Central Venous Catheters

CVCs are divided into two categories: non-tunneled and tunneled. Each catheter type has specific line care needs, advantages, disadvantages and complications (Table 17.2). Selection of the optimal type of CVC for use in a specific disease or treatment protocol is not standardized. Factors to consider in catheter selection include the age and weight of the child, the length and intensity of therapy, frequency of blood sampling, anticipated supportive care interventions including transfusions, infusions and nutrition, level of patient activity, body image, and family ability to understand teaching and properly care for the line.

17.2.1 Peripherally Inserted Central Catheter

A peripherally inserted central catheter (PICC) is the most frequently inserted non-tunneled CVC for short-term intravenous therapy and can remain in place for weeks to months. A PICC is the ideal central access device for oncology patients that present acutely ill and too unstable for anesthesia (e.g., mediastinal mass, airway compromise). Some institutions prefer a PICC during induction therapy for acute leukemia due to concern of an increased risk of catheter thrombosis associated with asparaginase therapy. The thin flexible silicone or polyurethane catheter is typically inserted into the basilic vein due to the ease of threading within this vessel. The catheter tip is placed into a large vessel, typically the distal superior vena cava (SVC), allowing for rapid dilution of medications and prevention of vessel damage from vesicants and hyperosmolar solutions (Pettit 2002; Burns 2005). Insertion complications include curling of the catheter, difficulty threading the catheter, multiple attempts to place the catheter, malposition or failure to insert the catheter and medial nerve damage (Pettit 2002; Burns 2005; Alomari and Falk 2006). Post-insertion imaging either with a chest radiograph or fluoroscopy should be obtained to document proper placement of the catheter tip.

Advantages of PICCs include the ability to insert at either the bedside or in interventional radiology, ability to remove at the bedside, decreased cost and decreased potential complications related to anesthesia or a surgical procedure. After insertion, the external portion of the catheter is measured and documented. Remeasurement with each dressing change ensures proper positioning. Smaller gauge (larger diameter) PICCs allow for blood sampling and red blood cell transfusions. The manufacturer's recommendations and established institutional guidelines should be strictly followed. Disadvantages of a PICC include the need for sterile dressing changes, frequent flushing and a risk of phlebitis. The catheter lacks a cuff for stabilization creating an increased risk of dislodgement. Securing a PICC line is especially important in young or unstable patients. A sutureless securement device, StatLock®, is a housing unit that clips the PICC line suture wings into place with an adhesive patch, improving stabilization over tape. A prospective,

Table 17.1 Summary of recommendations for prevention of infectious complications with central venous catheters (CVCs)

	Recommendation	Level of evidence[a]
Insertion	Hand hygiene with soap and water or waterless alcohol gel	1A
	Maximal sterile barrier precautions: cap, mask, sterile gown, sterile gloves, sterile full body drape	1A
	Skin antisepsis with 2 % chlorhexidine	1A
	Trained, competent provider to insert or oversee inexperienced personnel	1A
	No prophylactic antibiotic	1B
	Use of totally implanted device whenever possible due to decreased risk of infection	1B
	Use of ultrasound-guided assistance not recommended with subclavian line placement	2A
	Subclavian site is the preferred insertion site	2C
	CVC placement can occur with ALL induction or be delayed	2C
Site care	Hand hygiene with soap and water or waterless alcohol gel	1A
	Use either sterile transparent semipermeable dressing or sterile gauze and tape dressing (especially if diaphoretic or bleeding from site)	1A
	Change sterile transparent semipermeable dressing every 5 days or when loose, wet, or soiled	1C
	Change sterile gauze and tape dressing daily or if loose, wet, or soiled	1C
	Chlorhexidine gluconate for exit site antisepsis	1A
	Monitor site for evidence of infection	1C
	No topical antibiotic at exit site	1B
	Use of StatLock® for securement of PICC line	1B
	Antiseptic-impregnated catheters are not routinely recommended	2C
Hub care	Scrub hub for 15 s with either 70 % isopropyl alcohol or 2 % chlorhexidine in 70 % isopropyl alcohol prior to every access	1B
Assessment	Daily assessment of site for evidence of infection	1C
	Daily assessment of need for CVC	1A
Locking line	External catheters: daily (when not in use) and after intermittent use with heparinized saline (concentration/volume per institutional policy)	1C
	Totally implanted device: monthly and after intermittent use with heparinized saline (concentration/volume according to institutional policy)	1C
Education	Dedicated CVC team to evaluate current literature	1B
	Ongoing training for personnel of new policies, procedures, equipment	1B
Infection	Antibiotic ointment alone should not be used for exit site infections	1B
	Catheter removal is indicated for tunnel infection	2A
	Port catheter removal is indicated for pocket infection	1A
Occlusion[b]	Utilization of tPA dwell for CVC occlusion	2A
	Low-dose systemic tPA if tPA dwell unsuccessful	2C
	Imaging with compression US with Doppler and CT with venography if US nondiagnostic with a high level of suspicion	2A

ALL acute lymphoblastic leukemia, *PICC* peripherally inserted central catheter, *tPA* tissue plasminogen activator, *US* ultrasound, *CT* computed tomography
[a]Per Guyatt et al. (2006); see Preface
[b]See text for further detail

randomized trial to evaluate the use of StatLock® versus sutures found an overall reduction in complications and specifically with a significant decrease in bloodstream infections (Yamamoto et al. 2002).

17.2.2 External Tunneled Central Venous Catheter

A Broviac catheter is the most commonly inserted external tunneled CVC in pediatrics (other external

Table 17.2 Advantages and disadvantages of central venous catheters (CVCs)

Type of CVC	PICC	Broviac	Implanted port	Powerline
Advantages	Immediate access	Immediate access	No required daily care (when not accessed)	Immediate access
	Bedside insertion	Painless blood sampling	Blood sampling (when accessed)	Blood sampling
	Bedside removal	External portion repairable	Lower infection risk	Compatible with CT power injection
	Blood sampling with ≥2.8 F		No restriction of activities	Use for stem cell pheresis
	Transfusions with ≥4.0 F			
Disadvantages	Frequent flushing	Surgical placement	Needle required for access	Surgical placement
	Sterile dressing changes	Daily flushing		Daily flushing
	Phlebitis	Sterile dressing changes	Potential needle dislodgement	Sterile dressing changes
		Increased infection risk		Bathing limitations
		Bathing limitations		No swimming
		No swimming		Potential for self-removal
		Potential for self-removal		External portion not repairable
		Impact on body image		Impact on body image

PICC peripherally inserted central catheter, *F* French, *CT* computed tomography

tunneled CVCs include Hickman, Groshong, Leonard, Hemocath and Powerline) and is available in either a single- or double-lumen system. Tunneled catheters are placed into a vein in the chest or neck and tunneled under the skin to secure for long-term use. Made of silicone or polyurethane, Broviac catheters are surgically inserted into either the internal jugular vein or subclavian vein with the tip placed into the distal SVC. The line is tunneled under the skin and exits on the anterior or lateral chest. A Dacron cuff stimulates tissue growth stabilizing the line in place while inhibiting bacterial migration. The cuff may be felt under the skin approximately 2 cm above the exit site.

A Powerline is a newer less frequently used cuffed polyurethane tunneled CVC available in single-, dual- or triple-lumen systems. In addition to the advantages of an external CVC, a Powerline is compatible with power injection of CT contrast (as needed for imaging) with a maximum flow rate of 5 mL/s and can be utilized for stem cell harvesting (BARD website 2014). Routine daily line care is similar to a Broviac though Powerlines are made of a firmer material and breaks in the external portion are not repairable, thereby requiring removal.

Advantages of an external CVC include easy access for delivery of intravenous therapies and painless blood sampling. In the event of tears or blockages, the external portion of the catheter is repairable with kits available from the manufacturer. Repair kits for each CVC size should be kept in stock at the institution. Disadvantages of an external CVC are requirement of surgical placement with anesthesia, increased risk of infection and thrombosis compared to implanted catheters, requirement for sterile dressing changes, daily heparin flushes, risk of kinking and breaking particularly with larger gauge (smaller diameter) sizes, limitations on activity (swimming and bathing), impact on body image, and potential for self-removal, especially with infants and toddlers. External CVCs carry a greater risk of infection than implanted ports as a result of the external site of the hubs and possibly secondary to the frequency of access for infusion, line flushing and blood sampling (Adler et al. 2006; Maki et al. 2006; Perdikaris et al. 2008).

17.2.3 Implanted Port

A port is a totally implanted tunneled CVC consisting of two sections, a plastic or titanium reservoir with a self-sealing rubber septum and a silicone or polyurethane catheter. The reservoir is placed in a surgically created pocket in the subcutaneous tissue below the clavicle and sutured to the fascia to ensure stabilization. The reservoir should not be placed directly beneath the surgical incision as accessing through the incision may lead to infection or skin breakdown (Baggott et al. 2002). The catheter is tunneled and inserted into either the internal jugular or subclavian vein with the tip in the distal SVC. The use of a non-coring Huber needle prolongs the life of the septum to approximately 2,000 punctures with a 22 gauge needle and 1,000 punctures if using a 19 gauge needle (BARD website 2014). If the port is to be used immediately, the surgeon may access the device in the operating room prior to development of postoperative swelling thereby preventing patient discomfort.

Advantages of an implanted port include decreased risk of infection, ease of blood sampling when accessed for use, no restrictions on swimming or bathing and no required daily care when not accessed (O'Grady et al. 2002; Adler et al. 2006). A disadvantage, particularly in small children, is the requirement for needle access through the skin. A lidocaine-based topical anesthetic cream (or ethyl chloride "cold" spray) is frequently used prior to access to decrease the discomfort of needle insertion. While accessed, site assessment is necessary as dislodgment may occur due to the patient's activity or use of an inappropriate length Huber needle, potentially leading to infiltration or extravasation of infusions. Implanted ports may stay accessed for long periods of time, but it is recommended to reaccess with a fresh needle every 7 days. Mechanical complications, although quite rare, include damage to the port reservoir, separation of the catheter from the reservoir and erosion of the reservoir through the skin (Schulmeister 2010).

17.3 Catheter Insertion

Though rare, complications during insertion can arise and cause significant morbidity and include pneumothorax, hemothorax, chylothorax, malpositioning, arterial puncture and failure to place. Factors associated with complications include physician inexperience, multiple insertion attempts, prior catheterizations, patient anatomy, prior surgery or radiation in the area and a high body mass index (Mansfield et al. 1994; Lefrant et al. 2002; Kusminsky 2007). An insertion failure rate of up to 43 % and complication rate up to 24 % occurs with ≥3 insertion attempts leading to a recommendation of limiting each operator to a maximum of two unsuccessful attempts (Mansfield et al. 1994; Eisen et al. 2006). The definition of an "attempt" varies among studies ranging from one puncture to multiple punctures by one operator at one site making comparisons difficult (Eisen et al. 2006; Balls et al. 2010).

Several studies have been completed evaluating the advantage of using real-time ultrasound-guided assistance (UGA) rather than the anatomic landmark technique for placement of a CVC (Augoustides and Cheung 2009; Pittiruti et al. 2009; Balls et al. 2010). A meta-analysis by Randolph et al. (1996) concluded that this technique led to an improved insertion success rate and a decrease in complications in both internal jugular and subclavian vein insertions. McGee and Gould (2003) found that UGA is effective in catheterization of the internal jugular vein with a decreased incidence of mechanical complications and placement failure. However, they found no benefit using this technique with subclavian vein insertions as the clavicle lies directly over the vessel, impeding visualization. In their studies, Mansfield et al. (1994) and Troianos et al. (2011) reached a similar conclusion. A retrospective observational study by Balls et al. (2010) assessed 1,222 CVC placement attempts concluding that the use of UGA did not improve the success of placement on the first attempt but overall saw a reduced number of total attempts. Further study is required to determine whether the routine use of UGA is

feasible due to the high cost of equipment, required personnel training and equipment maintenance (Randolph et al. 1996).

Catheter insertion in the subclavian vein carries a higher risk of pneumothorax, malpositioning and failure to place compared to internal jugular insertion, while internal jugular catheterization is associated with a higher incidence of arterial puncture and hematoma (McGee and Gould 2003; Eisen et al. 2006). Although the subclavian vein carries the greater risk of insertion complications, it remains the preferred approach due to a lower rate of infection noted in some studies (McGee and Gould 2003). A prospective, observational study by Deshpande et al. (2005) found no difference in CVC infection rates for subclavian, internal jugular or femoral vein insertion sites in adult patients. The 2011 Centers for Disease Control (CDC) Guidelines for the Prevention of Intravascular Catheter-Related Infections declined to make a recommendation for the preferred CVC insertion site leaving the issue unresolved (O'Grady et al. 2011).

Children with acute lymphoblastic leukemia (ALL) often present with neutropenia and thrombocytopenia theoretically putting them at increased risk for complications with CVC placement. However, two separate studies evaluating 172 and 98 children, respectively, found no increased rate of complication with early CVC placement in newly diagnosed ALL patients (Handrup et al. 2010; Gonzalez et al. 2012). Platelet thresholds for CVC placement are undefined (see Chap. 2). Handrup et al. (2010) also concluded that the nonelective removal rate was similar between early and later placed CVCs. A retrospective analysis of 362 patients with ALL assessed complication rates between timing of insertion (early, ≤day 15 of induction, vs. late, >day 15 of induction) and type of CVC (ports vs. external CVCs) and found that early placement was associated with an increased risk of a positive blood culture and external CVCs were associated with an increased risk of positive blood cultures, thrombotic complications, and early removal (McLean et al. 2005). Due to the conflicting evidence, institutions providing initial care of newly diagnosed oncology patients must decide on the benefit of CVC placement timing, with ongoing monitoring for early complications and of line care in this setting.

17.4 Infection

Infection remains the major complication of an indwelling CVC, with bloodstream infection causing the most significant risk of morbidity and mortality. Terms used to describe intravascular catheter-related infection are confusing with central line-associated bloodstream infection (CLABSI) and catheter-related bloodstream infection (CRBSI) often used interchangeably. CLABSI is defined as an infection occurring in the patient with a CVC and not related to an infection at another site and is the term used by the CDC National Healthcare Safety Network (NHSN). CRBSI is a clinical definition requiring specific laboratory testing, quantitative blood cultures, differential time to positivity or culture of a segment of the removed catheter (O'Grady et al. 2011). Common organisms causing CLABSI include *Staphylococcus epidermis*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Candida albicans*. See Chaps. 1 and 14 for prevention, recognition and treatment of suspected infection or sepsis.

Most CVC-related infections are thought to occur by one of two methods: colonization at the exit site with pathogen migration along the external catheter surface or hub contamination leading to intraluminal colonization with spread into the circulation (McGee and Gould 2003). Within hours of CVC placement, a protein-rich sheath begins developing, covering the external and internal surfaces of the catheter. The protein sheath allows adherence of microbes which then produce a slimy substance (biofilm) becoming embedded in the matrix (Raad et al. 1993). Pathogens within a biofilm behave differently with an increased rate of reproduction and a greater resistance to antimicrobial therapy (Raad et al. 1993; Donlan 2011).

Antiseptic-impregnated catheters (AIC) coated with either chlorhexidine and silver sulfadiazine (CSS) or minocycline-rifampin (MR) have been studied in an effort to determine their effectiveness in decreasing the rate of CLABSI. Randomized clinical trials have generally not shown these catheters to be beneficial (McGee and Gould 2003). In a randomized clinical trial evaluating 232 catheters inserted in 180 critically ill hospitalized adult patients in use <10 days, there was no significant difference in the rates of colonization between antiseptic-impregnated and non-impregnated catheters (Theaker et al. 2002). Separate meta-analyses reviewing randomized controlled trials comparing AICs and non-AICs with a median insertion duration of 7–12 days concluded the efficacy of CSS catheters to be <2 weeks with MR catheters being effective somewhat longer (Mermel 2000; Walder et al. 2002). The results of numerous studies are difficult to compare with no type of catheter showing a definitive advantage. The CDC recommends that institutions develop strategies to provide education of personnel who insert and maintain catheters, with use of maximal sterile barrier precautions (i.e., cap, mask, sterile gown, sterile gloves and a sterile full body drape for line insertion) and skin antisepsis with >0.5 % chlorhexidine with alcohol for insertion. The use of antimicrobial-coated catheters is recommended at institutions where implementation of these CDC strategies fails to decrease CLABSI rates (O'Grady et al. 2011). Maki et al. (2006) determined that institutions with a baseline CLABSI rate of >2 % would benefit from use of AICs as this was the threshold at which AICs would decrease overall costs.

17.4.1 Exit Site Infection

An exit site infection is characterized by the presence of erythema, tenderness, induration or drainage within 2 cm of the catheter exit site, without signs or symptoms of systemic infection (O'Grady et al. 2011). Culture of the site should be obtained. Though not evidence-based, generally Gram-positive infections may be treated with oral antibiotics, while broad-spectrum parenteral antibiotics are indicated for Gram-negative organisms and for children with neutropenia (Baggott et al. 2002). Once the organism is identified, antibiotic therapy should be tailored to sensitivities. An exit site infection due to waterborne organisms, such as *Pseudomonas* spp., or fungus generally requires catheter removal as these organisms are notoriously difficult to clear. Antibiotic ointment alone should not be used at the exit site as this significantly increases the risk of *Candida* spp. infection and promotes antibiotic resistance (Zakrzewska-Bode et al. 1995; O'Grady et al. 2011).

17.4.2 Tunnel Infection

A tunnel infection is defined as tenderness, erythema, drainage or site induration >2 cm from the catheter exit site along the subcutaneous tract in the absence of concomitant CLABSI (O'Grady et al. 2011). Blood cultures from the CVC and skin cultures should be obtained. Catheter removal is indicated and parenteral antibiotics tailored to sensitivities of the cultured organism are given for 7–10 days (Mermel et al. 2009). A PICC may be placed to complete the recommended course of antibiotics.

17.4.3 Pocket Infection

A pocket infection involves erythema, tenderness and swelling over the site of an implanted port with purulent fluid noted in the subcutaneous tissue. Drainage or necrosis of the overlying skin may be present (O'Grady et al. 2011). Drainage should be obtained and cultured. Removal of the port is indicated with debridement, if necessary. A course of parenteral antibiotics is essential with medication tailored to the sensitivity of the infecting organism (O'Grady et al. 2002). Prior to insertion of another CVC, the wound should be healed, the course of antibiotics completed and the child should have defervesced. Consideration may be given to

placement of a PICC should a CVC be needed to complete therapy.

17.4.4 Prevention of Infection

A CVC bundle is a set of evidence-based care practices implemented to decrease the risk of infection due to the presence of a CVC. Components include hand hygiene, selection of the optimal insertion site, use of maximal barrier technique, chlorhexidine skin antisepsis and prompt removal of the catheter when it is no longer needed (O'Grady et al. 2011). Development of institutional guidelines and ongoing staff education are essential in decreasing infection rates (O'Grady et al. 2011). Each institution's infection control department is instrumental in tracking rates of CLABSI. Cooperation with the hematology/oncology service is imperative for ongoing evaluation with changes to institutional practices as indicated. A local expert on CVC care and management and infection control will enhance education, monitor adherence to policy, follow rates of infection and evaluate the current literature (Teichgraber et al. 2011). Placement of the institution's hand hygiene guidelines in patient care areas is a great reminder for practitioners, patients and family members. Further discussion of prevention of CVC line infection is detailed in Chap. 14.

17.5 Occlusions

A functioning CVC is a catheter that flushes easily, infuses without difficulty and has brisk blood return (Baskin et al. 2009). Occlusion is the most common noninfectious complication of CVCs with an occurrence rate of 25 % and resulting in delays in the administration of chemotherapy and supportive care (Stephens et al. 1995). Rapid assessment is needed to determine both the cause of the obstruction and the appropriate interventions. Causes of CVC occlusion include mechanical complications, drug precipitate or lipid residue and thrombosis. Each of these problems can result in either partial or complete obstruction of the catheter. A partial occlusion allows for fluid infusion but either a sluggish or complete inability to withdraw blood (ball-valve effect). A complete occlusion allows neither fluid infusion nor blood withdrawal. An unusual problem may occur with implanted ports allowing blood withdrawal but not fluid administration due to a thrombus inside the reservoir at the outlet port (a reverse ball-valve effect).

17.5.1 Mechanical Occlusion

The cause of a mechanical obstruction may be as simple as a closed clamp, a kink in the external portion of the line or an exit site suture that is too tight, all of which are easily corrected after careful inspection and manipulation. An improperly inserted Huber needle is corrected by re-accessing the implanted port. A "pinch-off" syndrome (Fig. 17.1) can occur with catheter compression between the clavicle and first rib at a reported 1 % incidence rate. This complication is associated with insertion into the subclavian vein via an infraclavicular approach (Fazeny-Dorner et al. 2003; Baskin et al. 2009).

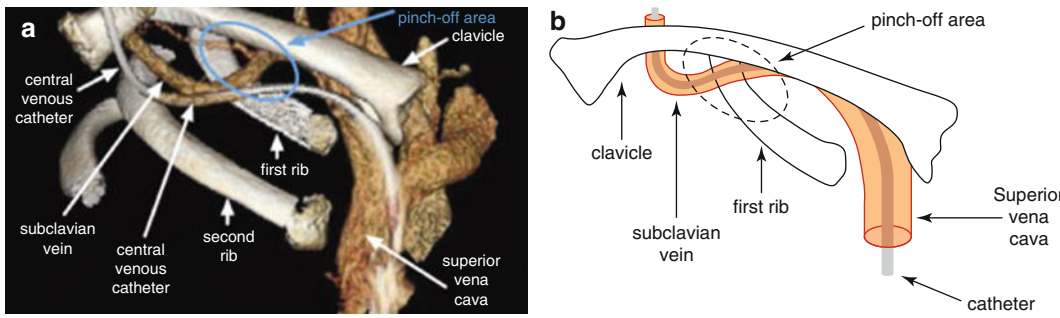

Fig. 17.1 Pinch-off syndrome (with permission from Baskin et al. [2009])

Rolling the shoulder forward or raising the arm on the opposite side may allow blood withdrawal. Over time, compression may lead to fracture of the catheter. A chest radiograph or fluoroscopic examination aids in diagnosis with immediate removal indicated if confirmed. A rare but life-threatening complication is fragmentation of a distal portion of the catheter with migration to the heart or pulmonary artery. Symptoms include shoulder and chest pain, palpitations and arrhythmias (Nace and Ingle 1993). Patients may be asymptomatic except for pain with attempted infusion (Dillon and Foglia 2006). Retrieval of the embolized catheter is generally accomplished by interventional radiology or cardiology using loop snares, baskets or guide wires (Sagar and Lederer 2004).

17.5.2 Drug Precipitate or Lipid Residue Occlusion

An intraluminal occlusion may result from precipitation of incompatible medications or lipid residue. Review of the patient's medications and parenteral nutrition formula may assist in evaluating the cause of occlusion. Precipitation resulting from calcium phosphate crystals or medications with a low pH may be cleared with 0.1 % hydrochloric acid (Baskin et al. 2009). However, many institutions refrain from this practice due to concern of catheter wall damage. Precipitations caused by high pH medications have been cleared by the use of sodium bicarbonate or sodium hydroxide (Baskin et al. 2009).

17.5.3 Thrombotic Occlusion

Fibrin begins forming on the external catheter wall within 24 h of insertion, starting at either the catheter entrance site into the vessel or where infused fluid comes into contact with the vessel wall. Blood cells adhere to the fibrin potentially interfering with blood flow and promoting bacterial growth. A variety of thrombotic occlusions are reported including fibrin sheath, mural thrombus and intraluminal thrombus (Fig. 17.2). Risk factors include prior catheterization of the same vessel, difficulty with insertion, poor tip placement, high catheter to vessel size ratio, suboptimal catheter care, underlying malignancy and type of chemotherapy (Kuter 2004). A fibrin sheath develops on the external catheter wall covering the catheter tip and resulting in withdrawal occlusion (Baskin et al. 2009). The sheath may extend up the entire length of the catheter with infused fluid traveling a path upward between the fibrin sheath and the catheter. Extravasation of medications and fluids is possible if the thrombus extends up to the site where the catheter enters the vessel (Mayo 1998). An intraluminal occlusion develops as a result of the buildup of fibrin and blood products with development of either a partial or complete occlusion. The incidence is decreased with strict adherence to institutional flush guidelines (Baskin et al. 2009). A mural thrombus forms as fibrin on the vessel wall attaches to fibrin covering the catheter. A withdrawal occlusion develops, but more significantly a mural thrombus may lead to venous thrombosis (Baskin et al. 2009).

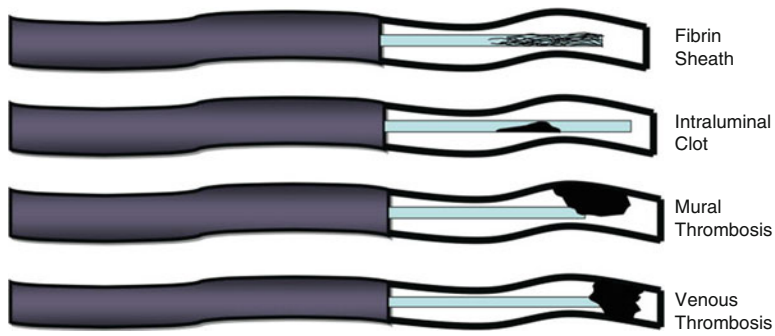

Fig. 17.2 Pictorial representation of central catheter occlusion and thrombosis (with permission from Baskin et al. [2009])

A suspected CVC-related thrombus may be evaluated by a radiographic study such as a dye study, computed tomography (CT) or ultrasound with Doppler flow (Fig. 17.3). However, common initial practice for treatment of a suspected thrombotic occlusion is instillation of a thrombolytic, most commonly tissue plasminogen activator (tPA) (Baskin et al. 2009). tPA converts plasminogen to plasmin resulting in local fibrinolysis (Fig. 17.4). tPA is simple and safe to use as well as being cost-effective. Our local institutional protocol for administration of tPA for dwell and infusion is summarized in Table 17.3.

17.6 Central Venous Catheter-Related Deep Vein Thrombosis

A catheter-related thrombus (CRT) is generally the result of a mural thrombus that has enlarged, leading to complete occlusion of the vein. Kuter

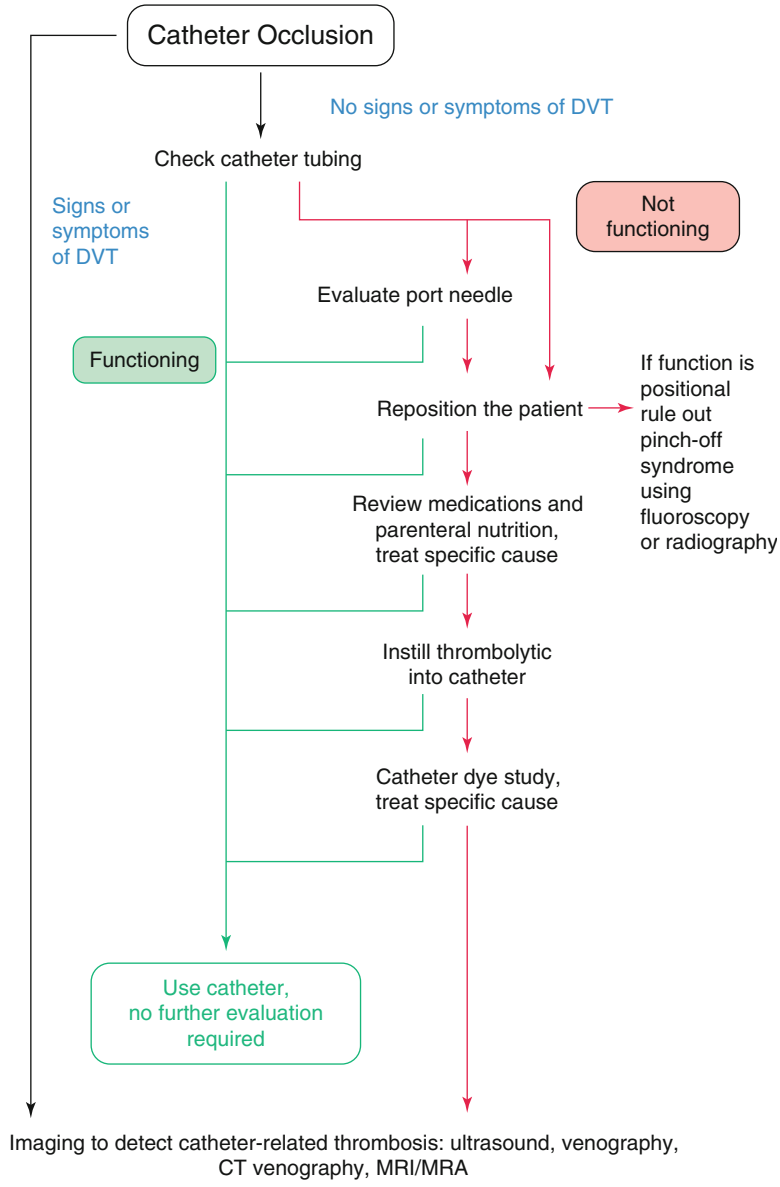

Fig. 17.3 Assessment of catheter occlusion (with permission from Baskin et al. [2009]). *DVT* deep venous thrombosis, *CT* computed tomography, *MRI* magnetic resonance imaging, *MRA* magnetic resonance arteriography

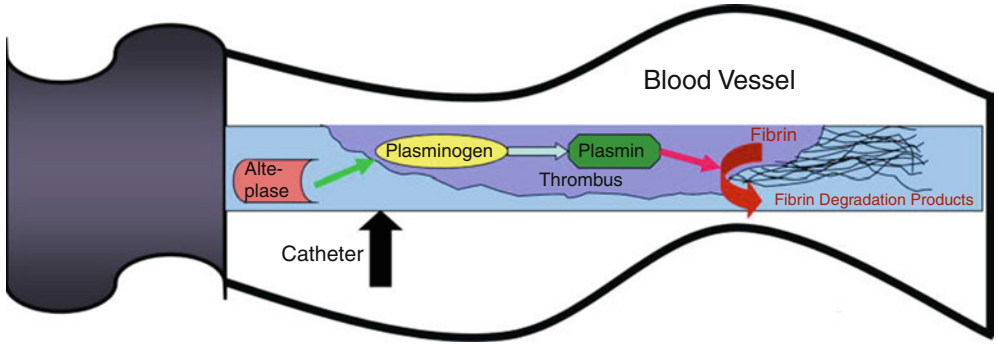

Fig. 17.4 Mechanism of action for tissue plasminogen activator (tPA) (with permission from Baskin et al. [2009])

(2004) reported an incidence of 5–41 % with differences related to a wide variety of catheter types, tip position, duration of insertion and underlying disease. Male et al. (2002) found a thrombosis rate of 29 % in a study of 66 children with ALL and a tunneled CVC. Clinical signs of a CRT include jaw, neck, chest, or shoulder pain, warmth, swelling, or development of visible collateral circulation. The majority of CRTs (up to 71 %) are asymptomatic, being diagnosed by imaging obtained to determine the cause of obstruction or with the occurrence of a pulmonary embolism (Kuter 2004).

17.6.1 Evaluation of Catheter-Related Thrombosis

Although the reference standard for the diagnosis of a CRT is contrast venography, compression ultrasound (CUS) with Doppler and color imaging is frequently used as CUS is noninvasive and does not require contrast medium (Rooden et al. 2005). In the patient with a negative CUS but a high clinical suspicion of a CRT, contrast venography is indicated (Rooden et al. 2005). Evaluation of the etiology of the CRT (in addition to the presence of a CVC) may guide treatment and prevention. A detailed family history of thrombosis will assist in determining the need for an evaluation for thrombophilia (see Chap. 8 for more detail). Other risk factors to consider are immobility, dehydration and administration of medications with thrombotic risk, particularly steroids and asparaginase (Table 17.4).

17.6.2 Treatment of Catheter-Related Thrombosis

Treatment of CRT is discussed in detail in Chap. 8 and is based on the 2012 American College of Chest Physicians (ACCP) guidelines with the following principles (Monagle et al. 2012):

- Anticoagulation therapy for 3 months following a first CRT.
- Continued anticoagulation with prophylactic dosing until removal of the CVC.
- For recurrent thrombosis during prophylaxis, increase to therapeutic dosing until line removal (but for a minimum of 3 months).
- A CVC that is no longer functional or required should be removed; a minimum of 3–5 days of anticoagulation at therapeutic dosing should be given prior to removal.

If a replacement CVC is medically indicated, consideration should be given to prophylactic anticoagulation to prevent recurrence of a thrombus. Low-molecular-weight heparin (LMWH) is an excellent anticoagulant for use in pediatrics due to predictable dosing (based on weight), limited need for blood level monitoring and short half-life. The updated 2012 ACCP guidelines recommend no routine monitoring of LMWH levels (Monagle et al. 2012). However, infants who are gaining weight and children with renal insufficiency do require monitoring to ensure appropriate levels. LMWH levels should be drawn 4 h after a dose (peak level) with a therapeutic target of 0.5–1 unit/mL. At least two to three doses should be given to reach steady state prior to obtaining a peak level.

Table 17.3 tPA dwell administration guidelines

General instructions
• Reconstitute tPA with 2.2 mL sterile water for injection (not bacteriostatic water) yielding a concentration of 1 mg/mL
• A 10 mL syringe is used for all dose administrations
• Instill one dose into each lumen of the catheter and allow to dwell for 30–120 min (optimal efficacy is achieved with a 120 min uninterrupted dwell time)
• A second dose is indicated if unable to obtain a brisk blood return after the initial treatment and dwell time
Broviac catheters
• Children <10 kg: dilute 0.5 mL tPA with 0.5 mL 0.9 % NaCl; instill 1 mL (0.5 mg) for each lumen
• Children ≥10 to <30 kg: 1 mL (1 mg) tPA for each lumen
• Children ≥30 kg: 2 mg (2 mL) tPA for each lumen
Implanted ports
• Children <10 kg: draw up 2.5 mL of 0.9 % NaCl into a 10 mL syringe and mix with 0.5 mL (0.5 mg) reconstituted tPA; total volume is 3 mL (0.5 mg) tPA
• Children ≥10 kg: draw up 1 mL 0.9 % NaCl into a 10 mL syringe and mix with 2 mL (2 mg) reconstituted tPA; total volume is 3 mL (2 mg) tPA
Completely occluded CVC
• Remove cap, cleanse hub per institutional policy and attach a 3-way stopcock to the catheter
• Attach tPA syringe to one of the stopcock ports
• Attach a 10 mL syringe to the remaining port
• Turn the stopcock off to the tPA syringe
• Gently pull back the plunger of the 10 mL syringe to the 3–5 mL mark and clamp the catheter to maintain negative pressure
• Turn the stopcock off to the 10 mL syringe
• Unclamp the catheter and allow tPA to be drawn into the line
• Clamp catheter, remove stopcock, apply positive pressure cap and allow tPA to dwell for 120 min
• May repeat a second dose of alteplase if needed
tPA (alteplase) infusion
If the CVC occlusion is not cleared after a second tPA dwell, a tPA infusion (6–24 h) may be indicated based on radiographic findings
Alteplase 0.03–0.06 mg/kg/h for 6–24 h
• Initial infusion 0.03 mg/kg/h for 6 h; if no clinical improvement (working line) may sequentially increase dose to 0.06 mg/kg/h (max 2 mg/h)
• Do not exceed 48–72 h of infusion
• Monitor patient for signs of sepsis as bacteria may be released into the bloodstream with dissolution of the thrombus
• Monitor labs including: PT, aPTT, fibrinogen, plasminogen, D-dimers, platelets; replete plasminogen with FFP for concentrations <50 %
• Repeat radiographic study to assess for improvement in dissolution of thrombus every 24 h
• Remove the catheter if the thrombus is not cleared after 48–72 h of tPA infusion (based on radiographic findings and functional improvement)

tPA tissue plasminogen activator, *PT* prothrombin time, *aPTT* activated partial thromboplastin time, *FFP* fresh frozen plasma

Table 17.4 Proposed risk factors for central venous catheter (CVC)-related thrombotic occlusions

Change in normal blood flow	Vascular endothelial damage	Hypercoagulable state
Immobility	Traumatic insertion	Malignancy
Large catheter to vessel ratio	Multiple insertion attempts	Sepsis
Dehydration	Catheter tip malposition	Chemotherapy
Compression of vessel by tumor	CVC placement time >14 days	Thrombophilia
Left-sided insertion		

17.6.3 Special Considerations During Anticoagulation Therapy

- LMWH should be held for 24 h prior to and 12 h after a lumbar puncture.
- LMWH should be held for 24 h prior to and 24 h after a minor surgical procedure.
- LMWH should be held during periods of thrombocytopenia (i.e., platelets $<50\times10^9$/L).

17.6.4 Contraindications of Anticoagulant Therapy

- Intracranial hemorrhage
- Ongoing hemorrhage
- Uncorrected coagulopathy
- Hypersensitivity to heparin or pork products
- Poor renal function (i.e., creatinine clearance < 30 mL/min)

17.7 Catheter Maintenance

Catheter maintenance refers to all activities undertaken to keep the line functioning properly while decreasing the risk of infection. CVC insertion bundles have dramatically reduced infectious complications related to surgical placement. Development of a maintenance bundle with institutional policies on hand hygiene, site cleansing, dressings, line flushing, hub care and line stabilization enhance catheter longevity and decrease morbidity (O'Grady et al. 2011). Hand hygiene, an inexpensive and easily implemented strategy, is the most effective measure in decreasing healthcare-associated infections (see Chap. 14) (Kline 2005).

17.7.1 Skin Antisepsis

Chlorhexidine has been shown to be a superior cleansing agent prior to CVC placement and for skin antisepsis with routine dressing changes. Chaiyakunapruk et al. (2002) reviewed 8 randomized controlled trials, totaling 4,143 catheters, comparing efficacy of chlorhexidine gluconate with povidone-iodine for skin disinfection. Results revealed a significant reduction in bloodstream infection with chlorhexidine.

17.7.2 Central Venous Catheter Dressings

CVC dressings serve a dual purpose: prevention of infection and stabilization of the line to decrease accidental removal. Semipermeable transparent and sterile gauze with tape are the two most commonly used types of dressings. The transparent dressing allows for evaporation of moisture and direct visualization of the site. Dressing changes are required every 5–7 days or more frequently as needed if the dressing becomes loose, wet, or soiled, which may decrease skin irritation and breakdown. A sterile gauze and tape dressing is recommended when there is bleeding or drainage at the site and for patients who are diaphoretic, requiring changes every 1–2 days. The literature has shown no difference in CLABSI rates between semipermeable transparent and sterile gauze and tape dressings (Mermel 2000; Gillies et al. 2003; O'Grady et al. 2011). The choice of dressing may be left to institutional guidelines or patient preference. Chlorhexidine has been shown to be the superior choice for skin antisepsis prior to CVC insertion (O'Grady et al. 2011). In the past decade several studies were undertaken to determine the effectiveness of a chlorhexidine-impregnated dressing (BIOPATCH, Johnson & Johnson, Somerville, NJ) in reducing rates of CLABSI. Findings revealed that although colonization was decreased there was no difference in the rate of CLABSI between semipermeable transparent dressings and BIOPATCH (Levy et al. 2005; Hatler et al. 2009).

17.7.3 Hub Care

Needleless connectors were introduced 20 years ago in an effort to decrease the incidence of needlestick injuries among healthcare workers.

Since then, emphasis has been placed on developing connectors that lessen the risk of CLABSI. Currently, several types of connectors are available, each with unique recommendations for flushing, locking and clamping the catheter. Strategies to decrease occlusion and CLABSI related to the use of needleless connectors include use of a single product within the institution, education on proper use including disinfection prior to access, and adherence to institutional policy for flushing and clamping.

Catheter hub colonization and contamination is a significant cause of CLABSI (Sannoh et al. 2010). In an observational study by Soothill et al. (2009), a change in catheter hub cleansing agent to 2 % chlorhexidine in 70 % isopropyl alcohol significantly decreased the rate of bloodstream infections in pediatric patients undergoing hematopoietic stem cell transplant. CDC guidelines recommend scrubbing the hub with friction for 15 s using 70 % isopropyl alcohol or 2 % chlorhexidine in 70 % isopropyl alcohol (O'Grady et al. 2011).

17.7.4 Central Venous Catheter Flushing and Locking

CVC flushing with normal saline is instrumental in assessing catheter patency and clearing the catheter after medication administration (preventing precipitation from incompatible drugs), blood sampling and blood transfusions. Locking a catheter, typically with heparinized saline, prevents reflux of blood into the catheter. However, wide variation exits in the frequency, concentration and volume of heparin utilized, with the majority of data from adult patients (Stephens et al. 1997; Hadaway 2006; Cesaro et al. 2009). Following institutional guidelines with ongoing assessment of efficacy and intermittent review of the literature will aid in decisions to change clinical practice. Examples of guidelines are in Tables 17.5 and 17.6.

Healthcare providers need to be cognizant of rare but potentially significant complications related to heparin locking solutions, specifically heparin-induced thrombocytopenia, heparin-induced thrombosis and bleeding. The cost and risk of replacing an occluded catheter outweigh the potential risks of heparin locks. A safe practice is strict adherence to institutional policy, awareness of potential complications and development of local expert resources.

17.7.5 New Strategies to Prevent Central Line-Associated Blood Stream Infection (CLABSI)

17.7.5.1 Chlorhexidine Bathing

Chlorhexidine has been shown to be effective in decreasing cutaneous colonization and is the recommended skin antiseptic prior to CVC insertion (O'Grady et al. 2002). Researchers are now investigating the effect of daily chlorhexidine bathing of pediatric oncology patients. Initial studies have demonstrated a significant decrease in CLABSI rates (Munoz-Price et al. 2009; Popovich et al. 2009; Montecalvo et al. 2012). A meta-analysis by O'Horo et al. (2012) concluded that the CLABSI rate is decreased in medical intensive care units with daily chlorhexidine bathing, whether 2 % chlorhexidine-impregnated cloths (Sage® products) or a 1:2 dilution of 4 % chlorhexidine was used. A current two-armed, randomized, double-blind study through the Children's Oncology Group is assessing the efficacy of 2 % chlorhexidine gluconate bathing in prevention of CLABSI in children with cancer and in those undergoing hematopoietic stem cell transplantation.

Table 17.5 Heparin lock guidelines

Device	Heparin strength, volume and frequency
PICC	2 F: 1 mL heparinized saline (10 U/mL) every 6 h
	2.6 F and larger: 2–3 mL heparinized saline (10 U/mL) every 12 h
Tunneled catheter	2 mL heparinized saline (10 U/mL) every 24 h
Implanted port	If locked >1 time daily: 5 mL heparinized saline (10 U/mL)
	Daily to monthly flush: 5 mL heparinized saline (100 U/mL)

PICC peripherally inserted central catheter, *F* French

Table 17.6 Example of central venous catheter (CVC) maintenance bundle

Care practice	*Bundle recommendations*
Hand hygiene	Hand hygiene performed before and after CVC insertion, care, and catheter entry or after contact with any inanimate object; use clean gloves for all CVC access as needed; glove use does not preclude use of hand hygiene
Surface disinfection	Clean work surfaces with germicidal wipe prior to CVC care
Use of maintenance kits/CVC cart	Procedure kits/carts containing supplies help to ensure all required supplies are available at the time of the procedure, including those required for insertion, dressing change and CVC removal
Insertion	*Bundle recommendations*
Hand hygiene	Hand hygiene is followed by waterless surgical scrub application
Maximal sterile barrier precautions	Patient is covered from head to toe with sterile drapes; mask, cap, sterile gown and sterile gloves during insertion procedure; all staff (including the assistant and family members) to wear regular face mask and cap when within 3 ft of sterile field
Skin antisepsis	Skin disinfected with chlorhexidine gluconate; apply back and forth friction scrub for 30 s and allow to dry completely for 30 s (2 min scrub for wet sites, such as the groin); site must be dry before skin puncture
Universal protocol utilized	Staff observers are skilled in monitoring elements of sterile technique; staff empowered to stop non-emergent procedure if sterile technique not followed
Assessment	*Bundle recommendations*
Ongoing assessment of catheter site	Inspect catheter site for cleanliness and dressing integrity; assess CVC site for complications hourly when infusing solutions and every 4 h when locked
Daily assessment of need for CVC	Discuss ongoing need for CVCs daily with medical team during rounds; assess patient for appropriateness of their vascular access device based on infusates/length of therapy and available vessels; promptly remove unnecessary CVCs
Catheter site care/management	*Bundle recommendations*
Skin antisepsis	Use clean gloves for all CVC access; maintain clean disposable towel or 4×4 gauze under CVC access port before accessing; skin disinfected with chlorhexidine gluconate; apply back and forth friction scrub for 30 s and allow to dry for 30 s (2 min scrub for wet sites, such as the groin)
CVC dressing assessment and change	Routine dressing changes performed by clinicians with demonstrated competency; use of catheter securement device with PICC dressing changes; mask and sterile gloves for dressing changes; dressing change frequency: transparent dressing, every 7 days and as needed for soiled dressing or loss of integrity; gauze and non-occlusive dressing, every 48 h and as needed
Antisepsis of needleless connectors, IV junctions and catheter hub	Vigorously scrub needleless connectors, IV junctions and hub (diaphragm and sides) prior to accessing with an alcohol swab using friction for a minimum of 15 s
CRBSI criteria	*Bundle recommendations*
Blood culture sampling	Consider DTP protocol when drawing blood cultures with significant time differential of CVC culture versus peripheral culture positivity of >2 h; generally peripheral blood cultures are not drawn on oncology patients who have central lines (see Chap. 1)
Administrative	*Bundle recommendations*
Education	Education of clinicians responsible for managing CVCs to include: care and maintenance strategies, identification and management of complications
Routine surveillance of CVCs	Collect and benchmark outcome data with the National Healthcare Safety Network

PICC peripherally inserted central catheter, *IV* intravenous, *CRBSI* catheter-related bloodstream infection, *DTP* differential time to positivity
Adapted from Mermel (2000), Marschall et al. (2008), Horan et al. (2011)

17.7.5.2 Antiseptic Needleless Connectors and Antiseptic Port Barrier Caps

Contamination of the CVC hub is the main source of CLABSI 10 days after insertion. Novel products are now available to decrease the incidence of this complication. Three such devices are currently marketed. *V-link with VitaShield* protective coating (Baxter) is a needleless connector with an antimicrobial coating (silver) on the interior and exterior surface. *Curos*® port protector is a barrier cap with a sponge saturated with 70 % isopropyl alcohol (IPA). Disinfection occurs 3 min after being threaded onto the connector. The cap may be left in place up to 7 days protecting the connector from airborne and contact contamination. Caps should be placed on all needleless injection sites and changed after each access. *Saralex-CL* (Menyhay) is an antimicrobial barrier cap that threads onto the needless connector bathing the connector in 2 % chlorhexidine gluconate in 70 % IPA. Disinfection occurs in 5 min and may be left in place up to 96 h. The cap protects the connector from airborne and contact contamination. A new cap is applied after each access.

A prospective simulation study by Menyhay and Maki (2006) evaluated the efficacy of cleansing a CVC hub with 70 % alcohol compared to the use of a Saralex barrier cap. One hundred five needleless connectors from three manufacturers were tested. The septum of each device was contaminated with *Enterococcus faecalis* and allowed to dry for 24 h. A control group of 15 connectors were not disinfected, 30 were cleansed with a 70 % alcohol swab and 60 had a Saralex barrier cap applied and removed after 10 min. Nutrient broth was injected through each connector, collected and cultured. Cultures from all control connectors were positive. Twenty connectors (67 %) with conventional disinfection with 70 % alcohol were culture positive, whereas only 1 (1.6 %) of the connectors disinfected with use of the Saralex cap was culture positive. Further study through randomized trials is needed to determine if practice changes are indicated.

17.8 Summary

CVCs are a central component in the care of pediatric oncology patients and allow for safe and effective administration of chemotherapeutic agents in addition to antibiotics, blood products, parenteral nutrition and multiple additional medications. Blood can be easily drawn from externally tunneled CVCs and in accessed implanted ports. Infection and thrombosis are the most common risk factors with CVC placement, and practitioners must be aware of the clinical signs and symptoms associated with these complications, methods to prevent these side effects, and treatment of these problems. Generally, practice and management are based on consensus guidelines and expert opinion as robust evidence is lacking, especially in pediatric patients.

References

Adler A, Yaniv I, Steinberg R et al (2006) Infectious complications of implantable ports and Hickman catheters in paediatric haematology-oncology patients. J Hosp Infect 62:358–365

Alomari A, Falk A (2006) Median nerve bisection: a morbid complication of a peripherally inserted central catheter. J Vasc Access 7:129–131

Augoustides JG, Cheung AT (2009) Pro: ultrasound should be the standard of care for central catheter insertion. J Cardiothorac Vasc Anesth 23:720–724

Baggott CR, Kelly KP, Fochtman D, Foley GV (eds.) (2002) Nursing care of children and adolescents with cancer, 3rd edn. Elsevier Saunders, Philadelphia

Balls A, LoVecchio F, Kroeger A et al (2010) Ultrasound guidance for central venous catheter placement: results from the Central Line Emergency Access Registry Database. Am J Emerg Med 28:561–567

Bard Access Systems. https://www.bardaccess.com. Accessed 21 Apr 2014

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

Burns D (2005) The Vanderbilt PICC service: program, procedural, and patient outcomes successes. J Assoc Vasc Access 10:183–192

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

Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S (2002) Chlorhexidine compared with povidone-iodine

solution for vascular catheter-site care: a meta-analysis. Ann Intern Med 136:792–801
Deshpande KS, Hatem C, Ulrich HL et al (2005) The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. Crit Care Med 33:13–20
Dillon PA, Foglia RP (2006) Complications associated with an implantable vascular access device. J Pediatr Surg 41:1582–1587
Donlan RM (2011) Biofilm elimination on intravascular catheters: important considerations for the infectious disease practitioner. Clin Infect Dis 52:1038–1045
Eisen LA, Narasimhan M, Berger JS et al (2006) Mechanical complications of central venous catheters. J Intensive Care Med 21:40–46
Fazeny-Dorner B, Wenzel C, Berzlanovich A et al (2003) Central venous catheter pinch-off and fracture: recognition, prevention and management. Bone Marrow Transplant 31:927–930
Gillies D, O'Riordan E, Carr D et al (2003) Central venous catheter dressings: a systematic review. J Adv Nurs 44:623–632
Gonzalez G, Davidoff AM, Howard SC et al (2012) Safety of central venous catheter placement at diagnosis of acute lymphoblastic leukemia in children. Pediatr Blood Cancer 58:498–502
Hadaway L (2006) Heparin locking for central venous catheters. J Assoc Vasc Access 11:224–231
Handrup MM, Moller JK, Frydenberg M, Schroder H (2010) Placing of tunneled central venous catheters prior to induction chemotherapy in children with acute lymphoblastic leukemia. Pediatr Blood Cancer 55:309–313
Hatler C, Buckwald L, Salas-Allison Z, Murphy-Taylor C (2009) Evaluating central venous catheter care in a pediatric intensive care unit. Am J Crit Care 18:514–520
Horan TC, Arnold KE, Rebmann CA, Fridkin SK (2011) Network approach for prevention of healthcare-associated infections. Infect Control Hosp Epidemiol 32:1143–1144
Kline AM (2005) Pediatric catheter-related bloodstream infections: latest strategies to decrease risk. AACN Clin Issues 16:185–198
Kusminsky RE (2007) Complications of central venous catheterization. J Am Coll Surg 204:681–696
Kuter DJ (2004) Thrombotic complications of central venous catheters in cancer patients. Oncologist 9:207–216
Lefrant JY, Muller L, De La Coussaye JE et al (2002) Risk factors of failure and immediate complication of subclavian vein catheterization in critically ill patients. Intensive Care Med 28:1036–1041
Levy I, Katz J, Solter E et al (2005) Chlorhexidine-impregnated dressing for prevention of colonization of central venous catheters in infants and children: a randomized controlled study. Pediatr Infect Dis J 24:676–679
Maki DG, Kluger DM, Crnich CJ (2006) The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin Proc 81:1159–1171
Male C, Chait P, Ginsberg JS et al (2002) Comparison of venography and ultrasound for the diagnosis of asymptomatic deep vein thrombosis in the upper body in children: results of the PARKAA study. Prophylactic Antithrombin Replacement in Kids with ALL treated with Asparaginase. Thromb Haemost 87:593–598
Mansfield PF, Hohn DC, Fornage BD et al (1994) Complications and failures of subclavian-vein catheterization. N Engl J Med 331:1735–1738
Marschall J, Mermel LA, Classen D et al (2008) Strategies to prevent central line-associated bloodstream infections in acute care hospitals. Infect Control Hosp Epidemiol 29:S22–S30
Mayo DJ (1998) Fibrin sheath formation and chemotherapy extravasation: a case report. Support Care Cancer 6:51–56
McGee DC, Gould MK (2003) Preventing complications of central venous catheterization. N Engl J Med 348:1123–1133
McLean TW, Fisher CJ, Snively BM, Chauvenet AR (2005) Central venous lines in children with lesser risk acute lymphoblastic leukemia: optimal type and timing of placement. J Clin Oncol 23:3024–3029
Menyhay SZ, Maki DG (2006) Disinfection of needleless catheter connectors and access ports with alcohol may not prevent microbial entry: the promise of a novel antiseptic-barrier cap. Infect Control Hosp Epidemiol 27:23–27
Mermel LA (2000) Prevention of intravascular catheter-related infections. Ann Intern Med 132:391–402
Mermel LA, Allon M, Bouza E et al (2009) Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 49:1–45
Monagle P, Chan AK, Goldenberg NA et al (2012) Antithrombotic therapy in neonates and children: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of chest physicians evidence-based clinical practice guidelines. Chest 141:e737S–e801S
Montecalvo MA, McKenna D, Yarrish R et al (2012) Chlorhexidine bathing to reduce central venous catheter-associated bloodstream infection: impact and sustainability. Am J Med 125:505–511
Munoz-Price LS, Hota B, Stemer A, Weinstein RA (2009) Prevention of bloodstream infections by use of daily chlorhexidine baths for patients at a long-term acute care hospital. Infect Control Hosp Epidemiol 30:1031–1035
Nace CS, Ingle RJ (1993) Central venous catheter "pinch-off" and fracture: a review of two under-recognized complications. Oncol Nurs Forum 20:1227–1236
O'Grady NP, Alexander M, Dellinger EP et al (2002) Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. MMWR Recomm Rep 51:1–29
O'Grady NP, Alexander M, Burns LA et al (2011) Guidelines for the prevention of intravascular

catheter-related infections. Clin Infect Dis 52:e162–e193
O'Horo JC, Silva GL, Munoz-Price LS, Safdar N (2012) The efficacy of daily bathing with chlorhexidine for reducing healthcare-associated bloodstream infections: a meta-analysis. Infect Control Hosp Epidemiol 33:257–267
Perdikaris P, Petsios K, Vasilatou-Kosmidis H, Matziou V (2008) Complications of Hickman-Broviac catheters in children with malignancies. Pediatr Hematol Oncol 25:375–384
Pettit J (2002) Assessment of infants with peripherally inserted central catheters: part 1. Detecting the most frequently occurring complications. Adv Neonatal Care 2:304–315
Pittiruti M, Hamilton H, Biffi R et al (2009) ESPEN guidelines on parenteral nutrition: central venous catheters (access, care, diagnosis and therapy of complications). Clin Nutr 28:365–377
Popovich KJ, Hota B, Hayes R et al (2009) Effectiveness of routine patient cleansing with chlorhexidine gluconate for infection prevention in the medical intensive care unit. Infect Control Hosp Epidemiol 30:959–963
Raad I, Costerton W, Sabharwal U et al (1993) Ultrastructural analysis of indwelling vascular catheters: a quantitative relationship between luminal colonization and duration of placement. J Infect Dis 168:400–407
Randolph AG, Cook DJ, Gonzales CA, Pribble CG (1996) Ultrasound guidance for placement of central venous catheters: a meta-analysis of the literature. Crit Care Med 24:2053–2058
Rooden CJ, Tesselaar ME, Osanto S et al (2005) Deep vein thrombosis associated with central venous catheters–a review. J Thromb Haemost 3:2409–2419
Sagar V, Lederer E (2004) Pulmonary embolism due to catheter fracture from a tunneled dialysis catheter. Am J Kidney Dis 43:e13–e14
Sannoh S, Clones B, Munoz J et al (2010) A multimodal approach to central venous catheter hub care can decrease catheter-related bloodstream infection. Am J Infect Control 38:424–429
Schulmeister L (2010) Management of non-infectious central venous access device complications. Semin Oncol Nurs 26:132–141
Soothill JS, Bravery K, Ho A et al (2009) A fall in bloodstream infections followed a change to 2 % chlorhexidine in 70 % isopropanol for catheter connection antisepsis: a pediatric single center before/after study on a hematopoietic stem cell transplant ward. Am J Infect Control 37:626–630
Stephens LC, Haire WD, Kotulak GD (1995) Are clinical signs accurate indicators of the cause of central venous catheter occlusion? JPEN J Parenter Enteral Nutr 19:75–79
Stephens LC, Haire WD, Tarantolo S et al (1997) Normal saline versus heparin flush for maintaining central venous catheter patency during apheresis collection of peripheral blood stem cells (PBSC). Transfus Sci 18:187–193
Teichgraber UK, Pfitzmann R, Hofmann HA (2011) Central venous port systems as an integral part of chemotherapy. Dtsch Arztebl Int 108:147–153
Theaker C, Juste R, Lucas N (2002) Comparison of bacterial colonization rates of antiseptic impregnated and pure polymer central venous catheters in the critically ill. J Hosp Infect 52:310–312
Troianos CA, Hartman GS, Glas KE et al (2011) Guidelines for performing ultrasound guided vascular cannulation: recommendations of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. J Am Soc Echocardiogr 24:1291–1318
Walder B, Pittet D, Tramer MR (2002) Prevention of bloodstream infections with central venous catheters treated with anti-infective agents depends on catheter type and insertion time: evidence from a meta-analysis. Infect Control Hosp Epidemiol 23:748–756
Yamamoto AJ, Solomon JA, Soulen MC et al (2002) Sutureless securement device reduces complications of peripherally inserted central venous catheters. J Vasc Interv Radiol 13:77–81
Zakrzewska-Bode A, Muytjens HL, Liem KD, Hoogkamp-Korstanje JA (1995) Mupirocin resistance in coagulase-negative staphylococci, after topical prophylaxis for the reduction of colonization of central venous catheters. J Hosp Infect 31:189–193